The contributions of sleep-related consolidation to emotional item and associative memory.

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Abstract

Extant empirical evidence of the past two decades suggests a pivotal role of sleep in system consolidation of episodic memory. Models of active system consolidation (Diekelmann & Born, 2010; Rasch & Born, 2013) propose that periods of restricted sensory processing that are pervasive during slow wave sleep (SWS) provide the opportunity of coordinated reactivations. These reactivations are assumed to result in subsequent redistribution of memory representations from intermediate maintenance in the hippocampus toward long-term storage in neocortical networks. However, newly emerging evidence (Genzel, Spoormaker, Konrad, & Dresler, 2015; Hutchison & Rathore, 2015) indicates that a consolidation process, which is highly distinct from the former framework, unfolds across periods of rapid eye movement (REM) sleep, fostering the selective enhancement of emotional memory retrieval. Critically, the interactions of both processes with regard to emotional associative memory have remained largely unexplored at present. This motivated the objectives of the present thesis, which aimed to generate a more comprehensive understanding of the differential contributions of consolidation processes during SWS and REM sleep to (non-)emotional item and associative memory retention. This was addressed in two consecutive experiments, which examined behavioral performance changes across different intervals of sleep, and aimed to link these to specific oscillatory features of SWS (sleep spindle activity) and REM sleep (right-frontal theta lateralization).

In experiment 1 consolidation processes were studied in a split-night-design, which contrasts the effects of early night sleep (entailing high amounts of SWS) with those of late night sleep (which is predominated by REM sleep episodes). In order to dissociate item memory from distinct retrieval of contextual features, participants performed a source memory task that ascertained the accurate recognition of (non-)emotional images, as well as the accurate retrieval of the initial screen location (right or left) during encoding. Analyses revealed a significant consolidation benefit for emotional images with regard to item recognition, irrespective of sleep. Source memory performance was differentially modulated across early and late night sleep as a function of stimulus valence. While early night sleep was associated with a selective retention benefit for neutral source memory, late night sleep yielded a selective benefit to emotional source recognition across sleep. This dissociation was further substantiated on a neurophysiological level, by means of selective correlations between spindle power (SWS) and neutral memory

performance in the early sleep group, which was complimented by a selective association between right-frontal theta laterality (REM sleep), and emotional source recognition in the late sleep group. As such, the results of experiment 1 genuinely revealed dissociable processes related to the consolidation of emotional and neutral source memory emerging across sleep. Moreover, this extends prior conceptions (Spoormaker, Czisch, & Holsboer, 2013) of consolidation processes during REM sleep, as these were believed to be confined to item memory reprocessing.

Experiment 2 attempted to address the generalizability of these previous findings with regard to the critical timing and duration of these consolidation processes, as well as concerning the effects of perceptual integration processes at the encoding stage. In order to examine performance changes across a restricted sleep interval entailing high proportions of REM sleep, an early morning nap paradigm was employed in which participants were randomly allocated to a wakeful control condition or to a 120-minute nap sleep condition in the early morning hours. As previous effects with regard to REM sleep (experiment 1) may be bound to certain preconditions at encoding (Murray & Kensinger, 2012), specifically to the inherent level of perceptual integration between emotional items and source features, experiment 2 adopted a different approach requiring the active integration of both components at the encoding stage. To this end, item and associative recognition were probed by means of a paired-associates task, which required the accurate retrieval of arbitrary object-scene-associations (entailing emotional or neutral scenes) formed during the encoding phase. Analyses yielded a selective, sleep-related retention benefit in associative recognition for both stimulus categories. However, this benefit in performance was again partially dissociable on a neurophysiological level as evident by selective correlations between spindle density during non-rapid eye movement (NREM) sleep and neutral associative memory performance. These results reinforce the former findings of experiment 1, demonstrating that similar consolidation effects related to SWS and REM sleep can be retained on a behavioral level after a brief interval of sleep during the daytime and in a dissimilar task design, requiring active integration of item and context at encoding. However, the lack of a robust correlation with regard to right-frontal theta lateralization signifies that the circadian modulations and neurophysiological specifics of REM sleep, place certain restrictions on the accurate assessment of related processes in diurnal nap paradigms.

In summary, the present thesis constitutes a first systematic approach towards dissociating the contributions of REM sleep and SWS to emotional associative memory consolidation, across two consecutive but dissimilar study designs. The yielded findings originally suggest that consolidation processes during both sleep stages are dissociable, but beyond this, contribute independently to memory retention of emotional and neutral associations. This was also substantiated on a neurophysiological level with regard to selective correlations between oscillatory features of both sleep stages and memory performance. Moreover, in support of previous conceptions (Hutchison & Rathore, 2015), it was genuinely established that REM sleep exhibits the unique capacity to influence associative memory of emotional stimuli. The exact mechanism by which this is accomplished remains to be elucidated in future experiments.

Zusammenfassung

Eine Vielzahl empirischer Befunde der letzten zwei Jahrzehnte belegen, dass der Schlaf eine tiefgreifende Rolle in der Gedächtniskonsolidierung zwischen unterschiedlichen Gedächtnissystems einnimmt. Sukzessive verfeinerte Modelle über aktive Vorgänge der „Systemkonsolidierung“ (Diekelmann & Born, 2010; Rasch & Born, 2013) legen nahe, dass Phasen eingeschränkter sensorischer Verarbeitung, die über den Tiefschlaf hinweg dominieren, ein Zeitfenster bieten in dem Gedächtnisspuren im Hippocampus in koordinierter Weise reaktiviert werden können. Diese Reaktivierungen gehen mit einer Integration der jeweiligen Gedächtnisinhalte in neokortikalen Netzwerken einher, die eine langfristige Aufrechterhaltung des Gedächtnisabrufs ermöglichen. Neue Befunde (Genzel et al., 2015; Hutchison & Rathore, 2015) legen allerdings nahe, dass sich ein weiterer Konsolidierungsprozess über den Schlaf hinweg vollzieht, der zu einer selektiven Aufrechterhaltung emotionaler Gedächtnisinhalte beiträgt. Dieser Prozess ist wiederum assoziiert mit dem Auftreten von REM-Schlaf (REM, engl. Rapid Eye Movement) Episoden. Bislang ist jedoch unklar, wie beide Konsolidierungsprozesse über unterschiedliche Schlafstadien hinweg miteinander interagieren in Bezug auf das emotionale Assoziationsgedächtnis. Dies bildete den Ausgangspunkt der vorliegenden Arbeit, die ein umfassenderes Verständnis hinsichtlich der Beiträge unterschiedlicher Konsolidierungsprozesse im Tiefschlaf und REM Schlaf in der Aufrechterhaltung des (nicht-)emotionalen Item- und Assoziationsgedächtnisses anstrebt. Dies wurde in zwei aufeinander aufbauenden Experimenten näher beleuchtet, in denen behaviorale Leistungsveränderungen über unterschiedliche Schlafintervalle untersucht wurden mit dem Ziel diese mit spezifischen oszillatorischen Merkmalen des Tiefschlafs (Schlafspindel Aktivität) und des REM Schlafs (Rechts-frontale Theta Lateralisierung) in Verbindung zu bringen.

In Experiment 1 wurden diese Konsolidierungsprozesse in einem „Split-night-design“ untersucht, das die Möglichkeit bietet, frühen Nachtschlaf (mit hoher Tiefschlafdauer) mit spätem Nachtschlaf (der von REM-Schlaf Episoden dominiert wird) zu kontrastieren. Um das Itemgedächtnis von dem distinkten Abruf kontextueller Merkmale dissoziieren zu können, wurde eine Quellengedächtnisaufgabe von den Probanden bearbeitet, in der sowohl das Wiedererkennen (nicht)emotionaler Bilder als auch der Abruf der initialen Bildschirmposition (rechts oder links) in der Lernphase erfasst wurde. Die berichteten Analysen weisen auf einen signifikanten

Konsolidierungsvorteil für das Wiedererkennen emotionaler Bilder über die Zeit hinweg hin, der jedoch unabhängig vom Schlaf auftritt. Die Quellengedächtnisleistung wird hingegen differentiell über den frühen und späten Nachtschlaf in Abhängigkeit von der Stimulusvalenz aufrechterhalten. Während früher Nachtschlaf mit einer selektiven Aufrechterhaltung des neutralen Quellengedächtnisses assoziiert war, konnte der späte Nachtschlaf mit einer selektiven Erhaltung des emotionalen Quellengedächtnisses in Verbindung gebracht werden. Diese Dissoziation war darüber hinaus auf neurophysiologischer Ebene nachweisbar anhand selektiver Korrelationen zwischen der Spindelaktivität im Tiefschlaf und der neutralen Gedächtnisleistung über den frühen Nachtschlaf und einer selektiven Korrelation zwischen der rechts-frontalen Theta Lateralisierung im REM Schlaf und der emotionalen Quellengedächtnisleistung über den späten Nachtschlaf. Die Ergebnisse des ersten Experiments eröffnen eine neue Perspektive, indem sie die Existenz zweier dissoziierbarer Prozesse in der Konsolidierung des emotionalen und neutralen Quellengedächtnisses über den Schlaf hinweg nahelegen. Im Zuge dessen erweitern die vorliegenden Ergebnisse vorangegangene Konzepte (Spoormaker et al., 2013) der Gedächtniskonsolidierung im REM Schlaf, die bislang eine eingeschränkte Wirkung auf das Itemgedächtnis prädizierten.

Das Ziel von Experiment 2 war es, diese neuen Ergebnisse auf ihre Generalisierbarkeit hin zu prüfen, insbesondere hinsichtlich der kritischen Zeitverlaufs und der Dauer der zugrundliegenden Konsolidierungsprozesse und in Bezug auf die Bedeutung perzeptueller Integrationsprozesse während der Enkodierphase. Um Veränderungen in der Gedächtnisleistung über ein kurzes Schlafintervall mit hohen REM-Schlaf-Anteilen zu untersuchen wurde ein Kurzschlaf Paradigma am frühen Morgen eingesetzt in dem Probanden einer Wachkontrollbedingung oder einer 120-minütigen Tagschlafbedingung am frühen Morgen zugewiesen wurden. Die vorangegangenen Ergebnisse aus Experiment 1 hinsichtlich der Effekte des REM-Schlafs könnten unter Zugrundelegung der Literatur (Murray & Kensinger, 2013) an bestimmte Bedingungen während er Enkodierungsphase gekoppelt sein, speziell an den inhärente Grad der perzeptuellen Integration zwischen emotionalen Items und ihren Quellenmerkmalen. Um dies zu prüfen wurde in Experiment 2 eine andere Herangehensweise mit einer Gedächtnisaufgabe, die eine aktive Integration beider Komponenten während der Enkodierung erforderlich machte, gewählt. Item- und Assoziationsgedächtnis wurden über das Behalten paarweise gelernter Assoziationen zwischen (nicht)emotionalen Bildern und Alltagsobjekten erfasst. Die korrespondierenden Analysen erbrachten einen selektiven, schlafbezogenen Vorteil in der Aufrechterhaltung der assoziativen Gedächtnisleistung über die Zeit hinweg in beiden Stimuluskategorien. Darüber hinaus war dieser Effekt erneut teilweise dissoziierbar auf neurophysiologischer Ebene, was sich in selektiven Korrelationen der Spindeldichte während des non-rapid eye movement (NREM) Schlafs zu der neutralen Assoziationsgedächtnisleistung wiederspiegelte. Diese Ergebnisse untermauern die vorangegangen Befunde aus Experiment 2, indem ähnliche Konsolidierungseffekte des Tiefschlafs und des REM Schlafs über ein kurzes Schlafintervall am frühen Morgen und innerhalb eines Aufgaben-Paradigmas, dass die aktive Integration während der Enkodierungsphase erforderte, auf behavioraler Ebene bestätigt werden konnten. Dennoch verweist das Ausbleiben einer robusten Korrelation zu der rechts-frontalen Theta Lateralisierung im REM-Schlaf darauf, dass zirkadiane Modulationen und neurophysiologische Besonderheiten des REM-Schlafs gewisse Begrenzungen in der akkuraten Erfassung dieser Prozesse innerhalb von Kurzschlaf-Paradigmen während des Tages setzen.

Die vorliegende Arbeit stellt eine erste systematische Annäherung an eine Dissoziierung der Beiträge des Tiefschlafs und des REM-Schlafs in der Konsolidierung des emotionalen Assoziationsgedächtnisses dar, die über zwei aufeinander aufbauende aber unterschiedliche Studiendesigns hinweg angestrebt wurde. Die daraus hervorgegangenen Ergebnisse legen erstmals nahe, dass Konsolidierungsprozesse über beide Schlafstadien dissoziierbar sind aber darüber hinaus gehend eigenständig zu einer Aufrechterhaltung der Gedächtnisleistung für neutrale und emotionale Assoziationen beitragen. Dies konnte auch auf neurophysiologischer Ebene über selektive Korrelationen zu oszillatorischen Merkmalen beider Schlafstadien substantiiert werden. Darüber hinaus konnte erstmalig nachgewiesen werden, dass Prozesse während des REM Schlaf über die Kapazität verfügen auf das assoziative Erinnern emotionaler Inhalte einzuwirken in Übereinstimmung zu neueren theoretischen Konzepten (Hutchison & Rathore, 2015). Der genaue Mechanismus über den dies bewirkt wird muss in zukünftigen Experimenten näher beleuchtet werden.

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I General introduction

‘I told you the truth,’ *I say yet again*, ‘Memory's truth, because memory has its own special kind. It selects, eliminates, alters, exaggerates, minimizes, glorifies, and vilifies also; but in the end it creates its own reality, its heterogeneous but usually coherent version of events; and no sane human being ever trusts someone else's version more than his own.’

Salman Rushdie

Midnight's Children

Human memory has always inspired fervent depictions in literary accounts, e.g. inciting Jane Austen to declare it as the *“one faculty of our nature [...] more wonderful than the rest”*. The capacity, which memory conveys, to recapitulate the past in the present moment is crucial to our adaptive subsistence, but contributes much more so to our outlasting sense of identity (Klein & Nichols, 2012). Strikingly, however, the particular ability to retain episodic details of past events (such as time or location) appears extremely susceptible; It is ontogenetically one of the latest to mature (Sprondel, Kipp, & Mecklinger, 2011), the first to decay (Shing et al., 2010) and less flexibly reorganized in response to injuries (Braun et al., 2008). Withal, it is vulnerable to interference on a fine-grained temporal scale, evolving over the time course of a single day (Day, Langston, & Morris, 2003). Research of the past decade reveals that a critical factor in preventing this rapid decay is established by active system consolidation during sleep (Diekelmann & Born, 2010). Sleep appears to offer the unique neurophysiological environment for selective reactivations of newly acquired memory traces in the hippocampus, which are subsequently redistributed to neocortical networks. This mechanism allows memory representations to remain accessible across remote periods of time, potentially persisting over the entire lifespan. Another aspect that critically contributes to the preservation of event recollection across time is the emotional impact these episodes exert on us (Kensinger, 2009). It appears immediately evident, that we will most likely forget the topping of the sandwich we had for lunch today, but quite definitely retain the flavoring of our own wedding cake. Moreover, when a caesura disrupts the continuity of our lives, such as a violent assault, this will be remembered with even greater certainty. These effects have a very refined neurophysiological basis that extends to the facilitation of consolidation processes (McGaugh, 2000). A recent line of research (Genzel et al., 2015; Hutchison & Rathore, 2015) suggests that these consolidation processes may likewise unfold across periods of sleep, however by highly different mechanisms than described above. The present thesis aimed to contribute towards a clear characterization of these consolidation processes by examining the effects of sleep on the maintenance of emotional associative memory across time.

In the present chapter, a theoretical introduction will be provided with regard to the human memory system in general (chapter I 1), and the way this is modulated by emotion (chapter I 2). Thereafter, concepts of system consolidation will be introduced (chapter I 3), as well as how these relate to the consolidation of emotional events in particular (chapter I 4). Derived from these considerations, chapter I will close on a brief outline of the present study objectives (chapter I 5). These will be further elaborated on in chapter II and III, which contain the unchanged manuscripts of experiment 1 and experiment 2 of the present dissertation project. The results of both experiments will be integrated and discussed conjointly throughout the general discussion (chapter IV). Finally, the present thesis closes on a summative evaluation (chapter IV 4) of the present findings in light of previous theoretical considerations and, thereby, proposes a preliminary working model entailing a new perspective on the consolidation of emotional and neutral events across sleep.

1. Human memory

It is widely acknowledged that human memory is not a unitary phenomenon, but rather consists of multiple memory sub-systems that operate in parallel, as well as independently, to support flexible and adaptive behavior of the individual throughout all disparate experiences encompassing life (Squire, 2004). A common distinction is made with regard to the declarative and non-declarative memory systems. The former is assumed to be related to conscious retrieval and thus acts on a representational level, providing a model of the external world (Squire & Zola-Morgan, 1991; Squire & Zola, 1996). In contrast, the non-declarative system entails facets of memory that do not imply conscious recollection and are expressed primarily through performance, which evolves over multiple repetitions and subsequent extraction of regularities (e.g. procedural memory). This distinction is also evident with regard to the brain structures supporting these discrete domains of memory (see Figure I 1; Squire & Zola, 1996).

Figure I 1[1]. Taxonomy of long-term memory systems and the neural structures which these are supported by. Taken from Squire, L. R., & Zola, S. M. (1996). Structure and function of declarative and nondeclarative memory systems. *Proceedings of the National Academy of Sciences of United States of America, 93*(24), 13515-13522.

The declarative memory system is further subdivided into episodic and semantic memory. While semantic memory entails factual knowledge, episodic memory refers to the recollection of events as well as relations of specific elements within an episode, such as the specific location or time at which an event took place, derived from the idiosyncratic experience of the individual (Squire, 2004). As such, both semantic and episodic memory afford the ability to infer unique information from a single trial, while the latter additionally encompasses autonoetic awareness (Squire & Zola-Morgan, 1991; Tulving, 1985).

1.1. Episodic memory

Episodic memory has been found to rely primarily on processes in the medial temporal lobe (MTL; see Figure I 2). Lesion studies suggest that the integrity of the hippocampal formation is crucial for the maintenance of episodic memory. In addition perirhinal (PRC) and parahippocampal (PHC) cortices appear to support distinct functions, with the PRC being involved in object-related (especially visual) memory, and the PHC being implicated

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[1] Zur Wahrung der Lizenzrechte des Verlages wird die Abbildung nicht dargestellt.

in memory for contextual aspects (particularly spatial memory) (Mayes, Montaldi, & Migo, 2007; Squire, Wixted, & Clark, 2007). These structures in turn receive projections from a variety of neocortical areas related to (uni- and polymodal) sensory processing (i.e. inferotemporal cortex and parietal lobe), strategic processes (prefrontal cortex) and ultimate long term storage (Squire & Zola, 1996).

Figure I 2[2]. Schematic view of the medial temporal lobe memory system. Taken from Squire, L. R., & Zola, S. M. (1996). Structure and function of declarative and nondeclarative memory systems. *Proceedings of the National Academy of Sciences of United States of America, 93*(24), 13515-13522.

Critically, the structures of the MTL and the neocortex make unique contributions to episodic memory at different stages of memory processing. Initial sensory processing is assumed to be accomplished primarily by neocortical processes and in relative independence of the MTL system (Squire & Zola-Morgan, 1991; Squire & Zola, 1996) . These early processing stages are commonly related to sensory and short-term memory and subsist as long as attention is focused (internally or externally) on a specific stimulus. In order to create an enduring internal representation, that is maintained across discontinued attention, encoding processes are required which critically rely on the engagement of the hippocampus[3] and its surrounding structures (Eichenbaum, Yonelinas, & Ranganath, 2007;

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[2] Zur Wahrung der Lizenzrechte des Verlages wird die Abbildung nicht dargestellt.

[3] For an account of rare conditions that do not require hippocampal involvement during the encoding of novel associations see Coutanche and Thompson-Schill (2014).

Yonelinas, 2002). The hippocampus is assumed to act as the hub of the episodic memory system, bearing the unique capacity to bind different constituents of an episode that are stored in disparate cortical sites (i.e. PRC and PHC; see Figure I 2; Yonelinas, 2013). As such, it encapsulates the “blueprint” of an episode, allowing the reconstruction of its inherent relations between multiple arbitrary elements at a later point in time. After successful encoding, initial memory representations are assumed to be in a labile state, requiring subsequent stages of consolidation to be strengthend and become resistent against retroactive interference (Frankland & Bontempi, 2005; Wang & Morris, 2010). These primary stages of (synaptic) consolidation are mostly related to local processes of long-term potentiation (LTP) resulting in structural changes at individual synapses and are assumed to progress in the first hours following encoding (Bergado, Lucas, & Richter-Levin, 2011; Clopath, 2012; McGaugh, 2000). Thereafter, memory retrieval of recent events is supported by the MTL system for an extended period of time, the exact duration of which remains to be characterized (Zola-Morgan & Squire, 1990). However, as the MTL system, particularly the hippocampus, enables the rapid and highly efficient acquisition of novel episodes it is also characterized by a high level of cellturnover (Kempermann, Song, & Gage, 2015; Yonelinas & Ritchey, 2015). In order to maintain memory representations over markedly extended periods of time, consolidation at the system level is thus required. During these processes of reorganization between different memory systems, memory representations are gradually redistributed from medium-term maintenance in the MTL system towards long term storage in neocortical networks (Diekelmann & Born, 2010). More precisely, hippocampal-bound relations of specific features of an event are assumed to be transposed into connections between neocortical modules storing these features. This process of redistribution is assumed to encompass structural changes at individual synapses as well as morphological growth (for a comprehensive account of these processes see I 3.2.; Wang & Morris, 2010). Consequently, while events are initially encoded in parallel within the MTL system and into neocortical networks (McClelland, McNaughton, & O'Reilly, 1995), the latter is assumed to serve as a permanent repository of episodic memory enabling retrieval of remote events across an individual’s lifetime (Squire & Zola, 1996). On a conceptual level, this entails the notion that, at some point, episodic memory retrieval is accomplished completely independent of the hippocampus and its surrounding structures within the MTL (however there is still considerable debate on this issue; Moscovitch, Nadel, Winocur, Gilboa, & Rosenbaum, 2006; Nadel & Moscovitch, 1997).

Notably, memory retrieval, specifically with regard to recognition memory, has been demonstrated to be supported by two discrete retrieval processes. Each of these processes is supported by differing sub-regions of the network described above (Eichenbaum et al., 2007). Moreover, similarly to the different sub-systems of human memory (declarative and non-declarative) these processes act in parallel and independently, providing distinct qualities with regard to the aspects of the retrieved event (Yonelinas, 2002).

1.2. Two distinct processes underlying recognition: Familiarity and recollection

Memory retrieval can be effected by means of free recall of a certain event (in response to a retrieval cue) or by recognition (identifying an episode as having previously occurred upon presentation). The latter is thought to be supported by two distinct processes referred to as recollection and familiarity[4] (Yonelinas, 1997; Yonelinas, 2002). Recollection is believed to critically depend on the hippocampus (as well as PHC), and describes the ability to retrieve details of an episode, thus allowing us to access its initial spatiotemporal context (Eichenbaum et al., 2007; Tulving, 1985; Yonelinas et al., 2010). Moreover, it is characterized by an effortful, prolonged retrieval process accompanied by a sense of autonoetic consciousness, as such, reflecting what has been essentially conceptualized as "episodic memory" (Tulving, 1985). Familiarity, on the other hand, is considered to reflect a fast-acting, automatic, process of recognition that is devoid of remembering any specific contextual details but is based on a distinct sense of "knowing" that an event has occurred in the past (Yonelinas, 2002). This process primarily relies on the PRC and is assumed to be continuous in the sense that it produces a varying signal of memory strength that is compared against an internal response criterion (c). If this criterion value is exceeded by an individual item's memory strength (such as a word or an image in a memory task) it is classified as "old" (Squire et al., 2007; Yonelinas et al., 2010). Recollection, in contrast, is not assumed to conform to such a continuous process as modelled by signal detection

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[4] In the current thesis, recognition memory and its underlying processes are discussed primarily based on the assumptions of the dual process signal detection model (Yonelinas, 1997), as empirical evidence from different areas and using different methods (see above) are in strong support of this account. Alternative single and dual process models make divergent assumptions on the underlying processes of recognition; however, a comprehensive discussion of these competing models exceeds the scope of the current thesis (for an overview see Mayes et al., 2007; Squire et al., 2007; Yonelinas, Aly, Wang, & Koen, 2010).

theory, but is only initiated when an individual item exceeds a high threshold with a discrete probability (Yonelinas et al., 2010).

These assumptions have been tested empirically by analyses of recognition memory performance (hit- and false-alarm-rates) at different confidence levels (6-point scale; from highly certain to highly uncertain). These analyses consistently yield a highly characteristic function of recognition performance, with the asymmetry (as determined by the intercept) of the resulting receiver operator characteristic (ROC) curve being reflective of the contribution of recollection to task performance (Yonelinas et al., 2010; but see Squire et al., 2007 for a different view on this). The role of familiarity in determining memory judgements is conversely signified by the degree of curvilinearity of the function (deviation from the chance diagonal), thus adhering to a continuous process that varies with confidence.

In addition to dissociating recollection and familiarity by means of ROC analysis, specific task designs have been proposed to measure the differential contributions to episodic memory that these processes make. One common task procedure (Remember-know-paradigm; Tulving, 1985; Yonelinas & Jacoby, 1994) dissociates both processes on the level of subjective experience by asking participants to indicate, whether a recognition judgement of an individual item was based on retrieving specific event details and accompanied by autonoetic awareness (“Remember”). Alternatively, participants are instructed to respond “Know” when merely recognizing the item without retrieving any associated features. The contributions of both retrieval processes can also be partially disentangled in task designs that explicitly probe recognition of the item itself (item memory) as well as the retrieval of a specific feature of the initial study episode (e.g. screen location of the item). Whereas the latter ability (often referred to as source memory) has been shown to rely exclusively on recollection, item memory can be supported by both processes alike (Glisky, Polster, & Routhieaux, 1995; Yonelinas, 1999). The unique capacity of recollection to access hippocampal-bound associative information can also be ascertained in paired-associates tasks, which require the relational encoding of two arbitrarily paired items (Bader, Mecklinger, Hoppstädter, & Meyer, 2010). During subsequent testing, the accurate retrieval of the association between constituents is probed by cued recall or by asking participants to distinguish intact from rearranged item pairs, rendering recollection critical to successfully accomplish the task (but see Mayes et al., 2007). However, it is important to note that specific variations within these particular task designs can result in the differential recruitment of both processes. For instance, it has been found that a reduced response deadline during retrieval results in an enhanced contribution of familiarity to recognition memory performance (due to the diverging time course of both processes; see Sauvage, Beer, & Eichenbaum, 2010). Also, providing an integrative concept during encoding or utilizing semantically-related item pairs can effectuate familiarity-based retrieval (referred to as unitization; see also I 2.2; Bader et al., 2010; Diana, Yonelinas, & Ranganath, 2008).

On a neurophysiological level, both processes have been found to elicit temporally and spatially dissociable effects during memory retrieval (Rugg & Curran, 2007). With respect to retrieval-related changes in electroencephalography (EEG) activity (event-related potentials; ERPs), familiarity has been brought into association with an early mid-frontal negative deflection (300-400 ms after stimulus onset), whereas recollection has been shown to elicit a late parietally distributed positivity (400-500 ms after stimulus onset). Notably, the amplitude of the former component has been demonstrated to correlate with confidence ratings (Woodruff, Hayama, & Rugg, 2006), affirming the assumptions of the dual process account. Functional magnetic resonance imaging (fMRI) data cumulatively suggests an involvement of the hippocampus in recollection as well as a corresponding link between the PRC and familiarity (Eichenbaum et al., 2007). Moreover, activity changes in these structures during familiarity-related as opposed to recollection-based retrieval have been found to follow fundamentally different regularities (increase vs. decrease in activity), thus adding further evidence to the notion of qualitatively different processes (Montaldi, Spencer, Roberts, & Mayes, 2006).

Based on this accumulated evidence, the binding of item and context (BIC) model proposes two segregated routes that are differentially related to familiarity- and recollection-based retrieval (Diana, Yonelinas, & Ranganath, 2007). The “what” stream is primarily related to item-specific information, receiving projections from unimodal sensory processing areas, which converge in the PRC and reach the hippocampus via projections to the lateral entorhinal cortex (ERC). The “where” stream processes contextual information that originates from polymodal cortical areas. This information regarding the spatiotemporal context of the item reaches the PHC and is ultimately projected to the hippocampus via the medial ERC (see Figure I 3). Consequently, both streams converge in the hippocampus where binding of item-based and contextual information is assumed to be supported by means of pattern separation processes (Hasselmo & Wyble, 1997). As such, this model illustrates the anatomical foundation of two retrieval processes operating independently of one another, and accessing different aspects of a previously acquired episode embedded in the MTL system.

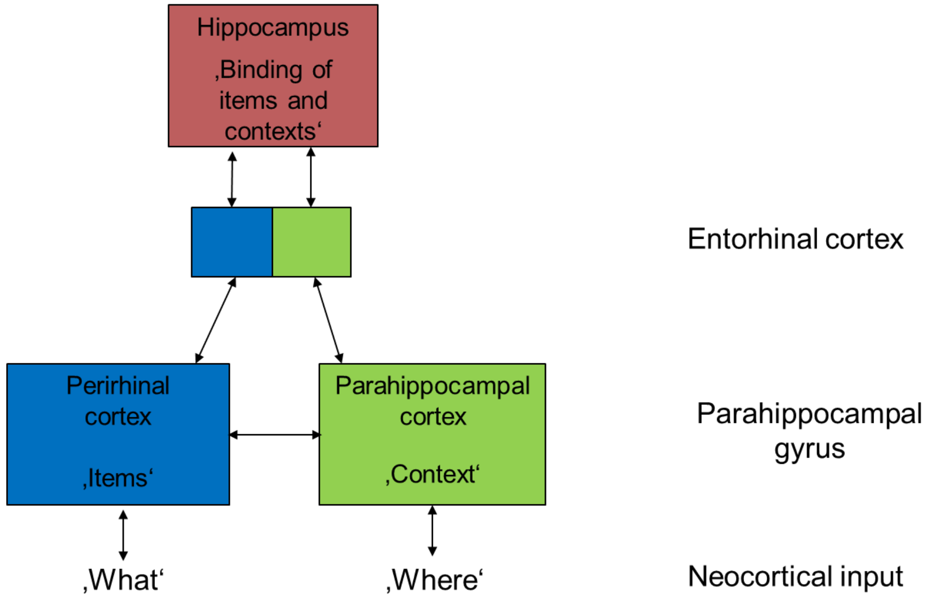

Figure I 3. The "Binding of item and context" model of recognition memory (adapted from Diana et al, 2007).

Beyond these processes confined to the MTL system, recent accounts (Ranganath, 2010; Buckner & Wheeler, 2001) emphasize the important role of the prefrontal cortex (PFC) in guiding retrieval processes, in implementing retrieved information into purposeful behavioral responses, and in selecting the aspects of a current experience that are critical to be retained in the future (during encoding). With regard to the latter, it is assumed that control processes relying on the ventrolateral (and also dorsolateral; see Simons and Spiers, 2003) PFC regulate the information that is fed into the MTL system, thus facilitating the encoding of restricted but distinct memory representations in order to adaptively guide prospective behavior (Ranganath, 2010).

2. Emotion and episodic memory

Another, yet dissimilar, process that profoundly alters episodic memory formation in the MTL memory systems relates to the emotionality[5] of the events that we experience. A plethora of empirical findings has demonstrated that episodes, that engage emotional processing, are integrated into the episodic memory system in a way that allows us to retain the vital aspects of these events across the duration of our lifetime (for reviews see LaBar & Cabeza, 2006; Phelps, 2004; Yonelinas & Ritchey, 2015). These processes are predominantly governed by the amygdala, a structure of the limbic system located adjacent to the hippocampus. The amygdala possesses the capacity to modulate processes in the MTL memory system, which has been recently integrated in a modified version of the BIC model (see Figure I 4; Yonelinas & Ritchey, 2015).

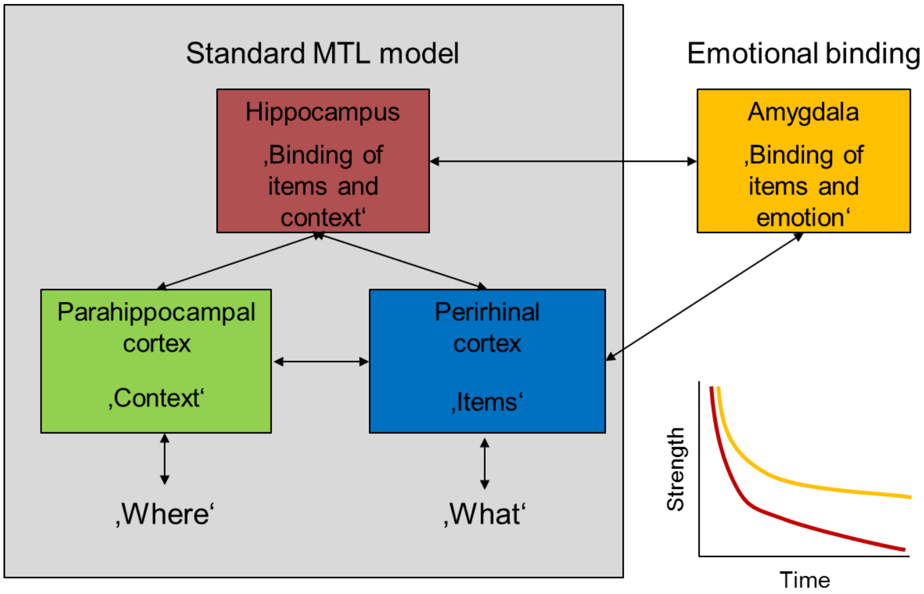

Figure I 4. The emotional binding model (adapted from Ritchey and Yonelinas, 2015). *Note:* In addition to the standard BIC model, this adaption incorporates modulatory effects of the amygdala on memory processes in the hippocampus and perirhinal cortex. The predictions that derive from these interactions are depicted in the lower right-hand corner; across time emotional bindings (supported by the amygdala, designated in orange) are less prone to forgetting as compared to neutral bindings (supported by the hippocampus, designated in red).

In this account it is assumed that the amygdala supports a unique binding mechanism, which results in an enhanced retention of emotional episode over time due to its anatomical (less cell turn over) and process-related (less interference due to restricted material entering

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[5] Throughout this chapter emotionality or emotional events will be discussed referring to negative valence, as a comprehensive account of diverging effects of positive valence is beyond the scope of the current thesis.

this processing route) features. These discrete binding processes are thought to be based on reciprocal connections of the amygdala to the hippocampus and PRC, thus inducing enhancements of specific aspects of episodic memory supported by these regions (see Figure I 4).

Despite its very simplistic assumptions, the model points out two very critical features of emotion-induced effects on episodic memory: First of all, these have been found to relate differently to specific stages of memory formation, thus producing different outcomes at different points in time. Secondly, these effects yield diverging outcomes with regard to the quality of the retrieved information (item vs. contextual memory). These two perspectives will be illustrated in greater detail in the following. In order to refer to the neuroanatomical foundations of these effects throughout the forthcoming sections, a brief overview of the main structures that support emotional memory processing, as well potential mechanisms of communication and critical connections to other regions will be provided first.[6]

2.1. Neuroanatomical network of emotional episodic memory

Animal studies as well as human lesion studies recurrently demonstrate that the integrity of the amygdala is essential for emotional memory formation. More specifically, studies have found that the characteristic effects of emotion at different processing stages are not evident when this structure is compromised (LaBar & Cabeza, 2006). Consequently, temporal lobectomy patients do not exhibit preferential retention of emotional material over time but uniform performance decrements of emotional and neutral stimuli (Cahill, Babinsky, Markowitsch, & McGaugh, 1995), emphasizing that the amygdala does not fulfill a general role in episodic memory (Squire & Zola-Morgan, 1991; Yonelinas et al., 2010). In contrast, it is predominantely believed that the amygdala selectively modulates processes supported by the structures of the MTL.

Located deep within the temporal lobe, the amygdala abuts on the anterior hippocampus and, as such, constitutes a region of the limbic system (LaBar & Cabeza, 2006). It is assumed to be the major subcortical structure involved in supporting the detection of emotionally significant stimuli (with regard to arousal), and subsequent modulation of

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[6] As an exhaustive account of the complete network involved in emotional processing and its different pathways exceeds the objectives of the present thesis only selected aspects, which will be referred to throughout the subsequent chapters, will be discussed.

different cognitive and behavioral processes (e.g. threat-related responses). In line with this very broad range of functions, it exerts its influence over a wide array of neural structures (see Figure I 5).

Figure I 5[7]**.** Schematic overview of the nuclei of the amygdala and their inputs to (green arrows)/ outputs from (purple arrows) other structures. Taken from Paré, D., Collins, D. R., & Pelletier, J. G. (2002). Amygdala oscillations and the consolidation of emotional memories. *Trends in Cognitive Sciences, 6*(7), 306-314. *Note:* Connections to and from the neuromodulatory systems of the brainstem and basal forebrain are not depicted. AHA= amygdalohippocampal area, OT= optic tract, PU= putamen, D= dorsal, V= ventral, L= lateral, M= medial.

On a more fine-grained level, the amygdala refers to a formation of different interconnected nuclei, which are neuroanatomically divided into the basolateral (BL) complex, the corticomedial group and a third anterior group (Paré, Collins, & Pelletier, 2002). As illustrated in Figure I 5 these sub-regions receive input from various sensory processing areas (relayed from the thalamus and cerebral cortex), and conversely innervate cortical and

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subcortical structures of diverse functions. Due to its most widespread projections encompassing all levels of the central nervous system, the BL complex has been frequently suggested to be a critical region with regard to modulatory effects of emotion on cognitive processes (Hubner, Bosch, Gall, Luthi, & Ehrlich, 2014; Paré et al., 2002; Pelletier, Likhtik, Filali, & Pare, 2005). Indeed, this region has been found to project to the hippocampus as well as ER and PR cortices, which reciprocally feed information to the BL and lateral nuclei (LaBar & Cabeza, 2006). The functional significance of these pathways is reflected by the predictive value of correlated activity in the amygdala and respective MTL regions at encoding with regard to subsequent emotional memory performance (for reviews see LaBar & Cabeza, 2006; Murty, Ritchey, Adcock, & LaBar, 2011; Phelps, 2004). Notably, these findings do not seem to generalize to the posterior PH region (Yonelinas & Ritchey, 2015; see I 2.3. for a discussion of potential implications).

The exact mechanism of interaction between the BL complex and the structures supporting episodic memory is not completely understood at present. Most accounts emphasize arousal-induced neurohormonal modulations mediated by the BL complex via efferent pathways of the hypothalamic–pituitary–adrenal (HPA) axis, the disruption of which has shown to suppress emotion effects on memory performance (see also I 2.2; LaBar & Cabeza, 2006; McGaugh, 2000). Another promising framework is based on the functional similarity of oscillatory patterns of the amygdala and MTL structures across different states (Paré et al., 2002). During emotional arousal, both amygdala and hippocampus have been shown to exhibit distinct rhythmic activity in the theta frequency range (4- 7 Hz). These coherent oscillations may facilitate synaptic interactions between structures (Bissiere et al., 2011). More precisely, during specific phases of the oscillation, BL amygdaloid neurons may generate depolarizations that induce synaptic changes in rhinal or hippocampal sites (Paré et al., 2002). However, it must be considered that both of the processes outlined above may be epiphenomenological and thus equate to the same mechanism.

Beyond the MTL structures that are critical for episodic memory, the amygdala interacts with a variety of areas related to early sensory processing, which in turn importantly contribute to memory processes at a very early stage. The amygdaloid nuclei receive visual information from different pathways originating from subcortical areas and from the sensory cortex, which are involved differentially in non-conscious and conscious perception of emotional stimuli respectively (Tamietto & de Gelder, 2010). The amygdala in turn projects back to cortical visual areas of the ventral visual stream as well as orbitofrontal, anterior cingulate, and frontoparietal cortices. In fact, the amygdala has connections to all cortical stages along the ventral visual stream up to the primary visual cortex (V1), thus potentially exerting its influence on different levels of sensory integration and object processing, but also on attentional processes (due to connections to frontoparietal regions of attentional control). Again, the functional relevance of these pathways is reflected by the contributions of encoding-related activity in temporo-occipital regions (such as the visual cortex as well as the fusiform gyrus; see Figure I 6) to the successful retrieval of visual detail as well as recollection-based retrieval of negative arousing material (see I 2.2. for a process-related discussion on this; Kark & Kensinger, 2015; Kensinger, Garoff-Eaton, & Schacter, 2007b; Mickley & Kensinger, 2008; Talmi, Anderson, Riggs, Caplan, & Moscovitch, 2008).

Figure I 6[8]. Overview of structures that critically contribute to modulatory effects of emotion on memory performance. Taken from Kensinger, E. A. (2009). Remembering the details: Effects of emotion. *Emotion Review, 1*(2), 99-113.

As in episodic memory formation in general (see I 1.3), top-down processes, particularly related to the orbitofrontal cortex (OFC)**,** have been found to modulate emotional memory processes (see Figure I 6). The OFC encompasses the ventral surface of the frontal lobe, as such, receiving projections from higher-order sensory processing areas (anterior inferior temporal cortices) but also sharing robust connections with subcortical structures, most

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prominently the amygdala (Barbas, 2000). Its functions appear ubiquitous, in that it serves as an environmental integrator (with regard to sensory input) and guides adaptive decision making (Stalnaker, Cooch, & Schoenbaum, 2015). Consequently, it allows us to adaptively apply emotional information to decisions, particularly when these originate from processes of mental simulation or inference, but also affords the ability to re-experience an emotion during recall of the pertaining event (Bechara, Damasio, & Damasio, 2000; Stalnaker et al., 2015). Thus, while not directly influencing the qualities of the encoded representation, the OFC may contribute to emotional memory formation by focusing and guiding encoding and retrieval processes (Kensinger, Garoff-Eaton, et al., 2007b). In line with this notion, studies demonstrate an absence of emotional memory enhancements in association with damages to this region (Kumfor, Irish, Hodges, & Piguet, 2013), as well as functional associations of orbitofrontal activity to successful encoding (Kensinger, Garoff-Eaton, et al., 2007b) and retrieval of emotional material (Smith, Stephan, Rugg, & Dolan, 2006).

It is important to note that certain aspects of top-down driven modulation of emotional memory relate differentially to valence- and arousal-dimensions of emotional material (Kensinger & Corkin, 2004). While arousal-induced enhancements are elicited by automatic processing mechanisms supported by the amygdala, preferential retention of negatively valenced stimuli (devoid of arousal) is functionally related to activity in the left inferior PFC, potentially reflecting the involvement of self-generated, controlled, processes of stimulus elaboration (see I 2.2. for a more detailed account on these processes).

2.2. Effects of emotion at different stages of episodic memory formation

As illustrated in the former section, effects of emotion on memory formation are already evident at very early stages of sensory processing and integration preceding actual encoding. In general, arousing material has been shown to be preferentially detected and attended to as reflected by differences in ERPs of arousing stimuli emerging as early as 100 ms after stimulus-onset (Olofsson, Nordin, Sequeira, & Polich, 2008).

Based on its extensive connections to sensory processing areas (see I 2.1.), the amygdala has been found to modulate attentional processes in response to emotional stimuli, resulting in an automatic capturing of visual attention. This is not just evident with regard to behavioral performance but is also reflected by eye gaze patterns (Mather, 2007) and ERPs (early posterior negativity, 200- 300 ms; see Olofsson et al., 2008 for a review) during processing of emotional stimuli. Consequently, limiting attentional resources during encoding, e.g. by means of divided attention manipulations, is not detrimental to the retention of negative arousing material, suggesting that attentional capture outweighs potentially diverting effects (Kensinger & Corkin, 2004; Kern, Libkuman, Otani, & Holmes, 2005). While the enhanced recruitment of attentional resources may be beneficial to the encoding of the arousing stimulus itself (e.g. a crashed car in a motor accident), it has conversely been shown to impair retention of the peripheral context (e.g. the highway of the motor accident). This secondary effect of attentional narrowing in response to arousing stimuli is commonly referred to as the "central/peripheral tradeoff effect", originating from the cue utilization hypothesis (Easterbrook, 1959). Across decades of research this effect has been extensively confirmed using highly matched neutral and negative arousing material[9]. Although the majority of these studies did not explicitly assess the associative link between emotional stimuli and their surrounding attributes (Kensinger, 2009) there are certain indications that attentional narrowing also produces differential outcomes with regard to item- and associative memory performance (see I 2.3.).

Despite the robust finding of focal memory enhancements as a result of attentional capturing, the extent of this "focality" is still under debate. Specifically, it is unresolved whether preferential processing of emotional items can encompass certain integral item features. In this regard, accounts commonly distinguish intrinsic from extrinsic features (Chiu, Dolcos, Gonsalves, & Cohen, 2013; Kensinger, 2009; Mather, 2007; Mather & Sutherland, 2011). While the former are integral to processing the item (such as color, location or visual details) the latter are more perceptually distant or conceptual in nature (such as peripheral objects or the thoughts that occurred during item presentation). It is important to note that this definition only yields an approximation in that what is essentially deemed "intrinsic" refers to the fraction of elements in a specific stimulus configuration which is processed in a holistic manner at a given time point, in a specific situation and by a specific individual (particularly with reference to its current goals; Mather & Sutherland, 2011). As such, the extent of focal elements that enters the ensuing route of preferential processing can vary substantially, as has been demonstrated with different encoding

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[9] But see Mickley Steinmetz, Waring and Kensinger (2014) for a recent account suggesting that this effect may not solely be based on attentional processes during initial encoding.

instructions (Kensinger, Gutchess, & Schacter, 2007; Mickley Steinmetz, Knight, & Kensinger, 2016).

During subsequent processing stages, arousal is assumed to exhibit an enhancing effect on sensory integration based on the widespread connections of the amygdala along the ventral visual stream (see I 2.1). These enhancements in sensory integration have been hypothesized to facilitate the binding of respective elements of an emotional episode into an integrated and thus less hippocampus-reliant representation (Kensinger, 2009; Murray & Kensinger, 2014). This conception is based on the unitization framework (see I 1.2), which assumes that associative memory retrieval can be supported by familiarity under the precondition that associations were encoded in an integrative process (intra-item binding), resulting in the formation of higher-order memory representations. While early perceptual integration is accomplished during serial stages of sensory processing, the PRC, which forms the culmination of the ventral visual "what" stream, supports the actual mnemonic encoding of unitized associations (Staresina & Davachi, 2010). As such, arousal processes may modulate the prerequisite of successful intra-item binding in the ventral visual stream, while conversely sharing robust connections to the ultimate encoding and storage site of these intra-item associations in the PRC. There is indeed accumulating evidence in favor of arousal-induced enhancements in memory formation via sensory pathways as increased encoding-related activity in these regions has been found to predict subsequent memory performance for emotional stimuli that are retrieved with visual detail or by means of subjective recollection (see I 2.1.). These specific outcomes suggest a qualitatively enriched retrieval process, which is compatible with the access to details of the integrated study episode provided by unitized representations (see also I 2.3.). Nonetheless, direct tests of arousal effects on unitization are currently restricted to one single study (Murray & Kensinger, 2012; Murray & Kensinger, 2014) demonstrating disproportionate activation within visual regions during successful integration of emotional item pairs, as well as enhanced retrieval of these emotional intra-item associations under limited encoding capacity (limited presentation time). This may indeed reflect a greater "ease" in intra-item integration of emotional stimulus configurations that may, however, not bear robust effects on retention when encoding capacity is less restricted.

