

## Imaging synaptic plasticity in therapeutic sleep deprivation for major depression (SleepLess)

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Staying awake for a night improves the mood for a lot of patients with depression very quickly. Unfortunately this beneficial effect often only lasts until the next sleep period. There are only a few other options in depression that show such a fast anti-depressive action. If the main players in this mechanism could be clarified, it is likely that this information could be used for novel treatments options or optimizations. A recent model of depression proposes that the connection between neurons (synapse) is strengthened during sleep deprivation which restores a deficit in the depressive brain. A novel brain imaging technique (Positron Emission Tomography (PET) imaging of the synaptic vesicle protein 2A (SV2A)) allows to monitor the amount of synapses in the living brain of humans and animals which suffer from depression.

A major problem in investigating animals inside a scanner is that they usually have to be immobilized, which is usually done by anesthesia. Since both anesthesia and sleep are subject to hamper with the parameter of interest, a stress free PET imaging method for awake animals will be developed.

We are convinced that synaptic density determined with PET has the power to become an indicator for the success of therapeutic sleep deprivation and thus providing means for future stratifications of different therapies in major depression. Identifying and understanding the mechanisms that mediate the effects of sleep restriction is necessary to develop effective interventions. This project will test a model that can be used to improve schedule design.