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Light your way up to better mood. How does light help us combat mood disorders?

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Bright light therapy is an efficient therapeutic method commonly used to treat mood-related disorders such as seasonal affective and major depressive disorders. Unfortunately, little is known about the molecular mechanism translating light exposure to positive changes in mood. The circadian clock is likely to be implicated, as light therapy is successfully applied to ameliorate circadian disturbances including jet-lag and sleep disorders. However, the suprachiasmatic nucleus, which is the master circadian pacemaker, was reported not to play a role in light induced mood-improvement. It is therefore prudent to look at other brain regions that receive light signals, one of those being the lateral habenula.

This thesis aims to decipher the molecular basis of bright light therapy and determine whether the lateral habenula is relaying the beneficial effect of light on mood. Using a mouse animal model it was demonstrated that *Per1* knock-out animals were more depressive-like than controls, and failed to positively respond to light treatment at the end of the dark phase in a despair based paradigm. Knowing that PER1 is a core clock component responsible for light resetting, its induction was tested in the lateral habenula. Indeed, this region increased *Per1* mRNA expression after a 30 min light pulse at ZT22, but not ZT14. Likewise, LHb-specific knock-down of *Per1* negatively impacted mood-related behaviour. Comparison of light induced genes in WT animals and *Per1* knock-out animals allowed the characterization of *Per1*'s role in mediating the effects of light treatment in the dopaminergic-mesolimbic system. Furthermore, in the nucleus accumbens, several downstream targets were identified. One of those, the g-coupled orphan receptor 88, was validated also on the behavioural level.

Overall, this research underlines the importance of *Per1* expression and induction in the LHb for mood-regulation. It describes PER1 as a mediator of positive effects of light therapy which inhibits expression of some genes. It also indicates its potential role as a modulator of the dopaminergic system in the nucleus accumbens. Lastly, it identifies downstream light pulse affected targets in the nucleus accumbens and the lateral habenula.

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