A slightly different account (Mather, 2007) also proposes that emotion may enhance associative memory formation, however by directly influencing hippocampal binding processes, rather than facilitating unitization processes, which bypass the hippocampus. More specifically, this account assumes that emotion enhances feature binding by modulating working memory (WM) processes, which are critically involved in hippocampal binding and thus long-term associative memory formation (see I 1.1.). It is assumed that maintaining visual feature conjunctions in WM is a highly demanding process and consequently very susceptible to interference (e.g. from novel material appearing in succession of the critical item-context-association). As arousing material effortlessly captures attention, which is also sustained under circumstances of divided attention, it may thus be more likely to be successfully maintained in working memory with its intrinsic features. However, empirical findings addressing this account are very inconsistent at present (Levens & Phelps, 2008; Lindstrom & Bohlin, 2011; Xie & Zhang, 2016; but see Bannerman, Temminck, & Sahraie, 2012; Bergmann, Rijpkema, Fernandez, & Kessels, 2012; Fairfield, Mammarella, Di Domenico, & Palumbo, 2015; Kensinger & Corkin, 2003).

On a functionally higher level, it has been proposed that emotion enhances elaboration during encoding resulting in more robust, thoroughly integrated, memory representations (Kensinger & Corkin, 2004). These effects are assumed to be reflected by encoding-related activation in the inferior frontal gyrus, thus acting relatively independent of arousal-related processes mediated by the amygdala (see I 2.1.; Murty et al., 2011). As emotional material is perceived to be highly salient, it may drive top-down-processes linking the present episode to past experiences (autobiographical elaboration), or to semantically related concepts (semantic elaboration) (Hamann, 2001; Kensinger & Corkin, 2004). Consequently, retrieval of the generated representations may be enhanced due to accessibility to highly potent retrieval cues. Examining combined effects of emotionality and a levels-of-processing manipulation (inducing different levels of elaboration during encoding) on subsequent memory performance, indeed yielded significant differences of neutral and negatively arousing items only in the shallow encoding condition (Ritchey, LaBar, & Cabeza, 2011). This may suggest that processes of stimulus elaboration are automatically initiated for emotional material in the absence of explicit encoding instructions, thus not resulting in beneficial effects when elaborative encoding is experimentally induced in neutral material alike. Additional factors, such as selective rehearsal (but see Guy and Cahill, 1999) as well as differential distinctiveness or relatedness of emotional stimulus material (see Talmi, Luk, McGarry, and Moscovitch, 2007 and Talmi & Moscovitch, 2004) can also contribute to preferential encoding of emotional material. However, as these effects are not inherently effectuated by emotion-specific modulations of neurophysiological processes, these will not be discussed in greater depth.

One of the most prominent characteristics of emotion effects on episodic memory, following encoding, is their time-dependent course (McGaugh, 2000). As formerly mentioned, selective retention has been shown to emerge after prolonged delays reaching from hours to days following initial encoding and, critically, co-occurs with profound changes in the underlying neural circuits. In fact, the contributions of initial amygdala activation and amygdala-MTL connectivity to subsequent memory performance have been found to increase over time (Ritchey, Dolcos, & Cabeza, 2008), and to persist over the length of a year (Dolcos, LaBar, & Cabeza, 2005). Consequently, accounts merely implying reduced retroactive interference of emotional material (Yonelinas & Ritchey, 2015) are insufficient in that these specificities are only plausible to arise from de novo processing of memory traces in previously implicated structures of the MTL (foremost the hippocampus and the anterior PH region) under influence of the amygdala. Most theoretical frameworks thus emphasize the role of consolidation processes, specifically with reference to early stages of synaptic consolidation, which are modulated by neurohormonal changes in response to encoding of arousal-inducing material (see also I 2.1; Hamann, 2001; LaBar & Cabeza, 2006). In brief, encoding of emotional stimuli is assumed to initiate the release of stress hormones from the adrenal gland, which influences memory formation via β-adrenergic receptors in the BL complex of the amygdala (BLA) (Hamann, 2001). Specifically, the release of norepinephrine in the BLA is assumed to elicit modulatory effects on previous encoding-related synaptic changes in adjacent structures of the MTL (particularly in the hippocampus). In this regard, the concept of “emotional tagging” (Bergado et al., 2011; Richter-Levin & Akirav, 2003) has been brought forward. This account assumes that secondary effects of amygdala activation (via catecholaminergic and cholinergic projections) may contribute to the release of plasticity-related proteins, which facilitate the maintenance of potentiated states in weakly tetanized synapses (early LTP elicited during encoding) and thus support progression into late phase LTP, enabling long-lasting changes in synaptic efficacy (Clopath, 2012). In support of the general framework, disrupting these processes in the consolidation phase by administration of β-adrenergic receptor antagonists has extensively been shown to eliminate selective consolidation benefits of emotional stimuli (Lonergan, Olivera-Figueroa, Pitman, & Brunet, 2013).

Beyond these processes of synaptic consolidation the prolonged time course of consolidation effects, exceeding the initial hours after encoding, suggests the relevance of system consolidation in establishing selective retention of emotional material (McGaugh, 2000). In this context, the formerly introduced concept of cross-regional communication via coherent theta oscillations may bridge the gap towards the initiation of system consolidation in the network of structures related to emotional episodic memory (Paré et al., 2002). As such, synchronized theta activity between the amygdala, hippocampus and rhinal cortices during arousal may prime networks to be reactivated during subsequent system consolidation. This notion indeed appears highly compelling, as the structures in question (as well as sub-regions of the PFC) have been shown to oscillate at the same (theta) frequency during specific stages of sleep, that have conversely been brought into association with system consolidation of emotional material (Popa et al., 2010). As these processes constitute the main subject of the current thesis they will be discussed in greater detail throughout section 4.2 of this chapter.

At a final stage, emotion also has been found to influence access to memory representations by guiding retrieval processes rather than just affecting the qualities of the retrieved material itself (see I 2.3.). In this regard, an ERP study found that successful retrieval of neutral items that were paired with emotional material during encoding elicited a distinct early positivity that critically emerged prior to the late parietal effect (associated with recollection; see I 1.2.; Smith, Dolan, & Rugg, 2004). As such, this effect has been interpreted to reflect a provisional recapitulation of the affective context of the item, which may potentially guide the retrieval process by serving as an internally generated retrieval cue (Buchanan, 2007). Furthermore, emotional material has been found to impact the primary search phase (initial accessing of critical information) but not subsequent elaboration (refined accessing of associatively-linked details) of the retrieval process (Ford, Morris, & Kensinger, 2014). Contrasting neurophysiological responses of emotionally- as opposed to neutrally-associated items during the search phase revealed increased activity in the left medial and lateral temporal lobes. This suggests, in accordance with the ERP data, that emotion may play a role in guiding retrieval search at a very early stage by facilitating initial access to the relevant event.

2.3. Effects of emotion on qualitative and quantitative aspects of episodic memory

As evident from the former section, emotion elicits multiple effects at different stages of episodic memory formation, which can produce diverging outcomes when assessed at different points in time and may overlay or even cancel out one another under specific conditions. Nonetheless, certain regularities have emerged with regard to emotional memory performance, the most robust being an enhancement of item memory in recognition tests employing various material across different modalities (e.g. words, pictures, sounds, narrated slideshows; Buchanan, 2007; LaBar & Cabeza, 2006; Phelps, 2004). An increase of recognition responses is often evident both with regard to studied items (“old”) and lures (“new”), resulting in an inflated false alarm rate when contrasted against neutral stimuli (i.e. Johansson, Mecklinger, & Treese, 2004; Maratos, Allan, & Rugg, 2000). This liberal response criterion with regard to arousing material has been interpreted to reflect an overcautious approach mode towards threatening stimuli (as potential omissions may put the individual at existential risk), but may also be partially based on high feature overlap within emotional as opposed to neutral stimulus categories, particularly in laboratory paradigms (Windmann & Kutas, 2001). Nonetheless, when accounting for this difference in bias (by means of the discrimination index Pr) performance rates of emotional stimuli have still been found to exceed those of neutral material (i.e. Ochsner 2000). Moreover, as previously noted, this enhancement of item memory performance has been found to increase over time such that certain studies do not find a difference in recognition immediately after encoding (Sharot & Yonelinas, 2008), but only after delays ranging from hours to days (i.e. Anderson, Yamaguchi, Grabski, & Lacka, 2006; LaBar & Phelps, 1998; Nishida, Pearsall, Buckner, & Walker, 2009; Rimmele, Davachi, Petrov, Dougal, & Phelps, 2011; Ritchey et al., 2008; Sharot & Phelps, 2004; Wang, 2014; Weymar, Löw, & Hamm, 2011). However, in some instances differences have been reported immediately after encoding (i.e. Dolcos & Cabeza, 2002; Kensinger & Corkin, 2004; Mickley Steinmetz, Schmidt, Zucker, & Kensinger, 2012) potentially reflecting contributions of emotion-related processing specificities that precede consolidation (such as elaboration during encoding, see above).

While the recognition benefit of emotional stimuli extends to the differentiation of encoded from new material with great visual specificity (i.e. discriminating studied objects from highly similar lures; Kensinger, Garoff-Eaton, et al., 2007b), the effects on associative memory are rather inconsistent, ranging from enhancements over impairments to the complete absence of any differences with reference to neutral material (Chiu et al., 2013). However, certain regularities have emerged with regard to the types of associative/source features that benefit from being encoded in the context of an arousing item. Perceptually-linked attributes such as item location, color or temporal position (i.e. D'Argembeau & Van der Linden, 2004; Mather & Nesmith, 2008; Schmidt, Patnaik, & Kensinger, 2011) have been found to exhibit preferential recognition whereas non-interacting background objects, tasks performed during item encoding and the color of a surrounding frame (i.e. Kensinger, Garoff-Eaton, & Schacter, 2007a; Kensinger & Schacter, 2006; Rimmele et al., 2011) have been found to coincide with diminished retrieval success in negatively arousing stimuli. This pattern of results empirically validates the notion of a selective benefit in retaining intrinsic rather than extrinsic features of emotional stimuli as a result of narrowed attention, which has been brought forward by multiple accounts (Chiu et al., 2013; Kensinger, 2009; Mather, 2007; Mather & Sutherland, 2011), albeit based on different assumptions regarding the qualities of the underlying memory representation. While the object-based framework (Mather, 2007) and its successive adaptions (Mather & Sutherland, 2011) propose that these effects are generally based on hippocampal-bound item-context-representations, a different line of accounts (Chiu et al., 2013; Kensinger, 2009; Murray & Kensinger, 2014) attributes this pattern to an emotion-induced facilitation of intra-item binding that bypasses the hippocampus (see also above). Although, a preliminary series of experiments directly addressing this latter interpretation (Murray & Kensinger, 2012; Murray & Kensinger, 2014) yielded promising results, this controversy presently remains unresolved. Of note, the theoretical distinction as to whether arousal-driven processes actually result in the modulation of strictly hippocampus-reliant memory representations also has important implications with regard to the involvement of familiarity and recollection during emotional memory retrieval.

In this regard, many studies have examined the effects of emotion on subjective recollection by means of the Remember-know-paradigm (see I 1.2.). Employing this paradigm has consistently yielded selective enhancements of recollection (Phelps, 2004; Yonelinas & Ritchey, 2015), reflecting a very vivid and enriched retrieval experience for emotional material. However, there has been considerable debate, whether this finding truly conveys the contribution of recollective processes to emotional memory retrieval as it is often not paralleled in objective measures of context memory within the same experiment (Rimmele et al., 2011; Sharot & Yonelinas, 2008). This may of course be resolved by assuming that participants retrieved event details of emotional material that were simply not probed in the task procedure (non-criterial recollection; Yonelinas et al. 2010). However, this interpretation is not supported by signal-detection-based analyses of the characteristics of emotion-induced “remember” responses. Resulting ROC curves have been demonstrated to exhibit an sufficient fit to the underlying assumptions of a high-threshold process, but rather suggest that remember responses to emotional stimuli are driven by familiarity-based recognition (Dougal & Rotello, 2007; Kapucu, Rotello, Ready, & Seidl, 2008; but see Ochsner, 2000; Ritchey et al., 2008 for accounts addressing this). Moreover, neuroimaging data suggests a double dissociation between the MTL structures supporting subjective recollection of neutral and emotional stimuli. While the former is correlated to activity in the posterior parahippocampus, which has extensively been shown to be associated with the retrieval of event details, the latter is associated with increased amygdala activation (Phelps, 2004). In this regard it is noteworthy to readdress that, the widespread reciprocal connections of the amygdala to surrounding structures of the MTL strikingly spare the PHC (Yonelinas & Ritchey, 2015), suggesting highly restricted, if any, interactions. As such, the coinciding enhancement of amygdala activation during remember responses may reflect the provisional recapitulation of the affective context during the search process, as it has been found in ERP studies (Buchanan, 2007). This may result in a highly vivid subjective retrieval experience that is nonetheless unrelated to subjective recollection in a veridical sense.

However, as subjective measures of recollection rely on the individual's accurate understanding of the underlying concept, it is often argued that their validity is restricted and may vary considerably between different studies. ERP studies, which provide an objective measure of recollection, have predominantly found successful recognition of emotional items to be associated with an enhanced late parietal positivity (i.e. Inaba, Nomura, & Ohira, 2005; Johansson et al., 2004; Righi et al., 2012; Weymar, Low, Melzig, & Hamm, 2009), and only seldomly with increases of the early mid-frontal negativity (but see Dolcos & Cabeza, 2002). The former effect was found to be abolished under administration of a β-adrenergic receptor antagonist, suggesting that this modulation in retrieval ERPs is closely related to the underlying mechanisms of emotional memory processing (Weymar et al., 2010). While this is suggestive of an enhanced recruitment of recollective processes during successful recognition, empirical evidence with regard to source memory retrieval is again less conclusive. In detail, one account (Newsome, Dulas, & Duarte, 2012) was able to demonstrate an enhanced late parietal effect during source retrieval of negatively arousing material while others have found no significant differences to neutral material (Cui et al., 2016; Koenig & Mecklinger, 2008). Moreover, some studies have reported a complete absence of the late positive component in negative stimuli for specific source features (Koenig & Mecklinger, 2008; Mao, You, Li, & Guo, 2015). This highly inconsistent pattern of results regarding the electrophysiological correlates of emotional source memory retrieval closely resembles the inconsistencies observed with respect to behavioral performance. A unified integration regarding the effects of emotion on hippocampus-dependent memory formation, and contiguously on the process of recollection, is thus not to be accomplished at present.

It may be the case that emotion exhibits the capacity to influence both (hippocampus-dependent) relational feature binding of intrinsic details within an emotional episode, as well as unitization processes, which result in the formation of intra-item representations (supported by the PRC). These distinct effects may be bound to specific circumstances and to intervening processes that presently remain undisclosed. Consequently, future research is needed to exhaustively characterize the processes that yield this wide range of behavioral outcomes (see above) as well as its neurophysiological correlates. Nonetheless, in the context of the current thesis it is important to emphasize that the affective processing network, therein most certainly the amygdala, appears to dispose of a unique route to influence the encoding and subsequent retention of certain event features. This necessarily builds the foundation of ensuing processes of system consolidation (see I 4.), during which resulting memory representations are reactivated and reprocessed.

3. Sleep and memory consolidation

Prior to focusing on the role of sleep in system consolidation of emotionally salient events (see I 4.), a general summary of the effects of sleep in episodic memory consolidation will be provided. As these have been found to relate to fundamentally different processes based on the specific neurophysiological signatures of particular sleep stages, a brief introduction to sleep physiology will be given first.

3.1. Neurophysiological characteristics of sleep architecture

Figure I 7[10]. Somnogram of the typical distribution of sleep stages across the course of a night. Taken from Inostroza, M., & Born, J. (2013). Sleep for preserving and transforming episodic memory. *Annual Review of Neuroscience, 36*, 79-102. The lower panel depicts characteristic EEG features of SWS and REM sleep. *Note:* W= Wake, REM= REM sleep, N1= NREM stage 1, N2= NREM stage 2, N3= NREM stage 3 (corresponding to SWS).

Sleep refers to the cyclic alternation of highly heterogeneous neurophysiological states referred to as sleep stages. These stages are organized in an ultradian cycle (lasting between 90 and 120 minutes), which is repeated across the course of the night under the modulatory

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[10] Zur Wahrung der Lizenzrechte des Verlages wird die Abbildung nicht dargestellt.

influence of circadian and homeostatic processes (see Figure I 7; Izac and Eeg, 2006). A common distinction is made between non-rapid eye movement (NREM) and rapid eye movement (REM) sleep, the former being additionally distinguished into stage N1-3 (AASM, 2007). Stage N1 is conceptualized as a transitory state between wakefulness and stable sleep onset, which is marked by a discontinuance of the dominant alpha rhythm expressed during wakeful relaxation (with closed eyes) and characterized by relatively low-voltage, mixed-frequency (4- 7 Hz) EEG activity. This tonic rhythm is retained (often further decelerated) during succeeding stage N2 with the additional emergence of sleep spindles (11- 16 Hz), waxing-and-waning field potentials propagating from reticular thalamic neurons, and K-complexes. During stage N3 (also referred to as slow wave sleep) EEG activity is dominated by high voltage low frequency oscillations (slow oscillations; 0.5- 2 Hz), globally reflecting a state of neuronal silence and highly synchronized activation across large populations of neocortical neurons. Spindle events recurrently disrupt this uniform slow rhythmic activity, however, appearing less visually discriminable as they emerge superimposed on slow waves (Mölle, Marshall, Gais, & Born, 2002). The sequence of increasing sleep depth is disrupted by the transition to REM sleep, which is commonly preceded by a short intervening phase of N2 (Izac & Eeg, 2006). The neurophysiology of REM sleep is highly distinctive in that it features a low-voltage mixed-frequency EEG pattern that strongly resembles wakeful EEG activity and is dominated by oscillations in the theta frequency range (4- 7 Hz). Moreover, its onset is associated with muscle atonia and transiently reoccurring horizontal eye movements (AASM, 2007). Consequently, global activation is desynchronized and considerably high, specifically in visual association areas, which may relate to dream experiences that strongly accompany REM sleep (Izac & Eeg, 2006). As referred to above, circadian and homeostatic processes modulate the sleep cycle across the night such that REM sleep and slow wave sleep (SWS) duration are disproportionately distributed between both night halves. While homeostatic processes result in an enhanced SWS duration embedded within the sleep cycles of the first night half, circadian factors contribute to an increased REM sleep duration over the second half of the night (see Figure I 7). Beyond the overt dissimilarities of global activation patterns during REM sleep and SWS, both stages are further signified by the differential involvement of the cholinergic and aminergic neurotransmitter systems. While cholinergic activity is at a minimum during SWS, it is considerably enhanced during REM sleep, often exceeding the level observed during wakefulness (Diekelmann & Born, 2010). A similar pattern is evident with regard to glucocorticoid concentrations, which rise over the course of the night concomitant with successively prolonged REM sleep phases (Altevogt & Colten, 2006; Izac & Eeg, 2006). Aminergic activity on the other hand, reaches an intermediate level during SWS but is strongly reduced in and may, in fact, act to suppress REM sleep (see I 4. for potential implications of this).

These disparities of REM and NREM sleep (particularly SWS) with regard to neurophysiological features are reflected by the diversity of their functions. SWS is assumed to provide vital restorative functions (i.e. neurophysiological and immunological; Besedovsky, Lange, & Born, 2012; Tononi & Cirelli, 2014) whereas REM sleep mentation may prepare the organism to adaptively respond to environmental threats in the future (McNamara, Barton, & Nunn, 2010). Intriguingly, both of these highly distinct neurophysiological states contribute to consolidation within the episodic memory systems in unique ways. This will be further elaborated upon throughout the succeeding chapters.

3.2. Prevailing models of sleep-dependent consolidation of episodic memory

Across the past two decades, accumulating empirical evidence has established a vital role of sleep in memory formation such that it supports the transfer of recent events from intermediate maintenance in the MTL system to long-term integration in neocortical networks. This must inevitably succeed in order to afford retention of remote events across a lifetime (Squire & Zola, 1996) and is intricately interwoven with neurophysiological process occurring during sleep (Diekelmann & Born, 2010). As referred to earlier (see I 1.1.), episodic memory is assumed to be supported by two complementary memory systems (Frankland & Bontempi, 2005), one of which enables rapid acquisition but only features limited storage capacity (hippocampus), while the other principally allows unlimited storage but relies on very gradual integration processes (neocortex). Prevailing models (i.e. the active system consolidation account; Diekelmann & Born, 2010) assume that the interaction between both systems (also referred to as system consolidation) must occur in an “offline” mode during which internal processing in respective structures as well as external input cannot interfere with the fine-tuned process of subcortical-cortical transmission (see Figure I 8). These conditions are critically met during SWS, when responsiveness to sensory stimulation is at its lowest and neurophysiological activity is globally reduced but highly synchronized. Herein, neocortical slow oscillations (~ 0.8 Hz) presumably triggered by residual activation changes of initial encoding (see I 3.3.), are assumed to drive the replay of newly acquired hippocampal-bound memory traces. This replay is assumed to be reflected by emerging SWR complexes, which have indeed been shown to underlie a temporally compressed sequence of place cell firing that closely resembles precedent encoding of a novel environment (Colgin, 2016; Wilson & McNaughton, 1994). These hippocampal sharp-wave ripples have been found to be temporally aligned to the propagation of sleep spindles (11-15 Hz) in the thalamus, which are in turn fed back to the neocortex (Steriade & Wyzinski, 1972). While the exact mechanism supported by the spindle oscillation in the succession of memory redistribution is not exhaustively characterized, its functions may be twofold; it may prime neocortical synapses for subsequent plastic changes and, additionally, enable ensuing, intrinsically cortical consolidation processes by means of its inherent gating mechanism, thus preventing interference (Peyrache, Battaglia, & Destexhe, 2011; Ulrich, 2016).

Figure I 8[11]. Illustration of the active system consolidation framework. Taken from Born, J., & Wilhelm, I. (2012). System consolidation of memory during sleep. *Psychological Research, 76*(2), 192-203. **(A)** Schematic depiction of two independent memory stores (Frankland and Bontempi, 2005). While a temporary store (hippocampus) initially supports the encoding of novel episodes, these are subsequently required to be transferred to a long-term store (represented by the neocortex). **(B)** Schematic illustration of the temporal alignment of hippocampal ripples and thalamo-cortical spindles, which are driven by neocortical slow oscillations. These spindle-ripple events, in turn, feed back into neocortical slow oscillations and, by this, transfer hippocampal bound information to neocortical stores.

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[11] Zur Wahrung der Lizenzrechte des Verlages wird die Abbildung nicht dargestellt.

As these coupled spindle-ripple events arrive at the cortex while neocortical networks are in the depolarized up-state, this corroborates the idea that spindles may initiate processes of synaptic plasticity (Batterink, Creery, & Paller, 2016). However, these processes are not assumed to directly result in the induction of LTP, which is required to produce long-lasting changes in synaptic strength. As immediate early gene (IEG) expression that is necessary for synaptic potentiation is strongly reduced during SWS, it is assumed that sleep spindles may only generate transient tags at individual synapses without actually initiating required processes of synaptic consolidation. These are in turn believed to occur during subsequent REM sleep, which has been found to feature marked increases of IEG-activity and provides an ideal state for local synaptic processes due to global disengagement of memory systems (Diekelmann & Born, 2010). As such, specific neurophysiological characteristics of sleep stages, rather than the stages themselves, provide distinct functions in sleep-related consolidation that act in concert to enable a fine-tuned neocortical-hippocampal dialogue. Importantly, this top-down driven mechanism of reactivation and subsequent integration is assumed to operate in a gradual manner resulting in the extraction of invariant features over multiple iterations.

While the active system consolidation framework (Diekelmann & Born, 2010) has received a lot of indirect support from numerous behavioral studies, there have been recent advances in establishing the validity of the underlying neurophysiological mechanisms. In this regard, the specific temporal coupling of oscillatory features (e.g. temporal nesting of hippocampal ripples in the troughs of thalamocortical sleep spindles) during SWS has been confirmed by means of intracranial EEG recordings of epilepsy patients (Clemens et al., 2011; Staresina et al., 2015). The functional significance of these oscillations is reflected by a wealth of empirical studies demonstrating correlations between sleep-related retention benefits and sleep spindle density (recorded non-invasively at frontal and centroparietal scalp sites) during intervening SWS (i.e. Hennies, Lambon Ralph, Kempkes, Cousins, & Lewis, 2016; Schabus et al., 2004; Tamminen, Payne, Stickgold, Wamsley, & Gaskell, 2010). Furthermore, in a seminal series of studies (Rasch, Büchel, Gais, & Born, 2007) the presentation of associated cues of the initial learning phase by means of targeted memory reactivations (TMR)[12], elicited highly specific activation changes in the left hippocampus during SWS affirming the notion of stimulus-specific hippocampal replay. The assumption that this replay is initiated during the depolarizing up-state of neocortical slow oscillations is supported by the differential effects of TMR during up- and down-states on subsequent memory performance (Batterink et al., 2016). Moreover, the causal role of slow oscillations in system consolidation has been substantiated through the successful enhancement of slow oscillations by in-phase auditory stimulation, which not only boosted overnight retention but also enhanced phase-locked spindle activity (Ngo et al., 2015; Ngo, Martinetz, Born, & Molle, 2013).

Provisionally, it may thus be concluded that extant evidence supports the mechanisms implicated by the active system consolidation account. However, the predictions over time, particularly regarding the gradual disengagement of the hippocampus, have not been tested extensively. In preliminary support of this prediction, activation patterns during retrieval of material that had undergone sleep-related consolidation (contrasted against sleep deprivation) across multiple testing delays, suggest a declining relevance of functional connectivity between the right hippocampus and the medial PFC (mPFC) and, conversely, an enhanced reliance on mPFC activation (Gais et al., 2007). Moreover, spindle density has been found to be predictive of the reduction of activity in the right hippocampus for remote (encoded prior to sleep) as opposed to recent recollection (Hennies et al., 2016). These neurophysiological effects should, however, be evident on a behavioral level in terms of a decontextualization, which evolves as invariances of encoded material are gradually extracted into neocortical networks. However, a recent study explicitly testing this assumption (Jurewicz, Cordi, Staudigl, & Rasch, 2016) was not able to demonstrate a corresponding pattern of results. On the other hand, the extraction of relational inferences (e.g. from overlapping item pairs) has been found to increase over sleep thus indirectly disclosing a gradual integration of invariant features into neocortical networks (see also I 3.3.; Lau, Alger, & Fishbein, 2011).

While the exact qualities of restructured memory representations arising over multiple iterations of this sleep-dependent system consolidation process remain to be characterized,

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[12] Stimulus presentation during encoding is temporally coupled with a non-intrusive, contextual cue such as a specific odor. This cue is subsequently presented during sleep to systematically induce reactivations of the respective memory trace.

a different objection concerns the fundamental assumptions of global activation patterns during SWS (Tononi & Cirelli, 2014). Competing accounts have pointed out that the neurophysiological state of SWS is marked by a predominance of long-term depression (LTD) -related signaling rather than by processes related to the expression of LTP (see above). Therefore, SWS may support global synaptic downscaling as opposed to promoting synaptic growth. This process may proactively prevent saturation of synapses, hence supporting learning processes during subsequent wakefulness, and improve the signal-to-noise-ratio with regard to strongly-encoded material (Tononi & Cirelli, 2003, 2014). However, this account is reconcilable with the active system consolidation view by assuming that global processes of LTD coincide with isolated and highly specific reactivations of previously encoded memory representations. These isolated reactivations occur in synchrony to the depolarizing upstate of slow oscillations and thereby may evoke synaptic changes in local neocortical circuits. Thus, while one process may dominate over the other on a global level, this does not dismiss the potency of the minor process to act in a fundamentally different way on a local scale. Building upon this, other alternative models of sleep-dependent consolidation can also be integrated with the assumptions of the active system account. The sequential hypothesis (Giuditta et al., 1995) emphasizes the importance of cyclic alternations of SWS and REM sleep episodes in sleep-related consolidation, which corresponds to the notion of ensuing processes of synaptic consolidation during REM sleep in the active system consolidation account. The dual-process hypothesis (Maquet, 2001), on the other hand, posits a selective role of SWS in declarative, particularly episodic, memory consolidation as well as a complementary facilitation of procedural memory related to REM sleep. The latter observation may relate to the specificities of procedural memory, as it is known to evolve over repeated refinements of activation patterns in locally circumscribed neuronal circuits. Consequently, this memory domain may benefit to a greater extent from REM sleep-dependent (local) synaptic consolidation as opposed to preceding SWS-related interactions between memory systems (Diekelmann & Born, 2010). Moreover, the first aspect of the dual process hypothesis is in close accordance with the mechanisms of SWS-inherent reactivations implicated by the active system consolidation account. As previously described, these reactivations are assumed to originate from the hippocampus, which in turn is known to uniquely support the binding of disparate features of an episode (see I 1.1.). As such, it is evident that declarative memory, but most prominently associative memory, should benefit profoundly from SWS-dependent reactivation and the ensuing interactions between distributed memory systems.

Indeed, behavioral studies very consistently demonstrate selective sleep-related effects on associative rather than item memory tests (i.e. Studte, Bridger, & Mecklinger, 2015; van der Helm, Gujar, Nishida, & Walker, 2011) as well as a selective enhancement of recollection as opposed to familiarity-based recognition (i.e. Daurat, Terrier, Foret, & Tiberge, 2007; Drosopoulos, Wagner, & Born, 2005). Moreover, these enhancements are commonly observed over the first (SWS-rich) as opposed to the second (REMS-rich) night half (Groch, Zinke, Wilhelm, & Born, 2015; Plihal & Born, 1997) and are closely linked to SWS-related features (Daurat et al., 2007; Studte et al., 2015), thus affirming the critical role of inherent mechanisms in associative memory retention. Intriguingly, it has recently emerged that the selectivity of SWS-related consolidation mechanisms (as implied by the active system consolidation account) is not merely evident with regard to the retention of specific aspects of previous events (e.g. contextual features), but also extends to the preferential enhancement of memory representations that are anticipated to be of prospective relevance (see I 3.3). This line of research will be briefly presented in the succeeding section.

3.3. Sleeps selectivity in memory consolidation

As recently reviewed by Stickgold and Walker (2013), sleep-dependent consolidation operates in a highly refined manner rather than uniformly enhancing all newly formed memory representations to the same extent. This has been established in terms of selective sleep-related retention benefits for material associated with high monetary incentives (Bennion, Payne, & Kensinger, 2016; Fischer & Born, 2009; Igloi, Gaggioni, Sterpenich, & Schwartz, 2015; Studte, Bridger, & Mecklinger, 2017), as well as for items cued to be remembered (by means of the directed forgetting paradigm) during encoding (Rauchs et al., 2011; Saletin, Goldstein, & Walker, 2011). Moreover, merely instructing participants about the ensuing test phase prior to sleeping, but after encoding has been completed, is equally effective in establishing selective consolidation (Lo, Bennion, & Chee, 2016; Wilhelm et al., 2011). Similarly, sleep has been found to enhance the successful execution of intended actions (prospective memory), however with the requirement that the intention must be induced in close temporal proximity to the encoding phase and is not fully executed prior to sleeping (Barner, Seibold, Born, & Diekelmann, 2017; Diekelmann, Wilhelm, Wagner, & Born, 2013; Diekelmann & Born, 2010). Taken together, this has been interpreted to reflect the generation of salience tags (Stickgold & Walker, 2013) during or shortly after encoding, which coordinate subsequent reactivation during sleep. In correspondence to this claim, selective retention benefits have been brought into association with spindle density as well as slow oscillation activity (0.68– 1.17 Hz) during SWS (Saletin et al., 2011; Studte et al., 2016; Wilhelm et al., 2011), suggesting a direct link to oscillatory features implicated in the active system consolidation account.

The underlying mechanisms by which these "tags" are generated during wakefulness, and instated during subsequent SWS remain obscure at present. It has been insinuated that regions of the PFC that are involved in strategic encoding processes (see I 1.2) may mediate these effects, as the mPFC is also strongly involved in the generation of slow oscillations during SWS (Diekelmann & Born, 2010; Inostroza & Born, 2013). In greater detail, controlled processes of selection and maintenance during encoding are known to be mediated by the PFC[13], and assumed to be preferentially initiated for material associated with a strong learning intention (Ranganath, 2010; Simons & Spiers, 2003). Critically, related activation changes in the PFC during encoding may result in residual synaptic activity within these particular local circuits after encoding has been completed, which in turn, may trigger the generation of slow oscillations during subsequent SWS (Bazhenov, Timofeev, Steriade, & Sejnowski, 2002). Specifically, the depolarizing up-state of the slow oscillation may be driven by the summation of miniature excitatory postsynaptic potentials (EPSPs) in these local synaptic circuits (Inostroza & Born, 2013). While this notion of residual activation changes driving subsequent reactivations can account for the observation that salience tags deteriorate over time when sleep is not initiated (Rauchs et al., 2011), its underlying assumptions have not been thoroughly empirically validated at present. Moreover, it cannot conclusively explain the retrospective effects of learning intention observed in certain studies (Barner et al., 2017; Fischer & Born, 2009; Wilhelm et al., 2011). A different view (Stickgold & Walker, 2013) proposes that tagging of specific items

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[13] In instances involving monetary incentives this may extend to frontal-subcortical circuits enclosing the mesolimbic system, see Perogamvros and Schwartz (2012).

may be accomplished by differential hippocampal activation during encoding, as this has been found to predict recognition memory after sleeping (Rauchs et al., 2011). However, this is at odds with the assumption that reactivations are initiated by top-down-mechanisms, specifically by the depolarizing up-state of the slow oscillation, which has been confirmed across a wide range of findings (see I 3.2.). Consequently, generation of salience tags likely results from a dialog between the PFC and hippocampus (Diekelmann & Born, 2010; Inostroza & Born, 2013), which is epiphenomenologically reflected by an enhancement of hippocampal activation during encoding. Furthermore, the notion that tagging underlies the enhanced recruitment of strategic processing during encoding is supported by findings that weakly encoded material (Creery, Oudiette, Antony, & Paller, 2015; Drosopoulos, Schulze, Fischer, & Born, 2007; Kuriyama, Stickgold, & Walker, 2004), as well as highly demanding stimuli (Schmidt et al., 2006), are selectively enhanced over sleep. On the whole this may reflect that cognitive effort (and its secondary processes) critically determines whether sleep-dependent consolidation is instated or not.

Alongside these modulatory effects of learning intention, it is currently emerging that there are specific preconditions regarding the accessibility of newly formed, declarative memory representations to sleep-dependent reactivation and redistribution. In this regard, a certain degree of prior knowledge as to the semantic concept of the to-be encoded stimulus appears to be necessary for sleep-dependent consolidation to succeed (Durrant, Cairney, McDermott, & Lewis, 2015; Groch, Schreiner, Rasch, Huber, & Wilhelm, 2017). On the other hand, when stimuli have already been successfully integrated into existing neocortical networks at the initial encoding stage, thus bypassing intermediate storage in the MTL, sleep-dependent consolidation does not appear to be initiated (Himmer, Müller, Gais, & Schönauer, 2017). As such, it appears that stimuli amenable to sleep-dependent consolidation have to bear the potential to be integrated into preexisting semantic networks without this integration actually having succeeded prior to sleep. This also supports the predictions regarding the outcomes of sleep-dependent system consolidation (Diekelmann & Born, 2010), ultimately culminating in a complete assimilation into neocortical networks (see I 3.2.).

In summary, the underlying mechanisms of sleep’s selectivity in episodic memory consolidation are presently not exhaustively characterized. The conception of a secondary effect of learning intention that is mediated by prefrontal regions has been proven to be helpful in accounting for empirical observations, and will serve as a preliminary working model in the context of this thesis. While it may be tempting to subsume emotionality in this model as a potential influential factor of learning intention, empirical regularities observed in this regard strongly diverge from the mechanisms described in this chapter. As this constitutes the main subject of this thesis, the following chapter will provide a comprehensive account of sleep-related effects on emotional memory consolidation.

4. Emotional memory and sleep

In this final chapter extant empirical findings on the potential involvement of sleep in emotional episodic memory will be reviewed (see I 4.1.). Theoretical assumptions and frameworks that have been derived therefrom are presented and discussed in the succeeding section (see I 4.2.). Finally, a provisional integration of empirical and theoretical accounts is attempted with regard to the question, whether REM sleep-related processes boast the capacity to enhance associative memory of emotional material (see I 4.3.).

4.1. Empirical findings: Behavioral evidence and neurophysiological correlates

In parallel to the accumulation of findings on the role of sleep in the consolidation of episodic memory, embedded in a framework of SWS-inherent processes, a separate line of research has evolved demonstrating a superior retention of emotional as opposed to neutral events after sleep. This objective was strongly inspired by animal studies, wherein learning paradigms are often inherently emotional (e.g. fear conditioning), and which consistently found aberrations in sleep, but particularly in REM sleep physiology, to be closely related to the failure of retrieving an acquired reaction (see also I 4.2.). These sleep-dependent processes were shown to relate to the human episodic memory system by demonstrating superior recall of emotional, as opposed to neutral, texts after sleep, which was evident specifically after the second (REM-sleep-rich) but not across the first night half (Wagner, Gais, & Born, 2001). Moreover, this selective effect persisted across a delayed retention interval of four years signifying the profound alterations of the underlying memory representation occurring during sleep (Wagner, Hallschmid, Rasch, & Born, 2006). Many ensuing studies focused on the retention of emotional as opposed to neutral item memory and predominantly found a selective enhancement of the former (but see Baran, Pace-

Schott, Ericson, & Spencer, 2012; Cairney, Durrant, Power, & Lewis, 2015), which was critically dissociable from the general retention benefit of emotional material across generic wakefulness (see I 2.2.; Cunningham et al., 2014; Hu, Stylos-Allan, & Walker, 2006; Nishida, Pearsall, Buckner, & Walker, 2009; Payne, Chambers, & Kensinger, 2012; Payne & Kensinger, 2010; Payne, Stickgold, Swanberg, & Kensinger, 2008; Prehn-Kristensen et al., 2009; Prehn-Kristensen et al., 2013). Moreover, this selectivity is not merely evident across emotional and neutral trials but also emerges within a single affective experience as reflected by a sleep-related enhancement of recognition memory for emotional foreground objects superimposed on background scenes (Cunningham et al., 2014; Payne et al., 2012; Payne & Kensinger, 2010; Payne et al., 2008). In line with the general central/peripheral tradeoff effect (see I 2.2.), this coincides with impaired item recognition of the background (Payne et al., 2012; Payne et al., 2008), suggesting that emotion-specific sleep-related consolidation effects operate in a highly selective manner.

Beyond these behavioral specificities, sleep-related effects on emotional memory consolidation have been found to underlie fundamentally different neurophysiological processes to those implicated in episodic memory in general (see I 3.2.). This is reflected by strong associations between behavioral performance benefits and REM sleep duration (Groch, Wilhelm, Diekelmann, & Born, 2013; Nishida et al., 2009; Payne et al., 2012; Wiesner et al., 2015 but see Payne et al., 2015) as well as REM-sleep-specific microstructural features (Gilson et al., 2015; Nishida et al., 2009; Prehn-Kristensen et al., 2013). In a seminal study, Nishida et al. (2009) examined memory retention of emotional and neutral images in a nap paradigm while simultaneously assessing specific oscillatory features in the critical consolidation phase during sleep. Behaviorally, recognition memory of neutral and emotional images encoded prior to (remote) and after sleep/ sustained wakefulness (recent) differed significantly between both groups. While the control condition exhibited similar retention rates across both stimulus categories, a significant benefit in retention (remote– recent) across sleep emerged selectively for emotional images in the nap group, albeit not significantly exceeding remote recognition performance of the wake group. However, within-group variance in this retention benefit (remote- recent) for emotional stimuli was significantly related to REM sleep duration, as well as REM sleep latency of the intervening nap which strongly supports the functional significance of the observed effect. Moreover, the authors were able to establish a link between the consolidation benefit for emotional images and right-frontal theta (4- 7 Hz) dominance[14] (µV²/Hz) during REM sleep. This strong correspondence (r= .88) between behavioral performance and the oscillatory signature of REM sleep originally substantiated that an active reprocessing of previously encoded emotional material must occur during epochs of REM sleep. Furthermore, the specific frequency range (4- 7 Hz) of oscillatory activity as well as its frontal distribution is remarkably aligned with the mechanisms that have emerged in animal studies examining the effects of sleep on fear conditioning (see also I 4.2.). In support of this novel finding, Prehn-Kristensen et al. (2013) were able to establish a similar association between the benefit of recognizing emotional as opposed to neutral images following sleep ($PR_{Emotional}$- $PR_{Neutral}$), and absolute theta power (µV²) at electrode F4. While it may be argued that these studies (Nishida et al., 2009; Prehn-Kristensen et al., 2013) merely constitute isolated findings, a corresponding line of evidence suggesting an active reprocessing of emotional memories during REM sleep can be drawn from studies employing neuroimaging techniques.

In fact, a profound neuronal reorganization of emotional memory has been found to emerge over sleep as reported by Sterpenich et al. (2007) for the first time. By contrasting retrieval of neutral and emotional images following sleep-related consolidation or disruption thereof[15], the authors found larger responses in the hippocampus and ventromedial PFC (vmPFC) as well as an enhanced functional connectivity between these regions specific to the rested sleep condition. While this suggests that a redistribution towards neocortical networks progresses over sleep, it may also signify a stronger engagement of controlled processes within the emotional memory network (see I 2.1.) during retrieval after sleep. This latter aspect was also reflected in activation patterns of the sleep-deprived group, which disclosed an enhancement of activation in the amygdala during retrieval. Moreover, when retrieval processes were reexamined after 6 months (Sterpenich et al., 2009), a similar region of the vmPFC was strongly engaged during emotional memory retrieval in the former rested sleep group, while differential effects on hippocampus activation were no longer retained. This may tentatively be interpreted to reflect the accomplishment of sleep-

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[14] This measure is derived by subtracting theta power at electrodes F4 and F3, as such reflecting the difference in activation in the right hemisphere.

[15] One group was sleep deprived during the night following encoding. Both groups were tested after 3 days and were not impacted by acute effects of sleep deprivation and fully recovered during retrieval testing.

related system consolidation in the rested sleep group, which over time culminates in retrieval processes that are supported by the neocortex and no longer require the hippocampus (see also I 3.2.). On a general level, these findings (Sterpenich et al., 2007; Sterpenich et al., 2009) were confirmed by a succeeding study (Payne & Kensinger, 2010) demonstrating the emergence of a refined network including the vmPFC during successful retrieval of emotional images after sleep, but not after an identical period of wakefulness. Intriguingly, Cairney et al. (2015) were able to establish that the increase in hippocampal-neocortical connectivity, in this study specifically between the right hippocampus and superior frontal gyrus, during the successful retrieval of emotional stimuli after sleeping was linearly related to the amount of intervening REM sleep. This may suggest that these alterations in retrieval-related activation may revert to the same REM-sleep-related mechanisms as disclosed in the studies of Nishida et al. (2009) and Prehn-Kristensen et al. (2013).

A slightly different emerging line of findings delineates an enhanced recruitment of visual processing areas during successful retrieval of emotional material following sleep in close association to REM-sleep-dependent processes (Bennion, Payne, & Kensinger, 2017; Sterpenich et al., 2014). By employing a task design entailing neutral and emotional foreground objects embedded in neutral background scenes, Bennion et al. (2017) found that successful retrieval of neutral background scenes that were previously encoded with an emotional object elicited differential activation in the middle occipital gyrus in participants who had slept in the critical retention period. Moreover, a selective correlation between activity in various regions along the ventral visual stream during successful retrieval of emotionally-associated neutral background scenes, and REM sleep duration, was evident in the sleep group. This finding is complemented by the preceding results of Sterpenich et al. (2014), which established a link between TMR during REM sleep and enhanced retrieval-related activation in visual processing areas (i.e. culcerine sulcus and fusiform gyrus) to emotional as opposed to neutral images. In considering the interactions of emotion with visual processing at early stages of encoding (see I 2.2.), it is tempting to speculate that sleep-related consolidation expands on these arousal-induced effects on primary visual integration (see I 4.3. for a more detailed discussion). While there are currently no empirical accounts directly addressing this interpretation, it may, nonetheless, be broadly concluded that a reorganization of emotional memory over sleep is evident both with regard to an enhanced involvement of the mPFC as well as visual processing areas during subsequent memory retrieval.

Whereas many studies have focused on the effects of sleep on emotional item recognition, it has rarely been addressed how these processes may relate to associative memory formation and recollection-based retrieval. Some studies have examined whether sleep differentially impacts recollection by means of the remember-know-new paradigm with inconsistent results (Atienza & Cantero, 2008; Cairney et al., 2015; Hu et al., 2006; Sterpenich et al., 2007; Sterpenich et al., 2014). In a 12-hour-sleep/wake-design, Hu et al. (2006) found a significant retention benefit for emotional stimuli after sleep which was driven by familiarity-based responses. Subjective recollection, on the other hand, was equally enhanced for emotional images across 12 hours entailing wakefulness or a night of sleep. Other studies, however, failed to find any differences in subjective familiarity and recollection of emotional material in response to sleep (Atienza & Cantero, 2008; Cairney et al., 2015). Moreover, Sterpenich et al. (2007) even found recollection of negative material to be protected across post-encoding sleep deprivation in the critical consolidation phase resulting in similar recollection estimates for negative but not neutral images in the sleep-deprived and rested sleep groups (but see Atienza and Cantero, 2008 for different findings in a similar study design). Finally, Sterpenich et al. (2014) found a significant enhancement of recollection over familiarity for emotional material after sleep, however this was evident across different conditions of TMR (applied in different sleep stages) and thus may not genuinely relate to sleep-related processes but reflect effects of generic consolidation (see I 2.2.).

A slightly different approach to the veridicality of retrieved memory representations is provided by the same-similar-task (see Kensinger, Garoff-Eaton, et al., 2007b for a detailed description) in which stimuli of the initial learning phase (“same”) have to be detected among lures that are highly similar to other stimuli of the learning phase (“similar”; i.e. different exemplar of the same category), and ordinary lures (“new”). Subsequent analyses can be based on a generalized index of memory performance (Same+Similar|Same), as well as detailed recognition performance (Same|Same). Utilizing this task design in a 12-hour-sleep/wake-design (Payne et al., 2008) and a 24-hour-wake-first/sleep-first-design (Payne et al., 2012), disclosed selective effects of sleep on emotional foregrounds both for general and specific memory, albeit more pronounced for the latter (only a trend of the critical interaction emerged for general memory in Payne et al., 2012). This lack of a selective effect on specific recognition[16] of emotional material is not highly suggestive of a differential engagement of recollection in sleep-related emotional memory enhancements but, nonetheless, does not dismiss the possibility. When ascertaining item memory it is possible to study the contributions of underlying retrieval processes by means of ERPs, which was applied in the present context by Groch et al. (2013). The authors employed a within-subject split-night-design, contrasting early SWS-rich sleep in the first night half with late REM-sleep-rich sleep in in the second night half (see Figure II 1). Complementing prior findings the authors found a beneficial effect of REM sleep (in the second night half) on emotional recognition memory, which was associated with an early frontal positivity (300- 500 ms). The topography and time window of this effect may suggest an enhancement of familiarity for emotional images. However, this was not fully substantiated by a direct test comparing the amplitudes elicited by hits to emotional stimuli between early and late sleep conditions.

