Factors associated with chronic insomnia in bipolar disorder outpatients

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Aims

Chronic insomnia is a major problem for many bipolar disorder (BD) patients, but causal mechanisms and secondary effects remain poorly understood. We conducted an exploratory, matched case-control study to identify factors associated with chronic insomnia in BD outpatients, focusing especially on inflammatory, HPA axis, metabolic, genetic, and clinical factors.

Aim: Compare clinical, biological, and psychosocial variables in BD outpatients with and without chronic insomnia, but matched on age and gender (I=Insomniacs vs. NI=Non-insomniacs).

Methods

We recruited 44 adult BD outpatients of a private outpatient clinic in Sacramento, California, who were in various stages of treatment and clinical status. Twenty-two of the patients had chronic insomnia (I) treated with daily hypnotic medications for at least 2 months. Each insomniac was pair-matched with a BD patient of the same gender and similar age (+/- 11 years), but without chronic insomnia, to assemble a group of 22 noninsomniac (NI) controls. Data on paired subjects were collected in the same season. Twelve pairs of women and 10 pairs of men participated, with average age of 52.

We collected data on both groups from medical records, biological samples, and questionnaires and used univariate conditional logistic regressions to compare the I group with their matched NI controls. Out of 95 variables tested, we present the variables that were most robustly associated with chronic insomnia (OR>=3 and p<.05).

Variables most strongly associated with chronic insomnia in paired BD
outpatients with (I), and without (NI), chronic insomnia but matched on
and gender: descriptive statistics and odds ratios.

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Variable	l mean +/-SD	Paired I-NI mean+/-SD	OR(CI) ¹	p ²	
Daytime anxiety medication (0=None, 1=As needed, 2=Daily)	.82+/9	.73+/8		.00009*	
Elevated fasting blood sugar (>=100mg/dL: 0=No, 1=Yes)	.32+/5	.32+/5		.02*	
Blood relatives with insomnia (For >= 2 months, 0=No, 1=Yes)	.73+/5	.36+/6	9.0(1-70)	.02*	
Waking cortisol (Saliva 3-day average: mcg/dL)	.15+/09	083+/1	.13(.037)	.002*	
TERT genotype (rs2736100: 0=CC, 1=AC, 2=AA)	1.1+/8	0.71+/9	5.4(1-20)	.002*	
Cortisol diurnal slope (Saliva 3-day average: mcg/dL/hr)	0061 +/006	.0043 +/007	4.6(1-20)	.01*	
TNF-α (Serum 2-week average: pg/mL)	1.1+/2	.13+/2	3.7(1-10)	.01*	
IL-8 (Serum 2-week average: MFI)	12+/-3	1.6+/-3	3.7(.9-20)	.03*	
Night-time rumination (DBAS-10 Item 10: 0-10 scale)	5.8+/-3	2.7+/-4	3.6(1-10)	.007*	

Age and gender group



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Results



These findings in BD patients are consistent with features of chronic insomnia observed in the general population by showing associations between insomnia and being medicated for daytime anxiety, having a family history of insomnia, and experiencing night-time rumination (i.e. out of control racing thoughts at night).

Some of these findings also suggest novel associations with chronic insomnia in BD patients. The association with the TERT A allele raises the question of whether this genotype plays a causal role in insomnia in BD. The associations with elevated fasting blood sugar, two components of the cortisol diurnal rhythm (waking cortisol and cortisol slope), and two cytokines (TNF-α and IL-8) suggest that BD patients with chronic insomnia may be at heightened risk for metabolic dysfunction, HPA axis alterations, and systemic inflammation.

Hypothesis-based research is needed to confirm these associations and elucidate the roles each of these factors may play in the underlying pathophysiology that causes chronic insomnia in BD — or in its secondary effects — in order to to develop more effective preventative measures, assessments, and treatments for BD patients with chronic insomnia.

from the Wald test. ⁵University of California, San Diego **Contact:** bonnie.dixon@ronininstitute.org





Conclusion

Notes: ¹Dashes indicate odds ratios that were indeterminate due to complete separation of the data by outcome group. ²Due to small sample size, p-values are from the likelihood-ratio test. So they don't have the usual relationship with the odds ratio 95% confidence intervals, which are

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