

P-163 - P2RX7: EXPRESSION RESPONDS TO SLEEP DEPRIVATION AND ASSOCIATES WITH RAPID CYCLING IN BIPOLAR DISORDER TYPE 1

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Introduction: Rapid cycling (RC) is a severe form of bipolar disorder (BD) with an increased rate of episodes. Circadian disturbances are common in BD, and those with RC might be even more vulnerable.

Aims: To investigate if the *P2RX7* gene would be involved in the circadian rhythm and in part thereby be implicated in RC.

Methods: Gene expression was analyzed in peripheral mononuclear cells (PBMCs) from healthy volunteers (n=8) at the sleep research center, University of California, Irvine Medical Center, USA. Swedish outpatients recruited from psychiatric clinics for BD, diagnosed with BD type 1 (n=569; RC: n=121) and anonymous blood donor controls (n=1,044) was investigated in case-case and case-control SNP/haplotype association analyses.

Results: *P2RX7* RNA levels were dramatically increased during sleep deprivation in PBMCs from the healthy volunteers ($p=2.3 \times 10^{-9}$). The *P2RX7* rs 2230912_A allele was more common (OR=2.2, $p=0.002$) and the ACGTTT haplotype in *P2RX7* containing the protective rs2230912_G allele was less common, among RC cases compared to nonRC bipolar patients and blood donor controls.

Conclusions: Sleep deprivation activates *P2RX7* expression in healthy persons which suggests that *P2RX7* is involved in, or downstream, circadian rhythm regulation. The putatively low-activity *P2RX7* rs2230912 allele A variant was associated with RC in BD which supports earlier findings of *P2RX7* associations to affective disorder.