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CLOCK GENES AND MOOD DISORDERS: WHICH ROLE?

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The Circadian Locomotor Output Cycles Kaput (CLOCK) gene is thought to be involved in the regulation of circadian rhythms, with its protein products driving transcription of other genetic components of the molecular oscillator. The possible role of 3111T/C CLOCK gene polymorphism and a number of other variants in psychiatry is currently under investigation. A polymorphism in the 3' flanking region of the CLOCK gene have been shown to affect mRNA stability and half-life, with possible significant effects on the level of protein finally being translated. In mice, a mutation of CLOCK gene, called "C" variant, has been shown to lead to a lengthened circadian period and in healthy humans the CLOCK\*C allele has been investigated as a predictor of "eveningness." Finally, a significantly higher recurrence rate of illness episodes has been found in bipolar patients homozygous for the C variant. In a series of studies, we investigated the possible effect of CLOCK variants in mood disorders and drug response.

Taken together, this evidence suggests that CLOCK gene variants modulate mood disorders in a subtle but consistent way, causing liability to a shorter and disrupted sleep, which is reflected in poorer sleep improvement during antidepressant therapy and eventually in a higher frequency of episodes. This also suggests the clinical usefulness of social rhythm therapy particularly in this subgroup of patients.