Finally, attempts have been made to disambiguate the potential contributions of REM sleep to emotional associative memory by examining performance on source or associative memory tests. Some studies examined source memory performance by means of location memory with mixed results (Cairney, Durrant, Hulleman, & Lewis, 2014; Groch et al., 2015; Stenstrom, 2010). In a study employing a virtual reality task in which emotional or neutral events occurred at different locations of a virtual environment, successful retrieval of emotional location memory was significantly impaired in a group that was deprived of REM sleep in the critical consolidation phase (Stenstrom, 2010). A different study (Cairney et al., 2014), on the other hand, did not find any beneficial effect in retrieving the initial location of emotional stimuli emerging across a period of sleep. However, this study was designed with the intention of inducing TMRs and thus did not include a wake control group, limiting potential comparisons. Moreover, memory performance did not decline significantly in either stimulus category over time, which may signify ceiling effects due to

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[16] Neither of both studies reported analysis contrasting general and specific memory performance. However, as effects were similar in magnitude and direction, a significant interaction involving this factor (as well as emotionality and sleep) is unlikely.

overtraining prior to sleep. Groch et al. (2015) ascertained location memory (one of four quadrants on the screen) of emotional and neutral stimuli while simultaneously probing memory of a color frame (one of four colors) that preceded item presentation during the encoding phase. Memory performance was contrasted prior to and following sleep in the first SWS-rich (early sleep condition) and second REM-sleep-rich (late sleep condition) night half (see Figure II 1 for illustration). Converging with prior accounts, item recognition of emotional images was found to be selectively retained in the late sleep condition. Analysis of location memory yielded no effects of sleep-related consolidation in either condition. The validity of this finding is however compromised by significant baseline differences between early and late conditions prior to sleeping. With regard to the successful retrieval of color frames, a significant beneficial effect emerged selectively for neutral images across early SWS-rich sleep. However, it is difficult to derive clear implications from this with regard to REM-sleep-related mechanisms as color memory was found to be generally impaired for emotional images (significant main effect of emotion), thus potentially precluding any beneficial add-on effects of REM-sleep-dependent reprocessing. Moreover, as source memory is naturally constrained by the amount of correctly recognized old images, it is important to account for this dependence in subsequent analysis which was neglected in the present study. Analysis on absolute source hits may thus have been biased by differential item recognition rates across early and late night sleep (see above). Nonetheless, it is noteworthy that SWS-related consolidation processes over the first night half did not result in a general retention benefit of source memory across item categories, but may have only been initiated for neutral images. In light of this unexpected finding, Groch et al. (2015) performed a follow-up study employing the same paradigm but additionally varying motivational salience of emotional and neutral stimuli during encoding (by introducing high vs. low monetary incentives). This resulted in an equal retention benefit of emotional source memory over the first half of the night as for neutral material. This account of variable effects depending on external enforcement of learning motivation highlights that tagging mechanisms preceding SWS-dependent reactivation (see I 3.3.) may be differentially initiated in relation to specific stimulus features.

Complementing this line of findings, recent attempts have been made to ascertain the effects of (REM) sleep in associative memory tasks entailing emotional and neutral material (Alger & Payne, 2016; Lehmann, Seifritz, & Rasch, 2016; Lewis et al., 2011). In a series of studies Lewis et al. (2011) examined the effects of a 12-hour-sleep/wake-manipulation and of a circadian-controlled nap manipulation on the retention of associations between neutral everyday objects and context scenes, which were either emotional or neutral. Memory was ascertained prior to (immediate), and after the respective retention interval (delayed) by means of a recognition test of isolated objects. Associative memory was additionally probed by asking participants to retrieve the encoding context of objects (emotional, neutral or unknown). While main effects of valence on object and context memory were inconsistent between experiments, sleep as opposed to wakefulness was consistently found to enhanced context memory equally for both valence types without producing any beneficial effects on object recognition. On a neurophysiological level, successful retrieval of emotional contexts elicited enhanced activation in the left amygdala, right anterior PH region and the vmPFC only after sleep had occurred in the respective consolidation interval. Moreover, sleeping was associated with an enhanced connectivity between the left amygdala and right anterior PH region during retrieval of emotional contexts, suggesting a reorganization of associative memory across sleep-related consolidation, which is genuine to emotional material. However, it cannot be inferred from these results which processes (in relation to specific sleep stages) effectuated these changes in activation patterns. Lehmann, Seifritz, et al. (2016) similarly utilized a 12-hour-sleep/wake-design to examine the retention of associations between verbally presented words and images of varying valence (neutral or emotional). In a cued recall procedure, the authors found a beneficial effect of sleep on the retention of images across valence categories. However, as this procedure involves the retrieval of bound features across different modalities, it may not recruit the same processes as the formerly discussed studies ascertaining memory within a single modality (Mayes et al., 2007). Lastly, a very recent study by Alger and Payne (2016) employed a paradigm aimed at assessing associative recognition of emotional and neutral object-face pairs. The faces of these associations were always neutral and overlapping[17] between two stimulus pairs of the same valence category,

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[17] At encoding two different faces (A and C) were presented with the same object (B) in separate trials. During retrieval phases participants were probed with a face and had to choose the corresponding object in a forced-

thus yielding an additionally measure of relational memory for the indirect association. Within an afternoon nap design, the authors found a consolidation benefit of emotional associations across both groups, whereas nap sleep resulted in a genuine retention benefit for neutral associations across time. This differential pattern was not evident with regard to relational memory, which was enhanced across both valence categories in the nap group, albeit without accounting for performance immediately after encoding. Interestingly, the finding of a selective facilitation of neutral associative memory performance across sleep resembles the effects reported by Groch et al. (2015) and thus enforces the idea that SWS-dependent processing may only limitedly result in the strengthening of emotional associations.

Two further studies that can only be partially considered in this context ascertained memory performance with regard to the temporal order (Groch et al., 2011) and spatiotemporal details (Gilson et al., 2015) within emotional and neutral stories, however with a low level of standardization during encoding (Groch et al., 2011) and retrieval (Gilson et al., 2015; Groch et al., 2011). While the former study found emotional context memory to be disrupted by noradrenergic suppression during SWS, albeit only examining the first half of the night with inherently low levels of REM sleep, the latter found a selective correlation between emotional context memory and density of rapid eye movements during REM sleep.

Prior to attempting an overarching integration (4.3.) of these findings under consideration of theoretical accounts (4.2.) it may be summarized that empirical results with regard to source and associative memory are highly heterogeneous. Some studies suggest that emotional associative memory is supported by the same mechanisms as they generally apply to sleep-related associative memory consolidation (Cairney et al., 2014; Lehmann, Seifritz, et al., 2016), whereas others imply that these are only limitedly initiated for valenced stimuli (Alger & Payne, 2016; Groch et al., 2015). On the other hand, certain studies rather vaguely indicate that REM sleep may contribute to successful episodic memory retrieval beyond mere item recognition (Gilson et al., 2015; Stenstrom, 2010). As such, it is important to consider potential neurophysiological processes during REM sleep

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choice procedure. At delayed (post nap) retrieval, participants performed a separate test in which relational memory was probed by presenting a face for which the indirectly linked face had to be identified again in a forced-choice procedure.

that are assumed to enhance emotional item recognition in order to deduce, how this may extend to other aspects of episodic memory.

4.2. Theoretical frameworks on REM sleep and emotional memory consolidation

In light of the predominant associations between emotional memory consolidation and REM sleep-related characteristics emerging with regard to item memory, it has been proposed that the underlying mechanism must be fundamentally different to the processes implicated in the active system consolidation view (Diekelmann & Born, 2010). In an attempt to integrate these empirical particularities in reference to the neurophysiological features of REM sleep, Walker and van der Helm (2009) introduced the "*Sleep to forget and sleep to remember*" (SFSR) model of emotional memory processing, which emphasizes both neuroendocrinological and oscillatory processes of wakefulness and REM sleep (see I 3.1.). In line with the general episodic memory literature, the model assumes that successful encoding processes in the wake state (see Figure I 9 left) result in the formation of a memory trace that is supported by the hippocampus and neocortical structures in parallel. The multiple elements of this representation are stored in different neocortical modules and bound into a coherent episode by the hippocampus. If the episode in question is perceived as emotional, this is assumed to elicit an arousal-induced enhancement of encoding processes by coinciding activation of the amygdala and, on a neuroendocrinological level, by aminergic and cholinergic modulations (see also I 2.2.). Moreover, these arousal-related mechanisms are assumed to result in a prioritization of newly formed memory representations at subsequent processing stages, particularly related to the phase of consolidation. During subsequent sleep, and therein specifically during REM sleep, newly formed memory representations are assumed to be reactivated in this emotional memory network (see Figure I 9 middle).

Figure I 9[18]**.** Illustration of the sleep to forget and sleep to remember (SFSR) model of emotional memory processing. Taken from Walker, M. P., & van der Helm, E. (2009). Overnight therapy? The role of sleep in emotional brain processing. *Psychological Bulletin, 135*(5), 731-748. *Note*: The upper panel illustrates neurohormonal concentrations while the lower panel depicts putative neurophysiological processes during successive stages of memory encoding, consolidation and retrieval.

On a global level, this is believed to be reflected by the marked enhancement of activation in the limbic system observed during REM sleep (Brown, Basheer, McKenna, Strecker, & McCarley, 2012; Nofzinger, 2005). On a local level, these interactions may be mirrored by theta oscillations (4-7 Hz) propagating from synchronized activation across different regions (see Figure I 9 middle). The coinciding shift in neurohormonal concentrations at the onset of REM sleep, particularly the inhibition of aminergic tone (see Figure I 9 upper panel), is assumed to be of functional significance in this regard as it is thought to alleviate the affective charge associated with the reactivated memory representation. Moreover, the enhancement of cholinergic activity (see Figure I 9 middle) during REM sleep closely resembles modulations of this transmitter system observed during wakeful encoding of emotional material (see I 2.2.) and may reflect consolidation processes on a neuroendocrinological level (but see Hutchison and Rathore, 2015 for a different view on this). While the model makes no clear assumptions regarding the specific aspects of memory retrieval which benefit from this REM-sleep-dependent reprocessing, it assumes that reactivations enable interactions of disparate brain regions storing contextual features of different sensory modalities (Goldstein & Walker, 2014). These interactions are believed to result in a gradual redistribution towards hippocampus-independent, neocortical storage

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[18] Zur Wahrung der Lizenzrechte des Verlages wird die Abbildung nicht dargestellt.

(see Figure I 9 right) and also in a strengthening of distributed aspects of emotional memory representations. Consequently, the model implicitly assumes an enhancement of associative memory during subsequent wakefulness. Moreover, coincidental reprocessing of the episode’s affective charge is proposed to effectuate an attenuation of emotional reactivity during wakeful retrieval, as denoted by decreased co-activation of the amygdala (see Figure I 9 left). In summary, the model predicts that memory retrieval of emotional episodes is enhanced in response to REM sleep (sleep to remember), whereas the affective charge is successively attenuated (sleep to forget). However, empirical evidence with regard to the latter is highly inconsistent at present and has led recent reviews to de-emphasize this aspect (Rasch & Born, 2013; Werner, Schabus, Blechert, Kolodyazhniy, & Wilhelm, 2015). Nonetheless, the notion that emotional memory benefits from REM-sleep-related processing mechanisms that are reflected by theta oscillations is receiving growing support (see I 4.1.). Walker and van der Helm (2009) substantiate this in their framework by referring to Paré et al. (2002) who originally suggested that the reoccurrence of theta oscillations during REM sleep may reflect reactivations of previously primed networks during wakeful encoding of emotional events. This interpretation receives its cogency from the observation that theta oscillations exclusively emerge in the amygdala under two highly specific conditions; during states of intense arousal, for instance during presentation of a conditioned stimulus (Seidenbecher, Laxmi, Stork, & Pape, 2003), and during REM sleep (see I 2.2.).

Nonetheless two fundamental assumptions must be critically examined in this regard; one being that REM sleep theta causally underlies the neuronal replay of previously encountered episodes, and the other being that this replay genuinely relates to emotional episodes and their subsequent retention. Accordingly, REM sleep theta activity has been demonstrated to underlie coordinated firing of previously activated place cells in the hippocampus which appears to progress at the same time scale as during initial encoding (Louie & Wilson, 2001; Peyrache, Lacroix, Petersen, & Buzsaki, 2015; Poe, Nitz, McNaughton, & Barnes, 2000). Moreover, there is evidence of an experience dependent phase shift of reactivations of place cells coding specific locations that become successively more familiar over multiple learning sessions (Poe et al., 2000). After a place cell initially codes a novel location (during encoding), it preferentially fires during the peaks of theta oscillations (during REM sleep), whereas, with growing familiarity, firing is more likely to occur during the troughs, with conceivable implications on the (de-)potentiation of the respective synaptic circuits during REM sleep (Huerta & Lisman, 1995). With reference to the second assumption, that theta-embedded replay during REM sleep is related specifically to emotional episodes, previous research has yielded considerable insights. Following avoidance learning, but not in a non-learning control condition, Fogel, Smith, and Beninger (2009) found significant increases in theta power during discrete post-training periods of succeeding REM sleep, which are known to be critical in successfully retaining an acquired response (often referred to as REM sleep windows). Moreover, Popa et al. (2010) demonstrated that theta coherence between the amygdala, mPFC, and hippocampus during REM sleep, was correlated with the (inter-individually varying) retention of a conditioned fear response across a 24 hour interval. Beyond this, Boyce, Glasgow, Williams, and Adamantidis (2016) were able to establish the causal relevance of theta oscillations by selectively silencing cells of the medial septum, which are critically involved in the generation of the theta rhythm, by means of optogenetics. When theta activity was selectively reduced during REM sleep this resulted in an impairment of fear-conditioned contextual memory, whereas silencing outside of REM sleep episodes had no effect on subsequent freezing behavior. These accounts are particularly noteworthy as they did not involve the disruption of memory consolidation by means of deprivation procedures, which inherently result in considerable methodological confounds (Genzel et al., 2015; Rasch & Born, 2013).

While extant evidence suggests that REM-sleep-inherent neuronal replay embedded in specific phases of the theta oscillation does exist, some authors (Rasch & Born, 2013; Spoormaker et al., 2013) have noted that this replay may only be relevant to plastic changes in highly constricted circuits, as such not contributing to system consolidation per se, due to the reduced cross-regional coherence in global activation during REM sleep. However, in opposition to this claim, Montgomery, Sirota, and Buzsáki (2008) demonstrated that the emergence of phasic REM episodes create short recurring time windows during which intra-hippocampal theta synchronization may induce output to downstream cortical targets. In fact, the emergence of hippocampal theta activity in general may be restricted to phasic (as opposed to tonic) REM epochs (Cantero et al., 2003), which are characterized by sympathetically driven rapid eye movements, muscle twitches and cardiovascular irregularities (Carskadon & Dement, 2005). On an oscillatory level this state is signified by the propagation of pontine-geniculo-occipital (PGO) waves, which are intense bursts of synchronized activity arising from the pontine brainstem to the lateral geniculate nuclei of the thalamus and the occipital cortex (Diekelmann & Born, 2010). Although the existence of these field potentials has not been fully established in the human brain (Rasch & Born, 2013), animal studies intriguingly suggest that PGO waves critically contribute to the retention of conditioned fear responses (Datta, Li, & Auerbach, 2008; Ulloor & Datta, 2005) as well as successful fear extinction (Datta & O'Malley, 2013).

As recently proposed by Hutchison and Rathore (2015) PGO waves may enhance synaptic plasticity in areas they pass through, including the hippocampus and amygdala, potentially by increasing expression of plasticity-related genes in the respective structures (Datta et al., 2008; Ulloor & Datta, 2005). This is corroborated by findings demonstrating that PGO waves occur phase-locked to (and potentially driven by) theta oscillations, and that their density is reflective of coincidental theta synchronization between the hippocampus and amygdala (for a review see Hutchison and Rathore, 2015). Taken together this suggests that both PGO waves and theta oscillations may be epiphenomological of one unitary memory process that appears to intricately relate to emotional memory retention across sleep. Moreover, this process, although involving a partially overlapping network of structures, appears to be highly distinct from the SWS-dependent mechanism, as pointed out by Genzel et al. (2015). Their theoretical integration (see Figure I 10) also expands on the marked difference in cholinergic tone between SWS and REM sleep (Hasselmo 1999; see Bergmann and Staresina, 2017 for a summary), which may relate to different processing modes in the hippocampus; either supporting hippocampo-neocortical information flow and, thereby, system consolidation (during SWS) or enhancing neocortico-hippocampal flow, enabling re-encoding or adaption of hippocampal memory traces (during REM sleep). However, it is important to note that the concurrent suppression of aminergic chemistry during REM sleep may conversely enhance excitatory feedback within neocortical networks, as noted by Hutchison and Rathore (2015).

Figure I 10[19]. Illustration of different oscillatory mechanism and concomitant changes in neurohormonal concentrations which have been established for NREM-dependent consolidation (left) and which may be of potential relevance in REM-sleep-dependent consolidation of emotional episodes (right). Taken from Genzel, L., Spoormaker, V. I., Konrad, B. N., & Dresler, M. (2015). The role of rapid eye movement sleep for amygdala-related memory processing. *Neurobiology of Learning and Memory*, *122*, 110-121. *Note:* SO= slow oscillations, SWR= sharp-wave ripples, NREM= Non-REM sleep, REM= REM sleep, PGO Waves= pontine-geniculo-occipital waves, HPC= hippocampus, mPFC= medial prefrontal cortex.

To summarize, enhanced cholinergic tone and attenuated aminergic activity may globally set the stage for cortico-cortical reorganization of emotional memory representations during REM sleep. However, transiently reoccurring periods of phasic REM may conversely result in increased theta coherence between the hippocampus and neocortex, which could enable information exchange by replay of activity to the neocortex. As such the globally disengaged activation patterns across different regions observed during REM sleep do not dismiss the possibility of transient windows of subcortical-cortical synchronization, which are required for system consolidation. It is important to note that the ambiguity of these considerations results from the lack of any direct empirical investigations in human subjects. Thus, all of the present considerations rely on theoretical assumptions and findings of animal studies that are not easily translated to the human memory system (Genzel et al., 2015). Nonetheless, the succeeding section will provide a preliminary integration of the current state of research as to the potential effects of REM sleep-dependent consolidation on associative memory retention. Moreover, it will be discussed, how sleep-dependent consolidation in general may support emotional associative memory

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[19] Zur Wahrung der Lizenzrechte des Verlages wird die Abbildung nicht dargestellt.

by different processes (related to SWS and REM sleep) with regard to different underlying memory representations (intra- or inter-item associations).

4.3. Integration of theoretical and empirical accounts

Early accounts of sleep-related consolidation have promoted a dichotomous view on the contributions of SWS and REM sleep to memory performance (Maquet, 2001). While the former was advocated to enhance declarative memory, the latter was subsumed to provide a function in other, essentially non-episodic memory domains, such as procedural memory. Hence, it has often been concluded that REM sleep-dependent processes do not contribute to hippocampus-dependent associative memory, both in general as well as with regard to emotional stimuli (Marshall & Born, 2007). However, as evident from the literature (see I 4.1.), emotional memory paradigms that have been employed in this context seldomly probe associative/source memory retrieval, which has precluded the emergence of any strong empirical evidence to base these assumptions on. Nonetheless, many authors (Rasch & Born, 2013; Spoormaker et al., 2013) do not intuit a role of REM sleep in associative memory consolidation due to the inherent involvement of interactions across different memory systems (specifically between the hippocampus and neocortex). These interactions require a fine-tuned subcortical-cortical information flow and are thus confined to states of neuronal silence, which dominate during SWS (Axmacher, Helmstaedter, Elger, & Fell, 2008). Contrary to this, global activation patterns during REM sleep do not suggest high levels of cross-regional synchronization and intra-hippocampal synchrony (Grosmark, Mizuseki, Pastalkova, Diba, & Buzsáki, 2012). In the opinion of Spoormaker et al. (2013), this does not corroborate a specific role of REM sleep in the transfer of hippocampus-dependent memory traces, but rather in subsequent stages of generic memory processing and integration into preexisting neocortical schemes (Stickgold & Walker, 2013). These stages of memory reprocessing likely succeed SWS-dependent system consolidation and may entail incidental outputs of the hippocampus to neocortical sites through sporadic bursts of activity (Spoormaker et al., 2013).The conception that REM sleep does not provide a generalized function to system consolidation is also supported by earlier studies in rodents, revealing effects of REM sleep deprivation on cued, but not contextual (hippocampus-dependent) fear extinction (Fu et al., 2007; Silvestri, 2005).

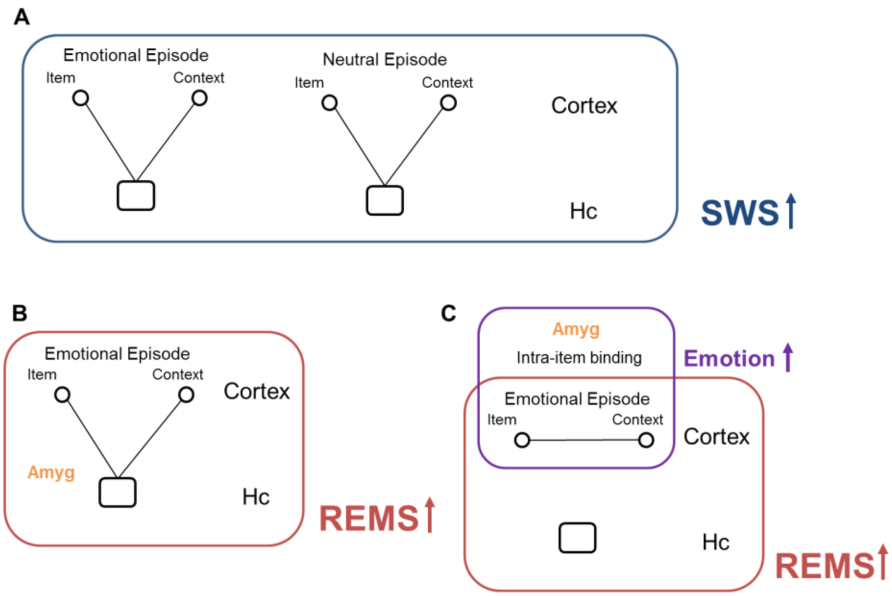

Figure I 11. Illustration of three different pathways by which sleep may support emotional associative memory consolidation. **(A)** SWS may enhance memory performance for emotional associations in similar vein to neutral associations. **(B)** Emotional associations may be supported by a distinct consolidation mechanism accomplished across REM sleep. This process may critically entail cooperative activation changes in the amygdala (Amyg). **(C)** Emotional associative memory may be supported by REM sleep via the selective consolidation of emotional intra-item associations. Modulatory influences of amygdala activation may facilitate intra-item binding processes at the encoding stage for emotional associations. These may then be subsequently reprocessed independently of the hippocampus (Hc) during REM sleep. *Note:* Amyg= amygdala, Hc= hippocampus, SWS= slow wave sleep, REMS= REM sleep.

Following this line, it would be argued that the effects of REM sleep on emotional memory retention are based on the reprocessing of memory traces that previously underwent SWS-related consolidation, thus enhancing item recognition (see I 4.1. for empirical findings supporting an enhancing effect in recognition tests) without genuinely contributing to system consolidation of emotional associations. Rather, this latter function would be supported by SWS-dependent processing resulting in a benefit analogous to neutral material (see Figure I 11.A for an illustration).

However, as previously discussed, newly emerging rodent studies do suggest a role of REM sleep in contextual fear consolidation (Boyce et al., 2016). Moreover, models of REM-sleep-related processing mechanisms are being successively refined and have incorporated field potentials (PGO waves) that may mediate cross-regional changes in plasticity and thus bear the potential to support hippocampal-neocortical information exchange (Genzel et al., 2015; Hutchison & Rathore, 2015). Furthermore, computational models suggest that the cholinergic tone during REM sleep toggles the information flow in the neocortico-hippocampal direction (Bergmann & Staresina, 2017), which, although fundamentally deviating from the processing mode during SWS, may induce encoding-like changes in synaptic connectivity related to theta oscillations (Hasselmo, 2006). Moreover, the findings of Nishida et al. (2009) and Prehn-Kristensen et al. (2013) yield corresponding evidence of a functional role of REM sleep theta in the human memory system, albeit restricted to the examination of item recognition. Although it may be argued that these findings are not informative as to processes within the MTL system, the coherence of theta activity in the hippocampus, amygdala and mPFC (Popa et al., 2010), suggests that theta activity during REM sleep assessed by scalp EEG may be indicative of synchronized activation between these structures (Hutchison & Rathore, 2015). In this context, it is also important to highlight the characteristic activation changes in the limbic system during REM sleep (Nofzinger, 2005), which may mark selective reactivations and subsequent reorganization of emotionally-laden episodes during transient windows of phasic REM sleep. Based on this competing line of evidence, it would be hypothesized that REM sleep exhibits the capacity to support the transfer of initially hippocampus-dependent memory representations in a network of structures that overlaps with that implicated in the active system consolidation framework but critically includes the amygdala (see Figure I 11.B).

While this notion entails that REM-sleep-inherent processing mechanisms revert to the consolidation of hippocampus-dependent item-context-associations there is, in fact, another possibility. As described throughout section I 2.2., arousal-induced modulations in early visual integration may facilitate the encoding of intra-item associations when an emotional episode is encountered. These integrated representations are likely to encompass perceptually linked features of an arousing stimulus as well as details that are of functional significance with regard to its affective character. When considering that REM-sleep-related (as well as generic wakeful) consolidation of emotional material is likely initiated by encoding-related residual activation changes (see emotional tagging), it is conceivable that these intra-item associations may be drawn upon during subsequent REM-sleep-related reprocessing. Although there is no direct evidence suggesting an enhancement of emotional associative memory in response to REM sleep that is mediated by the preferential encoding and subsequent reactivation of intra-item associations, neuroimaging findings (Bennion et al., 2017; Sterpenich et al., 2014) have yielded certain insights in this regard. These findings suggest that successful retrieval of emotional material following sleep-related consolidation coincides with an enhanced recruitment of activation in visual processing areas (see I 4.1.). This is of particular relevance in this context as areas along the ventral visual stream are both critical for sensory integration (Staresina & Davachi, 2010) and share strong reciprocal connections to the amygdala (see I 2.1.). Critically, Bennion et al. (2017) were able to demonstrate a selective correlation between specific activation enhancements in these areas for emotionally associated background scenes and preceding REM sleep duration. This may indicate that REM-sleep-related processes selectively pertain to emotional intra-item bindings, which were previously processed along the ventral visual stream, resulting in post-sleep modulations of neurophysiological activation in these respective areas. Another aspect to consider in this regard is the critical role of PGO waves in fear conditioning studies. As these field potentials originate in the brainstem and culminate in the occipital cortex[20] this could provide a potential "crossroad" along which REM-sleep-related processes may interact with the visual processing system and more critically, induce structural changes. In summary, this view would suggest that REM-sleep-related cortico-cortical reprocessing produces "add on" effects with regard to emotional intra-item associations. As this conception does not implicate a transfer of uniquely hippocampus-dependent memory traces to neocortical storage it does not posit a role of REM sleep in system consolidation per se (see Figure I 11.C). This should result in a retrieval benefit of emotional associations, which is restricted to specific types of intrinsic item features, for which REM sleep bears the genuine capacity to induce enhancements. This notion may account for the inconsistencies of empirical findings, which yield some indications of a REM-sleep-related effect on emotional associations (Gilson et al., 2015; Stenstrom, 2010) but also opposing results in other paradigms (Cairney et al., 2014; Lehmann, Seifritz, et al., 2016). These inconsistencies could plausibly be the result of a differential effect of REM-sleep-dependent processing, which benefits emotional intra-item but not inter-item associations. This is of course grounded on the theoretical assumption that emotional stimuli are preferentially processed in a unitized manner. Neutral stimuli, on the other hand, should not exhibit this specificity in mnemonic processing and thus be

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[20] Although these regions are not primarily involved in ultimate memory storage of integrated memory representations (this is critically supported by the PRC) activation in specific areas of the ventral visual stream (e.g. fusiform gyrus) remains to be related to subsequent retrieval success (Staresina & Davachi, 2010).

predominantly encoded in reliance on the hippocampus and benefit from SWS-dependent consolidation (see Figure I 11.A).

In conclusion the current state of empirical findings does not allow us to infer which of these assumptions is accurate, and they may indeed be partially reconcilable with one another, particularly the first (Figure I 11.A) and last (Figure I 11.C) conception. As there is clearly a lack of empirical findings ascertaining general effects of REM sleep on associative memory performance of emotional and neutral episodes, this motivated the current thesis to explore potential effects, their relation to oscillatory features of different sleep stages, and their boundary conditions with regard to specific study and task designs.

5. Research objectives of the present thesis

The current thesis aimed to examine the contributions of consolidation processes emerging across SWS and REM sleep to the retention of emotional and neutral associative memory. As a wealth of studies has demonstrated the pivotal role of SWS in system consolidation of hippocampus-dependent associative memories (Diekelmann & Born, 2010; Rasch & Born, 2013), it has be assumed that emotional associations are supported by this process alike (Spoormaker et al., 2013). Alternatively, however, the retention of this distinct class of associations may be accomplished by means of an independent process related to REM sleep, in similar vein to emotional item recognition (Hutchison & Rathore, 2015; Walker & van der Helm, 2009). This constitutes an open issue in the present literature with many associated ambiguities, e.g. as to the question whether both processes produce additive effects on emotional associative memory performance. This objective was addressed in the present thesis across two consecutive experiments, ascertaining item and associative memory of neutral and emotional images prior to, and following, putative processes of sleep-related consolidation. While the explicit examination of binding processes at the encoding stage (see above) was omitted in this approach, it was nonetheless a clear aim in designing both experiments to accommodate the specifics of emotional memory processing (Chiu et al., 2013; Kensinger, 2009; Mather, 2007; Murray & Kensinger, 2013), which have been neglected in former studies. Moreover, in order to attain insights into the neurophysiological processes of consolidation emerging during SWS and REM sleep, polysomnographic recordings were ascertained during critical sleep intervals of both experiments. Based on the considerations that have been elaborated throughout the present chapter, it was assumed that sleep-related consolidation in general should be particularly beneficial to associative memory retention. Despite unequivocal preexisting evidence in this regard, it was further hypothesized that emotional associative memory performance would be supported by consolidation processes during REM sleep. Neutral associations, on the other hand, were hypothesized to exhibit a clear retention benefit in response to SWS. Both of these hypotheses were further tested by means of correlational analysis, linking post sleep behavioral performance to spindle activity during NREM sleep as well as right-frontal theta lateralization during REM sleep.

In experiment 1 these objectives were addressed in a split-night-design, ascertaining the effects of early night sleep as opposed to late night sleep on subsequent memory performance. This rationale enables a partial dissociation of the effects of SWS and REM sleep, as the former prevails during the first night half, whereas prolonged REM sleep episodes are reliably detected to set in throughout the second night half (see Groch et al., 2013 and Groch et al., 2015 for a similar approach). Memory performance was assessed in a source memory paradigm, which entailed the encoding of emotional and neutral images at different screen locations, thus enabling the joint assessment of item and source recognition in the retrieval phase. Successful retrieval was probed prior to and after sleeping in the respective night half which allowed us to examine performance decrements across time within each group. In addition, post sleep performance differences were contrasted between groups. In order to disambiguate the findings of experiment 1 with regard to potential contributions of wakeful consolidation, a follow-up experiment was conducted implementing the same task but enclosing a retention interval of sustained wakefulness during the day (experiment 1a).

The findings of experiment 1 partially motivated the design of experiment 2, which aimed to examine how SWS and REM sleep support memory consolidation of emotional and neutral associations across a brief sleep interval during the daytime. Additionally, the experiment was designed to test whether previous effects generalize to a task procedure with different requirements during associative feature processing. In order to address this, an early morning nap design was employed, which contrasted performance changes across sustained wakefulness under low-interference conditions, with a 120-minute sleep opportunity aligned to the circadian phase that favors REM sleep occurrence (in the early morning hours). To explore whether previous findings are restricted to item-context-associations that are inherently processed in an integrated manner due to their perceptual intertwining (as in the case of spatial location), a dissimilar task design was utilized in which perceptual integration was required to be actively initiated during encoding. As this task design yielded unexpected results with regard to stimulus valence in experiment 2, a follow-up study (experiment 2a) was conducted to scrutinize differential effects of emotionality on encoding processes of items and item-context-associations respectively.

In the following chapters (II and III), the manuscripts based on experiments 1 and 2 are enclosed consecutively in their original form (including minor changes in formatting and the integration of supplementary materials at appropriate positions).

II Experiment 1. Remembering specific features of emotional events across time: The role of REM sleep and prefrontal theta oscillations

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1. Introduction

Sleep has been shown to have a profound effect on episodic memory consolidation that goes beyond mere protection from retroactive interference (Diekelmann & Born, 2010). Recent research affirms this notion by demonstrating the remarkable selectivity with which sleep-inherent processes operate to yield an enhanced retention of memory representations that are of specific future relevance (Stickgold & Walker, 2013; Studte et al, 2017). Contemporary models (Diekelmann & Born, 2010) assume that these effects critically relate to SWS, which is believed to offer a window of opportunity for reactivations of newly acquired memory representations. These reactivations are presumed to originate from the hippocampus, which is reflected on an oscillatory level by the propagation of SWR complexes. These SWR are believed to enclose compressed hippocampal reactivations and, thereby, may enable a partial redistribution towards long-term storage in the neocortex (Buzsáki, 2015). This process is mediated by thalamocortical sleep spindles (11- 15 Hz), whereas neocortical slow oscillations (< 1 Hz) are believed to drive the initial reactivation of memory representations in the hippocampus (Diekelmann & Born, 2010).

Interestingly, sleep’s selectivity in memory consolidation also pertains to different aspects of episodic memory, specifically item and associative memory processes. While item memory, which refers to the recognition of a previously acquired stimulus, seems to benefit only mildly from SWS, associative memory appears to benefit profoundly from SWS in the consolidation phase (Mednick et al., 2013; Studte et al, 2015). Associative memory refers to the retrieval of contextual or source features of a study episode and thus entails the binding of multiple features to represent an event (Yonelinas, 2002). These binding processes at the encoding stage have been found to rely critically on the hippocampus (Staresina & Davachi, 2009; Yonelinas, 2013). Consequently, the observation that SWS selectively enhances associative recognition aligns well with the active system consolidation account (Diekelmann & Born, 2010) which assumes that reactivations during SWS emerge specifically from the hippocampus. Moreover, the disproportionate involvement of system consolidation in hippocampus-based memory processes can also be observed when item memory performance is distinguished with regard to different retrieval processes (Daurat et al, 2007; Drosopoulos et al, 2005). According to dual process models of recognition memory (Yonelinas, 2002) item memory is supported by two distinct memory processes referred to as recollection and familiarity. These are assumed to operate in distinct neurophysiological circuits, with only the former relying on the retrieval of hippocampal-bound associative information (*see above*). In accordance with the evidence of a selective involvement in associative memory, sleep has thus been found to enhance subjective recollection ("remembering") rather than familiarity ("knowing") in item memory tests (Daraut et al, 2007; Drosopoulos et al, 2005). Critically, this selective involvement is also evident on a neurophysiological level: As mentioned in the foregoing, the process of redistribution in system consolidation may be retraced on an oscillatory level by the temporal coupling of hippocampal SWRs and thalamocortical sleep spindles (Staresina et al, 2015). This process can be partially ascertained by examining EEG activity in the spindle frequency range (11- 15 Hz) during SWS (Mednick et al., 2013; Studte et al., 2015), which has yielded complemental evidence of highly specific correlations between post sleep associative memory performance and spindle density during SWS (Studte et al., 2015).

Despite these converging findings across different approaches, evidence is not entirely unequivocal as to the selective redistribution of hippocampus-dependent memories during sleep-related system consolidation (e.g. Schönauer, Pawlizki, Köck & Gais, 2014, as well as Schönauer, Grätsch & Gais, 2015 and Payne et al, 2012 for divergent findings with regard to semantically related and unrelated word pairs). However, as item and associative memory tests may not yield process-pure measures of underlying retrieval processes (Yonelinas, 2002), this could partially account for inconsistent findings between studies employing different task procedures. On the whole, it is also important to note, that the process of redistribution results in dissimilar qualities of the represented information (more abstract and gist-like; Lutz, Diekelmann, Hinse-Stern, Born & Rauss, 2017) when system consolidation has been fully accomplished. Conversely, certain aspects of memory retrieval, particularly related to the retrieval experience itself, may remain to be supported by the hippocampus across time (Moscovitch et al, 2006). As such, redistribution during system consolidation does not imply an entire reallocation of the memory trace held within this system.

Sleep-related effects on episodic memory formation have been found to exhibit another highly distinctive feature, which pertains to the selective consolidation of emotionally significant episodes (Stickgold & Walker, 2013). Emotional - as compared to neutral - stimuli generally exhibit preferential consolidation over time (Yonelinas & Ritchey, 2015), but this effect is markedly enhanced by sleep (Hu et al, 2006; Nishida et al, 2009; Payne & Kensinger, 2011; Payne et al, 2008). This enhancement has been found to co-occur with profound changes in the neural circuits underlying emotional memory. After sleep, recollection of emotional material is associated with enhanced functional connectivity between the hippocampus and mPFC (Cairney et al, 2015; Sterpenich et al., 2007) as well as attenuated responding of the amygdala (Rosales-Lagarde et al., 2012; Sterpenich et al., 2007). These findings have been interpreted to reflect a decline of emotional reactivity that co-occurs with enhanced recollection of emotional stimuli over sleep (Walker & van der Helm, 2009).

Despite this evidence of a selective consolidation of emotional memories during sleep, remarkably little is known about the exact mechanism by which sleep modulates the consolidation of emotional memories. In contrast to the aforementioned effects of SWS on associative memory, emotional memory has been predominantly associated with REM sleep (Groch et al, 2013; Groch et al, 2015; Nishida et al., 2009; Wagner et al, 2001). Furthermore, preliminary findings indicate that emotional memory reprocessing during REM sleep is correlated with EEG theta activity (4- 7 Hz) and specifically with the extent of right-frontal theta lateralization (Nishida et al., 2009; Prehn-Kristensen et al., 2013). Complementary evidence from animal studies strengthens this notion of a pivotal role of theta oscillations during REM sleep by demonstrating a significant impact of theta coherence between the amygdala and hippocampus on retention of a conditioned fear response (Hutchison & Rathore, 2015; Popa et al, 2010).

Beyond the neurophysiological processes underlying emotional memory enhancements over sleep, only few studies have explored whether the beneficial effects of REM sleep are restricted to emotional item memory or if they do extend to emotional associative memory.

Initial studies did not find selective facilitating effects of sleep on associative memory for emotional items (Cairney et al, 2013; Lewis et al, 2011) but demonstrated a uniform enhancement of associative memory after sleep irrespective of stimulus valence (Lewis et al., 2011). This is in line with the predictions of the active system consolidation hypothesis and suggests that SWS-inherent processing mechanisms are equally instated for emotional and neutral associations. Interestingly, two recent studies demonstrate that sleep-dependent processing is only associated with enhanced associative recognition of neutral but not of emotional images (Alger & Payne, 2016; Groch et al., 2015), thereby indicating that SWS-dependent consolidation of associative memory may only emerge for neutral stimuli. Due to the inconclusiveness of empirical findings it is therefore an open issue whether emotional associative memory, similar to neutral associative memory, is supported by SWS or whether it benefits from REM sleep-dependent processing, similar to emotional item memory.

Taking differential effects of emotion on associative binding into account (Chiu et al, 2013; Kensinger, 2009; Mather, 2007), one might assume that REM sleep promotes the consolidation of emotional associative memory in particular when associative features are perceived as being intrinsic to the stimulus. The process of emotional binding implies the recruitment of a different network of neural structures, including the amygdala and the PH area (Kensinger & Corkin, 2004; Murray & Kensinger, 2013). In turn, this neural network exhibits markedly enhanced activation during REM sleep (Walker & van der Helm, 2009). Thus, REM sleep-dependent consolidation of emotional associative memory may act independently of the SWS-dependent system consolidation processes. Indeed, initial evidence suggests that retrieval of emotional associative information following sleep is associated with an enhanced response of the emotional memory network as compared to retrieval after sustained wakefulness (Lewis et al., 2011).

The current study aimed to explore the role of REM sleep and SWS in the consolidation of emotional item and associative memory. In order to contrast the effects of SWS and REM sleep, participants were subjected to a between-subject split-night-manipulation, which entailed a consolidation interval of either early night SWS-rich or late night REM sleep-rich sleep. Memory performance was ascertained in a combined procedure probing item memory and associative memory by means of a source memory paradigm. Participants encoded emotional (as defined by high arousal and low valence) and neutral images of various semantic categories at different screen locations. Thus, accurately recognizing images served as our measure of item memory, whereas the successful retrieval of the source feature, the images' screen location, was employed as a measure of associative memory and will be referred to as source memory in the following. In addition, we chose to ascertain item memory in a remember/know procedure (Rajaram, 1993), which allows differentiating correctly recognized old images with regard to the subjective retrieval process (familiarity or recollection) guiding this decision. Based on the selective effects of SWS-related system consolidation (Diekelmann & Born, 2010) on hippocampus-dependent associative memory, and thus potentially on recollection (Yonelinas, 2002), it is highly relevant to examine whether the consolidation effects related to REM sleep and SWS differently modulate item memory of emotional and neutral images with respect to subjective recollection ("remember") and familiarity ("know").

In accordance with prior findings, we expected item memory for emotional stimuli to be supported by late night sleep, entailing high proportions of REM sleep. Moreover, we aimed to test whether emotional source memory would benefit from early night SWS-rich sleep, as would be predicted based on the active system consolidation account (Diekelmann & Born, 2010), or from late night REM sleep-rich sleep, consistent with findings on emotional item memory (Groch et al., 2013; Groch et al., 2015; Nishida et al., 2009; Wagner et al., 2001). Further, we investigated the neural underpinnings of sleep-related consolidation by analyzing theta power during REM sleep and spindle activity during SWS. Specifically we aimed to explore how both oscillatory features are related to post sleep memory performance. In addition, we examined whether REM sleep has a simultaneous decremental effect on the affective charge of previously acquired memories (Walker & van der Helm, 2009). To address this, we ascertained subjective valence and arousal ratings of emotional and neutral images following the post sleep memory test allowing us to contrast the effects of early night and late night sleep.

2. Materials and methods

2.1. Experimental design

The present study used a between-subject split-night-manipulation that allows a partial dissociation of the influences of REM sleep and SWS on processes of memory consolidation (Ekstrand, 1967; Groch et al., 2013; Groch et al., 2015; Menz, Rihm, & Buchel, 2016; Plihal & Born, 1997; Schreiner & Rasch, 2015). Due to homeostatic demands building up over sustained wakefulness, long phases of SWS dominate the first night half with very short intervals of REM sleep within the ultradian sleep cycle. In the second night half, when the homeostatic pressure is dissipated, successively prolonged amounts of REM sleep appear with only minor co-occurring amounts of SWS. This distribution of sleep phases over the course of the night is reliably found across different individuals and can therefore be systematically manipulated by varying the time points of encoding and retrieval respectively.

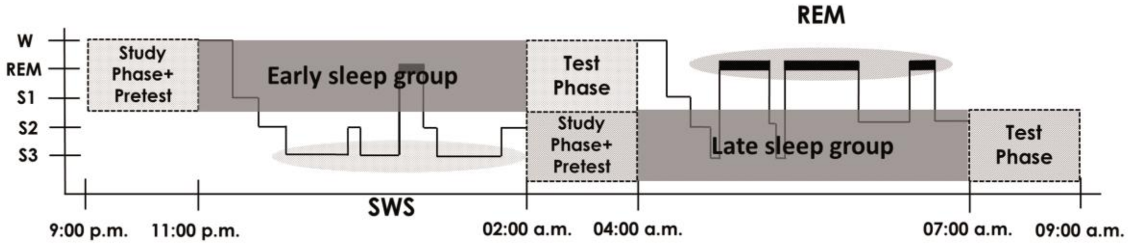

Figure II 1. Overview of the rationale of the split-night design. Participants of the early sleep group took the final post sleep retrieval test after sleep in the first night half, whereas participants of the late sleep group underwent post sleep testing subsequent to the second night half. Consequently, both groups slept during the entire night and only timing of learning and test sessions was varied between conditions.

In the current between-subject design, one group was subjected to an early night SWS-rich (“early sleep”) sleep, whereas the second group underwent late night REM sleep-rich (“late sleep”) sleep in the critical consolidation phase (see Figure II 1). The timing of the respective study- and test phases was determined by first stable sleep onset of the participant, with the 3-hour-interval starting at the first epoch of N1 (NREM stage 1) succeeded by N2 (NREM stage 2). This allows for a comparable dissipation of SWS over the first night half in all participants.

2.2. Participants

41 subjects took part in the study. Participants were screened for neurological and psychiatric disorders, sleep disorders (Buysse, Reynolds, Monk, & Hoch, 1991), habitual sleep duration (≥ 7 hours), strong evening preference (Randler, 2013), alcohol and nicotine ingestion, regular shift work and left-handedness (Oldfield, 1971). Additional requirements for study participation were normal or corrected-to-normal vision, normal weight ($18.5< \text{BMI}< 25$) and no long-term use of medication. In order to exclude potentially confounding effects of menstrual cycle, only females under hormonal contraception for the preceding three months were included (Genzel et al., 2012). Participants were instructed to maintain a regular sleep-wake pattern over the two weeks preceding the experimental night, which was monitored by a sleep diary, and to refrain from drinking alcohol or caffeinated beverages 24 hours before coming to the laboratory. Furthermore, subjects were asked to rise at 7:00 a.m. latest on the morning of the experiment.

Prior to analyses, one participant was excluded due to meeting ICD-10 criteria of a moderate major depression as assessed by Patient Health Questionnaire (Kroenke, Spitzer, & Williams, 2001). Data from two additional subjects were excluded due to poor performance in source memory at posttest [1.5*interquartile range (IQR) below the lower quartile of the overall group; $N= 1$] and severe difficulties falling asleep (timing of posttest exceeded 1.5*IQR above the upper quartile of the late sleep group) leading to desynchronization in timing of post sleep procedures from the rest of the group ($N= 1$) (Tukey, 1977). The final sample consisted of 19 participants in the early sleep group (6 male; $M_{age}= 22.9$, $SD_{age}= 2.36$) and 19 subjects in the late sleep group (6 male; $M_{age}= 22.58$, $SD_{age}= 2.24$). All participants gave written informed consent and were paid 100 € for complete study participation.

2.3. Procedure

All experimental procedures were performed at the Interdisciplinary Sleep Laboratory at Pfalzklinikum (Klingenmünster, Germany) on subsequent weekend days. Prior to the experimental night participants underwent an adaption night in the sleep laboratory with complete electrode set-up and under identical conditions as during experimental procedures. Subjects reported to the laboratory at 6:45 p.m.. On arrival they completed tests of fluid intelligence (Formann, Waldherr, & Piswanger, 2011) as well as processing speed (Wechsler, 2008) and obtained an undisturbed sleep opportunity of 8 hours. Participants went to bed at 11:00 p.m. and were woken up at 7:00 a.m., thus recreating the sleep interval of the main experiment.

