

this, first-degree relatives represent an invaluable population for endophenotype research. In addition, endophenotype-oriented studies of psychiatric disorders are particularly supported by the Research Domains Criteria (RDoC), which has been recently proposed by the National Institute of Mental Health as an alternative to current research approaches.

Finally, the study of first-degree relatives also provides an ideal framework for analysis of the risk/resilience diathesis, considering that their genetic background has been shown to lead to a 10- to 20-fold increased risk of developing BD compared with relatives of healthy individuals. Longitudinal assessments of these individuals through the ages of peak risk of illness onset (15-24 and 45-54 years⁵) are particularly warranted, and should not only allow identification of biomarkers and/or environmental factors associated with resilience to BD, but can also provide predictive measures or pinpoint the most relevant prodromal symptoms for those that will ultimately develop a full-blown psychiatric diagnosis.

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Disclosure

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Psychosis: glia, immunity, and melatonin

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I read with interest the recent article by Duarte et al. reviewing the neurobiological underpinnings of bipolar disorder (BD).¹ Such work is part of a growing body of interest on the role of not only glia, but wider immunity, alterations in psychosis.² This places the regulation of immune responses as an important target in the pathophysiology of schizophrenia and BD. In this context, it should be noted that melatonin plays an important role in the regulation of both immune and glial cell reactivity, including through its autocrine effects, which world-leading work by Markus et al. in Brazil has shown.³

Melatonin is classically associated with night-time release by the pineal gland and thereby with the regulation of the circadian rhythm. However, a plethora of recent data shows that melatonin is synthesized in many, if not all, mitochondria-containing cells.² As such, the genetic associations of melatonin with BD are likely to be linked to changes in a wide array of organs and tissues, including the gut, as well as in glia and immune cell regulation. Likewise, the general decrease in pineal melatonin levels in schizophrenia is likely to represent alterations in central and peripheral sites, as well as in circadian regulation.

Given that melatonin may decrease the levels of metabolic dysregulation induced by mood stabilizers and antipsychotics, its immediate clinical utility in psychosis should be highlighted.

However, the targeting of local melatonin synthesis in glia and immune cells is now a significant pharmaceutical company target. The recent development of alpha-7 nicotinic receptor agonists as cognitive enhancers in schizophrenia, as well as in Alzheimer's disease, may also require the careful regulation of melatonin synthesis, given that melatonin regulates the levels and activity of this nicotinic receptor, again as shown by Markus et al.⁴ The alpha-7 nicotinic receptor is also a significant inhibitor of glial and immune cell reactivity, suggesting that its interaction with levels of melatonin is likely to modulate its clinical utility.

Most general practitioners and psychiatrists have an underappreciation of such wider roles of melatonin, and of its clinical utility across a host of psychiatric and other medical conditions. It is not unlikely that the pathophysiological changes underpinning the data

reviewed by Duarte et al. involve alterations in melatonin pathways.

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Impairments of kleptomania: what are they?

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Kleptomania, also known as compulsive stealing, is a rare disorder that occurs in roughly 0.3-0.6% of the population.¹ It is characterized by repeated failures in resisting impulses to steal items that are not needed for their value or personal use. One of the key aspects of the definition of a psychiatric disorder is that it results in clinically significant harms and/or impairments to the individual or society.² Kleptomania has been associated with a lower quality of life³ and high rates of comorbidity with other psychiatric disorders, including suicidality.⁴ However, it is unknown whether specific domains of functioning are impaired in individuals with kleptomania, other than the legal ramifications associated with shoplifting. In this report, we describe the association between kleptomania severity and psychosocial impairments in individuals diagnosed with kleptomania.

The present research included 37 participants (seven men, 18.92%; 30 women, 81.08%) with a mean age of 35.84 years (standard deviation [SD] = 15.83) who voluntarily sought treatment for kleptomania at the Impulse Control Disorders Outpatient Unit (Ambulatório Integrado dos Transtornos do Impulso, PRO-AMITI) in São Paulo, Brazil, between 2005 and 2015. All patients seeking treatment at this clinic are asked whether they would be willing to participate in research studies. Importantly, they

are clearly informed that treatment will not be contingent upon research participation. Seven patients did not take part in the study. The sample consisted predominantly of Caucasians (n=26; 70.3%). Most of the sample reported being single (n=26; 70.3%). The mean educational attainment was 13.85 years (SD = 4.01) of formal schooling. Just under half of the sample (n=18; 48.6%) reported being employed, with 12 (32.4%) employed full-time and six (16.2%) employed part-time.

Informed consent was obtained from all participants, who were interviewed by a registered psychiatrist specializing in impulse control disorders using a semi-structured clinical interview to confirm a diagnosis of kleptomania. Participants then completed a measure of kleptomania severity using the Portuguese-adapted version of the self-report Kleptomania Symptom Assessment Scale (P-K-SAS).⁵ Items are anchored from 0 to 4, with total scores ranging from 0 to 44. Higher scores indicate greater kleptomania problem severity. Potential harms were assessed with the Portuguese version of the Social Adjustment Scale – Self Report (P-SAS-SR).² The P-SAS-SR assesses seven domains of psychosocial functioning: work, social and leisure, extended family, marital, parental (i.e., children), family unit, and economic condition; the measure is anchored from 1 (normal) to 5 (severe maladjustment), with higher scores indicating greater impairment. Lastly, participants were asked to self-report whether they had incurred legal troubles from shoplifting.

The mean P-K-SAS score of the present sample was 29.97 (SD = 9.12), which is greater than the cutoff score for remission (≤ 11),⁵ suggesting that our sample consisted of severe cases. To test the association between kleptomania severity and psychosocial impairments, we first examined assumptions of normality using the Kolmogorov-Smirnov test on our variables of interest. The results suggested that impairments in work, leisure, parenting, and economic condition violated assumptions of normality. For variables that were normally distributed, we used Pearson's correlation. When normality was violated, we used Spearman's rho, a nonparametric test of correlation, instead. As shown in Table 1, the magnitude of positive correlations between kleptomania severity and the seven domains of psychosocial functioning ranged from small (0.16) to large (0.67). Statistical significance was reached for three areas of functioning, ranging from medium to large correlations. Specifically, kleptomania was associated with impairments in work ($p_{[34]} = 0.43$, $p = 0.012$), leisure ($p_{[35]} = 0.53$, $p = 0.001$), and parenting ($p_{[14]} = 0.64$, $p = 0.014$). No other psychosocial domain reached statistical significance. To test whether the results held when controlling for legal troubles, we conducted partial correlation analyses between P-K-SAS and P-SAS-SR, with legal troubles entered as a covariate. The pattern of results remained the same, suggesting that impairments in work, leisure, and parenting associated with kleptomania were independent of harms incurred from legal troubles.

In conclusion, our results provide preliminary support for the hypothesis that individuals with kleptomania may experience impairments other than legal ramifications. The lack of statistical significance in some of the examined