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## Chapter 13

# Your Imaging Group Has Coined the Term ‘Dream Imaging.’ Please Summarize the Concept in Relation to Dream Theory

Martin Dresler, Victor Spoormaker, Renate Wehrle, and Michael Czisch

The rise of modern imaging techniques has endowed neuroscience with a new quality to enquire into cognition and consciousness. In the 1990s, positron emission tomography (PET) was utilised for the first time to address sleep-specific questions and led to intriguing insights into the neural correlates of sleep. While the brain experiences widespread deactivations during slow wave sleep, REM sleep is again associated with increased cerebral blood flow in the thalamus, visual areas and limbic regions as well as attenuated metabolism in the dorsolateral prefrontal cortex (DLPFC), parietal cortex and the precuneus (Maquet et al. 1996, 1997; Braun et al. 1998). Such a pattern of activation has been related to the phenomenology of REM sleep dreaming. Activation of visual association areas is in line with vivid dream imagery, amygdala activation with dream emotionality, and DLPFC deactivation with the lack of insight, reflexivity and volition commonly experienced in dreams (Hobson and Pace-Schott 2002; Nir and Tononi 2009; Desseilles et al. 2011).

In contrast to PET, functional magnetic resonance imaging (fMRI) repeatedly allows non-invasive measurements of neural activity changes with high spatial resolution. However, fMRI faces several technical problems when applied to the study of sleep. While early fMRI sleep studies used behavioural measures to determine if the subject had fallen asleep (e.g. Hong et al. 2009), the development of MR-compatible EEG recording systems allowed us to obtain polysomnography in strong magnetic fields. Improvements in EEG postprocessing techniques have made it possible to substantiate that fMRI data were recorded during verified, unambiguous sleep (Czisch and Wehrle 2010). Consistent with PET findings, fMRI-measured cerebral activity in general decreases throughout NREM sleep as compared to wakefulness (Kaufmann et al. 2006). On the background of this globally decreased cerebral activity, dynamic increases in specific regional activity can be observed. In particular, neural correlates of sleep EEG microprocesses like

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slow-waves (Dang-Vu et al. 2008), K-complexes (Czisch et al. 2009; Jahnke et al. 2012; Caporro et al. 2012), and sleep spindles (Schabus et al. 2007; Andrade et al. 2011; Caporro et al. 2012) have been analysed using fMRI. Fast sleep spindles have been shown to be paralleled by increased neural activity e.g. in the thalamus, cingulate and prefrontal cortex as well as pre- and postcentral gyrus, while slow spindles show a similar, but much weaker activity pattern (Schabus et al. 2007; Andrade et al. 2011). It was further shown that during spindle activity, processing of external acoustic stimuli is suppressed (Schabus et al. 2012), while the functional coupling between the hippocampus and the neocortex is increased (Andrade et al. 2011). These findings may reflect a spindle specific brain state allowing for increased information transfer between brain regions related to memory processes, with external interference being minimized.

External acoustic (Czisch et al. 2002, 2004; Dang-Vu et al. 2008) or visual (Born et al. 2002) perturbations during sleep have been used to characterize arousal reactions, but also sleep stabilizing mechanisms. When acoustic stimuli were continuously applied (for about half a minute) in NREM sleep stage 2, the brain's response showed a deactivation not only in the primarily targeted auditory areas, but nearly throughout the entire cortex (Czisch et al. 2002, 2004). Visual stimuli, on the other hand, led to a deactivation close to the visual cortex in the cuneus (Born et al. 2002). In the case of acoustic stimulation, deactivation was paralleled by an increase of slow EEG frequencies suggesting sleep deepening. Such deactivation may therefore be interpreted as a sleep protective mechanism reducing the processing of perturbing but non-alarming stimuli. Using the presentation of individual tones during light sleep, deactivation of motor cortical regions and the amygdala was confirmed (Czisch et al. 2009). In the latter analysis, it was further shown that whenever a tone presentation evoked a K-complex, the brain was transiently in a state allowing for stimulus processing and engaging cerebral regions typically activated during novelty processing.

Classical neurophysiological studies suggest that during REM sleep, the brain functions as a closed loop system in which activation is triggered in pontine regions while sensory input is gated and motor output is suppressed (Hobson and Pace-Schott 2002). Cortical synthesis of internally generated sensorimotor perceptions was proposed to explain partially coherent narrative dream mentation (Hobson and McCarley 1977). Until recently, the triggering ponto-geniculo-occipital (PGO) waves of this model were traceable in the animal model only. With fMRI, by correlating the appearance of eye movements and BOLD signal fluctuations, it was possible to directly visualise PGO-related activity in human sleep (Wehrle et al. 2005; Miyauchi et al. 2009).

The classical definition of REM sleep relies on the intermittent presence of REMs, which signify transient phasic activations embedded in tonic periods with sustained high-frequency EEG activity and suppression of muscle tone (Rechtschaffen and Kales 1968). Combined fMRI and polysomnography revealed differences in sensory processing and in thalamocortical activity patterns during tonic and phasic REM sleep periods in humans (Wehrle et al. 2007). While acoustic stimulation elicits residual activations of the auditory cortex during tonic REM

sleep, periods containing bursts of phasic REM activity are characterized by a lack of reactivity to sensory stimuli. This difference is mirrored by different arousal thresholds during tonic and phasic REM sleep (Ermis et al. 2010). In addition, a thalamocortical network including limbic and parahippocampal areas is specifically active during phasic REM periods (Wehrle et al. 2007). Thus, REM sleep may have to be subdivided into tonic REM sleep with residual external stimulus processing, and phasic REM sleep with the brain acting as a functionally isolated and closed intrinsic loop. This neural difference might explain why external stimuli are sometimes incorporated into the dream narrative while at other times they are ignored or lead to awakening.