During the experimental night, which took place one week after the adaption night, subjects arrived in the laboratory at 6:45 p.m. to undergo electrode set-up and prepare for the night (see Figure II 1 for overview of the study procedures). Allocation to study conditions was performed pseudo-randomly in order to control for gender effects (Genzel et al., 2012). The "early sleep" group underwent encoding of the study material (starting at 9:00 p.m.) and a pretest followed by 3 hours of sleep in the first night half from 11:00 p.m. onwards, thus obtaining high amounts of SWS in the critical consolidation period. They underwent a final retrieval test as well as the emotional reactivity assessment at approximately 2:00 a.m.. Participants of the "late sleep" group watched a neutral non-narrated documentary movie (excerpts of "Samsara") without intentionally encoding the content before going to sleep at 11:00 p.m. for an identical sleep duration of 3 hours. Consequently, studying and pretesting took place following the first night half (approximately 2:00 a.m.) and post sleep memory performance and emotional reactivity were assessed in the morning at approximately 7:00 a.m.. Hence, participants were tested after a consolidation period high in REM sleep.

Prior to the respective study and posttest block, participants watched a 30-minute compilation of non-arousing film clips (taken from "Relaxing: The most beautiful landscapes on earth") in order to prevent an effect of initial sleep inertia on memory performance. Before performing the encoding task as well as the final retrieval test, measures of state sleepiness (Hoddes, Zarcone, Smythe, Phillips, & Dement, 1973) and general mood (Watson, Clark, & Tellegen, 1988) were ascertained to account for potential circadian effects.

2.4. Task design and sleep recordings

Stimulus material

Pictorial stimuli for the memory task were selected from the International affective picture system (IAPS; Lang, Bradley, & Cuthbert, 2005) and supplemented with pictures from the Nencki Affective Picture System (NAPS;Marchewka, Żurawski, Jednoróg, & Grabowska,

2014) in order to allow for a sufficient number of trials. Negative pictures were preselected to be low in valence (*M*= 2.53, *SD*= 0.66) and moderate to highly arousing (*M*= 6.25, *SD*= 0.67), whereas neutral stimuli were chosen to be medium in valence (*M*= 5.5, *SD*= 0.61) and moderate to low in arousal (*M*= 4.01, *SD*= 0.81). To ascertain the applicability of the norms in the current student population, a prerating of the pictures with an unrelated sample of participants (*N*= 10) was conducted. Neutral and negative stimuli were closely matched in luminance, animacy, the occurrence of faces and indoor/outdoor displays. The final amount of 200 negative and 200 neutral items was split into 4 parallel sets equal in valence, arousal and the aforementioned visual stimulus properties, which served as old and new items at pre- and posttest respectively and were counterbalanced across participants. To exclude the potential occurrence of primacy and recency effects and to allow adaption to task procedures 3 neutral and 3 negative pictures were presented prior to and following the target picture set. The order of stimulus presentation was pseudo-randomized with no more than two stimuli of the same valence category occurring in succession and each participant receiving an individual order.

Memory task

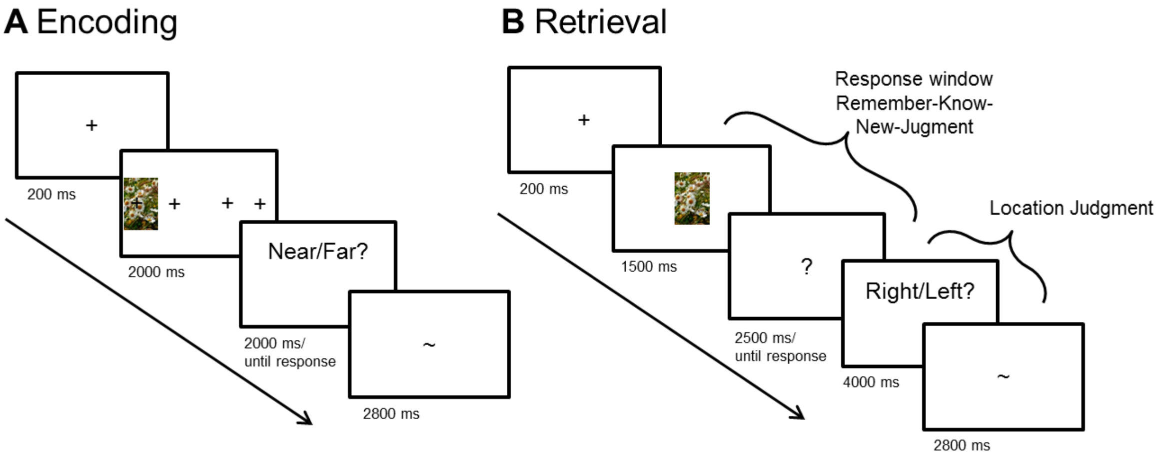

Figure II 2. Task design of **(A)** encoding procedure and **(B)** pre- and post sleep test procedure.

During encoding participants saw an initial fixation cross-hair (200ms) after which the stimulus was presented for 2000 ms. The source feature (screen location) was varied by presenting the stimulus on one of four different screen positions (right and left, as well as near or far from the screen center). After stimulus presentation, the participant’s judgment of the encoding task (“Is the stimulus perceived as being positioned near or far from the screen center?”) was ascertained (2000 ms) with the response keys counterbalanced across participants (see Figure II 2). This encoding procedure was chosen in order to ensure interactive encoding of the source feature and the respective item (Bergstrom, Henson, Taylor, & Simons, 2013). Encoding was intentional with participants being instructed to memorize the items and their respective screen locations (left/right) for a subsequent test phase.

Prior to the pretest phase, which took place 5 minutes after encoding was completed, participants received standardized instructions for remember(R)- and know(K)-judgements (Rajaram, 1993). They were informed on the differences of both retrieval processes and the critical relevance of the explicit access to episodic details in distinguishing recollection from familiarity. They were instructed to respond with a “Know” judgment in the absence of any recollective experience, thus whenever they sensed an indistinct “feeling” of having seen the respective image before without explicitly recapitulating its occurrence in the encoding phase. Different examples were provided of episodic details, which could be retrieved in the current experimental setting (e.g. a specific thought that came to the participants mind during initial image presentation or a specific sound coming from a different room that was heard by the participant during image presentation etc.). It was emphasized that the strength of the affective tone during the test phase was not relevant to this dissociation, but that a specific detail had to be retrieved in order to designate an image as “remembered”. After receiving these instructions, participants performed a series of practice trials, in which they were asked to verbalize and justify their judgements to the instructor to ensure full comprehension. Each test trial began with the presentation of an initial fixation cross-hair (200ms) that was followed by stimulus presentation (1500 ms) and an additional response window of 2500 ms at stimulus offset (blank screen). Participants were instructed to respond as fast and as accurate as possible with the onset of stimulus presentation giving a remember/know/new judgement. Response key assignment was again counterbalanced across participants. For items that were indicated to be old (R- or K-judgment) an additional prompt appeared (4000 ms) asking participants to retrieve the initial screen location of the item (right/left/unknown).

The procedures of the final post sleep retrieval test during which the other half of the encoded items (50 neutral and 50 negative) was presented intermixed with an equal amount of new items were kept identical to the pretest. The entire encoding procedure had an approximate duration of 45 minutes. The length of the retrieval tests varied between participants and lasted between 20 and 30 minutes.

Emotional reactivity

Emotional reactivity to previously encoded and new stimuli was assessed in a separate procedure in order to explore whether and how sleep affects the affective tone of events. Following the post sleep test a separate picture rating task was performed in which items of the posttest were presented in a different pseudorandomized order (1000 ms). After the initial presentation, the stimulus remained on the screen while ratings of valence (6000 ms) and arousal (6000 ms) were ascertained on a standard 9-point self-assessment manikin scale (Bradley & Lang, 1994).

Sleep recordings and spectral analysis

During both sleep intervals standard polysomnography recordings were performed according to the guidelines provided by the American Academy of Sleep Medicine (AASM, 2007) including EEG at frontal, central and occipital sites (F3, F4, C3, C4, O1, O2 according to the international 10- 20 system), submental electromyography (EMG) and horizontal electrooculography (EOG; lower right and higher left canthi). Signals were digitized at a sampling rate of 256 Hz (first-order high-pass and second-order butterworth low-pass filter: 0.3 and 75 Hz respectively, notch filter: 50 Hz) and amplified by SOMNOscreen amplifiers (SOMNOmedics GmbH, Randersacker, Germany). All electrodes were recorded referenced to Cz and were re-referenced offline to the contralateral mastoid for sleep stage scoring and to the average of both mastoids for spectral analysis. A 0.3- 35 Hz bandpass filter was applied offline.

Visual sleep stage scoring was performed by two trained raters independently in accordance with the criteria provided by the AASM (2007). The epoch length was set to 20 s to allow for overlapping windows of 4 s in the computation of spectral power density (see below). Each epoch was scored visually into NREM stage N1, NREM stage N2, NREM stage N3 (corresponding to SWS), REM sleep (stage R) and wake (stage W). Both the absolute amount of minutes spent in each sleep stage as well as the relative amount with reference to total sleep time (% TST) was determined for further analysis.

Spectral analysis was performed using the Matlab-based toolbox EEGLAB (http://www.sccn.ucsd.edu/eeglab/). Prior to analyses epochs were rejected semi-automated on the basis of automatic detection of extremely large fluctuations (> 1000 µV) and thereafter applying a threshold of 5 standard deviations followed by visual identification of muscle and eye movement artifacts. Spectral power density was computed for each epoch using the pwelch function (50% overlap, Hamming window) with a resulting frequency resolution of 0.25 Hz. Spectral power density was averaged for the theta band (4.0– 7.0 Hz) during REM sleep and slow (11.0- 13.0 Hz) as well as fast (13.0-15.0 Hz) spindle frequency ranges during SWS (Nuwer et al., 1998). For further analyses of theta power during REM sleep relative activity difference between the left- and right-prefrontal sites was computed by subtraction of activity at electrode F3 from F4 (F4- F3). To examine behavioral correlates of spindle density mean absolute power ($\mu V^2/Hz$) in the frequency bands of interest is reported for frontal and central electrodes where amplitudes of sleep spindles have been found to be largest (Schabus et al., 2007).

2.5. Statistical analysis

Memory task

Item memory performance was based on pictures correctly identified as new (correct rejections; CR) and old (hits) collapsed across R- & K-judgments. In order to account for individual differences in response bias, corrected recognition scores (Pr index; Snodgrass & Corwin, 1988) were calculated by subtracting percentage of erroneous responses to new images (false alarms; FA) from the percentage of correctly recognized old images. To further obtain an estimate of subjective recollection the proportion of new items erroneously receiving an R-judgment was subtracted from the proportion of old items correctly receiving an R-judgment ($R= R_{hits}- R_{FA}$). As the probability of making a K-judgment is constrained by R-judgments (participants are instructed to make a K-judgment in the absence of recollection when the item is perceived as being familiar) an estimate of familiarity was derived [$K= K_{hits}/(1-R_{hits})-(K_{FA}/(1-R_{FA}))$] according to Yonelinas & Jacoby, 1994. Source memory (SM) performance was calculated by dividing the probability of a correct source judgment by the probability of a correct "old" response ($SM= p_{correct\ source}/p_{correct\ source\ +\ incorrect\ source}$).

The behavioral data was subjected to Analyses of Covariance (ANCOVA) with the within-subject factors of “Time” (pre/posttest) and “Emotion” (negative/neutral) as well as the between-subject factor “Group” (early/late sleep group). Mean reaction times for hits and correct rejections of the item memory test were analyzed in an ANCOVA including the additional within-subject factor of “Item type” (hits/correct rejections). Pre-experimentally ascertained measures of fluid intelligence (Formann et al., 2011) and processing speed (Wechsler, 2008) were introduced as covariates in order to account for related variance in memory performance (Miller & Chapman, 2001).

Emotional reactivity

Emotional reactivity measures were aggregated to mean arousal and valence ratings separately for hits and correct rejections of the preceding item memory procedure. This was done to directly compare reactivity to emotional and neutral items that had undergone sleep-related processing (hits) to that of images which were newly presented after sleep (correct rejections). Mean ratings were analyzed in separate ANOVAs involving the within subject factors of “Emotion” (negative/neutral), “Item type” (hits/correct rejections) and the between subject factor “Group” (early/late sleep group).

Sleep physiology data

To explore the relationship between memory performance and sleep electrophysiological data Pearson correlation coefficients were computed between source/item memory and time spent in REM sleep, SWS and TST[21] as well as spectral power density during specific sleep stages. To allow for a stronger dissociation between effects of sleep on item and source memory partial correlations are reported controlling for shared variance whenever appropriate.

During sleep recordings electrodes F3 *(N*= 1 participants; early sleep group) and C4 (*N*= 2 participants; late sleep group) lost sufficient skin contact and respective power values were substituted (mean of surrounding electrodes) with exception of frontal laterality in theta power (F4- F3). Memory performance measures were adjusted when participants indicated to have erroneously pressed keys in specific trials according to item status (*N*=5 trials

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[21] To differentiate potential effects of respective sleep stages from effects of general sleep duration.

across all participants). Significant main effects and interactions were followed by post hoc t-tests and the significance level was set to $\alpha=0.05$ for all analysis.

3. Results

3.1. Behavioral data

A-priori group comparisons

Table II 1. Descriptive group measures

Measure	Early sleep group (N= 19)	Late sleep group (N= 19)	Test statistics
Accuracy Encoding task	**.98 (.04)**	**.99 (.01)**	**t_{36}= 1.22, p= .230**
SSS Encoding	**2.84 (0.96)**	**3.00 (1.11)**	**t_{36}= 0.47, p= 641**
SSS Posttest	**4.11 (1.29)**	**2.32 (0.89)**	**t_{36}= 5.00, p< .000**
PANAS Encoding	**1.04 (0.20)**	**1.09 (0.15)**	**t_{36}= 0.91, p= .368**
PANAS Posttest	**1.10 (0.13)**	**1.08 (0.17)**	**t_{36}= 0.40, p= .690**

Note: Accuracy in performing the encoding task is expressed as the percentage of correct responses (1 corresponding to maximal performance). SSS= Stanford Sleepiness Scale (single item measure ranging from 1*Feeling active, vital, alert, or wide awake* to 7 *No longer fighting sleep, sleep onset soon; having dream-like thoughts*). PANAS= Positive and Negative Affect Schedule, presented means are derived by computing the ratio of positive (positive affect subscale) to negative (negative affect subscale) mood (see Diener, 2000 for the reasoning behind this ratio and its advantages towards a disjunctive analysis of both subscales), a ratio of 1 indicates approximately balanced positive and negative mood, values >1 indicate a relative dominance of positive mood, values < 1 indicate a dominance of negative mood, positive and negative subscales each comprise 10 adjectives related to current mood state which are scored with regard to their current dominance on a scale from 1 *Not at all* to 5 *Extremely*). Standard deviations are given in parentheses.

Presleep item memory performance was analyzed in separate ANOVAs involving the factors Group and Emotion (see Table II 1). There was neither a main effect of Group ($F_{1,36}$= 0.20, p= .658) nor an interaction between Group and Emotion ($F_{1,36}$= 0.38, p= .539). In similar vein, source memory performance prior to sleep was not modulated by study condition (“Group”: $F_{1,36}$= 1.79, p= .189; “Group” x “Emotion”: $F_{1,36}$= 1.58, p= .218). Participants’ accuracy in the encoding task (correctly indicating the image location immediately after its presentation) was generally very high, as means of both groups approached full performance rates at 1.0. Also groups did not differ significantly in their performance of the encoding task (t_{36}= 1.22, p= .230). Groups were also closely comparable in covariate measures of fluid intelligence (t_{36}= 0.39, p= .697) and processing speed (t_{36}= 0.93, p= .359).

To examine potential contributions of circadian effects, ratio of positive to negative mood (Diener, 2000) was compared at pre- (prior to encoding) and posttest (before the final retrieval test) between both groups. Mood ratio was similar between groups across both time points (pre: t_{36}= 0.91, p= .368; post: t_{36}= 0.40, p= .690) as was subjectively reported sleepiness at encoding (t_{36}= 0.47, p= .641). Before post sleep memory testing participants in the early sleep group reported elevated levels of sleepiness as compared to the late sleep group (t_{36}= 5.00, p< .000; see Groch et al., 2015 for similar findings). However, none of the post sleep memory measures were significantly correlated with this subjective level of sleepiness (highest correlation: r= .14, p= .400 to neutral source memory performance), rendering this an unlikely cause of differential group patterns.

Item memory

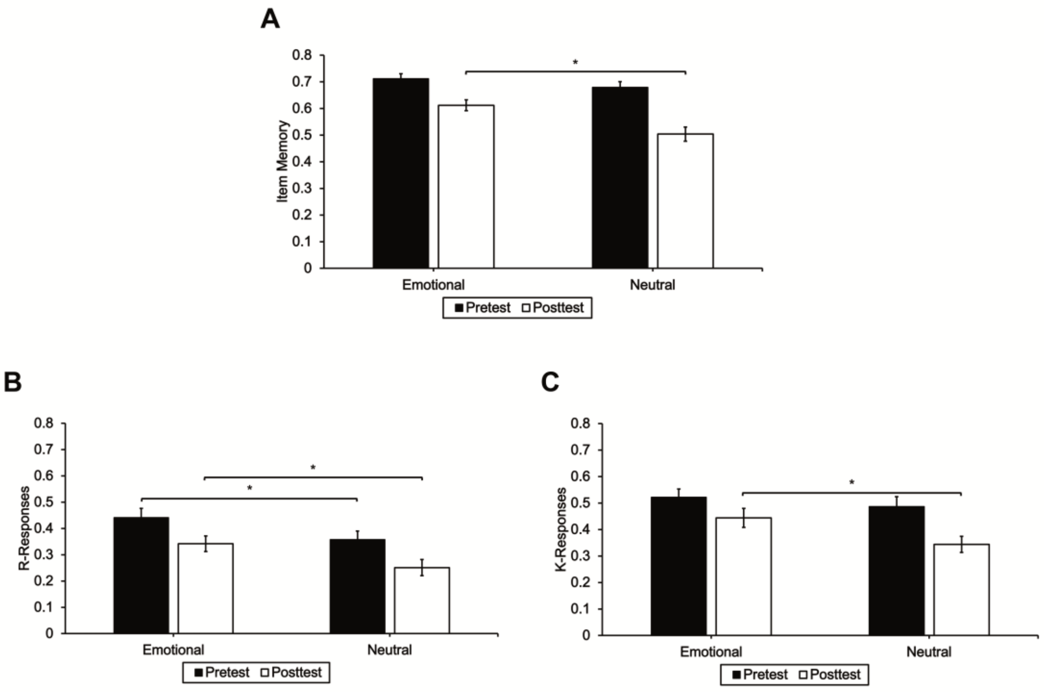

Figure II 3. Adjusted means of **(A)** item memory performance for emotional and neutral images and separately for **(B)+ (C)** R- and K- judgments at pre- and posttest, performance rates are collapsed across groups as there were no significant main or interaction effects involving the group factor. *Note:* Adjusted means were computed by means of multiple regression controlling for mean-centered scores of intelligence and processing speed.* indicates p< .05 for comparisons between valence categories at pre- and posttest. Significant effects over time are not illustrated for reasons of comprehensibility. Error bars represent standard error of the mean.

Analysis of item memory (Pr= hit rate– false alarm rate) revealed significant main effects of Time ($F_{1,34}$= 156.43, p< .000) and Emotion ($F_{1,34}$= 13.88, p= .001) as well as a significant interaction between both factors ($F_{1,34}$= 9.24, p= .005), pointing to an enhanced retention of emotional stimuli from pre- to posttest (see Figure II 3.A). Neutral item memory exhibited a stronger decline over time ($F_{1,35}$= 123.11, p< .000, ω^2= .77) as compared to emotional item memory ($F_{1,35}$= 34.31, p< .000, ω^2= .47). Consequently, while there was no significant difference in initial memory performance between the two valence categories at pretest ($F_{1,35}$= 2.48, p= .124), a significant difference emerged over time as evident at posttest ($F_{1,35}$= 19.5, p< .000). No significant main effect ($F_{1,34}$= 1.84, p= .184) or interactions (Time × Group: $F_{1,34}$= 0.08, p= .776; Emotion × Group: $F_{1,34}$= 1.48, p= .233; Time × Emotion × Group: $F_{1,34}$= 0.84, p= .366) involving the Group factor were found for item memory performance, suggesting that this memory benefit was not modulated by the early/late sleep manipulation.

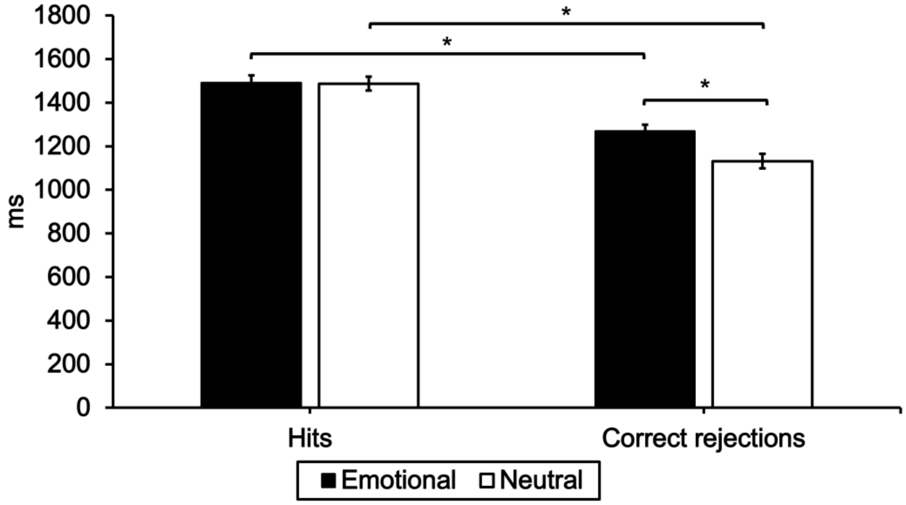

Figure II 4. Adjusted means of reaction times (ms) for hits and correct rejections to emotional and neutral stimuli. *Note:* Reaction times rates are collapsed across groups and time (pre- and posttest) as there were no significant main or interaction effects involving the group and time factors. * indicates p< .05 for comparisons between valence categories and item types. Error bars represent standard error of the mean.

Analysis of reaction times (ms) of hits and correct rejections of the item memory test revealed significant main effects of Emotion ($F_{1,34}$= 80.42, p< .000) and Item type ($F_{1,34}$= 130.74, p< .000) as well as a significant interaction between the two variables ($F_{1,34}$= 78.15, p< .000). Post hoc tests indicated that participants were generally faster when making correct "new" judgments as compared to correct "old" judgements ($F_{1,35}$= 125.16, p< .000).

Additionally subjects were significantly faster when responding correctly to new items when the stimulus was neutrally as opposed to negatively valenced ($F_{1,35}$= 129.63, $p <$ .000) (see Figure II 4). Again, no main effect of Group emerged in these analysis ($F_{1,34}$= 2.15, p= .152) as well as no interaction involving the Group factor (Time × Group: $F_{1,34}$= 0.06, p= .809; Emotion × Group: $F_{1,34}$= 0.04, p= .843; Item type × Group: $F_{1,34}$= 2.56, p= .119; Time × Emotion × Group: $F_{1,34}$= 1.79, p= .190; Time × Item type × Group: $F_{1,34}$= 0.20, p= .658; Emotion × Item type × Group: $F_{1,34}$= 0.01, p= .937; Time × Emotion × Item type × Group: $F_{1,34}$= 0.01, p= .934).

Remember- and Know-judgments

To further elucidate how this consolidation benefit for emotional images was reflected in recollection and familiarity measures separate ANCOVAs were performed (see Figure II 3.B and 3.C). Analysis of R-judgments revealed significant main effects of Time ($F_{1,34}$= 31.98, $p<$ .000) and Emotion ($F_{1,34}$= 20.85, $p<$ .000) indicating that R-judgments were more frequent at pretest than at posttest and that emotional images were more likely to evoke R-judgments than neutral images irrespective of time and sleep (Group: $F_{1,34}$= 1.44, p= .238; Group × Time: $F_{1,34}$= 0.90, p= .351; Group × Emotion: $F_{1,34}$= 0.12, p= .733; Group × Emotion × Time: $F_{1,34}$= 0.02, p= .893).

K-judgments were also modulated by Time ($F_{1,34}$= 38.23, $p<$ .000) and Emotion ($F_{1,34}$= 16.96, $p<$ .000). Furthermore, a marginally significant interaction between Time and Emotion ($F_{1,34}$= 4.09, p= .051) was apparent indicating again a differential decline of emotional and neutral item memory over time, as reflected by a significant difference in the retention rates of emotional and neutral items after sleeping ($F_{1,35}$= 17.43, $p<$ .000) but not before sleep ($F_{1,35}$= 2.29, p= .14). No main effect of Group ($F_{1,34}$= 0.30, p= .591) or interaction effect involving the Group factor (Group × Time: $F_{1,34}$= 0.02, p= .895; Group × Emotion: $F_{1,34}$=3.13, p= .086; Group × Emotion × Time: $F_{1,34}$= 0.35, p= .559) was evident in these analysis. Consequently, the retention benefit for emotional stimuli observed for item memory (see Figure II 3.A) mainly results from preserved familiarity-based recognition for these items at posttest (see Figure II 3.C; see also Hu et al., 2006 for similar findings).

Source memory

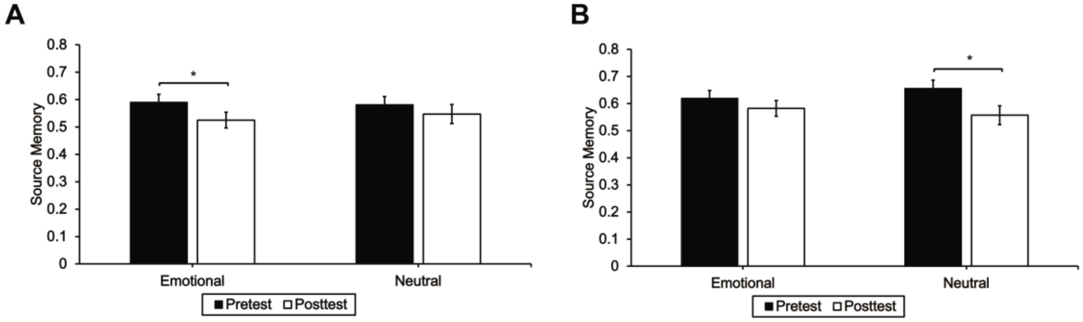

Figure II 5. Adjusted means of source memory performance (ratio of correct source judgments to item memory hits) for emotional and neutral items in the **(A)** early and **(B)** late sleep group at pre and posttest. *Note:* Within-group effects of differential memory retention in relation to valence category were qualified by a significant three-way-interaction of Group × Time × Emotion ($F_{1,34}$= 5.2, *p*= .029). Adjusted means were computed by means of multiple regression controlling for mean-centered scores of intelligence and processing speed. * indicates *p*< .05 for comparisons within valence categories from pre- to posttest. Significant effects between valence categories are not illustrated for reasons of comprehensibility. Error bars represent standard error of the mean.

Similar to item memory, source memory performance declined from pre- to posttest (main effect “Time”: $F_{1,34}$= 17.58, p< .000) with no effect of Emotion (main effect: $F_{1,34}$= 0.21, *p*= .652) nor an interaction between Time and Emotion ($F_{1,34}$= 0.63, *p*= .431) being evident. Furthermore, no main effect of Group ($F_{1,34}$= 1.30, *p*= .262) emerged in these analysis and no significant interaction was attained between Group and Time ($F_{1,34}$= 0.43, *p*= .519), nor between Group and Emotion ($F_{1,34}$= .01, *p*= .991). Notably, however, a significant three-way interaction between Time, Emotion and Group emerged ($F_{1,34}$= 5.2, *p*= .029)[22]. Planned comparisons between groups did not reveal any significant differences in source memory after sleep for both neutral ($F_{1,34}$= 0.42, *p*= .838) and emotional images ($F_{1,34}$= 1.93, *p*= .174). Group-specific analyses, however, revealed that source memory performance for emotional items declined significantly from pre- to posttest in the early sleep group ($F_{1,16}$= 8.24, *p*= .011) whereas for neutral source memory no significant decline ($F_{1,16}$= 2.43, *p*= .138) was evident (see Figure II 5.A). On the other hand, in the late sleep group source memory for neutral stimuli was found to decrease significantly ($F_{1,16}$= 14.67, *p*= .001) but remained preserved for emotional stimuli ($F_{1,16}$= 3.00, *p*= .103; see Figure II 5.B).

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[22] The three-way interaction remained significant without controlling for IQ and processing speed ($F_{1,36}$= 4.52, *p*= .04).

Table II 2. Adjusted means of memory performance in both groups for item and source memory

Memory Test	Performance Measure	Early sleep group (*N*= 19)		Late sleep group (*N*= 19)	
		Pretest	Posttest	Pretest	Posttest
Item Memory	$\mathbf{Hits_{Emo}}$	.84 (.02)	.75 (.03)	.79 (.02)	.73 (.03)
	$\mathbf{Hits_{Neut}}$	.76 (.03)	.61 (.04)	.70 (.03)	.56 (.04)
	$\mathbf{FA_{Emo}}$	.12 (.03)	.14 (.02)	.09 (.03)	.12 (.02)
	$\mathbf{FA_{Neut}}$	.06 (.01)	.07 (.02)	.04 (.01)	.08 (.02)
RK-Procedure	$\mathbf{R_{Emo}}$	.48 (.05)	.37 (.04)	.40 (.05)	.32 (.04)
	$\mathbf{R_{Neut}}$	.41 (.05)	.28 (.04)	.31 (.05)	.22 (.04)
	$\mathbf{K_{Emo}}$	.50 (.04)	.41 (.05)	.55 (.04)	.48 (.05)
	$\mathbf{K_{Neut}}$	.48 (.05)	.35 (.04)	.49 (.05)	.34 (.04)
Source Memory	$\mathbf{SM_{Emo}}$	.59 (.03)	.53 (.03)	.62 (.03)	.58 (.03)
	$\mathbf{SM_{Neut}}$	.58 (.03)	.55 (.04)	.66 (.03)	.56 (.04)

Note: Adjusted means were computed by means of multiple regression controlling for mean-centered scores of intelligence and processing speed. Hits= correctly recognized images of the item memory procedure, FA= false alarms to new images of the item memory procedure, R= estimate of recollection derived from the amount of correct remember-judgments of the item memory procedure, K= estimate of familiarity derived from the amount of correct know-judgments of the item memory procedure, SM= correctly recognized locations of items that had been correctly recognized in the preceding item memory procedure (correct source/overall hits). Standard errors of the mean are given in parentheses. None of the reported mean values reached the level of significance in between-group comparisons (p< .05).

By showing selectively enhanced retention of neutral source memory in the early sleep group, these results support the high relevance of SWS for the consolidation of hippocampus-dependent memory representations. Similar effects of SWS on source memory have recently been shown to be limited to neutral images (Groch et al., 2015). By showing that REM sleep on the other hand has the capacity to selectively support source memory for emotional stimuli, the current results extend these findings in an important way. Furthermore, these results also imply that emotional source memory benefits from a sleep-related consolidation mechanism that is different from the one mediating the consolidation of neutral stimuli.

Emotional reactivity

In order to examine potential simultaneous effects of REM sleep on the affective tone of emotional stimuli, valence and arousal ratings were subjected to separate ANOVAs. As expected valence ratings differed significantly between valence categories (main effect "Emotion": $F_{1,36}$= 354.24, p< .000) with negative images eliciting lower valence ratings than neutral images. In addition a significant interaction between Emotion and Item type (hit/correct rejection) emerged ($F_{1,36}$= 5.29, p= .027). The difference in ratings between new items (correct rejections) and old items (hits) was significantly larger for emotional images as opposed to difference values for neutral pictures (t_{37}= 2.29, p= .028). In other words, in the emotional valence category "old" images that had been initially presented prior to sleeping in the respective night half tended to be perceived as more aversive as compared to "new" images which were presented only during the posttest after sleeping (t_{37}= 1.93, p= .061; see Figure II 6.A). Analysis on valence ratings did not yield any significant main or interaction effects involving the Group factor (Main effect: $F_{1,36}$= 1.39, p= .246; Group × Emotion: $F_{1,36}$= 3.46, p= .071; Group × Item type: $F_{1,36}$= 0.18, p= .671; Group × Emotion × Item type: $F_{1,36}$= 1.26, p= .269).

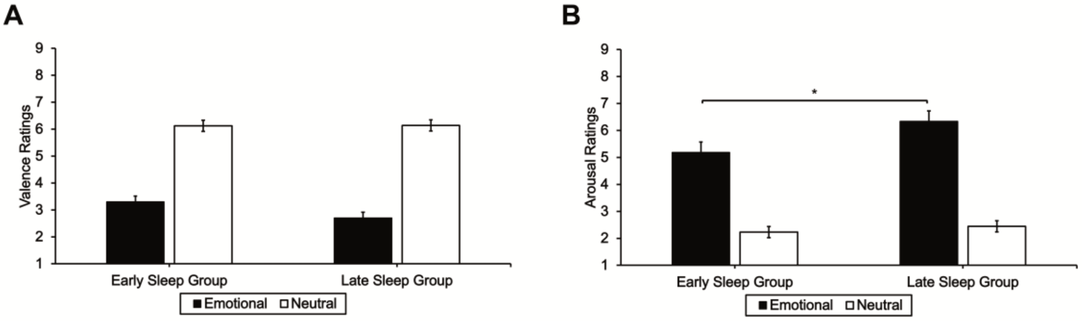

Figure II 6. Mean post sleep ratings of stimulus material separately for emotional and neutral items on **(A)** valence and **(B)** arousal dimensions for the early and late sleep group. *Note:* For reasons of consistency both ratings are collapsed across Item type (Hits/CR). * indicates p< .05 for comparisons between groups. Significant effects between item types are not illustrated for reasons of comprehensibility. Error bars represent standard error of the mean.

Analysis on arousal ratings also revealed the expected significant main effect of Emotion ($F_{1,36}$= 267.20, p< .000) signifying a markedly enhanced arousal response to emotional as opposed to neutral stimuli. Furthermore, it was found that old items were perceived as more arousing in comparison to new items across both valence categories (main effect "Item type": $F_{1,36}$= 7.36, p= .01). Additionally a significant interaction between Emotion and Group was apparent ($F_{1,36}$= 5.01, p= .032). While there was no significant difference in arousal responses to neutral stimuli between both groups (t_{36}= 0.72, p= .477) participants in the late sleep group indicated to perceive emotional stimuli as significantly more arousing when compared to subjects in the early sleep group irrespective of Item type (t_{36}= 2.11, *p*= .042; see Figure II 6.B). Thus, contrary to our hypothesis, that REM sleep has a reducing effect on the affective charge of emotional events, REM sleep was associated with an enhanced arousal response to emotional stimuli. This was found irrespective of whether these images had been initially presented prior to (hits) or following (correct rejections) sleep, which precludes that this effect results from memory processes during the consolidation period. No further main or interaction effects involving the factor "Group" emerged in these analyses (Main effect: $F_{1,36}$= 3.14, *p*= .085; Group × Item type: $F_{1,36}$= 0.06, *p*= .804; Group × Emotion × Item type: $F_{1,36}$= 1.21, *p*= .280).

3.2. Sleep physiology: Sleep stages

Table II 3. Sleep parameters in both study groups

	Early sleep group (*N*= 19)		**Late sleep group (*N*= 19)**		**Test statistics**	
Sleep parameters	**% TST**	**Time in min**	**% TST**	**Time in min**	**%TST**	**Time in min**
Wake	**1.74 (2.69)**	**3.11 (4.67)**	**0.97 (1.65)**	**1.78 (3.06)**	**t_{36}= 1.06, *p*= .295**	**t_{36}= 1.04, *p*= .308**
N1	**4.91 (2.42)**	**9.00 (4.42)**	**5.96 (3.31)**	**11.15 (6.08)**	**t_{36}= 1.12, *p*= .271**	**t_{36}= 1.25, *p*= .221**
N2	**40.78 (8.29)**	**75 (15.47)**	**44.29 (8.51)**	**82.55 (15.61)**	**t_{36}= 1.29, *p*= .206**	**t_{36}= 1.50, *p*= .143**
N3	**43.58 (10.68)**	**80.04 (19.3)**	**16.3 (7.49)**	**30.44 (14.14)**	**t_{36}= 9.12, *p*< .000**	**t_{36}= 9.04, *p*< .000**
REM	**10.73 (6.88)**	**19.87 (13.03)**	**33.44 (4.15)**	**62.49 (8.51)**	**t_{36}= 12.32, *p*< .000**	**t_{36}= 11.94, *p*< .000**
TST	**-**	**183.91 (6.77)**	**-**	**186.63 (6.48)**	**-**	**t_{36}= 1.26, *p*= .215**

Note: N1= NREM Stage 1, N2= NREM Stage 2, N3= NREM Stage 3 (corresponding to SWS), REM= REM sleep, TST= total sleep time. Standard deviations are given in parentheses.

Data on absolute and relative time spent in different sleep stages (in min, % TST) is presented in Table II 3. The critical manipulation of the split night design was confirmed by demonstrating highly significant differences in REM sleep (t_{36}= 12.32, *p*< .000) and N3/SWS (t_{36}= 9.12, *p*< .000) duration between the early and late sleep groups in the expected direction. Importantly, both groups did not differ significantly with respect to time spent in any other sleep stage and exhibited a similar TST (t_{36}= 1.26, *p*= .215).

Partial correlations between sleep physiology data and memory performance controlling for shared variance between item and source memory were computed separately for both groups. Contradicting prior findings (Groch et al., 2013; Nishida et al., 2009) there was no significant correlation between time spent in REM sleep and emotional memory performance after sleeping in the early (Source Memory: *r*= .02, *p*= .923; Item Memory: *r*= .16, *p*=.516) and late sleep group (Source Memory: *r*= .02, *p*= .927; Item Memory: *r*= .07, *p*= .772) respectively. However, the procedures of the split-night design result in a very narrow range in TST. Consequently, variance between subjects regarding time spent in different sleep stages within each condition is low, which may have prevented finding the respective correlations (see Groch et al. 2015 for similar results).

Correlational analysis between mean arousal and valence ratings and measures of sleep physiology yielded no significant associations for REM sleep or SWS with regard to emotional stimuli (see Table II 4). Only a single correlation was evident between SWS (in minutes) and mean valence ratings of neutral stimuli, denoting a more positive evaluation of neutral material in response to prolonged SWS durations over the first night half. Interestingly, TST correlated negatively with arousal ratings to emotional stimuli only in the early sleep group (*r*= -.54, *p*= .016) but not in the late sleep group (*r*= .21, *p*= .390). Hence, SWS-enriched sleep time in the first night half contributed to an attenuation of arousal responses, whereas this effect was absent across late night sleep in the second night half. Together with our behavioral finding of a reduced arousal response towards emotional stimuli in the early sleep group (see Figure II 6.B) this may suggest that REM sleep in the second night half leads to a disengagement of processes which contribute to a declining arousal response in the first night half (see Baran et al, 2012 and Werner et al, 2015 for similar findings regarding REM sleep in the second night half). As such, NREM sleep may provide a function in retaining a balanced emotional reaction by attenuating perceived arousal, which is obscured by consecutively appearing REM sleep episodes in the second night half and related affective processes.

Table II 4. Correlations of arousal and valence ratings with time spent in different sleep stages (min)

	Early sleep group (N=19)				**Late sleep group (N=19)**			
	Arousal		**Valence**		**Arousal**		**Valence**	
Sleep stage	**Emot**	**Neut**	**Emot**	**Neut**	**Emot**	**Neut**	**Emot**	**Neut**
N3	**.00**	**-.33**	**.39**	**.51**	**.26**	**.22**	**-.21**	**.10**
	***p*= .999**	***p*= .167**	***p*= .100**	***p*= .027**	***p*= .290**	***p*= .359**	***p*= .386**	***p*= .683**
REM	**-.38**	**-.08**	**.13**	**-.19**	**-.10**	**-.42**	**-.16**	**.14**
	***p*= .113**	***p*= .755**	***p*= .587**	***p*= .429**	***p*= .700**	***p*= .077**	***p*= .510**	***p*= .579**
TST	**-.54**	**-.63**	**.19**	**.18**	**.21**	**-.16**	**-.23**	**-.12**
	***p*= .016**	***p*= .004**	***p*= .446**	***p*= .450**	***p*= .390**	***p*= .501**	***p*= .336**	***p*= .615**

Note: Emot= Emotional stimulus category, Neut= Neutral stimulus category. Mean ratings were collapsed across both item types for correlational analysis as there was no significant group-related interaction involving the factor of Item type. Pearson correlations are reported with their respective significance levels below.

3.3. Sleep physiology: Spectral analysis

To test whether microstructural aspects of REM sleep physiology would be associated with behavioral memory performance correlations between memory measures and right-frontal theta lateralization (F4- F3) were analyzed based on the findings of Nishida et al. (2009). The correlational patterns mirrored behavioral results, by demonstrating no significant association between frontal theta lateralization and emotional item memory performance (*r*= -.36, *p*= .146). This is in line with the absence of any particular effect of late night sleep on emotional item memory performance. However, in the late sleep group, there was a significant positive correlation between right-frontal theta lateralization and post sleep source memory for emotional images (*r*= .55, *p*= .018). Critically, this was not evident for neutral source memory (*r*= .23, *p*= .369). Moreover, these correlations to emotional and neutral source memory performance were confirmed to differ significantly on a statistical level (z_{19}= 2.17, *p*= .015, one-sided test based on the procedure described by Eid, Gollwitzer, & Schmitt, 2010).

A more fine-grained analysis within each 0.25 Hz bin in the theta frequency range revealed the largest correlation in the 4.75– 5 Hz bin (*r*= .59, *p*= .011; see Figure II 7.B) and generally stronger correlations in the lower (<5 Hz) frequency range (see Figure II 7.A).

Analysis in the early sleep group did not yield any significant correlations between source (emotional: *r*= .19, *p*= .470; neutral: *r*= .14, *p*= .607) or item memory performance (emotional: *r*= -.40, *p*= .109; neutral: *r*= -.04, *p*= .866) and right-frontal theta lateralization. Thus, consistent with our behavioral findings, disclosing a selective retention benefit for emotional source memory after late REM sleep-rich sleep, we were additionally able to identify an electrophysiological process, right-frontal theta lateralization, which is specifically bound to the enhanced retention of emotional source memory.

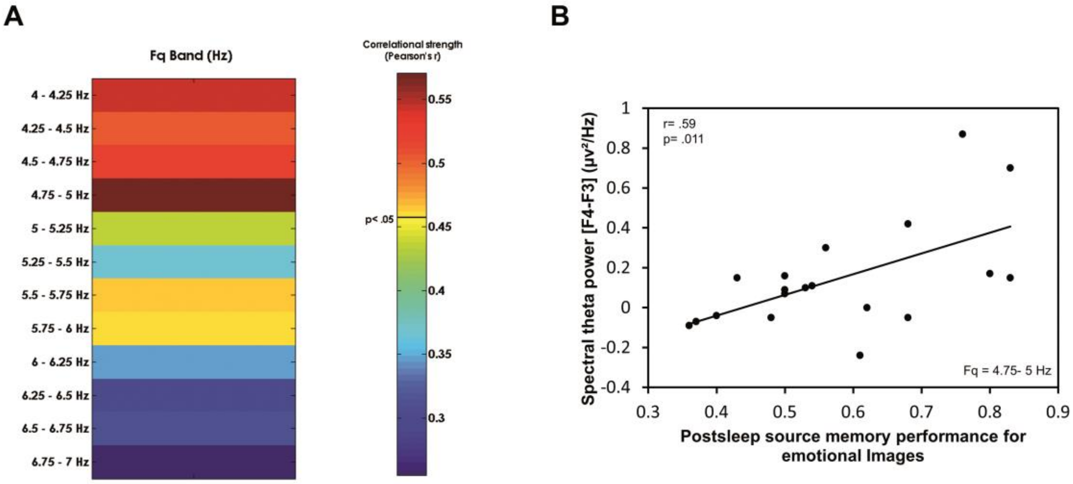

Figure II 7. (A) Correlations between emotional source memory (post sleep) in the late (REM rich) sleep group and right-frontal theta lateralization during REM sleep for each 0.25 Hz bin. Correlation strength is represented by the color range. **(B)** Scatterplot of peak correlation in the 4.75- 5 Hz bin. *Note:* Zero-order correlations are depicted for greater comprehensibility.

Based on the predictions of the active system consolidation view we further tested whether memory performance for neutral items would be correlated with spindle power during SWS. The analysis of fast (13– 15 Hz) and slow (11– 13 Hz) spindle frequency ranges in the early sleep group revealed no significant correlation with post sleep source memory performance (see Table II 5). However, post sleep neutral item memory performance was found to correlate significantly with slow spindle power and with fast spindle power at frontal electrodes (see Table II 5 and Figure II 8.A). This was not true for emotional item memory, providing further evidence for a selective role of SWS in memory consolidation for neutral items. This differential pattern with regard to stimulus valence was again confirmed by statistical analysis, directly contrasting the strength of correlations to emotional and neutral item memory for frontal fast spindle power and slow spindle power at all electrodes (see caption of Table II 5 for detailed statistics).

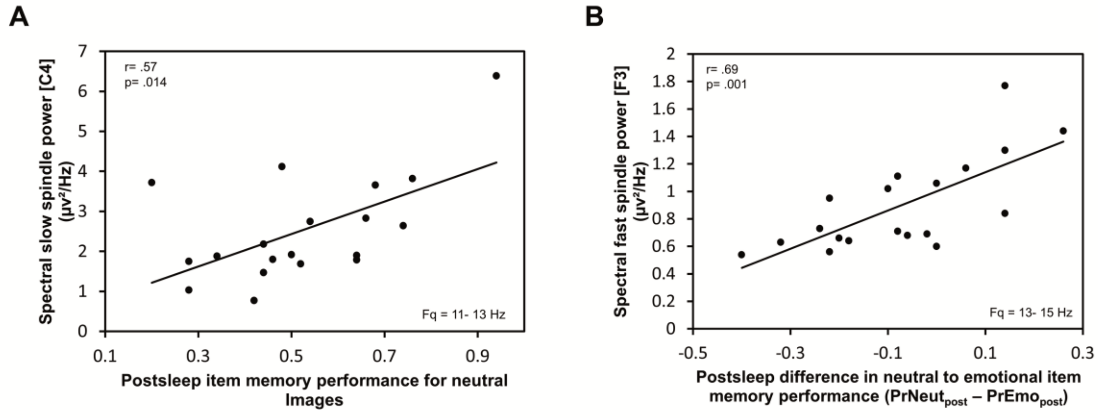

Figure II 8. Correlations between **(A)** slow spindle power (µV²/Hz) at C4 and neutral item memory performance and **(B)** fast spindle power (µV²/Hz) at F3 and retention benefit of neutral item memory relative to emotional item memory (PrNeut$_{post}$ – PrEmo$_{post}$) in the early sleep group. *Note:* Zero-order correlations are depicted for greater comprehensibility.

Interestingly, frontal fast spindle power (F3) also demonstrated a particularly high correlation with memory performance for neutral relative to emotional images (*r*= .69, *p*= .001)[23]. This signifies that higher spectral power in the fast spindle band (13- 15 Hz) during SWS was associated with a greater retention benefit of neutral over emotional item memory at posttest (see Figure II 8.B). Again no significant correlations were found in the late sleep group (see Table II 5).

