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Note

Slow wave sleep and accelerated forgetting

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ABSTRACT

We investigated whether the benefit of slow wave sleep (SWS) for memory consolidation typically observed in healthy individuals is disrupted in people with accelerated long-term forgetting (ALF) due to epilepsy. SWS is thought to play an active role in declarative memory in healthy individuals and, furthermore, electrographic epileptiform activity is often more prevalent during SWS than during wakefulness or other sleep stages. We studied the relationship between SWS and the benefit of sleep for memory retention using a word-pair associates task. In both the ALF and the healthy control groups, sleep conferred a memory benefit. However, the relationship between the amount of SWS and sleep-related memory benefits differed significantly between the groups. In healthy participants, the amount of SWS correlated positively with sleep-related memory benefits. In stark contrast, the more SWS, the smaller the sleep-related memory benefit in the ALF group. Therefore, contrary to its role in healthy people, SWS-associated brain activity appears to be deleterious for memory in patients with ALF.

1. Introduction

1.1. *Accelerated long-term forgetting*

Accelerated long-term forgetting (ALF) is a common symptom of transient epileptic amnesia (TEA) (Butler et al., 2007). People with ALF appear to learn and initially retain new information normally, but subsequently forget at an accelerated rate (Bell & Giovagnoli, 2007; Butler & Zeman, 2008). This phenomenon provides a novel opportunity to investigate post-encoding memory processes.

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1.2. Sleep and memory in health

In healthy people, post-encoding sleep is thought to play an important role in memory. This role is not fully understood, but may have both passive and active components. Sleep provides a temporary shield from potentially interfering cognitive stimulation. Cognitive stimulation during a wakeful retention interval may cause forgetting through a number of mechanisms – interference with access at the point of retrieval (e.g., Brown, Neath, & Chater, 2007); disruption of the memory trace (e.g., Wixted, 2004, 2010); and interference with certain consolidation processes (e.g., Mednick, Cai, Shuman, Anagnostaras, & Wixted, 2011; Wixted, 2004) – and so some part of sleep's benefit for memory retention is likely due to protection from this retroactive interference.

In addition to this passive, or permissive, benefit afforded by sleep, slow wave sleep (SWS) is thought to play an active role in declarative memory. In young healthy people, the more SWS that a period of sleep contains, the greater the benefit of that sleep for the retention of declarative memories (e.g., Alger, Lau, & Fishbein, 2012; Barrett & Ekstrand, 1972; Born, Rasch, & Gais, 2006; Diekelmann, Biggel, Rasch, & Born, 2012; Fowler, Sullivan, & Ekstrand, 1973; Lau, Tucker, & Fishbein, 2010; Plihal & Born, 1997, 1999; Yaroush, Sullivan, & Ekstrand, 1971). The disruption of slow wave activity during a post-learning nap adversely affects subsequent memory performance (Garside, Arizpe, Lau, Goh, & Walsh, 2015), while enhancement of the endogenous slow oscillation using electrical (Marshall, Helgadottir, Molle, & Born, 2006) or auditory (Ngo, Martinetz, Born, & Molle, 2013) stimulation improves memory for information learnt prior to sleep. Slow oscillations are thought to trigger the reactivation of recently-acquired, memory-related activity patterns in the hippocampus (Born et al., 2006; Marshall & Born, 2007) which strengthens the memories (e.g., Diekelmann, Buchel, Born, & Rasch, 2011; Rasch, Buchel, Gais, & Born, 2007; Rudoy, Voss, Westerberg, & Paller, 2009) and, when interleaved with reactivations of related older memories, helps integrate them with pre-existing knowledge (McClelland, McNaughton, & O'Reilly, 1995). Techniques designed to induce memory reactivation using sensory cues have demonstrated a benefit for memory if the cues are provided during SWS, but not if provided during rapid eye-movement (REM) sleep or active wakefulness (e.g., Diekelmann et al., 2011; Rasch et al., 2007; Rudoy et al., 2009). However, it should be noted that there is evidence to suggest that reactivation-based declarative memory consolidation does not happen exclusively during SWS; it also occurs during quiet rest (e.g., Axmacher, Elger, & Fell, 2008; Deuker et al., 2013; Ego-Stengel & Wilson, 2010; Groen, Sokolov, Jonas, Roebling, & Spitzer, 2011; Tambini & Davachi, 2013).