Another important but still under-recognised distinction besides tonic and phasic REM sleep is that between lucid and non-lucid sleep. During lucid dreaming, the sleeping subject becomes aware of his dreaming state, has full access to memory, and is able to volitionally control dreamed actions (LaBerge et al. 1981) while all standard polysomnographic criteria of REM sleep (Rechtschaffen and Kales 1968) are maintained. Lucid dreaming can be trained (LaBerge 1980), which makes this phenomenon a promising research topic despite its rarity in untrained subjects. Although REM sleep muscle atonia prevents overt motor behavior, lucid dreamers are able to communicate their state by predefined volitional eye movements clearly discernable in the electrooculogram (LaBerge et al. 1981). These volitional eye movements can serve as temporal markers, allowing fMRI analysis of lucidly experienced dream content. Dreamed clenching of the left and right hand could thereby be associated with neural activation of the contralateral motor cortices (Dresler et al. 2011).

Comparing lucid and non-lucid REM sleep, Edelman's distinction between primary and secondary or higher-order consciousness is of value, since the contrast between lucid and non-lucid dreaming mirrors the contrast between primary and higher-order consciousness (Dresler et al. 2009; Hobson 2009). In Edelman's (2003) words: "Higher-order consciousness allows its possessors to go beyond the limits of the remembered present of primary consciousness. An individual's past history, future plans, and consciousness of being conscious all become accessible." Lucid dreaming may be critical to fully understanding the neural correlates of higher-order consciousness, because in contrast to coma-wake and sleep-wake comparisons, there is no major shift in vigilance state as defined by formal criteria: lucid REM sleep still is REM sleep proper according to the classical Rechtschaffen and Kales (and new AASM) criteria. Lucid dreaming therefore provides the only phenomenon we know of that can contrast primary consciousness as experienced in dreams with full-blown higher-order consciousness (Dresler et al. 2009; Spooemaker et al. 2010a). Neural correlates of lucid dreaming therefore inform neurobiological approaches of consciousness research by revealing brain regions associated with higher-order consciousness. Quantitative EEG data show that lucid dreaming is related to an activation of the DLPFC (Voss et al. 2009), normally deactivated in REM sleep. fMRI data of lucid dreaming confirm these findings. In addition, the bilateral precuneus, parietal lobules, and occipito-temporal cortices

activated strongly during lucid dreaming as compared to non-lucid REM sleep (Dresler et al. 2011).

A growing body of research has studied the brain in the resting state during wakefulness. One of the described resting state networks, the so-called default mode network, has often been named as a precursor to consciousness. However, as research has shown that this network continues to fluctuate in light sleep, and can even be detected in deep sleep (Sāmān et al. 2011), coma (Boly et al. 2008), or in anesthetized monkeys (Vincent et al. 2007), its role has been redefined to subserve internal mentations associated e.g. with mental imagery, autobiographical memory, future envisioning and mind wandering (Buckner et al. 2008). This interpretation is strengthened by its pattern of anti-correlation with the so-called attention system, subserving external awareness (Fox and Raichle 2007). Interestingly, this anti-correlation disappears in deep sleep (Sāmān et al. 2011). Recently another resting state network, the so-called frontoparietal control system, has been proposed to allow switching between the default mode network and its opposed attention system (Vincent et al. 2008). Due to its proposed role as a kind of meta-network, the fronto-parietal control system might be seen as a prime candidate for underlying processes of metacognition – and therefore the emergence of lucidity in dreams. fMRI data of lucid dreaming indeed show strong overlap with the fronto-parietal control system (Dresler et al. 2012).

More recent network approaches study the sleeping brain with graph-theoretical analyses of EEG-guided fMRI data of sleeping subjects (Spoormaker et al. 2010b; Larson-Prior et al. 2011). It was shown that the capacity of the brain to integrate information (Tononi 2004) is reduced in both light and deep sleep, however through different mechanisms. Large-scale functional brain networks in light sleep stage 1 were characterised by increased cortico-cortical connectivity but exclusion of a critical hub, the bilateral thalamus. In contrast, a breakdown of long-distance cortico-cortical connectivity occurred in deep sleep (Spoormaker et al. 2010b). An increased clustering of local nodes was also observed in deep sleep, illustrating network configuration (a change in ‘small-worldness’) throughout sleep. The thalamus has been identified as a core region of the neural network of (primary) consciousness in a number of studies applying anaesthesia (Alkire and Miller 2005), as it is known to function as a relay station in the neural cascade of (sensory) information processing. Of note, Wehrle et al. (2007) showed an increase in thalamo-cortical networking in phasic REM sleep, which may be interpreted as an indication of increased consciousness underlying the vivid and self-centered scenarios during dreaming. Indeed, prototypical dreaming has been proposed to be bound to phasic REM sleep, while tonic REM sleep rather seems to be associated with dreaming activity qualitatively similar to that of NREM sleep (Molinari and Foulkes 1969).

In conclusion, neuroimaging of sleep is a potent tool in dream research. It can provide us with remarkable insights into mechanisms underlying fluctuating self-awareness and consciousness during sleep, and can even allow us to differentiate specific ‘dream’ contents as shown in lucid dreamers. Today, the application of neuroimaging methods for sleep research is still hampered by the complex

experimental procedure, which makes the collection of larger study samples a tedious process. As a few research groups have shown, these experimental drawbacks can be overcome, and the promise of combined EEG/fMRI is the combination of the high temporal resolution of EEG with the high spatial resolution of fMRI, such that investigations are not limited to cortical surface activity alone. Also due to the development of new analysis approaches, dream imaging is a quickly growing and highly promising field in sleep research that will offer new and deep insights into the dreaming brain.

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