In sum, we were able to identify dissociable neural correlates for the retention of neutral and emotional memories in both night halves. The selective retention benefit for emotional source memory in the late REM sleep condition was correlated with right-frontal theta lateralization whereas fast and slow spindle power, a key feature of SWS, was selectively correlated with neutral item memory in the early night SWS-rich condition. While this does not fully conform to the behavioral dissociation which we found with regard to source memory performance, it importantly corroborates, that memory processes of both night halves are selectively involved in the processing of neutral and emotional material respectively.

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[23] PrNeut$_{post}$ – PrEmo$_{post}$

Table II 5. Partial correlations between spindle power during SWS and post sleep memory performance

		Early sleep group (N=19)				**Late sleep group (N=19)**			
Sleep parameters		**Item Memory**		**Source Memory**		**Item Memory**		**Source Memory**	
		Emot	**Neut**	**Emot**	**Neut**	**Emot**	**Neut**	**Emot**	**Neut**
Slow spindle power (11-13 Hz)	**F3**	**.09**	**.61**	**.07**	**.22**	**-.05**	**.05**	**-.24**	**-.09**
		***p*= .723**	***p*= .007**	***p*= .777**	***p*= .386**	***p*= .857**	***p*= .850**	***p*= .348**	***p*= .733**
	F4	**.13**	**.57**	**.01**	**.18**	**-.15**	**-.04**	**-.12**	**-.04**
		***p*= .601**	***p*= .013**	***p*= .976**	***p*= .480**	***p*= .555**	***p*= .865**	***p*= .628**	***p*= .864**
	C3	**.03**	**.67**	**.09**	**.27**	**-.13**	**.01**	**-.02**	**.16**
		***p*= .905**	***p*= .002**	***p*= .729**	***p*=. 282**	***p*= .604**	***p*= .975**	***p*= .942**	***p*= .530**
	C4	**-.04**	**.57**	**.18**	**.33**	**-.16**	**.03**	**-.06**	**.07**
		***p*= .866**	***p*= .014**	***p*= .489**	***p*= .184**	***p*= .515**	***p*= .895**	***p*= .819**	***p*= .782**
	Cz	**.00**	**.58**	**.14**	**.30**	**-.42**	**-.32**	**.01**	**.01**
		***p*= .986**	***p*= .011**	***p*= .577**	***p*= .226**	***p*= .085**	***p*= .193**	***p*= .957**	***p*= .969**
Fast spindle power (13-15 Hz)	**F3**	**.08**	**.58**	**.01**	**.08**	**.25**	**.17**	**-.27**	**-.07**
		***p*= .765**	***p*= .012**	***p*= .968**	***p*= .757**	***p*= .316**	***p*= .494**	***p*= .286**	***p*= .787**
	F4	**-.10**	**.54**	**.05**	**.24**	**.10**	**.01**	**-.09**	**-.03**
		***p*= .706**	***p*= .020**	***p*= .841**	***p*= .346**	***p*= .682**	***p*= .982**	***p*= .725**	***p*= .912**
	C3	**-.23**	**.43**	**.03**	**.09**	**.03**	**.12**	**-.05**	**.17**
		***p*= .353**	***p*= .073**	***p*= .923**	***p*= .736**	***p*= .902**	***p*= .651**	***p*= .842**	***p*= .493**
	C4	**-.14**	**.39**	**.12**	**.25**	**.16**	**.15**	**-.16**	**.10**
		***p*= .586**	***p*= .115**	***p*= .628**	***p*= .315**	***p*= .531**	***p*= .567**	***p*= .519**	***p*= .689**
	Cz	**-.46**	**.10**	**.11**	**.13**	**-.28**	**-.44**	**-.08**	**.01**
		***p*= .056**	***p*= .699**	***p*= .676**	***p*= .611**	***p*= .259**	***p*= .066**	***p*= .739**	***p*= .966**

Note: Emot= Emotional stimulus category, Neut= Neutral stimulus category. Pearson correlations are reported with their respective significance levels below. Statistical comparisons (according to Eid et al, 2010) between the strength of spindle correlations to emotional and neutral item memory in the early sleep group for slow spindle power (SS) and fast spindle power (FS): SS(F3) z_{19}= 2.33, *p*= .010; SS(F4): z_{19}= 1.93, *p*= .027; SS(C3): z_{19}= 2.91, *p*= .002; SS(C4): z_{19}= 2.64, *p*=.004; SS(Cz): z_{19}= 2.51, *p*= .006; FS(F4): z_{19}= 3.76, *p*< .000; FS(F3): z_{19}= 3.01, *p*= .001.

3.4. Experiment 1a

In order to address alternative hypotheses for the behavioral effects of our main experiment, we conducted a follow-up study investigating consolidation in the same task design over a phase of wakefulness. Regarding the interaction effect of Time and Emotion on item memory, our main study design does not allow us to infer whether this retention benefit of emotional images was effected specifically across sleep-related consolidation. Alternatively, it may be argued that this reflects generic processes of consolidation, in the sense that emotional items show a benefit in retention over time irrespective of sleep. Thus, finding an interaction of Time and Emotion for item memory after a phase of wakefulness would indicate that our effect originates from sleep-independent consolidation mechanisms whereas a lack of a significant interaction would be a strong argument in favor of the sleep-specificity of our item memory effect. Secondly, with respect to our source memory results it is of interest to test whether the differential pattern of memory benefits for neutral and emotional images we observed is uniquely tied to the respective night halves, specifically the benefit of emotional source memory in the second night half. Of note, the decrease in emotional source performance in the early sleep group (M_{Diff}= .06; $F_{1,16}$= 8.24, p= .011) was considerably smaller than the deterioration of neutral source memory after late sleep (M_{Diff}= .10; $F_{1,16}$= 14.67, p= .001). As such, the passage of time may have resulted in a globally enhanced emotional source retention, which could have biased the results towards finding differential benefits for neutral and emotional memories across both night halves. However, finding a general decrease of source memory (main effect of Time and no interaction of Time and Emotion) over an identical interval of wakefulness would be strong support of our interpretation.

To test these hypotheses, 18 participants (9 male; M_{age}= 23.28; SD_{age}= 2.95) underwent identical procedures as the main study groups at 9:00 a.m. in the morning and took the final memory test following a 3 hour interval of wakefulness during which participants were permitted to leave the laboratory (approximately 13:30 a.m.). Analysis of item memory performance revealed main effects of Time ($F_{1,17}$= 55.32, p< .000) and Emotion ($F_{1,17}$= 5.91, p= .026) but no significant interaction between both factors ($F_{1,17}$= .001, p= .976) denoting no preferential consolidation of emotional material over time as observed in the sleep groups (see Figure II 9.A).

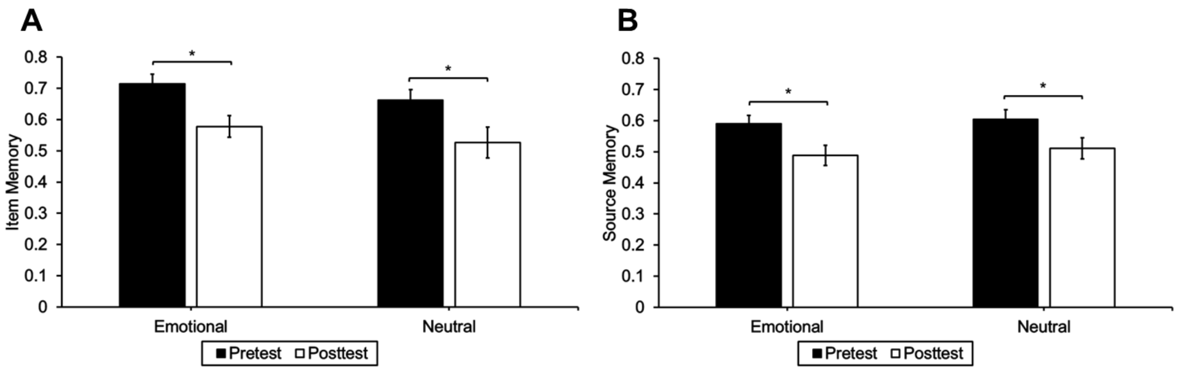

Figure II 9. Means of **(A)** Item and **(B)** Source memory performance at pre- and posttest in Experiment 1a (N= 18). *Note:* * indicates p< .05 for comparisons between valence categories at pre- and posttest. Error bars represent standard error of the mean.

Source memory performance on the other hand also exhibited a significant decrease over time ($F_{1,17}$= 12.92, p= .002) with no main effect of Emotion ($F_{1,17}$= 1.10, p= .310) and no significant interaction between Emotion and Time ($F_{1,17}$= 0.12, p= .736). Importantly, performance rates decreased similarly for emotional (M_{Diff}= .10; t_{17}= 3.24, p= .005) and neutral images (M_{Diff}= .09; t_{17}= 3.06, p= .007) not adhering to the differential patterns observed in both sleep groups (see Figure II 9.B and Table II 6).

Table II 6. Means of memory performance in Experiment 1a for item and source memory

Memory Test	**Performance Measure**	**Experiment 1a (n= 18)**	
		Pretest	**Posttest**
Item Memory	**Hits_{Emo}**	**.85 (.02)**	**.77 (.02)**
	$\text{Hits}_{\text{Neut}}$	**.76 (.03)**	**.64 (.04)**
	FA_{Emo}	**.14 (.03)**	**.19 (.03)**
	FA_{Neut}	**.10 (.02)**	**.11 (.03)**
Source Memory	**SM_{Emo}**	**.59 (.03)**	**.49 (.03)**
	SM_{Neut}	**.60 (.03)**	**.51 (.03)**

Note: Hits= correctly recognized images of the item memory procedure, FA= false alarms to new images of the item memory procedure, SM= correctly recognized locations of items that had been correctly recognized in the preceding item memory procedure (correct source/overall hits). Standard errors of the mean are given in parentheses.

This marked decrease across both valence categories is in favor of a sleep-specific interpretation of the retention differences in source memory in our main study and does not suggest the involvement of circadian or time-dependent factors. Critically, the comparable decrease of emotional and neutral source memory across wakefulness is in support of an active role of REM sleep in retaining emotional associations.

4. Discussion

On the basis of prior findings we aimed to explore by which mechanism sleep modulates the consolidation of emotional memories. While REM sleep has been consistently found to exert a beneficial effect on emotional item memory, a possible involvement in the retention of emotion source memory has not been examined extensively to date. Consequently, we tested whether emotional source memory is supported by SWS, similar to source memory for neutral material, or whether emotional source memory is supported by REM sleep-dependent consolidation mechanism, as has been demonstrated for emotional item memory retention.

In accordance with preceding accounts of a selective beneficial effect of sleep on emotional item memory, we found item memory for negative images to be preferentially retained across an interval of sleep as compared to neutral item memory. Surprisingly, however, this effect was not modulated by the early/late sleep manipulation. With respect to source memory performance, we found retention of emotional and neutral material to be differentially modulated across early and late night sleep. In line with the well-characterized memory function of SWS (Diekelmann & Born, 2010), source memory for neutral images was found to be selectively preserved over early night sleep. Late night REM sleep rich sleep, on the other hand, was associated with a selective preservation of source memory for emotional images. Moreover, the critical role of REM sleep in establishing this effect was confirmed by a significant correlation between emotional source memory at posttest and right-frontal theta lateralization in the late sleep group. On the other hand, spindle power during SWS exhibited selective correlations with item memory for neutral items in the early sleep group. These selective correlations substantiate a dissociation of emotional and neutral memory retention not just regarding early (SWS-rich) and late (REM sleep-rich) sleep, but also with respect to specific neurophysiological features of the respective sleep stages (Theta oscillations during REM sleep and spindle power during SWS).

4.1. Item memory

Despite no clear dissociation with respect to early and late sleep, we did find emotional item memory to be selectively preserved over time, as opposed to item memory for neutral images. Moreover, the results of Experiment 1a demonstrated no significant interaction of Time and Emotion after three hours of wakeful retention. This may suggest that the time-dependent advantage in retrieving emotional images was specifically related to sleep and does not reflect generic consolidation benefits over time (Bergado et al, 2011; Sharot & Yonelinas, 2008; Yonelinas & Ritchey, 2015). Nonetheless, it must be acknowledged that a main effect of Emotion on item memory was evident in Experiment 1a, which suggests that certain aspects of preferential processing of emotional material remained to be initiated regardless of sleep-dependent consolidation. Consequently, the present results cannot fully disclose how and by which exact mechanism the preferential retention of emotional item memory across time was established. Interestingly, the majority of former studies yielding time-dependent effects on emotional item memory entailed retention intervals of minimally 24 hours, thus including a full night of sleep (Anderson et al, 2006; Nishida et al., 2009; Ritchey et al, 2008; Sharot & Phelps, 2004; Sharot & Yonelinas, 2008; Ventura-Bort et al., 2016; Wang, 2014; Weymar et al, 2011; but see also LaBar & Phelps, 1998; Rimmele et al, 2011). This lends support to the notion of a time-dependent advantage that unfolds specifically as a result of sleep-related consolidation, which was similarly found by previous studies (Groch et al., 2013; Groch et al., 2015; Nishida et al., 2009; Wagner et al., 2001). While the exact mechanisms underlying the preferential retention of emotional item memory as well as the neural underpinnings require further exploration, the present results affirm the critical role of consolidation processes in establishing these effects.

The analyses of subjective recollection and familiarity in the present item memory procedure revealed a significant enhancement of R-judgments for emotional stimuli irrespective of time of testing. This is consistent with prior reports of an enhanced recollective experience for emotionally salient material (Johansson et al, 2004; Ochsner, 2000; Rimmele et al., 2011) independent of sleep-related consolidation mechanisms (Atienza & Cantero, 2008; Sterpenich et al., 2007). In addition, as for item memory in general, K-judgments to emotional items were selectively preserved over time as compared to K-judgments to neutral items. This suggests that the time-dependent advantage which was revealed in former item memory analysis (see above) is to be attributed to a preserved subjective familiarity rather than recollection of emotional images. Conversely, this may point towards a consolidation benefit of emotional material which emerges independently of hippocampal memory processes. This would conform to frequent findings of time-dependent advantages in emotional item memory which do not generalize to performance in associative, and thus hippocampus-dependent, memory tests (e.g. Sharot & Yonelinas, 2008; see Yonelinas and Ritchey, 2015 for a review). On the other hand, with reference to the potential involvement of sleep-related consolidation in establishing this effect, a former study by Hu et al. (2006) revealed a highly similar pattern of results. Across a 12-hour-sleep/wake-design the authors found a selective sleep-related enhancement of subjective familiarity to emotional images which was not evident in corresponding analysis of R-judgments. However, as the critical mechanism of the time-dependent advantage in item memory itself requires further clarification, this is similarly the case with regard to the present findings of an enhanced subjective familiarity of emotional material emerging across time.

4.2. Source memory

Examining the effects of REM- and SWS-rich consolidation on emotional source memory resulted in a significant three-way interaction that suggests differential beneficial effects for source memory across early and late night sleep for both valence categories. We found neutral source memory to be selectively preserved after early SWS-rich sleep which is generally in line with the active system consolidation account (Diekelmann & Born, 2010). Moreover, we found a similar preservation of emotional source memory over late night sleep, which extends previous findings and points to a specific role of REM sleep for the consolidation of emotional source memory.

Our first finding raises the question, why early SWS-rich sleep did not result in a similar beneficial effect on emotional source memory, as would be expected if SWS-dependent offline processing provided a generalized function in associative memory consolidation (Diekelmann & Born, 2010). Based on the finding that sleep-dependent benefits on associative memory only emerge when participants receive instructions about the subsequent test phase prior to encoding (Wilhelm et al., 2011), one may assume that the learning intention during encoding acts as the critical “tagging” mechanism, which determines whether sleep-related system consolidation is deployed. Such a specific learning experience, characterized by intentional encoding and the engagement of control processes may be associated with activation in the prefrontal cortex (Ranganath, 2010), which, in turn, contributes to the generation of slow oscillations and thus potentially impacts hippocampal reactivations during SWS (Batterink et al, 2016; Diekelmann & Born, 2010). The salience of emotional stimuli may have attenuated these tagging mechanisms during encoding as the material is perceived as highly distinctive and easily memorable, seemingly requiring less effort to successfully retain the item and its source feature (see Hourihan, Fraundorf and Benjamin, 2017 for evidence that emotional material influences metamnemonic judgements in this manner). On the other hand, neutral material may be perceived as less conspicuous, thus engaging more strategic processing mechanisms during encoding (see Alger and Payne, 2016 for a similar line of reasoning). In line with this hypothesis, Groch et al. (2015) reported an enhancing effect of early sleep on neutral source memory retention but not on emotional source memory retention in a similar split night study design. However, when the motivational value of the material was additionally varied (Experiment 2), a general retention benefit of both emotional and neutral source memory over early sleep emerged. Thus, the presumed enhancement of learning intention by motivational cues may have led to a similar and strong recruitment of tagging mechanisms during the encoding of emotional stimuli as in the case of neutral stimuli, and thus resulted in a similar initiation of system consolidation processes during SWS for neutral and emotional material. In fact, the findings of a recent study by Lehmann et al (2016) add to this notion by demonstrating a selective cuing benefit for emotional image-word associations across NREM sleep. Uncued neutral associations exhibited similar levels of memory retention as those that were reactivated during sleep by administration of external cues. In our interpretation this pattern of results may reflect that neutral association successfully engaged tagging mechanisms at the encoding stage, as such, not requiring external enforcement, which resulted in an absence of retention differences between uncued and cued neutral associations. Emotional associations, on the other hand, may have attenuated tagging mechanisms at the encoding stage and consequently exhibited a strong benefit from external cuing. In other words, when emotional associations are enforced by motivational cues (as in Groch et al., 2015) or directly cued during NREM sleep (as in

Lehmann et al., 2016) they gain access to SWS–related processing, whereas without such an external enforcement (as in the present study and in the uncued stimulus condition of the Lehmann et al. study), emotional associations do not exhibit preferential retention across early sleep.

While we did not find a beneficial effect of SWS on emotional source memory retention in the present study, possibly due to the factors outlined above, we did nevertheless find a selective preservation of emotional source memory over late night sleep. This is a novel finding and suggests that the well-characterized retention benefit in emotional item memory observed in association with REM sleep under the present testing conditions extended to the retention of source features of emotional material. In conjunction with the highly specific correlation between REM sleep's neurophysiological features and post sleep emotional source memory performance (see below for further discussion), we believe that the underlying process of consolidation may operate in a manner that is highly distinctive and distinguishable from SWS-related system consolidation. The precondition to this process may be the successful perceptually-based binding of the respective emotional item and its associative features at the encoding stage. This consideration is based on frequent accounts in the literature suggesting that emotional associations are preferentially retained only when they entail features that are "intrinsic", thus perceptually inherent, to the stimulus (such as color or location), whereas the process of associative binding appears to be impaired for "extrinsic" features (Chiu et al., 2013; Kensinger, 2009; Mather, 2007). Taking into account that REM sleep-related emotional memory processing may only occur as a sequel of arousal-induced changes in synaptic plasticity during initial encoding (Bergado et al., 2011; Richter-Levin & Akirav, 2003), enhancing effects of REM sleep may be limited to source features in spatiotemporal proximity of the respective emotional item (as in our study the screen location at which the pictures were presented). This could plausibly account for the absence of similar effects in other recent studies, such as the Lehman et al (2016) study, in which cuing emotional associations during REM sleep did not elicit any significant retention benefits in contrast to uncued associations. As the study employed associations between visually presented images and auditorily presented words this requires associative binding across different modalities (Mayes et al, 2007) which may not be accomplished by the perceptual binding mechanism proposed above. While this line of interpretation requires further elaboration in future studies, the neurophysiological dissociation we found regarding emotional and neutral memory retention and oscillatory features of REM sleep and SWS strongly supports the concept of independent processing mechanisms related to these two sleep stages.

4.3. Neurophysiological correlates of memory consolidation

Source memory retrieval of emotional images after sleeping was significantly and positively correlated with right-frontal theta lateralization in the late sleep group. This association strongly substantiates that specific processes during REM sleep are critical for emotional memory consolidation rather than general effects of time or sleep. The laterality of this effect at frontal recording sites merges with findings of episodic memory encoding and retrieval being related to activation of the right dorsolateral prefrontal cortex (Rugg, Otten, & Henson, 2002) and especially for complex pictorial stimuli (Brewer, Zhao, Desmond, Glover, & Gabrieli, 1998). Emotional processing of pictorial or image-related material has conversely been linked to right-lateralized amygdala activation (McMenamin & Marsolek, 2013). Furthermore, hemispheric asymmetry in frontal theta activity is generally been found to be a feature of REM sleep (Bolduc, Daoust, Limoges, Braun, & Godbout, 2003; Vyazovskiy, Borbély, & Tobler, 2002). Remarkably, analysis in each frequency bin revealed peak correlations in the 4– 5 Hz range which corresponds well with a recent finding from rodent research of 4 Hz oscillations in prefrontal–amygdala circuits coinciding with fear expression (Karalis et al., 2016). Also this distribution of correlations within the low theta frequency range corroborates the proposition of a lower frequency “slow” theta activity occurring in the human hippocampus during both wake and REM sleep (Hutchison & Rathore, 2015; Jacobs, 2014; Lega, Jacobs, & Kahana, 2012). This slower theta activity (~3 Hz) is considered to be more physiologically analogous to faster theta in rodents (4- 10 Hz), which is often implied to reflect encoding-related activity during the acquisition of new episodes (Hutchison & Rathore, 2015). Taken together, our findings, though preliminary, support the notion that phasic REM sleep may provide a critical window for large scale synchronized activation in the MTL system and thus support associative memory consolidation for emotionally salient information (Boyce et al, 2016; Hutchison & Rathore, 2015). This may also encompass the strengthening of distributed aspects of a memory representation and integration into preexisting neocortical schemes

(Stickgold & Walker, 2013) as supported by the recent findings of Alger and Payne (2016). Future studies are needed to disentangle the detailed mechanisms by which the oscillatory laterality effect, as it emerged in the present study, mediates the consolidation of emotional items and associated source features.

With regard to the neurophysiological correlates of SWS-dependent consolidation we found significant correlations between fronto-central slow spindle power as well as frontal fast spindle power and post sleep memory performance. These results are in line with prior studies showing that sleep spindle density constitutes a sensitive measure of system consolidation processes occurring during NREM sleep (Mednick et al., 2013; Studte et al., 2015; Studte et al., 2017). It is assumed that temporally coupled spindle-ripple events provide a physiological mechanism for a fine-tuned hippocampal-neocortical information transfer (Diekelmann & Born, 2010). Remarkably, we found selective correlations of spindle power with item memory performance for neutral images, but not for emotional images, affirming our behavioral results of a selective enhancement of neutral memory retention over early night SWS-rich sleep. However, contrary to our hypothesis this association was only evident for item memory performance and not neutral source memory, which does not parallel behavioral findings but nonetheless strengthens the notion of SWS selectively benefitting memory representations devoid of affective charge. Also, it must be considered that item and source memory were assessed in a combined procedure in the same test phase. Although we aimed to control for shared variance of item and source memory, our procedure may have created an overlap in both measures resulting in stronger correlations between item and source memory performance than in paradigms in which memory for items and associations are independently manipulated (e.g. Studte et al, 2015).

4.4. Emotional reactivity to previously encoded images

While we found REM sleep to be beneficial for memory retention of emotionally salient information, we found an opposing effect on emotional reactivity. Participants of the late sleep group rated emotional images to be more arousing irrespective whether these had been studied before sleep (hits) or encountered as lures in the post sleep retrieval test (correct rejections), thus initially presented after sleep. This contradicts the view that REM sleep-related offline memory processing is not just beneficial to emotional memory retention but also results in a successive reduction of the affective tone of these previously acquired stimuli (Goldstein & Walker, 2014; Walker & van der Helm, 2009). Conversely, this effect may indicate a general amplification of affective tone following REM sleep which is in line with a growing body of literature (Baran et al., 2012; Werner et al., 2015). A possible explanation of these divergent findings may lie in the subjective assessment of emotional response, which could have been confounded by the veracity of the emotional charge[24] (Walker & van der Helm, 2009). Indeed psychophysiological measures of arousal have been shown to be modulated by REM sleep in the expected (reduced affective tone) direction, whereas subjective ratings remained unchanged (Cunningham et al., 2014). Thus, psychophysiological measures may be better suited to track changes in emotional reactivity in a sleep study. We do not assume that the circadian discrepancy between the early and late sleep group can account for these findings. General circadian influences, if present, should be apparent on ratings of both valence categories (emotional and neutral) and on both stimulus dimensions (valence and arousal), which was not the case. Furthermore, the only control measure on which groups differed (post sleep sleepiness levels) was not significantly correlated with arousal ratings for emotional stimuli, neither in the early (*r*= .18, *p*= .467) nor in the late (*r*= .02, *p*= .924) sleep group.

4.5. Methodological considerations

Even though split-night designs are an established procedure to compare consolidation effects related to SWS and REM sleep respectively they also bear some inherent limitations. First of all, circadian influences arising from the split night manipulation are to be considered in the interpretation of findings on memory performance. Indeed circadian influences and concomitant rises in cortisol levels have been shown to modulate emotional learning (Lass-Hennemann & Michael, 2014; van Ast, Cornelisse, Meeter, Joëls, & Kindt, 2013), albeit with an inhibiting effect during memory retrieval (Bentz et al., 2013; Diekelmann et al, 2011). Consequently, this should have resulted in a detrimental effect on emotional memory performance rather than the observed relative retention benefit for emotional item-source-associations in the late sleep group. Secondly, it may be argued that the night half of sleep preceding encoding in the late group may impact comparability

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[24] Participants may respond by evaluating the affective character of the depicted scenes (which has been shown to become more salient in response to REM sleep; see van der Helm, Gujar, and Walker, 2010) rather than rating their subjective emotional responses.

between both groups regarding processes of initial encoding. In fact, SWS appears to subserve synaptic homeostasis and hence subsequent learning by providing a window for synaptic downscaling (Tononi & Cirelli, 2003). However, these influences should have been evident immediately following encoding, which was not the case as groups were closely comparable in performance measures at pretest (see a-priori group comparisons). Despite these limitations of the split-night-design it is noteworthy that it offers a unique approach by contrasting two conditions of sleep that merely differ in the relative amount of time spent in SWS and REM sleep respectively. Consequently, resulting behavioral differences are not prone to involve effects of interference or generic neurophysiological regeneration, as they likely occur in studies contrasting the effects of sleep against wakefulness, e.g. nap designs.

As such, we believe that the present study adds importantly to the existing literature by providing preliminary evidence of a sleep-dependent effect on emotional source memory in association with highly specific neurophysiological features of REM sleep (right-frontal theta lateralization) in a design contrasting memory retention processes under conditions that are closely comparable in the critical consolidation phase. Interestingly, these features (i.a. theta power during REM sleep) have been demonstrated to differ in individuals suffering from post-traumatic stress disorder (PTSD) opening up the possibility that these highly specific mechanisms in emotional memory consolidation may be of relevance in the development of psychopathological conditions (Cowdin, Kobayashi, & Mellman, 2014). Moreover, our results affirm the critical relevance of initial conditions and processes during encoding in determining subsequent processes, the involvement of different structures and, lastly, the outcomes of sleep-related memory consolidation. The complex interactions resulting from this are only beginning to be understood and open up intriguing perspectives for future study.

III Experiment 2. Early morning nap sleep preserves emotional and neutral associative memory: Evidence for dissociable consolidation processes.

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1. Introduction

When memory representations of specific events are initially formed, this merely constitutes the prerequisite to successful retrieval in the future. Subsequent stages of consolidation are critically for establishing which of these representations will persist over time. Sleep-dependent system consolidation is crucially involved in establishing this selectivity by enabling redistribution of memory representations between different memory sub-systems, which is required for successful retention over time (Diekelmann & Born, 2010; Stickgold & Walker, 2013). The present study examined the selective consolidation of neutral and emotional associative memory across an early-morning nap, with the central aim of exploring how particular sleep stages, namely SWS and REM sleep, contribute to the consolidation of these different classes of stimuli.

Contemporary memory models suggest that sleep-related system consolidation is largely accomplished during SWS. Within this neurophysiological state previously acquired memory representations are assumed to be partially redistributed from temporary storage in the hippocampus to long-term integration into neocortical networks (Diekelmann & Born, 2010). This process is reflected by the temporal synchrony of specific phases of oscillatory features in the hippocampus (SWRs), within the thalamocortical circuit (sleep spindles 11-15 Hz) and the neocortex (slow oscillations < 1 Hz). Accumulating evidence indicates that this mechanism may be particularly relevant to the consolidation of associative features of events (associative memory; Mednick et al., 2013; Studte et al, 2015; van der Helm et al., 2011). Associative memory has been found to rely critically on binding processes in the hippocampus, whereas mere recognition of the event itself (item memory) is supported by adjacent regions (Staresina & Davachi, 2009; Yonelinas, 2002; Yonelinas, 2013). The specific benefits of SWS-related consolidation to associative (and therefore hippocampus-reliant) memory are thus highly compatible with the assumed role of the hippocampus as a hub of temporarily-stored memory representations from which novel information is extracted and incorporated during sleep-related system consolidation (Diekelmann & Born, 2010).

A critical feature of sleep-dependent consolidation is the selectivity with which it operates to enhance memory representations that are crucial to be retained over time (Stickgold & Walker, 2013). This selective consolidation is assumed to be accomplished by means of top-down-processes, which are reflected on a neurophysiological level by the coordinated reactivation of specific hippocampal memory traces driven by neocortical slow oscillations (Batterink et al., 2016). These slow oscillations are assumed to originate as a result of residual activation changes in neocortical networks (e.g. related to learning intention during encoding) and, thereby, may give rise to the reactivation of relevant memory representations during subsequent SWS (Diekelmann & Born, 2010; Rasch & Born, 2013). This sequence in the generation of slow oscillations may constitute a mechanism by which memory representations are “tagged” at the initial encoding stage to be selectively reactivated and reprocessed during SWS. The process of “tagging” itself may be mediated by processes in the mPFC (Marshall & Born, 2007; Rasch & Born, 2013; Stickgold & Walker, 2013). In line with this idea it has been demonstrated that stimuli which are associated with monetary incentives (Studte, et al., 2017) or for which learning intention is enforced by study instructions (Saletin et al., 2011; Wilhelm et al., 2011), are selectively retained over sleep in close association to SWS-related oscillatory features, i.a. sleep spindle density (Saletin et al., 2011; Studte et al., 2017).

Whereas tagging at the encoding stage is crucial for neutral material so that SWS-dependent system consolidation is initiated and therewith the capacity for retrieval over extended time periods, emotional stimuli seem not to be retained by this process. In fact, emotional stimuli appear to enter an entirely different processing route of sleep-related consolidation, one which is related to rapid eye movement (REM) sleep physiology (Goldstein & Walker, 2014; Walker & van der Helm, 2009). Across various designs with different sleep durations, it has consistently been found that sleeping results in the selective enhancement of emotional item memory[25] (Groch et al., 2013; Groch et al., 2015; Hu et al., 2006; Nishida et al., 2009; Payne & Kensinger, 2011; Payne et al., 2008; Walker & van der

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[25] Mostly operationalized by contrasting negative and highly arousing with neutral and low arousing stimulus material.

Helm, 2009). This enhancement of emotional item memory has been linked to both REM sleep duration (Groch et al., 2013; Nishida et al., 2009; Payne et al., 2015) and the onset latency of REM sleep (Nishida et al., 2009). Furthermore, emotional memory retention is related to unique features of REM sleep physiology, specifically to the density of rapid eye movements (Gilson et al., 2015) and theta oscillations (4- 7 Hz), which characterize REM sleep on a neurophysiological level (Nishida et al., 2009; Prehn-Kristensen et al., 2013). These neurophysiological equivalents of sleep-related emotional memory consolidation were originally shown by findings of Nishida et al. (2009) who found a significant correlation of the offline difference in emotional memory performance across an afternoon nap and right-frontal theta laterality during REM sleep (difference in theta power at F4 and F3). Additionally, Prehn-Kristensen et al. (2013) found a significant correlation between absolute right-frontal theta power (F4) during REM sleep and the dominance of emotional over neutral memory retention after a full night of sleep in a sample of children and adults. These findings have been interpreted to suggest that theta oscillations (4- 7 Hz) and specifically their local (right-frontal) distribution reflect reactivations and subsequent reprocessing of affectively relevant events within limbic structures and neocortical networks (Walker & van der Helm, 2009). This assumption is supported by functional connectivity patterns during memory retrieval that point towards a sleep-related reorganization within the emotional memory network through enhanced connectivity between limbic areas, the occipital cortex, and vmPFC during post sleep recollection of emotional stimuli (Payne & Kensinger, 2011; Sterpenich et al., 2007; Sterpenich et al., 2009). Moreover, Bennion, Payne, and Kensinger (2017) showed that the enhancement of activation in visual processing areas elicited by successfully retrieved emotionally-linked stimuli after sleeping was linearly related to preceding REM sleep duration. This suggests an innate relationship between REM-sleep-related processes and subsequent sleep-dependent activation changes during wakeful memory retrieval.

Although there is substantial empirical evidence for a connection between REM sleep and enhanced emotional memory, it is not yet known which particular aspect of episodic memory retrieval profits from REM-sleep-related consolidation. More specifically, it needs to be established whether REM-sleep-based consolidation processes are only relevant to emotional item memory or whether they are also involved in the consolidation of emotional associative memory. Preliminary results suggest that REM-sleep-related consolidation mechanisms are involved in the preferential retention of emotional source memory, which represents a form associative memory (Sopp, Michael, Weeß, & Mecklinger, 2016). In a split-night-design, which contrasts memory consolidation processes across the first (SWS-rich) and second (REM-sleep-rich) night halves, we examined source memory (location) of emotional and neutral images.

In line with previous research, SWS in the first night half was associated with the retention of neutral source memory. Intriguingly, there was no corresponding benefit for emotional source memory, which is in line with former findings (Alger & Payne, 2016; Groch et al., 2015 but see Lewis et al., 2011) and suggests that the mechanisms which facilitate neutral associative memory retention over (SW-)sleep do not generalize to emotional stimuli. More specifically, these accumulating findings may reflect that the affective tone of emotional stimuli attenuates SWS-related tagging mechanisms. As emotional stimuli are inherently salient, this induces systematic effects on metamnemonic judgments during encoding (Hourihan, et al., 2017) which in turn may reduce learning intention. This systematic attenuation of learning intention may consequently influence SWS-related tagging mechanisms to selectively bypass emotional material as a result of its arousing qualities. Importantly, we further found a selective retention benefit of emotional source memory over the second night half, which was strongly associated with oscillatory features of REM sleep (right-frontal theta dominance). As such, the results revealed a complementary facilitation of emotional and neutral source memory retention by dissociable processes operating during early and late night sleep. Moreover, our finding of a consolidation process related to REM sleep, which resulted in selective facilitation of emotional source memory but operated independently of the above described SWS-related mechanism, is entirely novel and thus motivated the present study.

The present study aims to examine whether these results generalize to a different study design and to a different operationalization of associative memory. With regard to the first aspect, it investigates whether selective preservation of emotional associative memory also emerges in an early morning nap paradigm. An early morning nap design allows ascertaining consolidation-related effects after a brief sleep opportunity in a circadian controlled setting while still inducing high proportions of REM sleep (Carr & Nielsen, 2015; Deliens, Leproult, Neu, & Peigneux, 2013, 2013; Gilson et al., 2015; Groeger, Lo, Burns, & Dijk, 2011). Due to the circadian and homeostatic modulations of the sleep cycle, REM sleep propensity is greatest in the early morning hours and in close proximity to initial awakening from nocturnal sleep. Therefore, an early morning nap paradigm is ideal to examine the impact of REM sleep on memory performance. Moreover, a nap design allows testing whether effects of (REM-)sleep-dependent consolidation are similarly attained over a brief sleep interval during the daytime rather than being confined to extended periods of nocturnal sleep across an entire night half. Secondly, the study aims to establish whether the selective REM-sleep-related preservation of emotional source memory that we previously observed generalizes to associative recognition in a paired associate task. This task requires the active integration of two elements at the encoding stage (object-scene-pair) and is therefore an important extension to our former task, in which participants encoded single items with highly intrinsic features (spatial location). This potential extension is particularly relevant in the context of emotional memory as arousal has been found to narrow attention to central object features, also referred to as the "central/peripheral tradeoff effect" (Easterbrook, 1959). Whether elements of an emotional episode are encoded in a stimulus-driven manner or in an intentional integration process (Kensinger, 2009) may thus potentially set important preconditions for REM-sleep-dependent consolidation. Finally, the study assesses whether sleep-related effects persist over time by adding a second memory test on the following day (after a subsequent night of sleep). The temporal persistence of sleep-related effects on memory performance is rarely addressed in laboratory studies but yields important implications with regard to the sustainability of sleep-related consolidation effects. To measure potential effects on a neurophysiological level, we analyzed EEG recordings of the nap opportunity with respect to REM sleep (right-frontal theta dominance) as well as NREM sleep specific oscillatory features (sleep spindle density). We hypothesized that sleeping in the critical consolidation phase should be beneficial to the retention of associative memory from pre- to posttest. Moreover, we expected to find a neurophysiological dissociation between the retention of emotional and neutral associative memory. While the retention benefit of neutral associative memory should be selectively correlated to sleep spindle density (NREM), the retention benefit of emotional associative memory should be selectively associated with right-frontal theta dominance (REM).

2. Materials and methods

2.1. Subjects

Fifty-three subjects took part in the present study. Participation was restricted to individuals fulfilling the following criteria: sufficient sleep quality (PSQI≤ 5; Buysse et al, 1991), no extreme circadian preferences (neither strong eveningness nor strong morningness preference; Randler, 2013), habitual sleep duration ≥ 6 hours, absence of regular shift work, and pronounced right-handedness (as determined by Oldfield, 1971). Potentially confounding effects of menstrual cycle were minimized by selecting only females using hormonal contraception. Participants were further required to be native German speakers, aged between 18 and 30 years with normal or corrected-to-normal vision, and to be in good general health (BMI in the normal range, no chronic disorders, previous drug use or long-term medication).

The final sample for analysis comprised 23 participants (11 male; M_{age} = 22.46, *SD*= 2.60) in the nap condition and 23 participants (10 male; M_{age} = 24.31, *SD*= 2.54) in the control condition. Three participants were excluded as they did not meet criteria for required sleep/wake properties. In one subject of the control group N2 sleep was detected during the consolidation phase and two participants of the nap group did not show the minimum duration of 30 minutes NREM sleep. Additionally, three subjects were excluded due to poor associative recognition performance at pretest (1.5×interquartile range below the lower quartile of the overall group; *N*=2) and posttest emotional associative memory performance exceeding chance level (*N*=1)[26]. One participant failed to complete experimental procedures due to premature termination of study participation and was consequently discarded from analysis. All participants gave written informed consent and were paid 75 € for study participation.

2.2. Study design

The present study utilized an early-morning nap manipulation in order to facilitate REM sleep onset and establish a predominance of REM sleep over SWS duration (see Figure III 1; Carr & Nielsen, 2015; Deliens et al., 2013; Gilson et al., 2015; Groeger et al., 2011).

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[26] As pretest item memory performance was considerably high in all participants (PR_I> .50) outlier detection was based on associative memory performance at pretest solely.

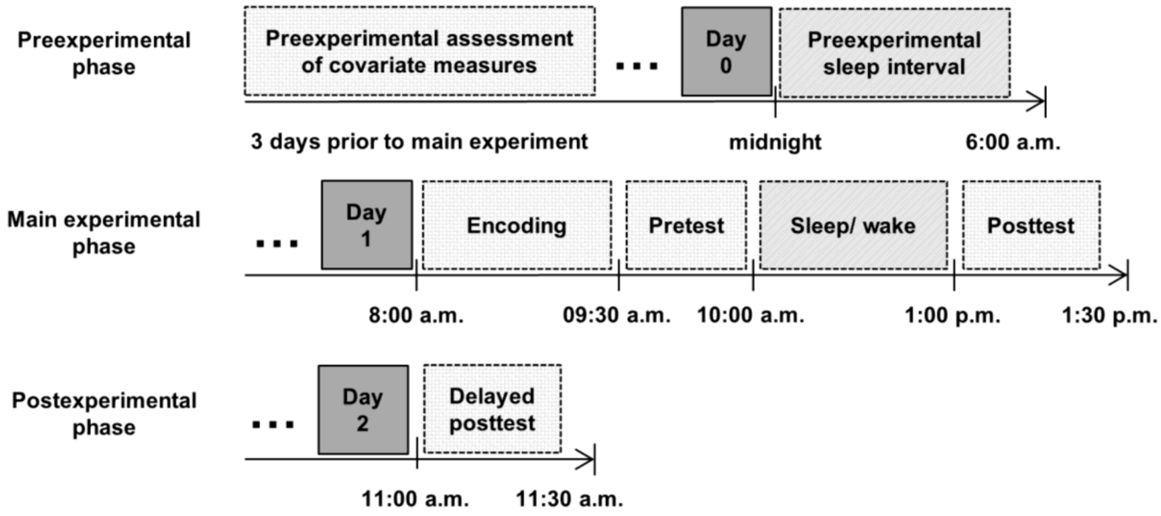

Figure III 1. Overview of the current study design. *Note:* In the main experimental phase participants were allocated to the nap or wake group in accordance with the rationale of an early morning nap design.

Three days prior to study participation, subjects were asked to complete covariate measures of trait anxiety and depression (Trait Anxiety Depression Inventory, STADI-T; Laux et al., 2013) as well as tests of fluid intelligence (Formann et al., 2011) and verbal memory (Schelling & Schächtele, 2001) in order to account for potential subject-specific variance in subsequent analyses. During the pre-experimental night participants were asked to restrict their sleep duration to 6 hours by going to bed at midnight and rising at 6:00 a.m. the latest (see Figure III 1). Adherence to procedures was monitored by accelerometers (Fitbit Flex, Fitbit, Inc.), sleep diary and confirmation of awakening by email. Additionally, participants were asked to refrain from alcohol, caffeine and nicotine intake as well as physical exercise starting from 24 hours prior to the experiment.

Participants arrived at the laboratory at 8:00 a.m. and were seated in a soundproofed testing booth facing a 27" LCD monitor (60 Hz refresh rate) at a viewing distance of about 65 cm. Upon arrival, they conducted the encoding phase of the experiment which was followed by the pretest procedure. Subsequently, participants were prepared for polysomnographic measurements during the succeeding nap (or monitoring of wakefulness during the corresponding interval in the control condition). Following this, participants were allocated to either the nap group or the control condition. Group allocation was determined in a pseudorandom fashion to establish balanced gender ratios in both groups (see Genzel et al., 2012 for accounts of differential sleep-related effects on memory consolidation between genders). At approximately 10:30 a.m. subjects of the nap condition obtained a 2-hour sleeping opportunity, whereas control participants were instructed to watch a non-arousing, low interfering and non-narrated documentary movie lasting two hours of the daily life in a monastery (Into Great Silence, Philip Groening) while remaining awake. At the end of the 2-hours interval, participants of both groups were seated in the laboratory for 30-minutes during which they watched excerpts of calming landscapes (taken from “Relaxing: The most beautiful landscapes on earth”) and they were served a standardized snack and drink. This phase was introduced to prevent potential detrimental effects of sleep inertia on immediate memory performance. Subsequently, participants underwent the posttest procedures at approximately 01:00 p.m. which were identical to the initial pretest, but comprised a different set of stimuli. Following completion of the posttest, participants were sent home and instructed to return on the following day at 11:00 a.m.. Sleep timing and duration between the two testing days were unrestricted and participants were asked to continue completing the sleep diary with regard to this second night. On day 2, participants completed the delayed posttest that was identical to pre- and posttest procedures, but entailed a different set of stimuli. This third assessment of memory performance was implemented to assess long-term effects of sleep-dependent consolidation. Covariate measures of state sleepiness (Karolinka Sleepiness Scale, KSS; Kaida et al., 2006) and current mood (State Anxiety and Depression Inventory, STADI; Laux et al., 2013) were ascertained at the onset of each phase of the experiment (encoding and test phases).

2.3. Memory task

The present task design was similar to the paradigms used by Ventura-Bort et al. (2016) as well as Luck, Leclerc, and Lepage (2014). Different object-scene-pairs were presented during encoding with the instruction to memorize these for a subsequent test phase in which old, recombined and new pairs were to be correctly classified by retrieving the initial associations (see Figure III 2).

Stimulus material

The stimulus material for the current experiment was selected from the IAPS (Lang et al., 2005) and the NAPS (Marchewka et al., 2014). Pictures were preselected in order to contrast memory performance for negative, highly arousing scenes (valence: *M*= 2.56, *SD*=

0.70; arousal: *M*= 6.35, *SD*= 0.71) with that of neutral scenes (valence: *M*= 5.55, *SD*= 0.58; arousal: *M*=4.14, *SD*= 0.79). All stimuli were rated in a separate sample of participants (*N*= 10) to preclude significant deviations from the original norms in the current population. Furthermore, scenes were matched with regard to luminance, animacy, the occurrence of faces and indoor/outdoor scenes both between lists and between valence categories (all *p*> .20). A total of 243 pictures were selected in each category (neutral and emotional) which were divided into nine parallel sets serving as old, recombined and new scenes at each time of measurement. The designation of these subsets was counterbalanced across participants and the order of stimulus presentation was pseudorandomized individually for each participant with no more than two scenes of the same valence category occurring consecutively

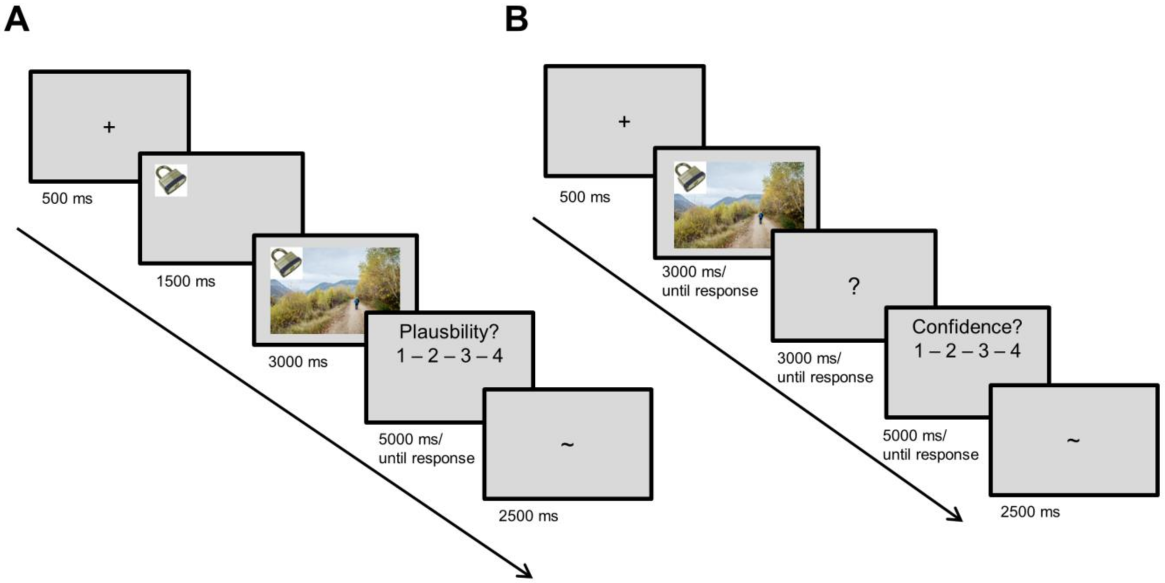

Figure III 2. Task design of **(A)** encoding and **(B)** test procedure. *Note:* The test procedure was identical at pre-, post and delayed post sleep times of measurement.

