

Insomnia and Emotional Memory

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ABSTRACT

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Insomnia is the second-most prevalent mental disorder and the primary modifiable risk factor for depression, anxiety disorders and PTSD (<u>Blanken et al., 2019</u>). In search of brain mechanisms, circadian and a homeostatic processes seem surprisingly intact. The hyperalert insomniac brain differs strongly from the hardly awake sleep-deprived brain (<u>Wei et al., 2016</u>, <u>Stoffers et al., 2014</u>). Big data psychometrics (<u>sleepregistry.org</u>) showed different insomnia types, all involving distributed deviations in brain circuits underlying stable characteristics of affect (<u>Blanken et al., 2019</u>).

HD-EEG, MRI and animal model studies converge to suggest that the core issue causing insomnia is a deficiency in overnight processing of memories of distressing experiences (Blanken et al., 2019, Wassing et al., 2019). Rapid Eye Movement (REM) sleep plays an important role in the reorganization of emotional memory circuits. Uniquely during the transition to REM sleep, and throughout REM sleep, the Locus Coeruleus (LC) is inhibited (Swift et al., 2018). This time window of low noradrenaline release facilitates synaptic depotentiation (Swift et al., 2018, Vanderheyden et al., 2014). Meanwhile, increased activity occurs in (para)limbic regions including amygdalae and anterior cingulate cortex, which is selectivly activated by the claustrum during REM sleep (Luppi et al., 2017).

However, in insomnia and related mental disorders, abundant EEG arousals during sleep indicate insufficient inhibition of LC activity. Abiding LC activity during sleep abolishes the only noradrenaline-free time window available to the brain including its unique balance between synaptic potentiation and depotentiation during nocturnal replay and

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neuronal network adaptation. We posit that this in particular interferes with overnight processing of emotional distress (Wassing et al., 2019, Wassing et al., 2019), resulting in daytime hyperactivation of salience- and emotional- circuits. This new model of circuits involved in insomnia is supported by GWAS (Jansen et al., 2019): risk genes for insomnia turn out to be expressed in cell types and brain areas identified with neuroimaging, including the claustrum and anterior cingulate cortex that activate during REM sleep (Stoffers et al., 2014, Wassing et al., 2019, Luppi et al., 2017, Altena et al., 2008).

People with insomnia have developed a brain optimally wired to stay alert, at the cost of suffering bad sleep.



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