Abstract*:*

Background: Reports of subjective sleep impairments have been replicated in adults with bipolar disorder (BD) and young BD patients. Furthermore, circadian rhythm alterations are a core feature of BD. Despite the impairment in circadian rhythms and altered sleep included in various heuristic developmental models of BD, thus far, biomarkers in population at risk for BD have not been sufficiently objectively validated.
Thus, we conducted: ***a)*** Explorative study of sleep and rest-activity circadian rhythm among offspring of BD parents. ***b)*** Study of sleep and rest-activity circadian rhythm among offspring of BD parents without the presence of psychopathology (except depression and anxiety disorders) based on our exploratory findings.

Methods: ***a)*** 14 days of actigraphic assessment and subjective scales (Pediatric Sleep Questionnaire, PSQ; the Morningness/Eveningness Questionnaire, MEQ; and The General Behavior Inventory Sleep Subscale, GBISS) to assess circadian preference, and to identify sleep impairment symptoms. Psychopathology was assessed using psychiatric interview.
b) ≥ 14 days of actigraphic assessment with advanced methods to assess the chronotype, social jet lag and sleep macrostructure, psychiatric interview and subjective psychometric scales to assess the full psychopathology profile.

Results: ***a)*** We investigated 42 offspring of bipolar parents and 42 sex and age matched controls. Prevalence of sleep disturbance symptoms was higher among OB than controls (headache after waking up, 17.9% vs. 2.4%, p= 0.03; excessive daytime sleepiness, 38.5% vs. 10.0%, p= 0.004; apparent tiredness at wake-up times, 43.6% vs. 15.0%, p= 0.007 and nightmares, 21.6% vs. 2.4%, p= 0.01), but the differences between groups were not significant after adjusting for current psychopathology. OB had higher GBISS total score (parental version, $p < 0.001$; self-assessment, p= 0.07) than the controls. OB had higher preference for eveningness than the controls (p= 0.047). According to the actigraphy, OB had longer sleep onset latency (p= 0.048) than the controls.
b) We investigated sample of child and adolescent OB (n= 43; 21 females; 11.0 ± 3.2 years) and controls (n= 42; 17 females; 11.1 ± 3.4 years) comparable in sex (p=0.4), age (p=0.7), and presence of current mood (p= 0.5) and anxiety (p= 0.6) disorders. The OB had shorter sleep time on free days (p= 0.007; effect size, Cohen´s d= 0.56), lower sleep efficiency on free days (p= 0.01; d= 0.47), lower prolongation of time in bed on free days (p= 0.046; d= 0.41), and lower social jet lag (p=0.04; d=0.5) than the controls. Other differences were found in the subgroup analysis (child OB vs controls; adolescent OB vs controls). A significant association with age, but not with the subsyndromal psychopathology, was found in majority of sleep variables. No significant differences were found in circadian rest-activity rhythm and chronotype. Between study sample overlap was 37% for OB (n=16) and 52% for controls (n=22).

Conclusion: Presence of psychopathology negatively impacts sleep of children and adolescents at risk for BD**.** The decreased physiological catch-up sleep on free days in the unaffected OB, which may indicate a decreased need for sleep in this population and poor sleep quality may represent an endophenotype of BD.

Key words: bipolar disorder, offspring, at risk, circadian rhythm, sleep, trait marker