The objects which were presented in conjunction with emotional and neutral scenes were chosen from the Bank of Standardized Stimuli (BOSS; Brodeur, Guérard, and Bouras, 2014) and from the Alternative Snodgrass and Vanderwart Stimulus Set (Moreno-Martínez & Montoro, 2012). Objects were selected to encompass a variety of different, instantaneously identifiable and inanimate objects from various semantic categories (e.g. tools, furniture, and clothing). Allocation to sub-lists was performed randomly with subsequent adjustments to prevent an imbalance of specific semantic categories of objects in single lists. Moreover, mean stimulus ratings of name agreement, familiarity, visual complexity and manipulability were matched across all 18 lists and also between lists ($p <$ .20), which were subsequently paired with neutral and emotional scenes. Object lists were assigned to sub-lists of emotional and neutral scenes at random but assignment within lists was manually corrected to ensure no semantic relation between scenes and their respective object. Lastly, the location of the object (upper right, lower right, upper left or lower left) was determined pseudorandomly to prevent objects from covering highly relevant aspects of the scene as they were presented in a superimposed manner. Location of object presentation was balanced within each list and across all 18 lists. The individual position of the object was retained over all phases of the experiment by creating recombined pairs only between object-scene pairs of the same location and again ensuring no semantic relatedness by the judgement of two independent raters. This process of stimulus generation resulted in a total of two parallel versions (serving as old or recombined pairs respectively) of 18 lists of 27 object-scene-pairs each. Objects and scenes were rescaled to 212×212 pixels and 950×713 pixels respectively. Throughout the experiment all scenes were presented at a horizontal visual angle of 15.3° and a vertical visual angle of 16.6°. During each phase of the experiment participants were familiarized to the task procedures with four trials consisting of object-scene pairs which were not included in subsequent analysis.

Encoding phase

Prior to the encoding phase of the experiment participants were instructed that they were going to see different scenes in conjunction with simple everyday objects, which they were to remember for a subsequent memory test (see Figure III 2.A). It was additionally emphasized that the successful accomplishment of the task would depend on retrieving the explicit association between the scene and its respective object. Each trial began with the presentation of a fixation cross (500 ms) that was succeeded by the presentation of the object in its respective location (1500 ms). Thereafter, the object-scene pair was presented conjointly (3000 ms) together with the instruction to imagine that the object is part of the scene. This task was chosen to enhance interactive encoding (Bergstrom et al., 2013) and facilitate perceptual intra-item binding processes by encouraging participants to create a composite image. Following stimulus presentation, participants were asked to rate the plausibility of the object-scene pair (5000 ms) on a scale ranging from 1 (implausible) to 4 (plausible). Trials were separated by an interstimulus interval of 2000 ms and were presented in four blocks with three self-paced pauses interspersed.

Test phases

Following encoding, participants immediately completed the pretest procedure to ascertain baseline memory performance independent of potential contributions of consolidation processes occurring over sleep or wakefulness (see Figure III 2.B). Participants were instructed to differentiate entirely new object-scene pairs from old and recombined pairs. While old pairs were presented in identical composition, recombined pairs comprised an object and a scene that had been presented in conjunction with a different scene or object during initial encoding. As a result of this manipulation, it is critical to retrieve the association between the scene and its object to successfully accomplish the task, which is assumed to require the involvement of the hippocampus (Yonelinas, 1997; Yonelinas, 2013). Thus, the correct classification of recombined item pairs should crucially reflect the contribution of hippocampus-dependent, recollective processes while entirely new pairs can be discriminated from pairs containing old objects and scenes by means of familiarity (Yonelinas, 2002). Prior to each test trial, a fixation cross (500 ms) was presented that was succeeded by the presentation of the object-scene pair (3000 ms). Participants were instructed to respond as fast and accurately as possible with the onset of the stimulus by indicating its status relative to the encoding phase (old, new or recombined). At stimulus offset an additional response window was introduced allowing participants to respond for an additional duration of 3000 ms. Subsequently, participants were asked to rate the confidence of their response (5000 ms) on a 4-point-scale (uncertain, rather uncertain, rather certain, certain). The inter-trial interval was set at 2000 ms and stimuli were presented in three blocks. Response keys of the old-new-recombined judgement were counterbalanced across participants and within each group.

Post- and delayed posttest procedures were identical to the sequence outlined above, but entailed different sub-lists of stimuli. Participants were explicitly instructed that item status was to be determined relative to the encoding phase and that “new” object-scene-pairs of prior test phases would not reappear in subsequent tests.

2.4. EEG recordings and analysis

In both experimental conditions standard polysomnography recordings (AASM, 2007) were performed including EEG (F3 and F4 according to the international 10- 20 system), EMG (submental) and horizontal EOG (lower right and higher left canthi). Signals were digitized at a sampling rate of 256 Hz (EEG and EOG) or 512 Hz (EMG) and amplified by a wireless SOMNOtouch amplifier system (SOMNOmedics GmbH, Randersacker, Germany) which was attached with a centered chest strap. Data were filtered online with a first-order high-pass filter at 0.3 Hz, a second-order butterworth low-pass filter at 75 Hz and a Notch-filter at 50 Hz. All electrodes were recorded referenced to Cz and were re-referenced offline to the average of both mastoids for sleep stage scoring, spindle analysis and spectral analysis. A 0.3- 35 Hz bandpass filter was applied offline for sleep stage scoring.

Visual sleep stage scoring was independently performed by two trained raters independently in accordance with the criteria provided by the AASM (2007) and using the Matlab-based toolbox FASST (fMRI Artefact rejection and Sleep Scoring Toolbox; Leclercq, Schrouff, Noirhomme, Maquet, & Phillips, 2011). The epoch length was set to 20 s to allow for overlapping windows of 4 s in the computation of spectral power density. Each epoch was scored visually into NREM stages N1-3, stage R and stage W. Both the absolute amount of minutes spent in each sleep stage as well as the relative amount with reference to TST (% TST) was determined for further analysis.

Sleep spindle density

Spindle density during NREM sleep was determined by means of the spindle detection algorithm implemented in the FASST-toolbox which is based on the method described by Mölle, Marshall, Gais, and Born (2002). In brief, the data of all three reference channels (F3, F4 and Cz) are bandpass filtered (8-20 Hz) and the root mean square (RMS) signal is computed. This signal is than transformed into a binary signal using individually computed spindle thresholds of each channel based on epochs scored as NREM 2. Thus bursts of activity in the frequency range of interest (determined by individual spindle thresholds) with a minimum duration of 400 ms are detected and considered as spindles. These potential spindle events were then reviewed visually with regard to the occurrence of artifacts (and excluded when necessary) by a research assistant who was unaware of the research question and individual performance rates. The average spindle density per epoch (NREM) was computed from the resulting matrix of spindle events across all channels and for each channel individually for statistical analysis.

Spectral analysis

Spectral analysis was performed using the Matlab-based toolbox EEGLAB (http://www.sccn.ucsd.edu/eeglab/). Prior to analyses, epochs were rejected semi-automated on the basis of automatic detection of extremely large fluctuations (> 1000 µV) and thereafter applying a threshold of 5 SD followed by visual identification of muscle and eye movement artifacts. Spectral power density was computed for each epoch of REM sleep using the pwelch function (50% overlap, Hamming window) with a resulting frequency resolution of 0.25 Hz. Resulting power estimates were averaged over respective epochs for the theta frequency range (4.0– 7.0 Hz) during REM sleep. For subsequent analyses of frontal theta laterality during REM sleep, relative activity difference between the left- and right-frontal sites was computed by subtracting activity at electrode F3 from that at F4 [F4- F3].

2.5. Statistical analyses

Memory task

Performance rates for old, recombined and new item pairs were analyzed to derive two separate measures of item and associative memory performance. Associative memory performance (PR_A) was defined as the probability of making a correct "old" judgement adjusted with reference to the probability of incorrectly classifying a recombined (rec) object-scene-pair as "old" [$PR_A = p(\text{Old}|\text{Old}) - p(\text{Old}|\text{Rec})$]. This definition of false alarms to recombined pairs is assumed to reflect the failure of retrieving the underlying object-scene-association, thus critically relating to hippocampus-dependent memory processes (see Luck et al., 2014) The discrimination index of item recognition (PR_I) was computed by subtracting the probability of making an "old" or "recombined" judgement to a new object-scene-pair from the probability of correctly identifying old object-scene associations as old by the judgement of "old" or "recombined" [$PR_I = p(\text{Old+Rec}|\text{Old}) - p(\text{Old+Rec}|\text{New})$]. The reasoning behind this operationalization is that recognizing both constituents as being “old” irrespective of their (non-)intact composition yields the closest approximation to item memory performance in this paired associate paradigm. In all subsequent analysis the experimental factor of “Emotion” is defined in reference to emotionality of background scenes within object-scene-associations.

Associative and item memory performance was subjected to separate ANOVAS including the within-subject factors of Time (pre-/ posttest) and Emotion (negative/ neutral background scene) as well as the between-subject factor Group (nap/ wake group). In order to follow-up on potential sleep-related effects after a subsequent night of sleep separate ANOVAS were performed with the within-subject factors of Time (post-/ delayed posttest) and Emotion (negative/ neutral) as well as the between-subject factor Group (nap/ wake group). Reaction time data were analyzed accordingly but including the additional within-subject factor of Item type (Old|Old/ Rec|Rec/ New|New).

Significant main effects and interactions were followed by post hoc t-tests and the significance level was set to $\alpha = .05$ for all analyses.

Sleep physiology and oscillatory EEG features

To link potential sleep-related behavioral effects to specific microstructural aspects of sleep physiology, Pearson correlation coefficients (*r*) were computed between memory performance (at pre-, post- and delayed posttest) and measures of oscillatory features derived from the analysis described above (spindle density and right-frontal theta dominance) in the nap group. Furthermore, explorative correlation analyses were performed with respect to time spent in REM sleep, SWS and TST as well as relative[27] theta power at frontal electrodes.

As individual participants failed to reach SWS (*N*= 2) and/or REM sleep (*N*= 5) corresponding sub-analyses were based on the remaining subset of participants. With regard to REM sleep specific analyses, one additional subject was excluded due to theta dominance strongly deviating from the groups’ distribution (3 × interquartile range below the lower quartile of the overall group).

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[27] Relative power refers to individual percentage of theta power in relation to power in the whole spectrum (in %).

3. Results

3.1. Sample characteristics

General characteristics

Table III 1. Descriptive group measures

Measure	Nap group (*N*= 23)	Control group (*N*= 23)
State		
KSS *Encoding*	**3.57 (0.84)**	**2.96 (0.98)**
KSS *Pretest*	**3.83 (0.72)**	**3.57 (1.12)**
KSS *Posttest*	**2.61 (0.94)**	**2.91 (0.95)**
KSS *Delayed Posttest*	**2.22 (0.67)**	**2.00 (0.60)**
STADI *Encoding*	**33.30 (5.23)**	**31.00 (5.24)**
STADI *Pretest*	**35.87 (7.17)**	**32.65 (6.56)**
STADI *Posttest*	**31.22 (5.12)**	**30.09 (4.70)**
STADI *Delayed Posttest*	**31.61 (7.54)**	**27.78 (3.57)**
Trait		
Gender	**♂:11, ♀:12**	**♂:10, ♀:13**
Age	**22.46 (2.60)**	**24.31 (2.54)**
IQ (WMT)	**10.00 (3.55)**	**10.91 (2.79)**
Verbal Memory (VVM)	**8.52 (3.92)**	**8.96 (3.61)**
Sleep Quality (PSQI)	**3.26 (1.32)**	**2.78 (1.35)**
Sleepiness (ESS)	**5.30 (3.10)**	**5.83 (3.49)**
Chronotype (rMEQ)	**13.27 (2.75)**	**13.43 (2.98)**
Trait Anxiety (STADI-T)	**18.09 (5.63)**	**20.30 (5.51)**
Trait Depression (STADI-T)	**17.39 (5.11)**	**18.00 (5.21)**

Note: KSS = Karolinska Sleepiness Scale, STADI= State-Trait Anxiety Depression Inventory, WMT= Wiener Matrizen Test [Viennese matrices test], VVM= Visueller und Verbaler Merkfähigkeitstest [Visual and verbal memory retention test- verbal subtest], PSQI= Pittsburgh Sleep Quality Index, ESS= Epworth Sleepiness Scale, rMEQ= reduced Morningness-Eveningness questionnaire. For state sleepiness (KSS) non-parametric test statistics are reported. Standard deviations are given in parentheses.

Trait characteristics of the current study sample were comparable between both conditions with regard to sleep-related and performance-related measures (see Table III 1; all *p*> .23). There was also no difference regarding trait anxiety and depression (*p*> .18). Groups did, however, differ in mean age (*p*= .019). To account for this difference in all subsequent between-group analyses the factor Age was introduced as a mean-centered covariate.

State measures of mood (STADI-S) and sleepiness (KSS) were obtained prior to the onset of each phase of the experiment (see Table III 1). Groups differed in state sleepiness prior to the encoding phase (*U*= 177.00, *p*= .04) with the nap group reporting higher sleepiness levels (*Mdn*= 4.00) as compared to the control group (*Mdn*= 3.00). However, this difference is contrary to the observed effects. Further, correlation analyses between state sleepiness and performance rates at all times of measurements yielded no significant results (all *p*> .23). Current mood states were comparable between groups with the exception of delayed posttest assessment. Participants of the nap group reported elevated levels of anxious and depressed mood as compared to control subjects (t_{44}= 2.20, *p*= .035), however this state measure (STADI delayed posttest) was unrelated to item and associative memory performance across the whole experiment (*p*> .10).

Sleep characteristics

Table III 2. Sleep parameters in the nap group

Sleep parameters	Time in min	% TST
Wake	**25.35 (19.67)**	**35.44 (43.03)**
N1	**11.23 (6.74)**	**12.61 (7.70)**
N2	**53.10 (16.08)**	**57.17 (13.32)**
N3	**10.81 (9.48)**	**12.45 (11.45)**
REM	**18.33 (15.13)**	**17.78 (13.77)**
TST	**93.48 (19.84)**	

Note: N1= NREM Stage 1, N2= NREM Stage 2, N3= NREM Stage 3 (corresponding to SWS), REM= REM sleep, TST= total sleep time. Standard deviations are given in parentheses.

Descriptive statistics of sleep characteristics in the nap group are summarized in Table III 2. As evident both in terms of TST as well as in absolute time, the amount of SWS (N3) and REM sleep obtained during the nap opportunity did not differ substantially with corresponding analysis failing to reach significance ($p > .05$). It is important to note that as expected REM sleep duration was considerably higher than in a standard afternoon nap paradigm (e.g. see Alger and Payne, 2016 or Studte et al., 2017).

Pre-experimental group comparisons

To address potential discrepancies in performance of the two groups prior to the experimental manipulation, data were subjected to ANCOVAS including only pretest recognition rates (see Table III 3). With regard to associative memory performance no main effect of Group or interaction effect involving the Group factor was evident ($p > .30$). However, a main effect of Emotion ($F_{1,34} = 23.54$, $p < .001$) emerged, reflecting significantly higher associative recognition rates for neutral object-scene-pairs as compared to emotional pairs. Analysis of item memory performance yielded no indication of a-priori differences between groups (main effect of Group: $p = .490$, Group × Emotion: $p = .991$). Notably, emotionality of background scene did not have a similar effect on item recognition (main effect of Emotion: $p = .126$) as in the case of associative memory performance.

Table III 3. Adjusted means of memory performance in both groups for item and associative memory

Performance Measure	Item condition	Nap group (N= 23)			Control group (N= 23)		
		Pretest	Posttest	Delayed Posttest	Pretest	Posttest	Delayed Posttest
PR_I	**Emotional**	**.89 (.02)**	**.84 (.02)**	**.73 (.03)**	**.87 (.02)**	**.82 (.02)**	**.72 (.03)**
	Neutral	**.91 (.02)**	**.84 (.03)**	**.75 (.03)**	**.89 (.02)**	**.79 (.03)**	**.75 (.03)**
PR_A	**Emotional**	**.63 (.04)**	**.51 (.04)**	**.29 (.03)**	**.58 (04)**	**.40 (.04)**	**.30 (.03)**
	Neutral	**.70 (.04)**	**.58 (.04)**	**.39 (.03)**	**.69 (.04)**	**.46 (.04)**	**.34 (.03)**

Note: PR_I= PR Item memory, PR_A=PR Associative Memory. Standard errors of the mean are given in parentheses.

3.2. Behavioral findings

Associative memory

Main analysis on associative memory performance (pre- and posttest) yielded significant effects of Time ($F_{1,43}$= 131.27, p< .001), Emotion ($F_{1,43}$= 27.88, p< .001) as well as a significant interaction of Time and Group ($F_{1,43}$= 8.16, p= .007). Like in the a-priori analysis on memory performance, emotionality of background scene exhibited an unexpectedly detrimental effect on associative memory performance of object-scene pairs. Importantly, this was found irrespective of time, with no consolidation benefit of emotional pairs emerging (Time × Emotion: p= .420). While the main effect of Time reflected a significant decline of performance rates from pre- to posttest (p< .001), this effect was modulated by the factor Group. In line with our hypothesis performance decrements were more pronounced in control subjects (t_{22}= 10.38, p< .001, d= 2.16[28]) than in subjects of the nap group (t_{22}= 6.01, p< .001, d=1.26). This was also mirrored by a significant between-subject difference in performance at posttest (t_{44}= 2.4, p= .021), which was not evident prior to the experimental manipulation (t_{44}= 0.63, p= .532; see Figure III 3).

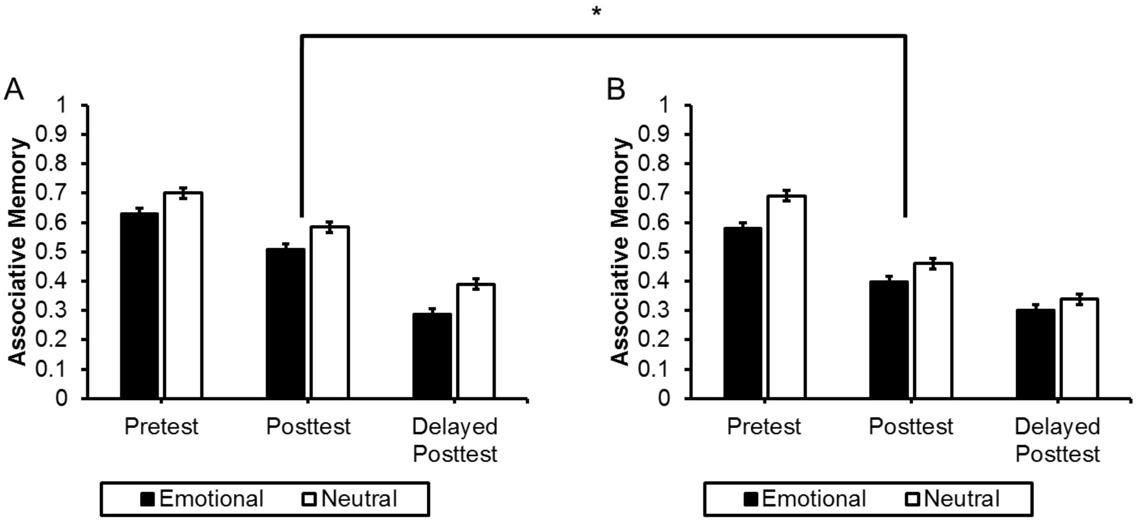

Figure III 3. Adjusted means of associative memory performance (PR_A) for emotional and neutral items in the **(A)** nap group and **(B)** control group at pre-, post- and delayed posttest. *Note:* * indicates the significant interaction of time and group (p< .05) for between-subject comparisons. Significant effects between item categories (neutral and emotional) are not illustrated for reasons of comprehensibility. Error bars represent standard error of the mean.

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[28] For all within-subjects effects *d* is corrected for dependence between means in accordance with Morris and DeShon (2002).

Item memory

With regard to item memory a main effect of Time ($F_{1,43}$= 28.78, p< .001) and a marginally significant interaction between Time and Emotion ($F_{1,43}$= 3.70, p= .061) emerged (see Figure III 4). The main effect of Time represented a significant decline of memory performance from pre- to posttest (t_{45}= 5.75, p< .001), which was not as pronounced (d= 0.80) as for associative memory (d= 1.58). The trend towards an interaction of Time and Emotion reflected an attenuated decline of emotional (t_{45}= 3.01, p= .004, d= 0.44) as compared to neutral item memory performance (t_{45}= 5.311, p< .001, d= 0.79) across both groups. While this trend may be interpreted to reflect a delayed forgetting of emotional item memory occurring both over sleep and wakefulness (Yonelinas & Ritchey, 2015), it is important to note the clear absence of a main effect of Emotion (p= .916) in the direction observed for associative memory performance. Thus Emotion exhibited differential effects on item and associative recognition, rather than impairing all aspects of memory retention. Furthermore, the absence of any effect related to the Group factor (all p> .44) importantly verified that morning nap sleep did not benefit item recognition.

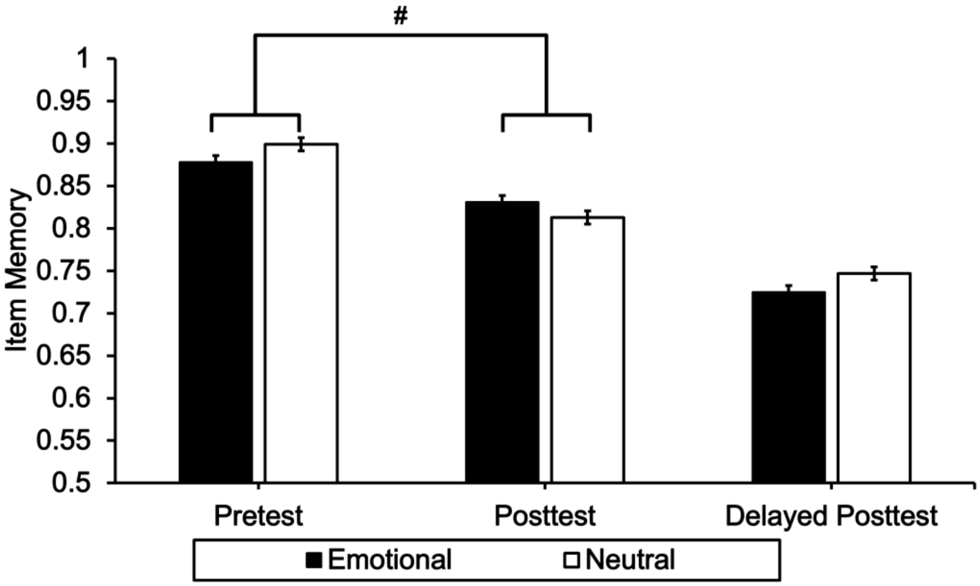

Figure III 4. Adjusted means of item memory performance for emotional and neutral images at pre-, post- and delayed posttest. *Note:* # signifies the trend towards an interaction of time and emotion (p< .10). Performance rates are collapsed across groups as there were no significant main or interaction effects involving the group factor.

Post experimental reassessment of memory performance

As expressed earlier, it is of great interest to reexamine potential sleep-related effects on memory performance after a delay without any experimental manipulation. In this regard, analyses of associative memory changes from post- to delayed posttest yielded significant main effects of Time ($F_{1,43}$= 74.62, p< .001) and Emotion ($F_{1,43}$=18.53, p< .001), paralleling the effects observed in the former analysis. Moreover, a significant interaction of Time and Group ($F_{1,43}$= 6.39, p= .015) emerged, signifying an equalization of performance rates between both groups from post- to delayed posttest. Accordingly, the significant performance benefit of the nap group at posttest in comparison to the wake group (t_{44}= 2.4, p= .021) did not persist after a subsequent night of sleep (t_{44}= 0.64, p= .529). This finding may indicate that sleep-dependent consolidation, which progressed from pre- to posttest in the nap group, similarly emerged in the former wake group when sleep was achieved with a greater delay, from post- to delayed posttest. Consequently, intermediate hippocampus-dependent storage of associative memory may have been robust enough to persist against intervening sources of interference across a complete daytime interval until sleep was initiated between post- and delayed posttest sessions. Alternatively, this pattern may suggest that sleep did not produce sustainable changes related to system consolidation, as these were abolished as soon as both groups were tested in a similar well rested state. Item memory performance, which was not modulated by nap sleep in the former analysis, solely exhibited a significant decline from post- to delayed posttest (main effect of Time: $F_{1,43}$= 45.54, p< .001) with no further main or interaction effects (p> .14).

Reaction times

Analysis of reaction times (in ms) from pre- to posttest yielded main effects of Emotion ($F_{1,44}$= 72.90, p< .001) and Item type ($F_{2,43}$= 132.32, p< .001). Emotionality of background scenes was associated with significantly slower response latencies. Additionally, correct reactions to recombined pairs (Rec|Rec) were given significantly slower as compared to correct responses to old or new item pairs (all p< .001). Furthermore, a significant interaction of both factors (Emotion × Item type: $F_{2,43}$= 13.89, p< .001) was evident, expressing that the difference between response latencies to emotional and neutral items was significantly larger for correct responses to entirely new as compared to rearranged item pairs (t_{45}= 3.30, p= .002). Reaction times to different item types were also differentially modulated across Time (Time × Item type: $F_{2,43}$= 13.89, p< .001). While correct responses to new object-scene-pairs were given significantly faster at posttest as compared to pretest (t_{45}= 2.42, p= .019), no significant differences emerged for correct reactions to old and recombined pairs from pre- to posttest (p> .05). Lastly, a significant interaction between Emotion and Group ($F_{1,44}$= 5.97, p= .016) emerged, reflecting a more pronounced difference in response times to emotional and neutral stimuli in the control group. Importantly, this was not attributable to a significant difference at pretest (p> .10) but only emerged across both times of measurements, likely reflecting unsystematic between-subject variance.

Corresponding analyses of reaction times from post- to delayed posttest revealed significant main effects of Time ($F_{1,44}$= 10.99, p= .002), Emotion ($F_{1,44}$= 39.79, p< .001) and Item type ($F_{2,43}$= 144.74, p< .001). While both Emotion and Item type exhibited effects in accordance with the former analysis, the main effect of Time reflected a significant increase in reaction times from post- to delayed posttest. A significant interaction of Emotion and Item type was also evident($F_{2,43}$= 8.78, p= .001), reflecting a significantly higher difference between reaction times to emotional and neutral stimuli when responding correctly to old as compared to rearranged item pairs (t_{45}= 3.30, p= .002).

3.3. Neurophysiological findings

Correlations between memory performance and sleep stage duration

To summarize, behavioral analyses revealed a beneficial effect of nap sleep on associative recognition of both emotional and neutral object-scene-pairs but no corresponding enhancement of item recognition. To explore potential associations between sleep macrostructure and post sleep memory performance, correlations were computed between item and associative memory indices and time spent in specific sleep stages that are of interest with regard to memory consolidation (SWS and REM sleep) as well as TST. None of these analysis yielded significant results with respect to post- and delayed posttest performance[29].

Correlations between memory performance and spindle characteristics (NREM)

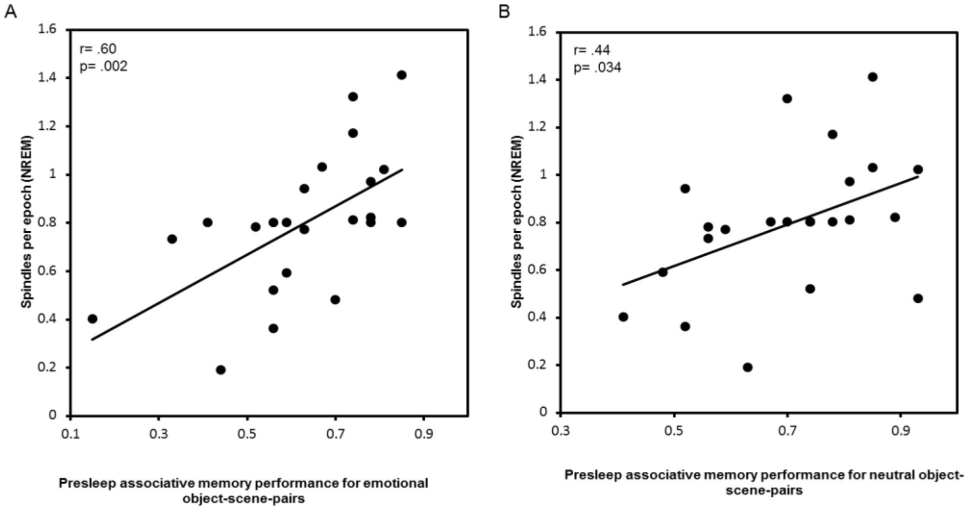

Figure III 5. Correlations between pretest associative memory performance for **(A)** neutral and **(B)** emotional object-scene-pairs and spindle density during NREM (mean number of spindles per epoch) in the nap group.

Analysis of pretest performance yielded significant associations of spindle density with both neutral (*r*= .44, *p*= .034) and emotional (*r*= .60, *p*= .002) associative memory (see Figure III 5). This may reflect a disparate aspect of spindle density which relates to general cognitive functions and cortical-subcortical network efficiency (Schabus et al., 2007).

Critically, spindle density was significantly correlated with post sleep associative memory performance for neutral (*r*= .50, *p*= .014) but not for emotional (*r*= .13, *p*= .569) stimuli (see Figure III 6). This correlation was also found to be significantly larger for neutral as compared to emotional associative memory (z_{23}= 1.96, *p*= .025[30]), suggesting that spindle density played a critical role in the consolidation of neutral object-scene associations but not with regard to pairs entailing an emotional scene. This selectivity with regard to spindle density was retained at delayed posttest as reflected by a significant association between

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[29] With regard to pretest performance, only a significant correlation between emotional associative memory and SWS duration both in minutes (*r*= -.60) and in % TST (*r*= -.49) emerged. This may reflect higher homeostatic demands for SWS in individuals with higher arousal-induced associative memory impairments. Speculatively, this variance in the magnitude of arousal-induced impairments may reflect different levels of engagement with the emotionality of the scenes. Consequently, this could results in differential requirements of emotional “rebalancing” during subsequent SWS (see Talamini, Bringmann, de Boer, and Hofman, 2013 for similar findings).

[30] One-sided calculation according to Eid, Gollwitzer, and Schmitt (2010).

spindle density and neutral associative memory performance (*r*= .44, *p*= .035) but no significant correlation regarding associative recognition of emotional object-scene associations (*p*> .13).

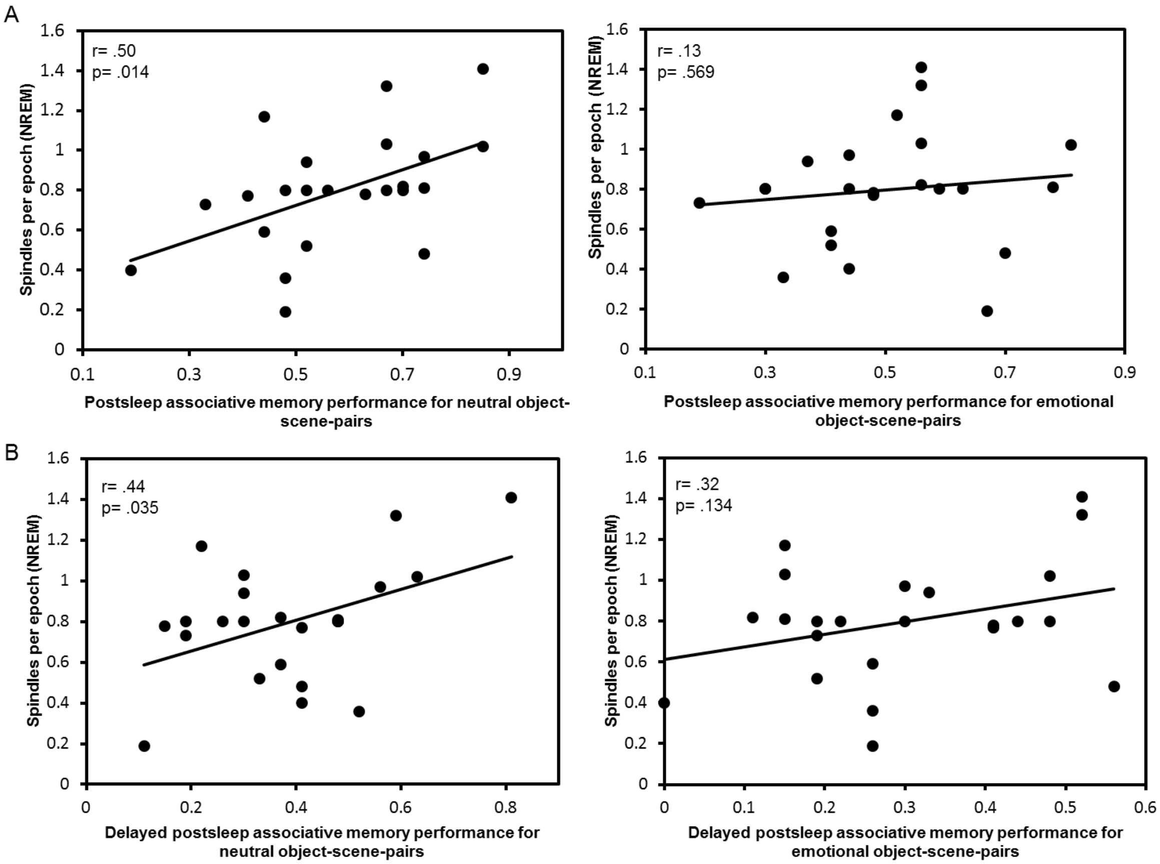

Figure III 6. Correlations between **(A)** post- and **(B)** delayed posttest associative memory performance for neutral and emotional object-scene-pairs and spindle density during NREM in the nap group.

With regard to item memory performance, this highly specific pattern of correlations to spindle density was not evident. The only significant association was found between spindle density and delayed posttest neutral item memory performance (*r*= .47, *p*= .024). As this remained an isolated finding, it may likely reflect a certain level of shared variance between item and associative memory performance in this combined task design.

Correlations between memory performance and theta power during REM sleep

Based on the prior findings of Nishida et al. (2009) and our previous results, we tested whether the sleep-dependent performance benefit regarding emotional associative recognition at posttest was related to right-frontal theta dominance during REM sleep [F4-F3]. Correlation analysis on theta laterality and post sleep emotional associative memory performance yielded no significant result (*r*= -.13, *p*= .632; see Figure III 7.A). Moreover neither item nor associative memory of either valence category across all three times of measurement showed any significant association with right-frontal theta laterality (*p*> .12). Exploratory analyses on relative REM theta power yielded a significant and negative correlation between false alarms to recombined item pairs (collapsed across emotional and neutral categories) at delayed posttest and relative theta power at F4 (*r*= -.51, *p*= .035, see Figure III 7.B), which is in line with the proposed role of REM sleep in the reorganization of long-term memory in order to maintain relational memory across time (Diekelmann & Born, 2010).

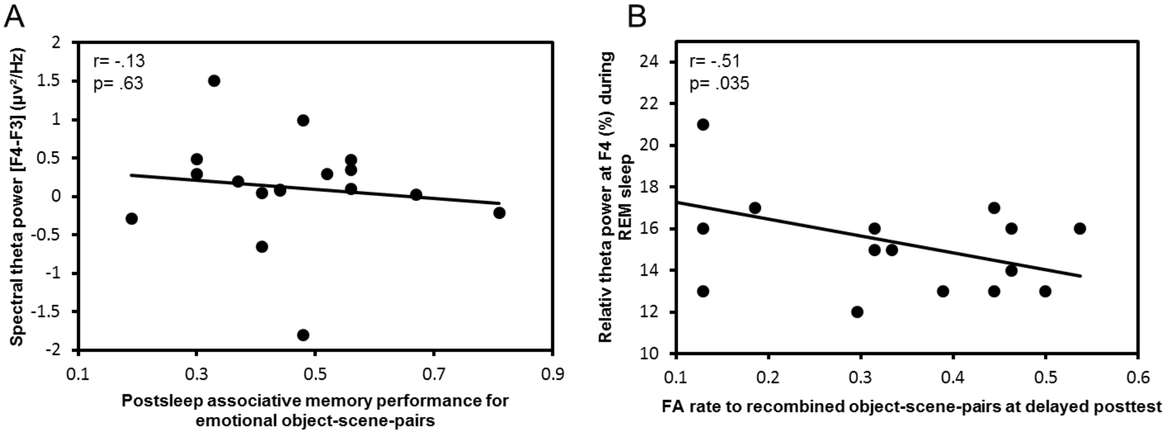

Figure III 7. Correlations between **(A)** post sleep emotional associative memory performance and right-frontal theta dominance (µV²/Hz) during REM sleep and **(B)** false alarm rates to recombined object-scene-pairs across both item types (p[Old|Rec]) at delayed posttest and relative theta power during REM sleep in the nap group. *Note:* Relative power refers to individual percentage of theta power in relation to power in the whole spectrum (in %).

4. Discussion

The present study aimed to further clarify the role of REM sleep in the consolidation of emotional associative memories. Critically, we wanted to test whether our former results (Sopp et al., 2016) generalize to a nap sleep design and to differing demands regarding feature integration at encoding. Thus, we assessed memory performance in a paired associate paradigm entailing negative and neutral background scenes prior to and following an early morning nap as opposed to sustained wakefulness. Memory performance was reassessed after a subsequent night of sleep to examine long-term consequences of sleep-dependent consolidation. We derived two separate indices of item and associative memory performance. Item memory was defined by the probability of correctly identifying emotional/ neutral background scenes and everyday objects irrespective of correctly retrieving their pairings. Associative memory was operationalized by the probability of correctly retrieving the associations of emotional/ neutral background scenes and paired objects. Consequently, "emotionality" refers to the affective character of the background scene within these object-scene-associations. In extension of our previous findings (Sopp et al., 2016), we expected to find a facilitating effect of REM sleep on emotional memory performance in the current task design, which required to actively form an association between a foreground object and an emotional background scene. Moreover, in line with system consolidation accounts (Diekelmann & Born, 2010), we hypothesized to find an enhancement of neutral memory performance in association to SWS-dependent processing mechanisms. On a behavioral level, we were thus expecting to find an enhanced retention of both emotional and neutral object-scene-associations emerging over sleep in the nap group. These enhancements should, however, be dissociable regarding the neural underpinnings of REM and NREM sleep (i.e. right-frontal theta dominance and sleep spindle density).

4.1. Effects of emotion

Emotionality of background scenes generally elicited different effects on item and associative memory. Item memory for emotional object-scene-associations exhibited a marginally significant retention benefit (p= .061) from pre- to posttest which was not modulated by sleeping, with no main effect of Emotion emerging (p= .916). However, analysis on associative memory performance revealed a significant impairment in successfully retrieving object-scene associations when the respective scene was from the negative and highly arousing stimulus category (main effect of Emotion: p< .001).

This does not adhere to our initial intention of creating a task in which emotion would facilitate binding processes and result in an enhancement of associative memory performance. As suggested by previous findings (Kensinger, 2009; Murray & Kensinger, 2013), arousal-induced activation changes in visual processing areas may facilitate binding processes and this effect may be critically drawn upon by sleep-related consolidation (Bennion et al., 2017). However, the recruitment of this facilitated-binding effect may be hampered by inverse effects of emotion-induced arousal on attentional processes that may hinder the successful formation of object-scene associations with emotional scenes. Consequently, empirical findings on the effects of emotion on associative memory are inconsistent and depend on variations of specific task features (Bennion, Ford, Murray, & Kensinger, 2013; Chiu et al., 2013; Mather, 2007). In view of these considerations and the pattern of our results, we believe that the unexpected detrimental effect of emotion in the current study is (1) related to processes in the initial encoding phase that (2) specifically impair successful binding between the scene and its respective object (rather than impacting mere item encoding). As such, attention may have been narrowed to the highly arousing scene, limiting resources required for successful binding of the object-scene-association. In fact, this effect of attentional narrowing may only be outweighed by providing encoding conditions in which the to-be-associated feature is of functional significance with regard to the arousing stimulus or, alternatively, highly integral to processing the stimulus itself (hence intrinsic, such as the screen location; Chiu et al., 2013; Kensinger, 2009). Although our encoding instructions ("Imagine that the object is part of the scene") as well as instructing participants to intentionally integrate both constituents were aimed exactly at inducing this functional significance, our experimental manipulation may not have been strong enough to counteract attentional narrowing. This interpretation is compatible with the slight retention benefit for item memory of pairs entailing an emotional scene that emerged across time. However, as our task design was mainly focused on providing a comprehensive assessment of associative memory performance, it is not possible to clearly deduce how memory performance of the isolated background scene was modulated by emotionality.

4.2. Experiment 2a

As memory for the (non-)emotional background scene was not exclusively relevant to accomplish the item memory task, this may also explain why beneficial effects of emotionality may have not emerged with sufficient clarity. In fact, accurate recognition of emotional background scenes may have been impeded due to conflicting memory signals elicited by superimposed objects which, in our interpretation, may have been impacted by attentional capturing of emotional background scenes during encoding. To explore this possibility and substantiate the claim that emotional backgrounds elicited an effect of attentional narrowing at the encoding stage we conducted a follow-up experiment.

Material and Methods

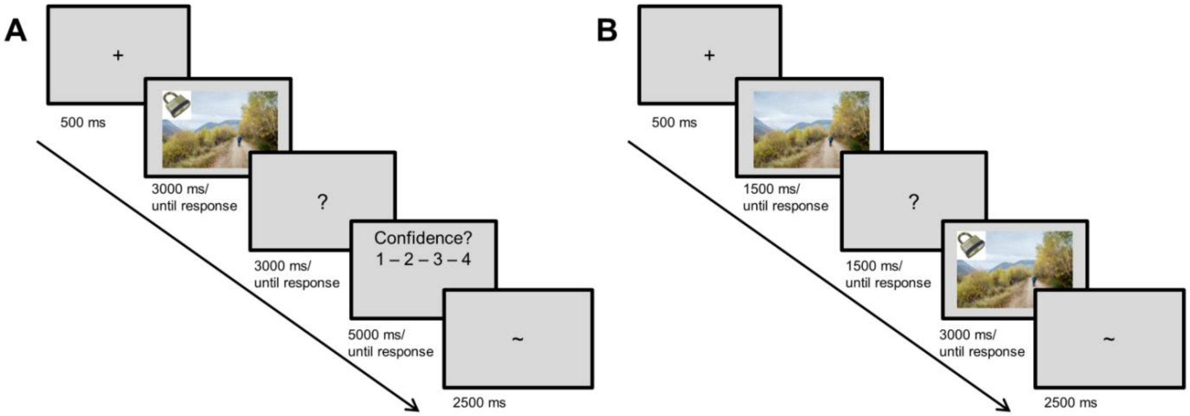

Figure III 8. Illustration of retrieval phases of the **(A)** main and **(B)** follow-up experiment, which was held constant across all times of measurement (pre and posttest).

The encoding phase was held identical to the main experiment, but we modified the retrieval phase to obtain an unbiased measure of recognition performance for background scenes. To achieve this, participants were asked to perform an old-new discrimination task with isolated background scenes of old, new and recombined pairs (see Figure III 8). Whenever subjects indicated that scenes had been encountered during the initial learning phase (old) the corresponding object (either old, new or recombined) was presented superimposed with the instruction to indicate whether this scene was previously presented in conjunction with the object (yes) or alongside a different object (no). By means of this sequential testing procedure we were able to analyze item memory performance of old background scenes derived of subsequently presented old and recombined pairs [$PR_I = p(\text{Old}|\text{Old+Rec}) - p(\text{Old}|\text{New})$] while still retaining a measure of associative recognition based on the rate of correctly recognized intact object-scene-associations adjusted by the rate of recombined object-scene-associations erroneously recognized as being intact [$PR_A = p(\text{Old}|\text{Old}) - p(\text{Old}|\text{Rec})$].

With reference to the attentional narrowing account, we predicted that item memory should be enhanced for emotional scenes but remain to be impaired for object-scene-associations entailing an emotional scene.

Participants

Twenty-three participants[31] were tested in this follow-up study of which two subjects were excluded due to substantially low pretest item memory performance for emotional scenes (1.5 × interquartile range below the lower quartile of the group; *N*= 2). Hence, the sample which was subjected to the final analysis comprised of 21 participants (3 male; M_{age}= 20.57, *SD*= 2.20).

Procedure

The study procedure was identical to the main experiment except for the exclusion of the delayed memory assessment (delayed posttest), thus resulting in an identical trial structure and number during encoding. The consequent pretest phase was modified to include the assessment of (isolated) scene as well as object-scene recognition (see Figure III 8), while again retaining the same amount of trials. Following task completion, participants left the laboratory and returned after 2.5 hours, recreating the retention interval of the main study. Upon returning, they performed the posttest procedure, underwent debriefing and were paid for their study participation (20 €).

Results

Item and associative PRs were analyzed analogous to the main experiment (see Figure III 9). Analysis of item memory performance including the factors Time (pre/ post) and Emotion (neutral/ emotional) yielded significant main effects of Time ($F_{1,20}$= 39.54, *p*< .001) and Emotion ($F_{1,20}$= 4.54, *p*= .046), but no significant interaction. As previously found, item memory decreased over time, however in contrast to our former findings, singularly presented emotional contexts elicited higher retention rates (*M*= .77, *SD*= .11) as compared to neutral contexts (*M*= .72, *SD*= .13), which was evident across both times of measurement. Corresponding analysis of associative memory performance resulted in main effects of Time ($F_{1,20}$= 40.83, *p*< .001) and Emotion ($F_{1,20}$= 15.32, *p*= .001) with no significant interaction emerging. While associative memory performance similarly

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[31] For practical reasons study eligibility for the follow-up experiment was assessed at study completion, thus five participants were excluded from any further analysis due to antidepressant or beta-adrenergic blocking medication (*N*= 3) and previous drug use (*N*= 1). One additional participant stated to be no native German speaker (*N*= 1).

decreased over time, object-scene pairs entailing an emotional scene were recognized less accurately (*M*= .44, *SD*= .18) as compared to neutral pairs (*M*= .59, *SD*= .21).

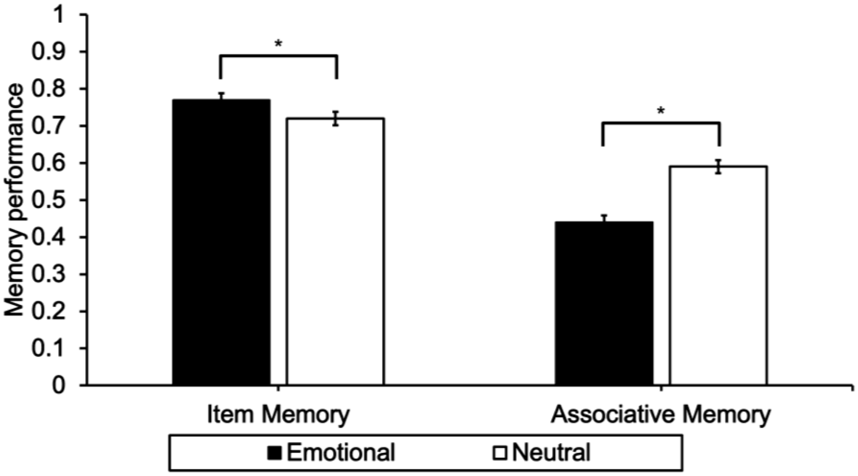

Figure III 9. Means of item and associative memory performance for emotional and neutral items collapsed across pre- and posttest in the follow-up study. *Note:* Significant effects of time are not illustrated for reasons of comprehensibility. * indicates the significant main effects of emotion ($p< .05$). Error bars represent standard error of the mean.

