Results: There was a trend toward increased tau accumulations in patients with late-life depression compared to healthy controls, while levels of Aβ depositions were equally low in patients and controls. Notably, patients with psychotic symptoms exhibited greater tau loads ($p < 0.01$) than those without psychotic symptoms. However, tau depositions were not significantly correlated with any of the clinical symptoms examined here.
Conclusions: The current findings implicate tau pathologies in the pathophysiology of late-life depression with psychotic symptoms, indicating a potential therapeutic approach to this disease based on PET-visible pathologies.
Keywords: TAU PROTEIN, Depression, PET, Late Life Depression, Neuroimaging

951. Changes in Resting-State Global Brain Connectivity in LSD-Induced Altered States of Consciousness are Attributable to the 5-HT2A Receptor

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Background: Lysergic acid diethylamide (LSD) is a prototypical psychedelic drug with agonist activity at various serotonin (5-HT) and dopamine receptors. Despite the therapeutic and scientific interest in LSD, the specific receptor contributions in particular to changes in brain connectivity have not been studied yet.
Methods: In a double-blind, randomized, counterbalanced, cross-over study 24 healthy participants received either 1) placebo+placebo, 2) placebo+LSD (100 μg po), or 3) ketanserin - a selective 5-HT2A receptor antagonist (40 mg po)+LSD (100 μg po) in three different sessions. Resting-state fMRI scans were acquired 75 and 300 minutes after the second substance administration. We analyzed resting-state functional connectivity with a data-driven global brain connectivity (GBC) method to facilitate discovery.
Results: LSD administration caused widespread alterations of GBC across cortical and subcortical regions. LSD decreased GBC in fronto-medial and lateral areas, as well as basal ganglia, but increased GBC in the occipital, temporal, and parietal cortex. Similar patterns were found when comparing LSD with ketanserin+LSD. Negligible differences were observed when comparing ketanserin+LSD and placebo.
Conclusions: Results revealed that LSD induces widespread GBC alterations that are predominantly attributable to its agonistic activity onto the 5-HT2A receptor. While LSD reduces connectivity in attention networks, it increased connectivity across sensory areas. Present results inform psychedelics' mechanism of action pinpointing targets of therapeutic value and reinforce use of data-driven neuroimaging methods for pharmacological imaging.
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Keywords: serotonin 2A receptor, Resting state functional connectivity, BOLD fMRI, Pharmacology

952. Light Therapy Facilitates Thalamo-Cortical Brain Recovery from Mild Traumatic Brain Injury

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Background: Mild traumatic brain injury (mTBI) or "concussion" is often associated with persistent problems with sleep for up to 50% of patients. We hypothesized that regular morning blue light exposure therapy may re-entrain the circadian rhythm and improve sleep, potentially enhancing brain repair and neuropsychological recovery.
Methods: Twenty-eight individuals (15 female; 18-48 years) with a documented mTBI during the preceding 18 months underwent a comprehensive neuropsychological assessment and multimodal neuroimaging. Participants completed 6-weeks of daily morning light exposure (30 min/day) with a light device fitted with blue (n=14) or amber wavelength (placebo; n=14) diodes, and returned for follow-up assessment and imaging.
Results: Blue light exposure led to an earlier bedtime and rise time, lower daytime sleepiness, and improved balance compared to placebo light ($p<.05$). Structural magnetic resonance imaging (MRI) showed that active blue-light treatment was associated with increased volume of the pulvinar nucleus bilaterally ($p<.05$, FWE corrected), while no difference was observed for amber placebo. Blue light was also associated with increased functional connectivity and greater integrity of white matter axonal pathways connecting the pulvinar to parietal regions compared to placebo ($p<.05$, FWE corrected). Changes in functional and structural connectivity correlated with improved neurocognitive performance.
Conclusions: Daily morning exposure to blue-wavelength light for 6-weeks led to improved sleep and associated alterations in thalamo-cortical structure, connectivity, and function compared to amber placebo light exposure. These preliminary findings raise the possibility that blue-light treatment may provide a novel method for improving recovery from some aspects of mTBI.
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Keywords: Light Therapy, Traumatic Brain Injury, MRI, DTI, Functional Connectivity

953. Reciprocal Disruptions in Cortico-thalamic and Hippocampal Connectivity in Youth at Genetic High Risk for Psychosis

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