Sleep spindles are associated with synaptic plasticity (Rosanova & Ulrich, 2005). Their incidence increases following learning (e.g., Gais, Molle, Helms, & Born, 2002) and has been found to correlate with overnight memory retention in some cases (Schabus et al., 2004). According to an influential model from Born and colleagues (Born et al., 2006; Marshall & Born, 2007), these sleep spindles are an important component of SWS-associated memory consolidation; these researchers propose that slow oscillations trigger spindles from the thalamus in tandem with reactivations in the hippocampus, and that it is these sleep spindles that allow the reactivations to induce plastic changes in the neocortex.

An alternative account for the benefit of SWS for declarative memory retention is that it downscales synaptic weights, improving memory by increasing the signal-to-noise ratio. That is, mechanisms reflected by slow waves may reduce the strength of synapses representing noise to such a level that they no longer interfere with memory retrieval (Tononi & Cirelli, 2003, 2006).

1.3. Sleep and ALF

It has frequently been suggested that memory in people with ALF may not benefit from sleep in the same way that it does in healthy people (e.g., Butler et al., 2009; Holmes & Lenck-Santini, 2006; Jansari, Davis, McGibbon, Firminger, & Kapur, 2010; Muhlert et al., 2011; Sud et al., 2014; Tramoni et al., 2011; Urbain, Di Vincenzo, Peigneux, & Van Bogaert, 2011; Zeman, Butler, Muhlert, & Milton, 2013). A recent study of ours, however, demonstrated that sleep can benefit memory retention in people with ALF just as much as it does in healthy control participants (Atherton, Nobre, Zeman, & Butler, 2014). Nevertheless, this benefit may be largely due to sleep's passive role in protecting against interference. It remains possible that SWS-specific *active* processes of sleep-related memory consolidation are disrupted in people with ALF.

There is some evidence to suggest that epileptic activity following learning is associated with poor memory retention in people with epilepsy (Fitzgerald, Thayer, Mohamed, & Miller, 2013; Jokeit, Daamen, Zang, Janszky, & Ebner, 2001; Mameniskiene, Jatuzis, Kaubrys, & Budrys, 2006; Ricci, Mohamed, Savage, & Miller, 2015; Ricci, Mohamed, Savage, Boserio, & Miller, 2015; Wilkinson et al., 2012). Interictal and ictal epileptiform discharges are enhanced during SWS, compared to wakefulness and REM sleep (Bazil, 2000; Bazil & Walczak, 1997; Goncharova, Zaveri, Duckrow, Novotny, & Spencer, 2009; Kotagal, 2001; Mayanagi, 1977; Nazer & Dickson, 2009; Romcy-Pereira, Leite, & Garcia-Cairasco, 2009; Rossi, Colicchio, & Pola, 1984; Sammaritano, Gigli, & Gotman, 1991), and could potentially interfere with the SWS-associated brain activity patterns that facilitate memory retention in healthy people (Galer et al., 2015; Shatskikh, Raghavendra, Zhao, Cui, & Holmes, 2006; Tassinari, Cantalupo, Rios-Pohl, Giustina, & Rubboli, 2009; Urbain et al., 2011; Verrotti, Filippini, Matricardi, Agostinelli, & Gobbi, 2014).

In people with transient epileptic amnesia, half of whom complain of ALF (Butler et al., 2007), the attacks of transient amnesia characteristic of the syndrome often occur upon waking from sleep, suggesting a link between seizure activity and sleep (Butler et al., 2007). Furthermore, electroencephalography in people with TEA is more likely to reveal epileptic abnormalities if performed while the person is asleep than whilst they are awake and alert (Butler et al., 2007; Zeman, Boniface, & Hodges, 1998).

1.4. Hypothesis

The objective of the current study was to investigate the role played by SWS in the benefit of sleep for memory retention seen in patients with TEA-associated ALF. We hypothesized