Discussion

The results of this follow-up experiment provide strong support to the view that negative and highly arousing scenes induced attentional narrowing at encoding (see Kensinger, Garoff-Eaton, & Schacter, 2007a; Kensinger, Gutchess, & Schacter, 2007; Kensinger, Piguet, Krendl, & Corkin, 2005 for similar results). While this may result in a superior retention of the affective component itself (item memory), it comes at the cost of an accurate representation of the component and its surrounding constituents (associative memory) as the successful creation of object–scene associations is hindered. In line with this hypothesis, we were able to replicate the detrimental effect of emotion on associative recognition in our follow-up experiment, which was evident across both times of measurement. However, with regard to memory of background scenes we did not find a similar interaction of time and emotion like in the main experiment, but rather a main effect of emotion across pre- and posttest, albeit using slightly different measures of item recognition in both studies. This may reflect that the characteristic time course of delayed forgetting for emotional stimuli was less pronounced in this high interference condition (participants left the laboratory between pre- and posttest) as compared to the low inference conditions evident in both control (watching a low inferring movie in a standardized setting) and sleep groups of our main experiment. This enhanced level of interjacent interference may have diverted consolidation processes during the retention interval (e.g. related to synaptic consolidation; see Bergado et al., 2011) resulting in a less pronounced time course of these critical effects and a more generic benefit of retrieving emotional scenes emerging over averaged performance rates of pre- and posttest.

4.3. General discussion

Integrating the results of the follow-up study with the findings of our main experiment discloses a diminished forgetting of emotional as opposed to neutral stimuli across (low interfering) wakefulness and not exclusively over sleep. While this effect is not in line with prior accounts of sleep-related enhancements of emotional item memory (Groch et al., 2013; Groch et al., 2015; Nishida et al., 2009), it is broadly consistent with the emotional binding model (Yonelinas & Ritchey, 2015), which predicts a permissive effect of time on the retention of emotional material due to amygdala-dependent storage. However, our results also exceed this account in suggesting that intervening processes of retroactive interference may impede a clear time-dependent course of delayed forgetting for emotional material. This may suggest that a particular stage of consolidation (perhaps related to synaptic consolidation; see Bergado et al. 2011) that occurs over wakefulness is critically modulated by emotionality.

4.4. Effects of sleep

Beyond the absence of differential effects on emotional item recognition, sleep did not exhibit any beneficial effect on item memory in general but resulted in comparable performance to the wake group. However, in line with our predictions, we did find a significant effect of sleep on associative memory, resulting in an enhanced retention of object-scene associations in the nap group as compared to the wake group at posttest (p= .021). This pattern of results lends strong support to the notion that the framework of sleep-dependent system consolidation applies specifically to the consolidation of associative aspects of previously acquired memory representations (Diekelmann & Born, 2010) as has also been found by former studies (Studte et al., 2015; van der Helm et al., 2011). Supportive evidence that our task required hippocampal binding processes during encoding comes from an fMRI study by Luck et al. (2014). Employing a highly similar task, the authors found that successfully retained - as opposed to subsequently forgotten - object-scene-pairs elicited an enhancement of hippocampal activation during encoding across different valence categories. These results confirm the relevance of hippocampal processing during successful encoding of relations between objects and scenes in this particular type of paired associate task.

4.5. Neurophysiological correlates

The observed sleep-related enhancement in associative performance was evident for both negative and neutral scenes. However, as stated earlier, the critical test in establishing a dissociation with regard to REM sleep and SWS-dependent processes in the current design lies in linking these enhancements in emotional and neutral associative memory performance to specific oscillatory features of both sleep stages (REM sleep theta dominance and NREM spindle density respectively). Therefore, we examined spindle density and its association to pre-, post- and delayed posttest performance. Results revealed significant and positive correlations between pre sleep associative memory performance of both stimulus categories and subsequent spindle density. Such a pattern of results has been observed in previous studies assessing pre sleep performance rates (Studte et al., 2015; Studte et al., 2017). The association of spindle density to memory performance prior to the onset of any putative effects of sleep-related consolidation is assumed to reflect a distinct “trait-like” characteristic of spindle density. Current accounts propose that spindle density can be regarded as a measure of cortical-subcortical network efficiency and is thus related to memory processes and general cognitive abilities alike (Fogel & Smith, 2011; Schabus et al., 2006). However, this general elevation of spindle density in highly gifted individuals has been shown to be dissociable from spindle increases related to sleep-dependent consolidation (Schabus et al., 2008) and thus does not impede the interpretation of post sleep spindle correlations.

In our main analysis, we found a significant and selective association between neutral associative memory performance and spindle density (*r*= .50, *p*= .014). While a general association was observed between associative memory performance prior to sleeping and spindle density, a selective and thus distinguishable variance in spindle density was shared with post sleep associative memory performance. Critically, the selective correlation between neutral associative recognition and spindle density suggests that SWS-dependent consolidation mechanisms (Diekelmann & Born, 2010) were only initiated for neutral object-scene pairs but not for emotional stimuli. This selectivity in SWS-dependent consolidation is in line with former studies (Alger & Payne, 2016; Groch et al., 2015; Sopp et al., 2016) which demonstrated selective (SW-)sleep related retention benefits for neutral associative memory in task designs with varying stimulus valence. However, none of these studies were able to directly link this selective retention benefit for neutral associations to NREM sleep-specific oscillatory features. As such, the present study makes a genuine contribution by demonstrating a selective correlation between spindle density and neutral associative memory performance in an emotional memory paradigm[32]. Moreover, the current pattern of results revealed that emotional associations were not merely bypassed by SWS-related tagging mechanisms, but also consolidated by means of an entirely independent mechanism. Consequently, emotional associations were preferentially retained in the nap group in the clear absence of any correlation between this behavioral benefit and spindle density. Based on the considerations outlined in the introduction, this finding may signify that the arousal elicited by emotional object-scene pairs attenuated tagging mechanisms to the extent that these associations were not reactivated and reprocessed during subsequent SWS, but may have conversely entered a different processing route of preferential consolidation. This conforms to the dissociation over both night halves, which we observed in our former study (Sopp et al., 2016) and supports the conception that neutral material preferentially captures learning intention (and related tagging) in mixed designs. On the whole, it is important to point out that the highly selective correlational pattern of spindle density was not found with regard to item memory performance. Firstly, this parallels our behavioral analysis in which no sleep-related enhancement of item recognition emerged. Moreover, this is in line with the active system consolidation account (Diekelmann & Born, 2010) in demonstrating a selective association between spindle density and associative memory performance.

While we accurately predicted that neutral associative memory performance would be maintained by SWS-dependent processing (as reflected by sleep spindle density), we assumed to find a complementary, REM-sleep-dependent process (related to right-frontal

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[32] See Göder et al. (2015) for a similar finding with regard to item memory without a corresponding effect on behavioral performance.

theta dominance) to support emotional associative memory over time. Contrary to this hypothesis, we found no such correlation between the retention benefit in emotional associative memory performance and right-frontal theta dominance (*p*> .63). This absence of a clear correlation is at odds with a recent finding of our own working group (Sopp et al., 2016) demonstrating a significant association between the superior retention of emotional source memory performance observed over the second night half and right-frontal theta dominance (see also Nishida et al. 2009 for similar findings regarding emotional item memory). This discrepancy with regard to previous findings may be related to methodological aspects. Specifically, the distribution of sleep stages in the early morning nap (see above) may have limited the emergence of sufficient variance in REM sleep and, consequently, theta dominance to yield a linear association to behavioral performance. This is a common constraint in reliably detecting microstructural effects in sleep studies (particularly nap paradigms) as some participants do not enter specific sleep stages or only express insufficient epochs to reliably derive measures of microstructural sleep architecture. Employing short sleep intervals during the daytime may thus result in a low signal-to-noise-ratio selectively with regard to measures related to REM sleep physiology (as this is expressed at the end of each sleep cycle and predominantly in the second night half). In the current study, participants spent an average of 18.33 minutes (*SD*= 15.13) in REM sleep, which diverges from the stable occurrence of REM sleep during nocturnal sleep. In our former study REM sleep comprised on average 33.44 % of TST (*SD*= 4.15) in the late night sleep group (Sopp et al., 2016), thus resulting in eligibility of the complete sample for subsequent correlational analysis.

As a considerable number of participants had to be excluded due to insufficient REM sleep epochs in the current study, corresponding subanalysis were based on a restricted subsample (*N*= 17). This limited sample size may have resulted in distortions of correlative patterns between emotional memory performance and right-frontal theta lateralization due to disproportionate influences of unrelated between-subject variance. In-depth analysis of the current data support this interpretation: When post sleep emotional associative memory performance was z-normalized within list conditions[33], to account for variance driven by differences between individual items, and when additionally controlling for interindividual

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[33] This refers to the counterbalancing of individual item assignment to pre, post and delayed posttest conditions and new, old and recombined test lists which resulted in nine list conditions.

variance in fluid intelligence (by introducing the Viennese Matrices test as a covariate) a positive association between right-frontal theta dominance and post sleep emotional associative memory was obtained ($r = .42$, $p < .05$ one-sided). For post sleep neutral associative memory this effect trended in the same direction but was not as pronounced ($r = .37$, $p > .05$ one–sided). We refrained from interpreting these correlations in terms of our main study results due to the post-hoc-driven approach in data analysis. However, in this context they indicate that unrelated between-subject variance may have prevented a clear “backtracing” of the sleep-related retention benefit in emotional associative memory to REM sleep theta dominance.

In summary, post-hoc correlation analyses on z-normalized emotional memory performance suggest very tentatively that frontal theta lateralization may constitute the neuronal correlate underlying sleep-related emotional associative memory consolidation in the current nap condition characterized by a low overall proportion of REM sleep. While this pattern of results was not sufficiently pronounced to draw any strong conclusions, it certainly does not dismiss the behavioral effect we found regarding post sleep emotional associative recognition and its relation to sleep-dependent consolidation. As such, we demonstrated a significant sleep-related retention benefit for emotional associative memory, which was markedly unrelated to SWS-related processing mechanisms (as reflected by sleep spindle density). Moreover, sleep-dependent processing mechanisms were initiated for emotional associations although these did not exhibit preferential retention in general (for similar results see Sopp et al. 2016). The beneficial effect of sleep on emotional associative memory is thus dissociable from general effects of emotionality on memory processing, but more so, highly distinct from SWS-dependent processes which support neutral associative memory retention. Corroborating evidence comes from the highly circumscribed correlational pattern between spindle density and associative memory performance, which neither generalized consistently to item memory nor to emotional associative memory performance at (delayed) posttest. However, the process by which this retention benefit was effected as well as its associations to REM sleep physiology require further exploration in future studies.

In conclusion, the main objective of generalizing our former findings (Sopp et al., 2016) was partially attained in the present experiment. We were thus able to confirm that sleep-related consolidation equally benefits emotional associations, which require active integration at encoding. Therefore, it can be assumed that the underlying mechanism in question is not restricted to the processing of perceptually-bound source features (such as item location). A generalization of previous effects to a shorter sleep interval in the daytime was not fully accomplished, albeit for methodological reasons rather than clear theoretical boundary conditions of REM-sleep-related effects.

4.6. Effects on delayed performance

Beyond immediate effects of sleep-related consolidation, we were also interested to explore how potential retention benefits are modulated by a subsequent night of sleep, or in other words, whether differences resulting from initial sleep-related consolidation are sustained across time. In line with the absence of immediate consolidation benefits in item recognition (at posttest), sleep-related consolidation did not yield any effects on delayed item memory performance. Corresponding analysis on associative memory performance suggested that the immediate effects of sleep on neutral and emotional associative memory were not maintained over time, as performance rates at delayed posttest did not differ significantly between the nap and wake group. However, in interpreting this effect it is critical to consider the correlation between the initial neurophysiological signature of the nap opportunity (spindle density) and delayed posttest performance. By demonstrating that this association is not only maintained across time but that it also retains its selectivity with regard to stimulus valence, we provide evidence that effects of initial sleep-related system consolidation produce long-lasting changes that reach beyond highly controlled laboratory conditions. In this context, the pattern of behavioral results may suggest that a delayed consolidation took effect in between post- and delayed posttest sessions in the control group, which emphasizes the role of the hippocampus as a temporary buffer of episodic memory (Bontempi, Laurent-Demir, Destrade, & Jaffard, 1999; Holscher, 2003; Zola-Morgan & Squire, 1990). While this temporary maintenance in reliance on the hippocampus may span moderate periods of time, as suggested by delayed consolidation in the current wake control group, its exact time course is currently unexplored. Consequently, future studies should further investigate at which delay sleep-dependent system consolidation critically supports long-term retention of a particular episode. From a different perspective, the finding that the selectivity of correlations between associative memory and spindle density in relation to stimulus valence persisted across time substantiates our interpretation of a selective SWS-related reprocessing of neutral material: Not only was neutral associative memory performance after sleeping selectively related to spindle density, but this selectivity was also evident after another night of sleep.

Similarly to posttest performance, we were not able to demonstrate a relationship between right-frontal theta dominance and emotional associative memory at delayed posttest. However, we found a significant negative correlation between relative theta power (F4) and false alarm rates to recombined item pairs of both stimulus types. This is consistent with the active system consolidation account, which implies that processes of REM-sleep-dependent consolidation enable local processes of synaptic consolidation following previous stages of SWS-related system consolidation (Diekelmann & Born, 2010). Moreover, theoretical frameworks of theta activity during wakeful memory encoding suggest a role in the sharpening of memory traces via phase-dependent expressions of LTD resulting in the selective strengthening of target memories (Hsieh & Ranganath, 2014). These encoding-related mechanisms may be similarly relevant to processing modes during REM-sleep-related consolidation. Intriguingly, the correlation between false alarms in associative recognition and relative theta power was not evident immediately after napping (posttest correlation: r= -.35, p= .163). Certain effects of sleep-related consolidation may thus emerge with a delayed time course, when other memory processes formerly supporting this specific aspect of episodic memory fail and can no longer compensate for deficiencies of non-accomplished system consolidation.

5. Main conclusion

In summary, the current findings demonstrate a sleep-related consolidation benefit for emotional and neutral associations emerging after an early morning nap of only 120 minutes. Furthermore, correlations between memory performance and oscillatory features suggest a selective facilitation of neutral associative memory related to SWS-dependent consolidation mechanisms that is retained over time (from post- to delayed posttest). Memory for emotional associations, on the other hand, appears to be supported by a distinct sleep-related consolidation process. Taken together, these findings suggest, that arousal at encoding disrupts the initiation of system consolidation during subsequent SWS. However, this disruption seems to be counteracted by a distinct process, which independently of

SWS-dependent consolidation, results in an equally successful retention of emotional stimuli over sleep. The underpinnings of this process remain to be fully disclosed by future research.

IV General discussion

1. Summary

The present thesis aimed to disentangle the contributions of SWS and REM sleep make to the consolidation of emotional episodic memory. Current evidence (Genzel et al., 2015; Hutchison & Rathore, 2015; Nishida et al., 2009; Prehn-Kristensen et al., 2013) suggests an enhancement of emotional memory across periods of sleep, which is effectuated by a mechanism that is highly distinct from the framework of active system consolidation (Diekelmann & Born, 2010; Rasch & Born, 2013). This mechanism seems to be closely related to REM sleep and its neurophysiological features, which aligns with the insights generated by animal studies of fine-grained oscillatory processes in the limbic system (see section I 4.2.) that emerge within this state (Hutchison & Rathore, 2015). However, a lack of investigations has been devoted to a clear characterization of these REM-sleep-related effects on the episodic memory system. In particular, it is not yet fully understood how these relate to item recognition as opposed to associative memory retrieval. Moreover, potential interactions or additive effects of REM-sleep-related processing, and SWS-dependent system consolidation specifically with regard to emotional associative memory retention, have not been examined. These theoretical gaps in the current literature motivated the present thesis to investigate how different sleep-related manipulations relate to the retention of item and associative memory for emotional and neutral stimuli. Furthermore, behavioral enhancements were subjected to in-depth analysis in order to retrace these to specific oscillatory features of SWS and REM sleep respectively.

In experiment 1 emotional memory consolidation was examined by means of a split-night manipulation, which contrasted the effects of otherwise identical intervals of early night (SWS-rich) and late night (REM-sleep-rich) sleep. Memory was ascertained in a source memory paradigm, which probed location memory of emotional and neutral images in combination with a remember-know-new procedure. This procedure was employed to additionally distinguish the contributions of subjective familiarity and recollection to item recognition. In a follow-up study (experiment 1a), task performance was assessed across an interval of wakefulness during the daytime to disentangle unique effects of sleep from generic effects of the passage of time. Experiment 2 aimed to test whether the effects that emerged in the former study generalize to a different study design, which entailed an early morning nap opportunity of 120 minutes rather than extended periods of nocturnal sleep, as well as a different operationalization of contextual memory. To examine whether REM-sleep-related consolidation mechanisms equally exert their influence on context features which require active integration at the encoding stage, a paired associate task was designed entailing either an emotional or a neutral scene. Memory performance was additionally reassessed after a consecutive night of sleep outside of the laboratory to address long-term consequences of sleep-related consolidation, which directly succeeded encoding. In a slightly modified follow-up experiment (2a) the unexpectedly detrimental main effect of emotion on associative recognition was expanded on, by probing item recognition in a sequential retrieval task. This experiment again included a retention interval of wakefulness under similar conditions as in experiment 1a.

In the succeeding sections the main results of experiments 1 (1.1.) and 2 (1.2.) will be reiterated in order to provide an integration (1.3.), which highlights the aspects in which the results of both studies are consistent or deviate from one another. Thereafter, it will be discussed how these findings contribute to a refined understanding of consolidation processes over wakefulness (2.1.), over SWS (2.2.) and, finally, over REM sleep (2.3.), with regard to emotional events. In addition, the limitations of the present empirical findings will be pointed out and perspectives for future research will be highlighted (3.). In a final conclusion (4.) of all these considerations, a preliminary model encompassing two routes, which support the joint retention of emotional and neutral associations across sleep, will be proposed.

1.1. Experiment 1

In experiment 1 item recognition was found to be retained differentially over time but equally across both night halves. While recognition rates were similar for both emotional and neutral images after initial encoding, a significant difference was evident at posttest reflecting an enhanced retention of emotional as opposed to neutral images. Separate analysis of “Remember” and “Know” responses revealed that this time-dependent advantage was attributable to an enhancement of accurate familiarity-driven responses to emotional images, whereas recollection-based retrieval was generally enhanced for emotional images regardless of time. Examining item recognition over a period of wakefulness (experiment 1a), did not yield a similar retention benefit across time as observed in the main study, but only resulted in a main effect of emotion across both times of measurement.

With regard to source memory a significant interaction of time, emotion and group emerged, signifying differential retention rates of emotional and neutral stimuli across early (SWS-rich) and late (REM-sleep-rich) night sleep. While emotional source memory was selectively preserved across the second night half, an isolated retention benefit for neutral location memory was evident across the first night half. Importantly, this pattern of results was entirely absent across wakeful consolidation (experiment 1a) resulting in a marked decline of both neutral and emotional source recognition from pre- to posttest. This excludes the possibility of time and sleep being confounded with regard to the main study results. Intriguingly, the behavioral dissociation observed across early and late night sleep was partially substantiated on a neurophysiological level with regard to oscillatory features of SWS and REM sleep respectively. Accordingly, post sleep emotional location memory in the late sleep group was found to be selectively correlated to right-frontal theta laterality ($\mu V^2/Hz$) during REM sleep. Spindle power ($\mu V^2/Hz$) during SWS, on the other hand, was found to be selectively correlated to post sleep neutral item memory performance in early (SWS-rich) sleep subject. Taken together, these results originally suggest a dissociation of contextual memory consolidation of emotional and neutral events with regard to REM-sleep- and SWS-dependent processes respectively. While this selectivity of SWS-related consolidation with regard to neutral associations in intermixed designs is beginning to emerge in the few studies addressing this topic (Alger & Payne, 2016; Groch et al., 2015), the enhancing effect of REM-sleep-related consolidation on emotional source memory constitutes an entirely novel finding, which extends previous conceptions on the scope of REM-sleep-related processing mechanisms.

1.2. Experiment 2

In experiment 2, which aimed to test the generalizability of the former findings, item memory analysis revealed a marginally significant interaction of time and emotionality across both wake and nap groups. This effect signified a preferential retention of emotional item memory as compared to neutral item recognition, albeit only from pre- to posttest and not across delayed testing. Employing the same encoding procedure but probing scene-recognition in a separate procedure in experiment 2a yielded a main effect of emotion. Emotional item memory was superior to neutral recognition memory, however without the time-dependent course that arose in the main experiment.

In the analysis of associative memory performance a main effect of emotion was evident, which unexpectedly reflected an attenuation of associative recognition performance for emotional pairs that also stably reoccurred in the follow-up experiment (2a). In addition, an interaction of time and group emerged from pre- to posttest, which signified a superior retention of both emotional and neutral object-scene associations across sleep compared to low-interfering wakefulness. As the current nap design, which contrasted wakefulness with sleep, did not permit a behavioral dissociation analogous to experiment 1, subsequent analysis of oscillatory features were aimed to disclose the contributions of SWS and REM sleep to this behavioral performance benefit for emotional and neutral associations. In line with the predictions, a selective pattern of correlations between neutral associative memory and sleep spindle density (NREM) emerged. This association also persisted over time, as reflected by a significant and selective correlation to neutral associative memory at delayed posttest. However, the corresponding correlation between post sleep emotional associative recognition and right-frontal theta laterality (REM sleep) failed to reach significance. In conclusion, a partial dissociation with regard to the preferential retention of emotional and neutral associations over sleep was established, albeit leaving ambiguities with regard to the exact contribution of REM-related consolidation processes.

1.3. Integration of findings

In both studies emotional item memory was preferentially retained across time, irrespective of sleep-related manipulations or, in fact, any sleep occurring in the critical consolidation phase at all (see experiment 2). Interestingly, this effect was not time-dependent but only emerged over averaged performance rates of pre- and posttest in follow-up studies 1a and 2a[34]. This may reflect differential effects of interference, as participants of both follow-up

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[34] Experiment 2a was no absolute replication of the main experiments task design and may consequently involve additional processes as the one proposed here.

studies left the laboratory in the critical consolidation phase (see section IV 2.1. for a discussion on this).

Table VI 1. Systematic integration of both experiments as to the effects of different consolidation processes.

Test	Process	Experiment 1	Experiment 2	Effect
Item Memory	Time (high interference)	Follow-up experiment 1a	Follow-up experiment 2a	General advantage in **item memory** for **emotional stimuli**
	Time (low interference)	Collapsed across early + late sleep groups	Collapsed across nap+ wake groups	Time-dependent advantage in **item memory** for **emotional stimuli**
Associative Memory	Predominance of SWS	Early sleep group	-	Selective consolidation of **neutral context memory**
	Predominance of REM sleep	Late sleep group	-	Selective consolidation of **emotional context memory**
	Conjoint occurrence of SWS+ REM sleep	-	Nap group	Selective consolidation of **emotional and neutral associations**

Note: The table integrates putative consolidation processes related to time (under low and high interference conditions), REM sleep and SWS as evident in different conditions of experiment 1 and 2 with regard to the retained effects on memory performance. This is summarized for tests of item and associative memory performance.

While both studies are aligned with regard to the effects of emotion on item memory, their results diverge with regard to associative memory. Whereas emotional and neutral source memory performance generally did not differ in experiment 1 (no significant main effect of emotion), emotional associations were retrieved less successfully as compared to neutral associations in experiment 2. This may likely be the result of dissimilar effects of attentional narrowing elicited within both memory paradigms (see section IV 2.1.). Regarding the differential effects of sleep on item and associative memory, both studies converge in demonstrating a significant impact of sleep on associative memory but a clear lack of any behavioral enhancement of item recognition. Moreover, they are compatible with respect to the differential contributions of REM sleep and SWS. While a predominance of SWS (in the first night half) resulted in a selective facilitation of neutral memory and a predominance of REM sleep (in the second night half) gave rise to an isolated retention benefit of emotional source memory in experiment 1, the conjoint occurrence of SWS and REM sleep in the early morning nap paradigm of experiment 2 resulted in a complementary facilitation of emotional and neutral associative recognition. Thus, on a behavioral level, the results of both studies are broadly consistent and can be integrated as to time- and sleep-dependent modulations of memory performance (see Table IV 1).

A conjoint interpretation of the oscillatory correlates of post sleep item and associative memory performance across both experiments is less easily accomplished. While post sleep emotional source memory was selectively related to REM sleep right-frontal theta dominance in the late sleep condition of experiment 1, this association was not retained in the nap condition of experiment 2. Conversely, while neutral memory performance was linkable to spindle power during SWS only with regard to item memory in experiment 1, a selective correlation between spindle density and neutral associative recognition emerged in experiment 2. These discrepancies may be partially resolved by methodological considerations. With regard to REM sleep theta laterality it is important to point out that while REM sleep duration in the late sleep group of experiment 1 encompassed 33.44% of TST (*SD*= 4.15) on average, this was considerably lower in the early morning nap of experiment 2 (*M*= 17.78%, *SD*= 13.77). The difference is even more pronounced with respect to absolute REM sleep duration which was on average threefold higher in the critical condition of experiment 1 (*M*= 62.49 min, *SD*= 8.51) as compared to experiment 2 (*M*= 18.33 min, *SD*= 15.13). Of particular note, the standard deviation of the mean in experiment 2 reflects a very high variability in REM sleep duration between participants, which is not uncommon in daytime sleep opportunities. Due to circadian modulations of the sleep cycle the sequential occurrence of sleep stages is less reliably induced in daytime naps as compared to conditions of nocturnal sleep (Cajochen, Kräuchi, & Wirz-Justice, 2003). As discussed in section III 4.5 this less stable induction of REM sleep severely restricted the eligible subsample of participants for REM-sleep-specific analysis. This may conversely have resulted in disproportionate influences of unrelated between-subject variance in correlational analysis that potentially masked a linear relationship between right-frontal theta dominance and memory performance. This was further supported by the results of post-hoc analysis. When accounting for certain sources of unrelated between-subject variance (effects of counterbalancing and general cognitive abilities) a positive association between REM sleep theta laterality and post sleep emotional associative memory was obtained that was not evident for neutral object-scene-pairs. Nonetheless, this constitutes a highly tentative finding of a post-hoc driven analysis approach, thus not permitting a stand-alone interpretation.

The inconsistent pattern of correlations between spindle power (SWS) and item but not source memory performance in experiment 1 (see above) may be ascribed to a high degree of shared variance between item and source memory measures in this particular type of retrieval task. As previously mentioned (see chapter I 4.2.), it is difficult to account for the inherent constraint of source memory performance within task designs that probe item and source memory sequentially. Despite all efforts to control for this overlap in variance, by means of adjusting source memory performance in a relative index of source recognition and computing partial correlations in succeeding analysis, it may have obscured a clear pattern of correlation to spindle power. In this regard, it must also be noted that spindle power constitutes a menially discriminative measure of spindle activity as it does not ascertain discrete spindle events of a specific duration. Moreover, as spectral power in the entire spindle frequency range is employed to reflect spindle-related activity, this likely includes unrelated voltage fluctuations, which can result in a low signal-to-noise-ratio. However, most spindle detection algorithms, by which discrete spindle counts can be obtained, rely on epochs of N2 sleep (and not isolated SWS) in determining individual spindle thresholds. This would have severely compromised a clear-cut comparison in experiment 1, as the early sleep group was characterized by an isolated enhancement of SWS duration, and not NREM duration in general, conforming to the rationale of the split-night-design. Consequently, analyses that aimed to trace the origin of behavioral retention benefits from early night sleep were focused exclusively on SWS-dependent processes and thus on spindle power during SWS.

Despite certain inconsistencies, the results of both studies are aligned on an overarching level in demonstrating that NREM-sleep-related neurophysiological measures were exclusively related to neutral memory performance, whereas REM sleep theta laterality was selectively related to emotional memory retention. The contributions that this dissociation makes with regard to theoretical models of sleep-related consolidation will be highlighted in the succeeding chapter along with resulting inferences on the preferential consolidation of emotional events across wakefulness (see IV 2.1.).

2. Contributions of different processes to the consolidation of emotional events

2.1. Contributions of wakeful consolidation to emotional item memory

Prior to addressing time-dependent effects on emotional memory performance it is important to point out the (ir-)regularities between both studies observed with regard to baseline performance preceding the retention interval. In general, item memory was not reliably enhanced for emotional stimuli after initial encoding, but exhibited its deferential retention in a time-dependent course (or averaged across successive times of measurement; see experiments 1a and 2a). The only clear benefit evident immediately after encoding was found with respect to the accuracy of remember-responses in experiment 1, which conforms to the well-documented effect of enhanced subjective recollection for emotional events (Yonelinas & Ritchey, 2015). However, there is still considerable debate as to whether this effect reflects recollection in a veridical sense (see section I 2.3), which is also mirrored in the current results revealing no parallel effect on source memory performance[35]. As such, accurate retrieval of the initial location at which images were presented (experiment 1) was unaffected by stimulus valence, denoting the absence of any immediate enhancement by putative effects of facilitated intra-item binding (see section I 2.2).

These effects were similarly absent in experiment 2 but additionally counteracted by a detrimental effect of attentional narrowing on baseline performance for emotional associations. This pattern of results emphasizes that the spatial relations between the arousing stimulus and its contextual feature crucially determine successful context encoding and retention. Whereas the location feature of experiment 1 was strictly intrinsic to the stimulus in the sense that it was not possible to process the image independently of

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[35] This divergence can potentially be the result of non-criterial recollection (Yonelinas et al., 2010). However, the overall pattern of results does not conform to this interpretation.

its location, this necessity was not established in the task procedure of experiment 2. Thus, attentional narrowing did not produce any effects in experiment 1 as the critical feature was encapsulated by the stimulus. However, attentional effects likely compromised the processing of peripherally presented objects in experiment 2 (see experiment 2a for supportive evidence). Contrary to this outcome, the manipulation of experiment 2 was designed with the intention of effectively inducing an analogous intrinsic processing of the object feature by providing integrative study instructions in a perceptually-linked presentation array of both constituents. However, this was apparently not sufficient to recreate the processing route that was established in a stimulus-driven manner in experiment 1, which emphasizes the intricate interplay of arousal-driven effects and specific sub-processes leading up to successful encoding. This is generally in line with the literature that demonstrates rather inconsistent effects of enhancements and impairments of contextual memory performance elicited by arousal, but most robustly the absence of detrimental effects for location features (Chiu et al., 2013; Mather, 2007). Future studies should aim to explore how top-down manipulations can recreate this stimulus-driven intrinsic processing mechanism by which contextual features are “spared” from the detrimental effects of attentional narrowing, in order to further a better understanding of the underlying mechanisms. From a very broad perspective, it is evident that item location constitutes a feature that is highly integral to the episodic memory systems and anatomically represented in a very refined way (Burgess, Maguire, & O'Keefe, 2002; Wheeler, Stuss, & Tulving, 1997). As such, spatial location may be processed very differently in the context of arousal compared to “artificial” feature conjunctions. Such “artificially” formed associations between experimental stimuli (see experiment 2) may not gain access to pre-dispositional processing routes, which are laid out within the episodic memory system for integral event features (e.g. time or location).

With regard to the time-dependent course of emotional and neutral associative memory retention, no effects emerged over wakefulness in either experiment, thus reflecting that emotional item-context associations were not preferentially consolidated over time. Prior accounts (Murray & Kensinger, 2013) have insinuated that intra-item binding processes may not consistently have been found to benefit from emotion in the literature as effects only emerge over time, when consolidation processes set in. The current experiments which examined consolidation effects under conditions of integrative processing do not provide support to this notion. However, as intra- and inter-item binding was not systematically varied in either study this precludes any strong inferences in this regard.

On the other hand, it was consistently found across both experiments, that emotional item memory was selectively retained across time but independent of sleep. As different frameworks have been brought forward to account for this delayed forgetting effect (Bergado et al., 2011; Yonelinas & Ritchey, 2015) it is important to take the results of experiments 1a and 2a into consideration in interpreting these findings. As both follow-up experiments did not yield a time-dependent recognition benefit for emotional images this reflects that the level of interference between pre- and posttest was an important factor in determining the time-dependent course of memory retention. This, however, contrasts with the assumptions of the emotional binding account (Yonelinas & Ritchey, 2015) which attributes the delayed forgetting of emotional material to an effect of reduced interference for this class of stimuli, hence unfolding permissively over time. This is clearly at odds with the dampened time course observed in experiments 1a and 2a, wherein participants left the laboratory in the critical retention phase and were thus subjected to an enhanced level of interference, which should have resulted in an even higher time-dependent advantage for emotional stimuli within this framework (Yonelinas and Ritchey, 2015). While a main effect of emotion was still evident in both of these studies, this likely reflects the residuum of the time-dependent advantage that only remained detectable across averaged performance rates. Consequently, the current pattern of results does not support a permissive effect of time on emotional memory retention but rather suggests the involvement of active consolidation processes in the delayed forgetting of emotional material, as these processes, in turn, have been found to be susceptible to interference. In light of the absence of any time-dependent modulations of associative/source memory in both experiments, it may be further assumed that the consolidation processes in question that facilitated emotional item memory retention over generic wakefulness did not relate to interactions of different memory systems. The involvement of system consolidation processes should have conceivably resulted in a similar or even more marked benefit for associative memory of emotional images over time. Complementing this line of interpretation, experiment 1 revealed that the delayed forgetting of emotional material across wakefulness was ascribable to an enhancement of subjective familiarity for emotional items across time, thus not entailing the recapitulation of specific event features during successful recognition. As such, it may be tentatively inferred that the interaction effect on item memory performance in experiment 1 and 2 was likely related to processes of synaptic consolidation as implied in the emotional tagging account (Bergado et al., 2011). This account assumes that memory traces initially remain in a labile state after encoding and are required to undergo consolidation to be retained across time. On a neurophysiological level this stage of consolidation is assumed to be reflected by the transition from early-phase to late-phase LTP, which must ensue within the first few hours after encoding in order to result in durable changes in synaptic efficacy within neural circuits encoding a newly acquired representation. As discussed in section I 2.2., neurohormonal changes elicited during the encoding of arousing material are assumed to interact with these processes resulting in a greater likelihood of successful synaptic consolidation of emotional stimuli.

While a comprehensive discussion of these processes exceeds the scope of the present thesis, it is important to point out that the shift in neurotransmitter concentrations that elicits these processes is markedly dissimilar to the neurohormonal “environment” of REM sleep (Walker & van der Helm, 2009). During wakeful encoding, adrenergic signaling is assumed to play a crucial role in initiating subsequent preferential consolidation of emotional material, as blockage of secretion following encoding has been found to inhibit successful retention (see McGaugh 2000 for a review). On the other hand, during REM sleep norepinephrine release from the locus coeruleus is inhibited, which has been taken to suggest that the mechanism of REM-sleep-dependent consolidation must operate in an entirely different way as compared to the consolidation process that favors the retention of emotional material across wakefulness (Walker & van der Helm, 2009). Conversely, the marked increase of cholinergic neurochemistry during REM sleep, which exceeds levels of wakefulness, has been speculated to contribute to this independent REM-sleep-related process of consolidation, albeit currently lacking a strong empirical foundation (see section IV 2.3. for further discussion).

In summary, the results of the present thesis emphasize that preferential consolidation of emotional material over wakefulness and sleep can be ascribed to two independent processes. These processes operate in distinct manners and progress over different time scales. It is particularly worth highlighting that wakeful consolidation selectively influenced emotional item memory, whereas REM-sleep-dependent consolidation selectively impacted emotional associative memory in conjoint task procedures. This pattern of results is strongly aligned with the assumption that wakeful consolidation primarily relates to synaptic consolidation processes (Bergado et al., 2011), which encompasses the strengthening of local synaptic circuits without facilitating interactions between different memory systems. These processes lend themselves to consolidation of item memory, which is not exclusively supported by bound information across different memory systems (Yonelinas et al., 2010), while bearing limited impact on associative memory. In contrast, system consolidation is believed to require the unique neurophysiological environment of sleep (Diekelmann & Born, 2010). Thus, it appears consistent that potential consolidation benefits of emotional associative memory should emerge specifically within this state. As such, the characteristics of REM-sleep-dependent consolidation with regard to emotional item and associative memory retention, which derive from the present thesis, may signify a unique contribution to the interactions between memory systems in similar vein to SWS-related processes (see section IV 2.3. for further discussion).

2.2. Contributions of SWS-dependent consolidation to neutral associative memory

As discussed previously, it is currently believed that system consolidation is mainly accomplished during sleep. This neurophysiological state is assumed to enable the communication between different memory sub-systems while the brain resides in an “offline” state. The active system consolidation account (Diekelmann & Born, 2010) assumes that these processes critically relate to SWS and the coordinated emergence of specific oscillatory features within different memory sub-systems. In line with this framework, the current thesis demonstrates a facilitation of memory consolidation across early night SWS-rich sleep (experiment 1) and in close association to spindle density during NREM sleep (experiment 2). Moreover, this behavioral facilitation was selectively evident with regard to associative/source memory rather than item recognition, thus adhering to the notion that SWS-dependent consolidation is particularly relevant to hippocampus-reliant memory representations (Marshall & Born, 2007; Rasch & Born, 2013). This is a regularity that has arisen with remarkable consistency over the last decade (e.g. Studte et al., 2015; van der Helm et al., 2011), albeit mostly without inspecting the particular time course of these effects beyond short retention intervals. Re-examining the effects of sleep (as opposed to sustained wakefulness) on associative memory performance over time, after sleep has equally occurred in the former control condition, bears important theoretical implications on the time sensitivity of sleep-related system consolidation. It is thus presently an open issue how long intermediate storage within the hippocampus can be sustained before system consolidation must be initiated to prevent decay or retroactive interference by newly acquired memory traces within the MTL system. The findings of experiment 2 contribute to a better understanding in this regard by demonstrating that the correlation between NREM spindle density and associative memory performance is maintained after a subsequent delay (at delayed posttest), thus suggesting that the initial processes of system consolidation remain to signify the qualities of retrieved memory representations across time. This finding was, however, not paralleled by a preservation of initial post sleep performance differences in associative memory between groups at delayed posttest. Consequently, it may be inferred that system consolidation was sufficiently accomplished after a greater delay between encoding and sleep in the present experiment. This contrasts preceding accounts demonstrating time-sensitive effects of sleep-dependent consolidation across intervals of >10 hours between encoding and sleep onset (Gais, Lucas, & Born, 2006; Talamini, Nieuwenhuis, Takashima, & Jensen, 2008; see Holz et al., 2012 for a dissimilar pattern after 7.5 hours). However, many potential specificities of individual study designs may account for this discrepancy to the present results and future studies are thus required to extensively characterize the time-dependent course of system consolidation.

The most intriguing contribution that the present results yield as to the current understanding of SWS-dependent system consolidation is the specificity of these processes with regard to stimulus valence. As prior accounts have begun to suggest (Alger & Payne, 2016; Groch et al., 2015) SWS-dependent consolidation processes were found to be markedly disengaged for emotionally salient stimuli in the present thesis. This was consistently observed across both experiments, emerging in terms of a selective retention benefit of neutral source memory over the first night half (experiment 1) and in the form of a selective correlation of sleep-dependent gains in neutral associative memory to spindle density in the nap condition of experiment 2. This may be interpreted to reflect that the arousal elicited by emotional material attenuates sleep-related tagging mechanisms that in turn determine the reactivation of specific memory representations during SWS. As summarized throughout section I 3.3., these tagging mechanisms are assumed to relate to the strength of learning intention during encoding and its secondary effects with regard to processes of selection and maintenance that are mediated by prefrontal regions (Ranganath, 2010; Simons & Spiers, 2003). Emotional material may attenuate these processes as it is perceived to be highly salient, thus not requiring any effortful elaboration to be successfully retained over time. This metamnemonic effect may, in fact, be grounded on the highly efficient processing of emotional material at early stages of visual integration that has been demonstrated to result in an enhancement of successful intra-item integration on a behavioral level under conditions of limited temporal resources in a series of studies by Murray and Kensinger (2012) (see Murray and Kensinger, 2014 for corresponding fMRI data). Importantly, this efficiency in integration was found to be reflected in participants' ratings of encoding success for emotional and neutral item pairs, thus likely corresponding to a subjective sense of “ease” in processing and integrating emotional material experienced at the encoding stage. In further support of this interpretation, Hourihan, Fraundorf, and Benjamin (2017) recently confirmed that emotion influences judgments of learning in the sense that participants predict better recall of negative and arousing stimuli as compared to neutral and non-arousing material during encoding. Interestingly, this effect was absent when valence and arousal of material was varied continuously in one learning list. This suggests that the effect on judgements of learnings is based on the perceived distinctiveness of emotional stimuli corroborating the notion that salience of arousing material may drive the differential processing of emotional and neutral stimuli. While these studies did not ascertain effects of sleep-related consolidation, their results likely relate to tagging processes elicited at encoding that are relevant to the instatement of SWS-dependent consolidation. Thus initial processing of emotional stimuli may result in the metamnemonic judgment that successful retention can be accomplished without the recruitment of additional resources. This may conversely evoke an intensification of learning intention and the compensatory investment of cognitive effort, in the encoding of neutral material, which is not accompanied by this feeling of “ease”. The secondary initiation of executive control processes may conversely result in a selective tagging of neutral stimuli for preferential reactivation during subsequent SWS.

As apparent from the above, the conception that arousing stimuli attenuate tagging and thereby fail to undergo SWS-dependent consolidation is based on many secondary assumptions for which there is no clear empirical evidence at present. The most “direct” evidence in this regard may be drawn from the findings of Groch et al. (2015) who found that introducing a reward-related manipulation counteracted the differential facilitation of neutral and emotional source memory across early SWS-rich sleep. Thus, both emotional and neutral material benefitted from SWS-rich retention when they were externally enforced with a monetary incentive, which presumably nullified stimulus-driven fluctuations in learning intention between both valence categories. A dissimilar but reconcilable pattern of results was reported by Bennion et al. (2016) who examined item recognition of emotional and neutral stimuli of which half were encoded intentionally while the other half was processed incidentally within a nap design. It was found that sleep only benefitted the retention of neutral stimuli and only did so under intentional learning conditions. As such Bennion et al. (2016) demonstrate that learning intention sets the precondition to a selective benefit of neutral material over nap sleep[36], presumably by means of selective tagging of neutral material at the encoding stage. This finding corresponds to the conditions and results of the main experiment in Groch et al. (2015). Moreover, it emphasizes that SWS-related effects on emotional memory retention may only be induced by strong external cues (e.g. monetary incentives; see follow-up experiment in Groch et al., 2015), which are sufficiently potent to nullify differential stimulus-driven metamnemonic effects during encoding of emotional and neutral stimuli.

Despite these supportive findings (Bennion et al., 2016; Groch et al., 2015), it nevertheless remains to be substantiated that the selective retention benefit of neutral material in response to SWS-dependent consolidation is established via the differential recruitment of tagging mechanisms. Future studies should thus aim to investigate how neutral and emotional material is “tagged” at the encoding stage and how this in turn relates to subsequent reactivation. As summarized in section I 3.2, encoding-related “tags” are

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[36] As sleep was manipulated by means midday nap opportunity, this likely did not include high amounts of REM sleep, thus not producing complementary effects on emotional memory performance.

assumed to underlie residual activation changes at previously engaged synapses, as these have been found feature a higher probability of miniature EPSPs that in turn drive slow oscillations and thereby the initiation of SWS-inherent reactivations (Diekelmann & Born, 2010; Gais & Born, 2004; Rasch & Born, 2013). Interestingly, it has been suggested that this process may be retraceable during initial encoding by examining stimulus-specific modulations in theta activity (Heib et al., 2015). In this regard, theta coherence in the prefrontal-hippocampal circuitry during learning is believed to underlie controlled processing and anticipatory attention and, thereby may determine the "sufficiency" of residing activation in local synapses (which encode the particular event) to drive subsequent reactivation during SWS (Rasch & Born, 2013). Applying this to emotional and neutral material, by linking potential differences in theta activity at encoding to subsequent consolidation-related performance differences, would establish a more direct link between stimulus valence, tagging and selective SWS-related consolidation. To be precise, such an approach would provide insights as to how arousal affects controlled processes, which culminate in successful tagging, on a single-trial basis. Another potential avenue to further explore the notion that arousal attenuates tagging may lie in applying the method of TMR to emotional and neutral associations during SWS. By this, the process of tagging that is assumed to occur "naturalistically" for neutral material could be recreated via external application of cues associated to emotional material during SWS. This should result in a greater cuing benefit for emotional as opposed to neutral material, as the latter do not require this additional external enforcement in order to be successfully reactivated. Consequently, retention rates of cued emotional associations should reach similar levels as uncued neutral associations, which has been similarly found in a recent study by Lehmann, Schreiner, Seifritz, and Rasch (2016), albeit applying TMRs during all stages of NREM sleep.

On a more general level, future studies are required to define the regularities with which prefrontal executive control functions mediate strategic processing at the encoding stage, and, thereby determine subsequent SWS-related consolidation. In this regard, it is noteworthy to point out the correlation between spindle density and presleep associative memory performance that was found in experiment 2 regardless of stimulus valence. This is a quite common finding in studies ascertaining presleep performance rates and may partially reflect the contributions of general cognitive factors to sleep-related consolidation (Ujma et al., 2015), which likely relate to the aforementioned processes of selection and maintenance during encoding. More specifically, it is assumed that highly-gifted individuals who excel at coordinated and strategic encoding will likely express higher immediate memory performance but are also superior in guiding their attentional resources towards the efficient tagging of particularly relevant information resulting in a greater probability of successful reactivation and consolidation across sleep (Studte et al., 2016). This trait-like characteristic is reflected by correlations between spindle density and general cognitive abilities (Fang et al., 2016; Ujma et al., 2015). Moreover, a recent study demonstrated a significant correlation between working memory capacity and sleep-related consolidation benefits with regard to associative memory (Fenn & Hambrick, 2012). Integrating these findings may serve to further close the gap between encoding related processes and tagging mechanisms: As such, dispositional and instantaneous factors determine the capacity for strategic processing during encoding under the influence of learning intention as well as anticipatory processes. These processes, potentially reflected by theta coherence, generate activation changes that drive selective reactivation during subsequent SWS. However, as this highly refined sequence of processes related to sleep-related tagging is only beginning to emerge within recent empirical investigations a conclusive characterization on a neurophysiological level beyond broader concepts is currently unattainable.

In summary, the empirical findings of the present thesis have been found to converge with prevailing models of SWS-related system consolidation (Diekelmann & Born, 2010; Marshall & Born, 2007; Rasch & Born, 2013) in many regards: It was confirmed that SWS-related consolidation selectively benefits associative/source, and thus hippocampus-dependent, memory rather than equally enhancing item memory. Moreover, these behavioral effects were found to relate to spindle activity, a frequently employed oscillatory marker of system consolidation, which also remained to predict memory performance across time. In addition, spindle density was correlated to baseline performance rates reflecting the inherent relations between system consolidation and general cognitive abilities as well as controlled processing at the encoding stage. This high degree of convergence to contemporary models of system consolidation (Diekelmann & Born, 2010) indirectly certifies the validity of the present findings on the whole, as it signifies that critical characteristic of sleep-dependent consolidation similarly surfaced within the specifics of the present study designs. However, the current results also bear a unique contribution by substantiating the selectivity of SWS-dependent consolidation with regard to stimulus valence across two different study designs. Moreover, this differential benefit was linked to a specific oscillatory feature of sleep-dependent consolidation (spindle density), which extends former accounts finding similar selective effects on a behavioral level, but no corresponding neurophysiological correlates (Alger & Payne, 2016; Groch et al., 2015). Although this notion requires further testing by future studies, the current effects may be provisionally interpreted to suggest that arousal attenuates sleep-related tagging mechanisms.

