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NEUROIMAGING AND GENETICS OF ANTIDEPRESSANT RESPONSE TO SLEEP DEPRIVATION: IMPLICATIONS FOR DRUG DEVELOPMENT

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Despite confirmed evidences about some neurochemical effects of antidepressant treatments, there is still an high level of uncertainty about which biological changes are needed to recover from a major depressive episode. Changes of monoaminergic neurotransmission are paralleled by profound changes in brain metabolism, neural responses to stimuli, sleep architecture, biological rhythms, and, at the intracellular level, neuronal signaling pathways regulating gene expression, neuroplasticity, and neurotrophic mechanisms.

Sleep deprivation targets the biological mechanisms which are responsible of the possibility, unique to mood disorders, of rapid switching between depression, euthymia, and mania. The rapidity of action of sleep deprivation enables the study of the correlates of antidepressant response at close time points, providing a good model to study the biological basis of the antidepressant response and of the patophysiology of affective illness.

Current knowledge suggests that multiple neurobiological effects of sleep deprivation are responsible for the clinical mood amelioration, suggesting a multi-target mechanism of action. An impressive group of brain imaging studies using different brain imaging techniques (positron emission tomography, single photon emission tomography, functional magnetic resonance imaging, proton spectroscopy, arterial spin labeling) showed that clinical response is associated with changes in the functioning of specific brain areas. The combination of these new methodological acquisitions with the classical neurobiological and pharmacogenetic perspective provides an evolving knowledge about brain changes associated with antidepressant response, and will then help to identify the real targets of antidepressant treatment.

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