

# Supporting CDKL5



## **Sleep, Plasticity and the Pathophysiology of Neurodevelopmental Disorders: The Potential Roles of Protein Synthesis and Other Cellular Processes. Brain Sciences 2014.**

This is an interesting review from the US about sleep and its relationship to the development of memory and learning. The “laying down” of memory processes can be categorized into three stages - encoding, consolidation and retrieval, and sleep is clearly more than just having a few zzzzzz's after a good night out! In normal development, sleep appears to be important for the consolidation of various types of memory and therefore can affect the development of learning. Sleep may be particularly important for memory consolidation during the periods of intense learning that occur throughout early development.

The drive for sleep at any point in time is determined by two processes: a circadian process that mainly controls REM sleep and a homeostatic process that is mainly confined to the description of non-REM sleep. There are a number of substances implicated as being sleep regulators, including adenosine, prostaglandins, nitric oxide and cytokines. There are also a number of cellular processes involved and one hypothesis suggests that sleep is required for synaptic pruning – NB) disorders of synaptic pruning have been implicated in neurodevelopmental disorders.

Having reviewed the normal processes of sleep, the authors discuss the disturbance of sleep in neurodevelopmental disorders, pointing out that recent data has revealed that sleep abnormalities are among the most prevalent and common symptoms and may contribute to the progression of these disorders. The authors review a number of neurodevelopmental disorders including Autism, Fragile X Syndrome, Rett syndrome, Prader-Willi and Angelman's Syndrome, where sleep disorders have been reported. They then go on to discuss the cellular consequences of normal and prolonged wakefulness and their effects on plasticity of the brain. The authors also point out that sleep has been thought of as a symptom of a wide variety of psychiatric and neurological disorders and that if the “primary” disorder was treated then the sleep disorder would resolve. However, this view is being replaced with the idea that the disordered sleep is not merely a symptom but that it can also play a role in the progression of the primary disorder. As the authors again point out, cell signaling and cortical connections are often altered in neurodevelopmental disorders so that the effects of any “perturbations” on neurons will be unpredictable. The combination of abnormalities of sleep and the altered brain conditions that are present might therefore lead to “synergistic and deleterious” effects. Finally, the authors note that there are very few sleep-dependent memory studies in patients with neurodevelopmental disorders or studies in any subject group that test whether social skills-learning is sleep-dependent.

Note – Theories around sleep and the disturbance of sleep in relation to memory and learning remain contentious as there appears to be conflicting experimental evidence. However, this is a good review around the subject and although CDKL5 isn't specifically mentioned, we all know how relevant this is to us. A difficult subject to study as there are many forms of memory and learning. The authors point out that more research into sleep disturbance in individuals with neurodevelopmental disorders is needed. Although future therapeutic strategies are discussed, this paper isn't giving us any practical answers yet into how we might deal with sleep disturbance. It is, however, making a very good case that managing and trying to improve sleep patterns should be a priority. There is quite a lot more technical stuff in the review so certainly worth a read.