2.3. Contributions of REMS-dependent consolidation to emotional associative memory

The current thesis aimed to explore how REM sleep and its inherent consolidation mechanisms relate to the retention of emotional associative memory, thus exceeding previous findings which, in the majority, focused exclusively on item recognition. As such, its most novel contribution overall lies in demonstrating that such an effect can be observed under specific conditions, further suggesting that REM-sleep-related consolidation mechanisms exhibit the potency of influencing associative memory of emotional material, beyond mere item memory performance. Complementing the absence of an effect of SWS-dependent consolidation on emotional material (see IV 2.2.), presumably resulting from attenuated tagging mechanisms, REM-sleep-related consolidation processes over the second night half gave rise to a selective facilitation of emotional source memory (see experiment 1). Moreover, this particular facilitation was found to be related to right-frontal theta lateralization during REM sleep, a previously discussed marker of emotional memory reprocessing within this state (see Genzel et al., 2015; Hutchison & Rathore, 2015 for review and Nishida et al., 2009; Prehn-Kristensen et al., 2013 for supportive empirical findings). This effect was markedly absent for item memory performance both behaviorally and regarding the neurophysiological correspondence to theta lateralization, which contrasts previous studies (see below for further discussion). In an attempt to further generalize these findings in experiment 2, the former pattern of results was not fully retained, mainly with respect to the lack of a clear correlation between the nap-sleep-related benefit in emotional associative recognition and right-frontal theta lateralization. As previously discussed (see IV 1.3.), this may revert to methodological aspects arising from insufficient statistical power for detecting REM-sleep-related effects. However, some other factors related to REM sleep physiology, and to specific features of both experiments are worth considering in this regard. These will be discussed in the following, prior to integrating the present findings with former accounts on emotional associative memory as well as the general literature on emotional memory consolidation during REM sleep. Finally, it will be discussed how the presently found effects may relate to neurophysiological processes of REM-sleep-dependent consolidation as well as the perspectives this bears with regard to the processing of hippocampus-dependent memory representations during REM sleep.

On a broader level as well as specifically with regard to the inconsistencies observed between both experiments, it is important to note that REM sleep as a neurophysiological state may be less reliably detected as compared to SWS. This is reflected by the notion of “covert” REM sleep processes (see Pace-Schott 2003 for a review). These may mark atypical NREM episodes that fail to fully conform to REM sleep criteria, as they are applied during sleep stage scoring (AASM, 2007). Consequently, these processes may equally give rise to consolidation-related processes but remain unaccounted for in quantitative measures of micro- and macrostructural sleep architecture. Additionally, these phases of covert REM sleep may be particularly prevalent early on, in the first sleep cycle (Pace-Schott, 2003) thus potentially exerting a higher impact on the precise detection of REM sleep in a nap opportunity (experiment 2) rather than across the second night half (experiment 1). Moreover, there are certain indications that theta activity during tonic and phasic REM sleep epochs may be functionally distinct (Hutchison & Rathore, 2015; see also section I 4.2). This differentiation is neglected in conventional sleep scoring, potentially obscuring subsequent analysis. Another source of variability between different studies may relate to the possibility that theta power actually constitutes a secondary feature of underlying consolidation processes. More specifically, Datta and O'Malley (2013) found that sleep did not exhibit an enhancing effect on the retention of fear extinction overall, but only in animals that expressed an increase in phasic pontine-wave (equivalent to PGO-waves in the primate brain) activity during REM sleep. This suggests that, in order to retrace effects of REM sleep to behavioral differences, it is required to ascertain the precise neurophysiological processes involved in consolidation at a very fine resolution. Thus, if emerging frameworks attributing the critical mechanism of REM-sleep-related consolidation of emotional material to the propagation of PGO waves prove to be applicable to the human episodic memory system (Hutchison & Rathore, 2015), this may entail that theta activity only poses a secondary process to these effects. Therefore, the degree to which measures related to theta power are sufficient to represent these underlying processes may vary across studies, which could have resulted in dissimilarly pronounced effects with regard to right-frontal theta lateralization retained across both experiments in the present thesis. As evident from these considerations, studying neurophysiological processes related to REM sleep poses certain challenges, which are not equally encountered in the context of SWS-related processes. This makes inconsistencies within the literature more reconcilable as to the validity of REM-sleep-related consolidation per se, but also highlights the requirement for future studies to apply more refined techniques (i.e. differentiating phasic and tonic REM sleep phases) in examining these effects.

A different line of considerations with regard to discrepancies in the clarity of correlations between right-frontal theta lateralization and behavioral enhancements of emotional associative/source memory arises from the different types of tasks that were employed in both experiments. As previously addressed (see IV 2.1.), the location feature of experiment 1 may have elicited different effects not just with regard to its interactions with arousal but also on a more general level. Specifically, as spatial location constitutes a particularly integral feature to the episodic memory system it may have been processed in stronger reliance on hippocampal binding mechanisms. Indeed, some accounts (Genzel et al., 2015; Hutchison & Rathore, 2015) have addressed that REM-sleep-related processing may be strongly related to emotional memory particularly with regard to spatial location as most animal studies, from which basic assumptions on underlying processes have been derived, almost exclusively employ spatial learning tasks. It has thus even been speculated that REM sleep exhibits a general role in processing spatial features of previously acquired material (Genzel et al., 2015). Related to these considerations, the test format of both studies may have resulted in the involvement of different retrieval processes, or rather a differential exclusion of familiarity-based retrieval. As probing location required a test format that differed from the initial learning presentation (all images were presented at central vision), this may have eliminated any effects of associative familiarity in supporting successful retrieval (reviewed by Mayes et al., 2007). In experiment 2 on the other hand, object-scene-pairs were presented in an identical arrangement, thus potentially enabling contributions of familiarity to task performance. These contributions may have been permissive in this experiment, in the sense that they did not alter performance to the degree that behavioral differences between groups were abolished. However, the inclusion of minor contributions of familiarity in associative task performance may nonetheless have obscured a clear correlational pattern of emotional associative memory with frontal theta oscillations arising from hippocampus-dependent consolidation. This consideration is of course based on the assumption that right-frontal theta lateralization underlies reprocessing of hippocampal-bound information for which the present experiments cannot provide direct evidence. This claim is further debatable from the theoretical viewpoint (see section I 4.2. and 4.3.) of neurophysiological specifics of REM sleep (for a more comprehensive discussion see below).

A different consideration that might account for dissimilarities between studies, relates to lateralization effects in spatial processing, which have frequently been reported for the right hemisphere (Bellgowan, Buffalo, Bodurka, & Martin, 2009; Burgess et al., 2002 but see Iglói, Doeller, Berthoz, Rondi-Reig, & Burgess, 2010 for a more complex pattern of results with regard to allocentric and egocentric processing). As encoding processes of emotional material have been found to be biased towards the right hemisphere as well (albeit not univocal, see Hamann 2001) it may be speculated that this corresponding lateralization in the hippocampus and the amygdala during spatial encoding of emotional material may produce different outcomes as during encoding of other types of object features (such as object identity that is processed more left-lateralized, see Bellgowan et al., 2009). This could be further speculated to exert downstream effects on REM-sleep-dependent consolidation. While this line of argumentation is based merely on theoretical assumptions, it may nonetheless be interesting to explore effects of lateralization as well as the broached interactions in the context of REM-sleep-dependent consolidation in future studies. Despite all of these considerations, it is important to emphasize that both experiments demonstrated a behavioral facilitation of emotional associative/source memory in association to (REM) sleep. On the whole this does not suggest that two entirely different processing mechanisms were “at work” in both task and study designs, but that these factors contributed to nuanced differences, if any.

Conversely, this consistently observed behavioral retention benefit for emotional material is at odds with the findings of preceding studies (Alger & Payne, 2016; Groch et al., 2015). In contrast to the alignment of the present with former findings as to selective SWS-dependent gains in neutral associative memory, prior studies did not find any indication of a beneficial effect of REM sleep on emotional associative memory performance. Taking the literature on the effects of emotion at various stages of memory formation into account (see section I 2.2), this discrepancy may relate to differences in integrative processing modes elicited by divergent task designs across these studies. This may be particularly relevant to the dissimilar results of Groch et al. (2015), as the authors employed a stimulus array that combined two different episodic features (location and frame color) without explicitly inducing an integrative processing strategy. This resulted in an absence of any sleep-related effects with regard to the retention of the location feature and an isolated benefit of early sleep on neutral picture-frame recognition. However, potentially beneficial effects of REM sleep may not have arisen in this particular design due to the low probability of engaging intrinsic stimulus processing on a single trial basis. This processing mode may in turn create the critical momentum by which co-occurring amygdala activation “marks” emotionally relevant associations (or single items) for subsequent REM-sleep-inherent reactivation. This interpretation is highly tentative, as there is currently no published data from a joint design varying intrinsic vs. extrinsic feature processing of emotional material in the context of sleep-related consolidation. Consequently, it poses an important future objective to identify the mechanism by which the structures relevant to emotional memory processing (see section I 2.1. for an overview) effectively “signal” to the sleeping brain during REM sleep, which newly acquired representations are relevant to be reactivated, analogous to the SWS-related tagging at the encoding stage. The substantiation of this mechanism is similarly important to account for the effects observed with regard to item memory performance by prior accounts and requires more theoretical as well as empirical elaboration in future studies. However, the view that intrinsic processing is an important, if not critical, precursor to REM-sleep-related consolidation is also reconcilable with the absence of any REM-sleep-related effect on emotional associations in the studies of Lehmann, Schreiner, et al., 2016 and Lehmann, Seifritz, et al., 2016. The authors used an associative learning paradigm combining (non-)emotional images with spoken neutral words (presented via headphones). As this task involves the binding of constituting elements across different sensory domains (Mayes et al., 2007) it likely induced an extrinsic processing mode (if not counteracted by bottom-up instructions), thus not conforming to the rationale proposed here. Also, the design involved multiple encoding cycles, which is commonly avoided in episodic memory research. Multiple repetitions of single trials can results in a strong engagement of strategic processing (Simons & Spiers, 2003), which does not resemble the instantaneous processes that are instated when an episode is encoded under real-world conditions (in a “single trial”-manner, see section I 1). Moreover, this encoding cycle entailed the assessment of expectancy ratings for spoken words, which places the paradigm in conceptual proximity to fear conditioning experiments, thus making it less comparable to the other studies discussed in this context.

On the whole, the discrepancies between the present and prior studies placed in the context of presumptive differences with regard to intrinsic feature processing raises an important trajectory for future research. Moreover, the fact that these mechanisms may have only made emotional material amenable to REM-sleep-dependent consolidation benefits without benefitting emotional memory processing per se (in terms of an immediate or delayed retention benefit irrespective of sleep) appears inconsistent and requires further clarification. It must also be considered that two further studies (Alger & Payne, 2016; Lewis et al., 2011) employing a highly similar task design as the one of experiment 2 did not find corresponding results regarding emotional associative recognition. However, in the study of Alger and Payne (2016) participants underwent an afternoon napping paradigm entailing a mean of approximately 60 minutes total sleep duration, which may have limited the emergence of sufficient REM sleep epochs in order to elicit corresponding behavioral differences between groups. With regard to the results of Lewis et al. (2011) it is important to bear in mind that differential effects of sleep for emotional material were evident in terms of neurophysiological correlates of memory retrieval (see section I 4.2.). Moreover, as the study entailed an entire night of sleep in the experimental group, it is conceivable that selective effects of REM-sleep-dependent consolidation were masked by complementary effects of SWS-related consolidation, thus yielding an enhancement of both neutral and emotional associative memory across sleep as similarly assumed with regard to the current findings of experiment 2. This emphasizes the complexity of interactions that may remain covert on a merely behavioral level, both regarding consolidation processes of different sleep stages as well as with respect to the effect of initial feature processing on the initiation of sleep-dependent consolidation.

On the other hand, potential interactions between task requirements and sleep-related consolidation may conversely account for the inconsistency of the present results to the broader literature. While the majority of preceding studies demonstrated an effect of (REM) sleep-related consolidation on emotional item memory (see e.g. Groch et al., 2013; Groch et al., 2015; Hu et al., 2006; Nishida et al., 2009; see Goldstein & Walker, 2014 for a review), the present findings (across both experiments) disclose a marked absence of any REM-sleep-related effect on emotional item memory performance. In accounting for this divergence from the general literature it is important to emphasize that the majority of these preceding findings exclusively focused on the assessment of item memory performance, thus likely entailing corresponding study instructions aimed at drawing participants' attention to the stimulus itself and not to the surrounding context of its presentation. Consequently, it may be speculated that the shift in task requirements in the present experiments, from the single item to the item-location/object-association, may have elicited a corresponding shift in the reactivated aspects of stimulus presentation during succeeding REM sleep. More specifically, in the present experiments attention may have been allocated to the association between the image and its respective location/object potentially exerting downstream effects on encoding processes. This may have resulted in an effective prioritization of item-feature-associations as opposed to isolated item representations with regard to subsequent consolidation. In support of this interpretation hippocampal activation has been found to differ on a single-trial basis during encoding trials focused on item as opposed to conjoint item-feature encoding (Mitchell, Johnson, Raye, & D'Esposito, 2000; Uncapher & Rugg, 2009). Although highly speculative, this difference in hippocampal activation, in concert with the coincidental changes in amygdala activation during the encoding of arousing stimuli, may translate to differential reactivations of emotional item-context-bindings rather than isolated item representations during REM sleep. This would be reconcilable with the observation that the present as well as prior experiments (Lewis et al., 2011) were not able to demonstrate simultaneous effects of REM-sleep-related consolidation on item and associative memory, as a task-induced “shift” in prioritized information occurs whenever associative memory is probed in a joint encoding procedure. In fact, the only study that derived estimates of item and associative recognition and found a beneficial effect of sleep on item but not source memory for emotional material was reported by Groch et al. (2015). However, the authors did not account for the inherent restrictions of source memory by prior item recognition in calculating source memory measures, rendering a concluding evaluation of the results of the late sleep condition difficult (see also section I 4.2.).

Expanding further on this conception, the differential pattern with regard to emotional item and associative memory retention in response to REM sleep may also be interpreted to point towards a selective effect of REM sleep on hippocampus-dependent memory consolidation. This dissociation may only be ascertainable when the task design entails a facet that strongly requires hippocampal engagement and may otherwise generalizes to item memory retention (as in prior studies focusing on item memory). This strongly relates to the theoretical gap pointed out in section I 4.3 as to whether and how emotional associative memory retention is supported by sleep-dependent consolidation. With regard to the first conception (see Figure I 11.A), it can be deduced from the present findings that the initiation of SWS-dependent consolidation mechanisms is overridden in a stimulus-driven manner for emotional material (see the former section IV 2.2 for a more detailed discussion). While the results of Groch et al. (2015) suggest that these mechanisms can be enforced to equally benefit emotional material when additional instructions are given, this does not appear to arise when emotional and neutral material are encoded in a conjoint task under naturalistic conditions (without manipulating learning intention to be equalized across valence types). Moreover, in the present experiments emotional associative memory was found to benefit from sleep independently of SWS-related mechanisms but in close association to REM-sleep-related features, corroborating the alternative conceptions summarized in Figure I 11.B and 11.C. However, with regard to the question by which of these potential mechanisms enhanced retrieval success for emotional associations was effected across REM sleep, the current results only provide limited indications.

As pointed out above, the selectivity of this REM-sleep-related enhancement that was evident for associative, but not for item recognition, can be integrated conceptually with the framework summarized in Figure I 11.B. This framework proposes that REM-sleep-related consolidation mechanisms exhibit the capacity to initiate system consolidation, however circumscribed to emotionally salient material. These effects may be mediated by activation changes in the amygdala during encoding that result in corresponding modulations of activation during subsequent REM sleep episodes. While this notion does not attribute any specific role to intrinsic or extrinsic processing, the predicted effects may only arise when emotional item-feature-conjunctions are processed interactively, thus outweighing potentially detrimental effects of attentional narrowing (see section VI 2.1). As a consequence, this process may require integrative processing, however, without resulting in a bottom-up driven process of intra-item binding that bypasses hippocampal item-feature binding as proposed by certain frameworks (Chiu et al., 2013; Murray & Kensinger, 2013). This interpretation can concurrently account for the absence of any overt beneficial effects of emotion on associative memory in the present experiments, which would have been expected to emerge irrespective of sleep based on the predictions of these referenced frameworks (Chiu et al., 2013; Murray & Kensinger, 2013). Thus it may be the case that the "protective" effect of integrative encoding of emotional item-context-associations, which has surfaced across experiments, may not ultimately relate to the encoding of unitized and thus hippocampus-independent item-context-representations. Instead, this integrative or intrinsic processing mode may support the "trespassing" of context features towards subsequent stages of higher-order visual processing by preventing disruptive effects of attentional narrowing at early stages of visual perception. On the whole, this illustrates a severe lack in conceptual clarity in the literature, which has not reached a circumscribed and unitary definition of what "intrinsic" item-context processing critically designates.

Nonetheless, the present findings do not allow us to strictly dismiss the alternative conception, that REM-sleep-related benefits in emotional associative recognition may revert to the selective strengthening of intrinsically-bound item-context associations (as depicted in Figure I 11.C). As discussed in section I 4.3., this notion would reconcile a behavioral retention benefit in associative recognition with certain specificities of REM sleep neurophysiology, which some authors have pointed out to be inapt in enabling a coordinated redistribution between memory systems (Rasch & Born, 2013; Spoormaker et al., 2013). However, the pattern of the present results is not easily integrated with regard to an underlying effect on intra-item associations. As increased associative familiarity should be beneficial to successful item and associative recognition (see Diana et al., 2008 for corresponding findings in a source memory paradigm), the selective strengthening of emotional intra-item associations during REM sleep should have equally exerted a beneficial effect on item recognition in the current task formats[37]. It may be argued that emotional item recognition was retained to a similar degree in the control or early sleep group respectively, due to the general consolidation benefit across time (see section IV 3.1.), which may have outweighed potential effects of REM sleep on behavioral performance in this regard. However, this claim is difficult to reconcile with prior studies demonstrating a beneficial effect of REM sleep on item memory performance in designs that likely encompassed similar effects of generic wakeful consolidation (e.g. Groch et al., 2013; Nishida et al., 2009). Alternatively and in similar vein to what has been discussed above, it could be proposed that the emphasis on the association between the item and its feature during encoding may have resulted in a prioritization of this associative aspect during REM-sleep-dependent reprocessing of these essentially intrinsically-bound associations. However, the conclusiveness of this argument appears much more evident in the context of a “shift” of hippocampal engagement from item encoding (in former studies) towards the encoding of the associative link between the respective item and its feature in the encoding procedures of the present experiments, which in turn effectuated a corresponding shift in REM-sleep-inherent consolidation mechanisms towards the reprocessing of this associative link specifically for emotionally salient stimuli. This interpretation is further reinforced by the considerations pointed out with regard to the differences of both task procedures that may account for disparities in correlational strength between right-frontal theta laterality and task performance (see above). As such, the task

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[37] As both item and associative/source recognition judgments were equally based on the presentation of either isolated items (experiment 1) or item-context-pairs (experiment 2) it is very unlikely that associative familiarity of the integrated item-context representation contributed differentially to performance on these measures within experiments, see e.g. Parks and Yonelinas (2015).

procedure of experiment 1 may have yielded the more sensitive estimate of source recollection and conversely exhibited a stronger association to REM-sleep-related consolidation processes and thus to theta laterality.

While this line of argumentation may plausibly account for the pattern of the present empirical results, it is not based on any direct evidence as this is not attainable from the present study designs. Consequently, this hypothesis needs to be addressed by future studies both with regard to the involvement of different processing mechanisms at the encoding stage (e.g. by varying intra- and inter-item-binding explicitly in a joint task procedure) as well as with respect to the exact consolidation processes during subsequent REM sleep. Moreover, future research should seek to establish a correspondence between REM-sleep-inherent oscillatory patterns and putative reprocessing of hippocampal memory traces in amygdala-hippocampal-prefrontal cortical circuits. In this respect, animal studies have furthered many intriguing insights. Most notably, Poe et al. (2000) were able to establish an experience-dependent phase-shift of place cell firing observed during REM sleep theta oscillations. During epochs of REM sleep it was found that place cells coding a novel location preferentially fire during the (depolarizing) peak of the theta oscillation whereas with growing familiarization to the environment the respective place cells exhibit a "shift" in firing patterns towards the (hyperpolarizing) trough of the oscillation in subsequent nights of sleep. This has led to the interpretation that consolidation processes during REM sleep may potentiate synaptic circuits encoding novel events while simultaneously de-potentiating hippocampal memory traces that have undergone successfully redistribution during SWS epochs of preceding nights (Diekelmann & Born, 2010; Hutchison & Rathore, 2015). Consequently, REM sleep may provide a crucial function in memory consolidation by freeing capacity for novel acquisition in the wake state. Intriguingly, Hutchison and Rathore (2015) point out the possibility that this phase-shift in the context of emotional memory may enable a simultaneous up-and-down-regulation of memory traces that were previously consolidated during SWS in relation to their emotional salience. More specifically, emotional memories may be prioritized by preferential nesting in the peak of the theta oscillation while representations of neutral material in the hippocampus may be actively degraded as a result of reactivation in the hyperpolarizing through. While this is merely an intriguing line of thought at present, it may explain how REM sleep related consolidation interacts with preceding SWS-dependent mechanisms and, critically, points out a mechanism by which REM-sleep-related processes may serve to selectively strengthen hippocampal memory traces. As such, these processes may not operate in parallel to SWS-related mechanism in that they might promote local changes in hippocampal memory traces without directly facilitating interactions between different memory systems. In fact, it appears quite intuitive that the process by which REM sleep supports emotional memory consolidation should be highly dissimilar to SWS-related processes, as these differ so substantially in their neurophysiological and neuroendocrinological signatures. This is reflected by the propagation of entirely different oscillatory features, such as PGO waves. At present, the indications that PGO waves, theta oscillations and the dominance of cholinergic chemistry during REM sleep contribute to the retention of emotional experiences across time appear rather “scattered”. However, on an integrated level, they signify that a very distinct mechanism during REM sleep must coordinate the preferential consolidation of emotional material across sleep and may do so by directly modulating hippocampal memory traces.

Within this context, it is also important to further clarify the functional role of right-frontal theta oscillations, which has emerged in human studies (Nishida et al., 2009; Prehn-Kristensen et al., 2013) and was critically substantiated in the present experiments. It can be directly inferred from animal research that theta oscillations should serve a critical function in this regard and that the underlying process reflected by these oscillations (although possibly restricted to plastic changes of hippocampal memory traces) encompasses cooperative activation changes not only in the amygdala but also in prefrontal cortical networks (Popa et al., 2010). However, the lateralization of this effect cannot be readily explained by preceding accounts or theoretical considerations. From a broader perspective, fMRI studies have demonstrated that specific types of episodic features elicit lateralized activation changes during encoding (Bellgowan et al., 2009). It could thus be speculated that the reactivation of respective memory traces effectuates corresponding differences in lateralization of theta power. However, this interpretation deviates from the present findings in that there was an indication (of differing magnitude) of a correlational association between right-frontal theta laterality and emotional associative memory performance for two highly dissimilar features (location and object-scene associations), which should have resulted in diverging laterality effects (cf. Bellgowan et al., 2009; Casasanto, 2003). A different consideration that may account for right-lateralized activation changes during REM-sleep-inherent consolidation of emotional material relates to the hemispheric asymmetries observed during processing of emotional material in the amygdala (McMenamin & Marsolek, 2013). Processing emotional, but particularly negative, material has repeatedly been shown to evoke activation changes in the right amygdala, which could relate to a laterality bias elicited during subsequent reactivation in REM sleep. However, these lateralization effects have not been established as univocally with regard to the prefrontal cortex (Killgore & Yurgelun-Todd, 2007), restricting the direct applicability of these findings in the context of the present results. Consequently, future studies are required to substantiate the functional correspondence of this effect to underlying processes in the limbic system, e.g. by ascertaining simultaneous EEG-fMRI recordings during REM sleep.

In summary, the interpretation of the present findings gives rise to several adjoining conceptual ambiguities, which need to be resolved by future research. Nonetheless, the present results originally substantiate a role of REM sleep in emotional associative memory consolidation, which was demonstrated behaviorally across two different study designs. Globally, this affirms the relevance of REM sleep in memory consolidation, which has been successively deemphasized in the literature of the past years. Moreover, the secondary findings of REM-sleep-related contributions to an enhanced processing of affective salience (experiment 1; valence ratings), as well as an increased maintenance of associative recognition across prolonged delays (experiment 2; explorative correlation to FA of recombined item pairs), suggest that consolidation processes within this state may reach even farther than presently assumed. This highlights several interesting perspectives for future studies that will be summarized in the subsequent section.

3. Limitations and outlook

While the present experiments extend prior accounts, in revealing an association between REM sleep and emotional associative memory, they also bear certain limitations. These relate to the individual study designs but also more generally to the approach of this thesis and will be enumerated consecutively.

In experiment 1 a split-night-design was employed in order to partially contrast memory retention across otherwise identical intervals of predominant SWS and REM sleep. Due to the circadian and homeostatic modulations of the sleep cycle (Carskadon & Dement, 2005) it is not possible to systematically manipulate the occurrence of SWS and REM sleep between conditions in a naturalistic[38] manner while simultaneously retaining the circadian alignment between both conditions. Within the rationale of the split-night-design it is thus required that the critical post sleep memory test is performed with a lag of approximately three to four hours between the early and late sleep conditions. This has been pointed out to result in confounds of potential sleep-related effects with regard to circadian modulations of neurohormonal concentrations. More specifically, the rise of cortisol levels during late sleep and in the early morning hours could be speculated to elicit an enhanced consolidation and/or retrieval success of emotional material. However, contrary to this notion the pharmacological suppression of cortisol levels during sleep has been found to evoke a more marked rather than an attenuated retention benefit for emotional stimuli (Wagner, Degirmenci, Drosopoulos, Perras, & Born, 2005). Moreover, confounding influences of the morning cortisol rise during retrieval are rendered unlikely due to the inhibiting effect of cortisol on memory retrieval (Diekelmann, Wilhelm, Wagner, & Born, 2011) which is found to be even more pronounced for emotional material (Rimmele, Besedovsky, Lange, & Born, 2015). This should have conversely yielded an attenuation of post-sleep emotional memory performance in the late sleep group, which was not evident in the present results. A different concern that has been raised in the context of the split-night-design is the proactive effect of SWS on memory encoding (Tononi & Cirelli, 2003, 2014). This proactive effect may exert unequal influences on encoding performance in the late sleep condition, as this group obtains three hours of sleep prior to encoding. To address this confound a pretest procedure was implemented, which did not yield any differential effects of the timing of encoding procedures (prior to or following the first night half) on immediate memory performance. Nevertheless, a potential confound in this regard cannot be fully precluded from the current analysis, particularly with regard to delayed effects of

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[38] More invasive techniques such as pharmacological interventions (Mednick et al., 2013) and partial sleep deprivation protocols (Morgenthaler et al., 2014) can accomplish a more marked discrimination without entailing concurrent circadian misalignments. However, the latter are known to produce high amounts of distress (with corresponding effects on neurohormonal concentrations), while the former bear considerable confounds with regard to secondary effects of administered pharmacological substances (e.g. antidepressant effects of selective serotonin reuptake inhibitors).

“well rested” encoding in the late sleep group. While it is difficult to explain why these proactive effects should result in differential performance benefits in relation to stimulus valence as observed in the late sleep group, future studies should aim to further account for this discrepancy in encoding timing. The current design could thus be improved by implementing control measures related to encoding performance (e.g. processing speed and working memory performance) and including control groups, which are held awake in the respective night halves. Respective control groups were omitted in the current design as this would have considerably enhanced the complexity of the design with only a restricted informative value. The interpretation of the results in control conditions is inherently confounded by effects of sleep deprivation in nocturnal sleep designs. As sleep deprivation considerably attenuates overall cognitive performance, a strict comparison between groups is often regarded as uninformative with regard to the effects of active memory consolidation during sleep. In light of the present results it would nonetheless be interesting to replicate experiment 1 while additionally including control groups across both night halves. This would allow testing whether the differential retention patterns in source memory performance emerge in the early and late control conditions irrespective of a general difference in performance levels between sleep and wake groups as a result of sleep deprivation.

With regard to experiment 2, a major but unexpected caveat lies in the high variability and overall low REM sleep duration in the early morning nap condition. This manipulation, similar to the late sleep condition of experiment 1, was designed to elicit marked enhancements of REM sleep duration by (1) restricting REM sleep duration during the night preceding the experiment[39] and (2) scheduling the experimental sleep opportunity in close proximity to awakening from nocturnal sleep. With regard to the latter it must be acknowledged that this was only accomplished to a limited extent as a result of the prolonged encoding procedure, which comprised a total of 324 individual trials. Consequently, participants of the nap group completed the final electrode set-up for the morning nap at approximately 10:30 a.m.. Although this broadly conforms to the timing employed by former studies (Carr & Nielsen, 2015; Deliens et al., 2013; Gilson et al., 2015; Groeger et al., 2011), the substantial lag between awakening from nocturnal sleep (at

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[39] This was implemented by restricting the pre-experimental sleep window from midnight to 6:00 a.m..

6:00 a.m.) and the onset of the morning nap (at 10:30 a.m.) may have resulted in a re-accumulation of homeostatic sleep pressure. These homeostatic demands may have been further enhanced due to the highly demanding encoding procedure (Maire, Reichert, & Schmidt, 2013) that posed a considerable strain on participants' continuous attention, as indicated by debriefing statements. Another consideration that may account for the great variability in REM sleep duration between participants regards the lack of strong experimental control over the sleep patterns of the preceding nights leading up to the experiment. In fact, newer models of sleep regulation (McCauley et al., 2009) have incorporated that sleep pressure is substantially modulated by cumulative effects of sleep restrictions evolving over multiple nights. While it was not feasible in the present study to comprehensively monitor pre-experimental sleep patterns, this possibility should be considered in future experiments. Moreover, limiting the amount of study trials by omitting the third delayed testing procedure may also contribute to a more stable enforcement of REM sleep episodes in the early morning hours for the reasons set out above. This would bear the potential of establishing a behavioral dissociation of REM-sleep-related effects on emotional associative memory performance, which was not attainable in the present experiment due to the balanced rates of SWS and REM sleep. Notwithstanding, it must be emphasized that the delayed assessment of memory performance in the present experiment yielded important insights that should be expanded upon in future studies. In particular, it is necessary to readdress whether the absence of between-group differences in associative memory performance after a consecutive night of sleep (at delayed posttest) can be directly ascribed to delayed consolidation processes by means of corresponding associations to sleep-inherent oscillatory features in the former control condition. However, this would require to ascertain polysomnographic measurements during the intervening night of sleep (between post- and delayed posttests), which was not practicable in the current design.

Beyond these specificities of both study designs, there are some limitations that are relevant to the interpretation of both experiments alike. Foremost, both studies did not explicitly manipulate intrinsic and extrinsic feature binding, which is of critical relevance in drawing direct conclusions as to the underlying mechanisms of REM-sleep-related consolidation. However, the current set of studies was aimed to serve as a first approach to systematically ascertain the effects of REM sleep on emotional associative memory consolidation across two different task- and study designs. The aspect of intrinsic/extrinsic feature binding in the context of emotional material, and its downstream effects on consolidation, was therefore not addressed in this first step to prevent the emergence of excessive variance in between-subject comparisons obscuring an overall association between REM sleep and emotional associative memory retention. As the present studies have substantiated a basis to assume that REM sleep contributes to the consolidation of emotional associations, future studies should thus aim to scrutinize these effects with regard to the underlying binding mechanisms at the encoding stage. In adaptation of prior study designs (Bader et al., 2010; Bastin et al., 2013) the trial procedure of the encoding task of experiment 2 could be modified to include the presentation of a sentence linking the arbitrary pairing of object (e.g. a styrofoam cup) and background scene (e.g. a boy sitting at the side of the road). This sentence could either describe both constituents in an interactive way (e.g. “The boy is playing with the styrofoam cup”), hence fostering intra-item binding, or alternatively in a non-interactive manner (e.g. “The boy is sitting at the side of the road while the styrofoam cup rolls past”). Contrasting these conditions in the context of emotional and neutral material may disclose potential differential contributions of REM-sleep-related consolidation mechanisms to task performance. Another related limitation, which arises from the current findings, is the lack of an objective neurophysiological measure of post-sleep retrieval processes. This may conversely yield important insights as to whether REM-sleep-related processing affects the engagement of hippocampal processes during successful associative memory retrieval of emotional stimuli. Thus, future experiments should aim to integrate electrophysiological measurements during retrieval procedures in order to derive ERP measures of recollection and familiarity.

On a more general level, the interpretation of the presently attained results is restricted by the correlative nature of the employed designs, which did not entail a direct manipulation of reactivations during respective sleep stages. Hence, the present findings do not permit to infer a strict causality of sleep-dependent processes (assessed by means of oscillatory features) with regard to post-sleep memory performance. Within newly developed paradigms this is usually achieved by directly cuing previously learned material during specific phases of sleep and linking oscillatory responses to subsequent post-sleep retrieval success of these specific items (e.g. Schreiner and Rasch, 2015). This method of targeted memory reactivations has yielded intriguing results and has been successively refined to induce reactivations during particular phases of characteristic oscillations (e.g. slow oscillations) of NREM sleep (Batterink et al., 2016). As such, it would be highly interesting to apply this technique in the context of emotional associative memory, by inducing respective reactivations temporally aligned to particular phases of REM sleep theta oscillations. This would allow future studies to further test the hypothesis that reactivations of emotionally salient material are preferentially “nested” in the (depolarizing) peaks of theta oscillations. As originally proposed by Hutchison and Rathore (2015), this specificity of temporal nesting may enable selective consolidation of emotional memories. Moreover, the potential specificity of reactivations with regard to the phase of theta oscillations may concurrently account for the non-effective cuing of emotional material during REM sleep reported by Lehmann, Schreiner, et al. (2016), as cues were presented arbitrarily interspersed during REM sleep epochs without considering the alignment to particular phases of theta oscillations.

Another aspect, which deserves further attention in future experiments, is the processing of neutral stimuli in the context of emotional material and its subsequent effects on sleep-related reactivations. The framework, which has been proposed here, that neutral associations may be preferentially tagged for subsequent reactivation as a secondary effect of an enhanced learning intention, needs to be tested more rigorously with regard to its underlying assumptions. Some potential perspectives have been pointed out previously (see section IV 2.2.), one of the most promising being the employment of encoding-related changes in frontal theta power as a potential marker of sleep-related tagging mechanisms (Rasch & Born, 2013). Moreover, these processes may be additionally approached on a behavioral level by investigating outcomes of different stimulus processing manipulations, such as processing depth. It would thus be interesting to employ a levels-of-processing manipulation (Craik & Lockhart, 1972) in the context of emotional and neutral stimulus encoding, in order to test whether this results in similar initiation of sleep-related tagging for neutral and emotional material or whether differential effects remain to persist in the semantic encoding condition. The latter outcome would suggest that the effects driving preferential tagging of neutral material exceed the mere enforcement of elaborative stimulus processing, thus allowing a further approximation to the putative mechanisms of learning intention on a behavioral level.

With regard to the potential applications of the present findings, it will pose an important objective to ascertain the long-term consequences of disrupted processes of REM-sleep-dependent consolidation on emotional memory formation. More specifically several accounts (Landmann et al., 2014; Walker & van der Helm, 2009) have raised the possibility that the co-occurrence of sleep disturbances in the context of certain psychiatric disorders (e.g. PTSD and major depression) may be more than coincidental. In fact, the concurrent disruption of sleep-related consolidation processes may be critically relevant to the etiology of these disorders which are signified by alterations in memory processes (van Marle, 2015). For instance, patients suffering from PTSD or trauma-related disorders have been found to exhibit selective impairments in associative memory performance, while demonstrating no corresponding deficits in item recognition tests (Guez et al., 2013; Guez et al., 2011). This impairment may be related to stress-induced structural changes (Saar-Ashkenazy et al., 2016), although evidence in this regard is not unequivocal at present. Primary attempts to apply theoretical accounts of (REM-)sleep-dependent consolidation to experimental models of post-traumatic stress disorders yield very heterogeneous results (Kleim, Wysokowsky, Schmid, Seifritz, & Rasch, 2016; Porcheret, Holmes, Goodwin, Foster, & Wulff, 2015; Werner et al., 2015). This may signify that interactions between basal processes of sleep-related consolidation and memory processes elicited by complex real-world events (e.g. traumatic incidents) are more intricate as incorporated in present accounts. Nonetheless, it would be highly interesting to examine these basal processes of REM-sleep-dependent consolidation of emotional associations, which emerged in the present thesis, in the context of trauma-related disorders, as this may potentially yield an important perspective in the progressive refinement of effective treatments.

4. Final conclusion

The present thesis aims to contribute to a more comprehensive understanding of the effects of REM sleep on emotional memory consolidation. This was motivated by certain gaps within the present state of empirical findings, which have been restricted to studying item recognition performance and are thus largely uninformative of the particular aspects of memory retrieval that benefit from REM-sleep-dependent consolidation. To this end, two consecutive experiments were conducted. These experiments systematically examined the contributions of SWS and REM sleep to emotional and neutral memory performance in terms of (1) item memory, (2) the qualities of the retrieval experience (Remember-Know-paradigm) and (3) associative/source memory. Both studies yielded the consistent finding that sleep in general is selectively involved in associative memory consolidation. Moreover, it was established that associative memory retrieval of emotional and neutral events is supported by two independent consolidation processes (see Figure IV 1). In line with the well-established framework of active system consolidation during SWS (Diekelmann & Born, 2010), it was found that SWS benefitted associative memory performance, however only for neutral associations (as evident in behavioral performance and correlations to spindle density). On the other hand, the present results illustrate that REM sleep, which was previously not believed to be involved in associative memory consolidation (Spoormaker et al., 2013), contributed to the retrieval of emotional association across sleep (as evident in behavioral performance and correlations to right-frontal theta dominance). While the underlying mechanisms of both processes remain obscure in certain respects, these findings nonetheless make a genuine contribution to the present literature and offer intriguing inferences with regard to the way in which SWS- and REM-sleep-dependent processes operate to maintain associative memory retrieval across time. As such, it appears that emotional associations achieve access to REM-sleep-dependent reprocessing by an instantaneous, stimulus-driven mechanism that may be mediated by activation changes in the amygdala. The successful initiation of REM-sleep-related consolidation may, however, be restricted by attentional processes at the encoding stage, as reflected in the results of experiment 2.

While emotional associations are required to critically pass through the “filter” established by attentional narrowing, material, that is not detected as emotionally salient enters an entirely different processing route. This route may be considered the “default mode” of associative memory consolidation that is supported by SWS-inherent reactivation and redistribution of hippocampal-bound memory traces (Diekelmann & Born, 2010). The initiation of these processes relies on tagging mechanisms at the encoding stage that, although not entirely characterized at present, seem to be determined by the intensity of learning intention attributed to a specific association (Rasch & Born, 2013; Stickgold & Walker, 2013). This aspect may be enforced for neutral associations due to their inconspicous characteristics and low memorability, which may influence metamnemonic judgments to induce compensatory efforts during encoding. This, by inference, could result in a preferential access of neutral material to this route of sleep-related tagging that culminates in an enhanced probability of successful reactivation during subsequent SWS. Emotional material, on the other hand, may not enter this route as an indirect result of its high inherent salience, which may conversely attenuate the strength of learning intention.

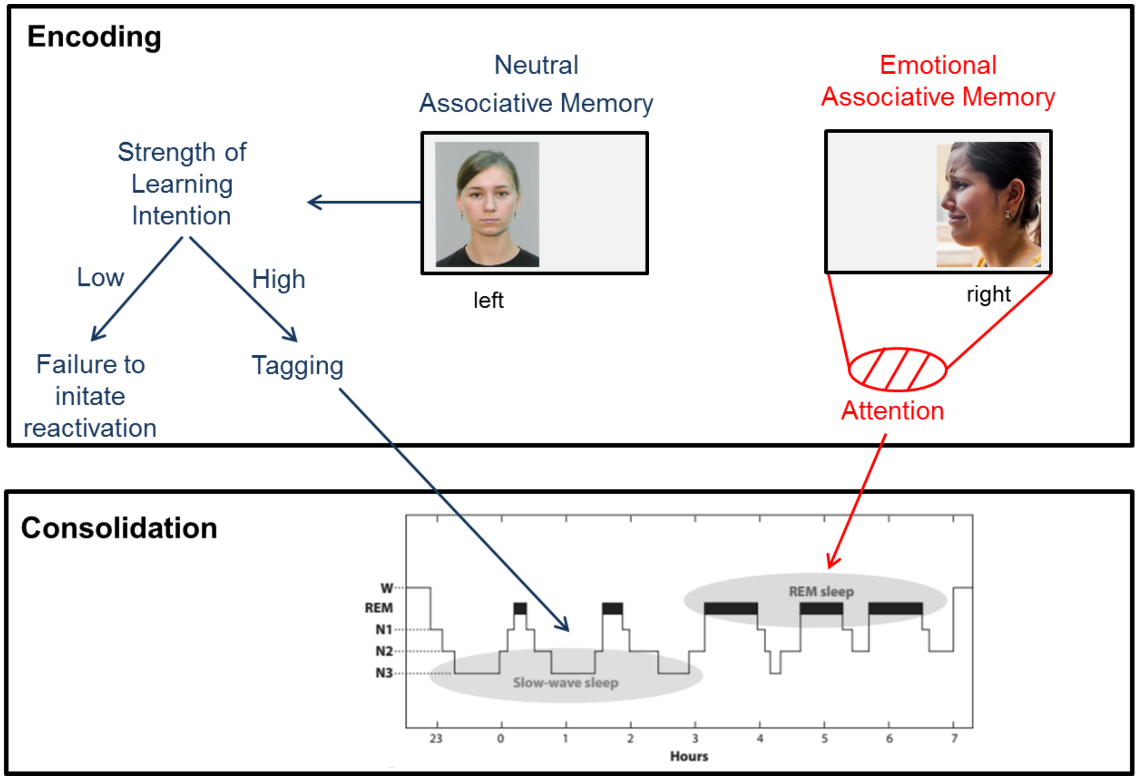

Figure IV 1. Schematic illustration of dissociable consolidation processes contributing to the selective retention of emotional and neutral associations over sleep. Neutral associations are retained via the selective recruitment of tagging mechanisms at the encoding stage, resulting in the initiation of system consolidation during SWS. This, however, depends on the strength of learning intention during encoding that may vary in a stimulus-driven manner. Emotional associations are required to withstand diverting effects of arousal on initial attention allocation during encoding. Required that this early processing stage is accomplished, consolidation processes during REM sleep facilitate retrieval across time.

Importantly, it would be inaccurate to infer from this preliminary working model that there are two discrete processes strictly confined to the consolidation of emotional and neutral material. Rather, this framework proposes a genuine route of REM-sleep-related consolidation for emotional associations, while the SWS-related route is potentially accessible to stimulus material of all valence categories alike. However, the extent to which neutral items gain access may systematically vary with the degree to which these are embedded in highly salient material, as a consequence of secondary effects on learning intention. Simply put, emotional material is consolidated in any instance, while neutral associations are required to engage learning intention to be successfully retained across time. This notion converges with the highly specific processing routes of emotional material laid out at different stages of stimulus processing in the cognitive system (Tamietto & de Gelder, 2010) which ensure that emotional material is readily detected and instantaneously attended to. As such, it appears plausible that a distinct consolidation process may guide memory formation to retain emotional events across times independently of generic event information.

This preliminary model (see Figure VI 1) leaves many questions unanswered. One major ambiguity regards the exact mechanism by which REM sleep processes accomplish the selective preservation of emotional associative memory. This may entail a direct reprocessing of hippocampal-bound associations (Hutchison and Rathore 2015) or, alternatively, revert to the selective reactivation of intra-item associations. Nonetheless, this preliminary, but non-exhaustive, working model may serve to guide future experimental investigations in generating new insights as to how emotional associations are reprocessed during sleep. As the field of system consolidation during sleep has seen striking advancements over the course of the last decades, the avenue established in the present thesis will hopefully disembogue in a comprehensive understanding in the future.

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VI Index of figures and tables

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VII Abbreviations

AASM	American Academy of Sleep Medicine
ANCOVA	Analysis of Covariance
ANOVA	Analysis of Variance
BIC	Binding of item and context model
BL	Basolateral
BLA	Basolateral complex of the amygdala
BOSS	Bank of Standardized Stimuli
CR	Correct rejections
EEG	Electroencephalography
EMG	Electromyography
EOG	Electrooculography
EPSP	Excitatory postsynaptic potentials
ERP	Event-related potentials
ESS	Epworth Sleepiness Scale
FA	False alarms
FASST	fMRI Artefact rejection and Sleep Scoring Toolbox
fMRI	Functional Magnetic Resonance Imaging
HPA	Hypothalamic-pituitary-adrenal
IAPS	International Affective Picture System
ICD-10	International Classification of Diseases
IEG	Immediate early gene
IQR	Interquartile range
K	Know
KSS	Karolinska Sleepiness Scale
LTD	Long-term depression
LTP	Long-term potentiation
mPFC	Medial prefrontal cortex
MTL	Medial temporal lobe
N1-3	Non-rapid eye movement stage 1-3
NAPS	Nencki Affective Picture System
NREM	Non-rapid eye movement

OFC	Orbitofrontal cortex
PANAS	Positive and Negative Affect Schedule
PFC	Prefrontal cortex
PGO	Pontine-geniculo-occipital
PHC	Parahippocampal cortex
PRC	Perirhinal cortex
PSQI	Pittsburgh Schlafqualitätsindex
PTSD	Post-traumatic stress disorder
R	Remember
Rec	Recombined
REM	Rapid eye movement
rMEQ	Reduced Morningness-Eveningness questionnaire
RMS:	Root mean square
ROC	Receiver operator characteristic
SFSR	Sleep to forget and sleep to remember
SM	Source Memory
SSS	Stanford Sleepiness Scale
STADI-S/T	State-Trait-Angst-Depressions-Inventar [State-Trait Anxiety Depression Inventory]
SWR	Sharp-wave ripples
SWS	Slow wave sleep
TMR	Targeted memory reactivations
TST	Total sleep time
V1	Primary visual cortex
vmPFC	Ventromedial prefrontal cortex
VVM	Visueller und Verbaler Merkfähigkeitstest [Visual and Verbal Memory Retention Test]
W	Wake
WM	Working memory
WMT	Wiener Matrizen Test [Viennese Matrices Test]

VIII Annotations

This doctoral thesis is based on two experiments, which are submitted or in preparation for publication as ‘Original Articles’ in international peer-reviewed journals. I am the first author of the articles but other authors contributed to the work and are listed below. Both articles are presented here in their original form, apart from changes in formatting (e.g. figures and labeling).

Chapter II

Sopp, R., Michael, T., Weeß, H.-G., & Mecklinger, A. (submitted). Remembering specific features of emotional events across time: The role of REM sleep and prefrontal theta oscillations.

Chapter III

Sopp, R., Michael, T., & Mecklinger, A. (in preperation). Early morning nap sleep preserves emotional and neutral associative memory: Evidence for dissociable consolidation processes.

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