LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

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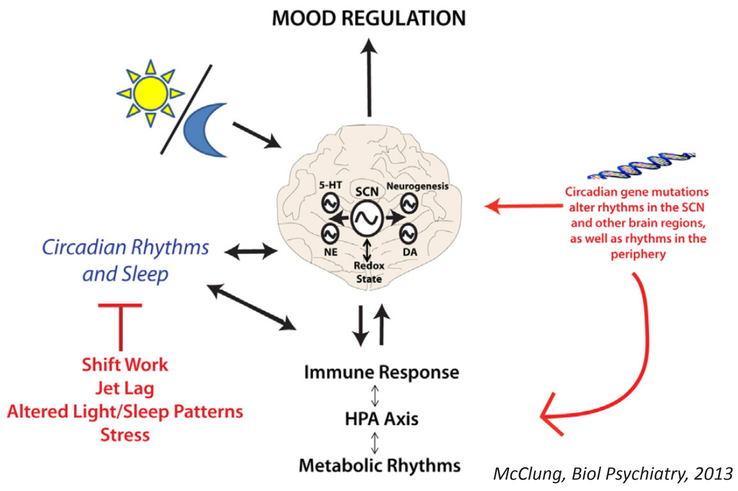
Large-scale resources for the study of circadian aspects in the etiology, course, and outcome in major mental illnesses

Background

Disturbances of the complex chronobiologial regulation have been linked to the etiology of psychiatric illnesess such as major depressive disorder (MDD), bipolar disorder (BDD), and schizophrenia (SCZ) (1, 2). Some circadian genes have been reported associated with these disorders (3, 4). There is a scarcity of research on how circadian mechanisms impact on course and outcome of mental illness beyond increasing the general risk to develop them. A better understanding of the complex interplay between chronobiology and the longitudinal course may, however, open a whole range of new therapeutic strategies.

Circadian aspects of psychiatric symptomatology



McClung, Biol Psychiatry, 2013

ConLi+Gen
The international Consortium on Lithium Genetics

KFO241

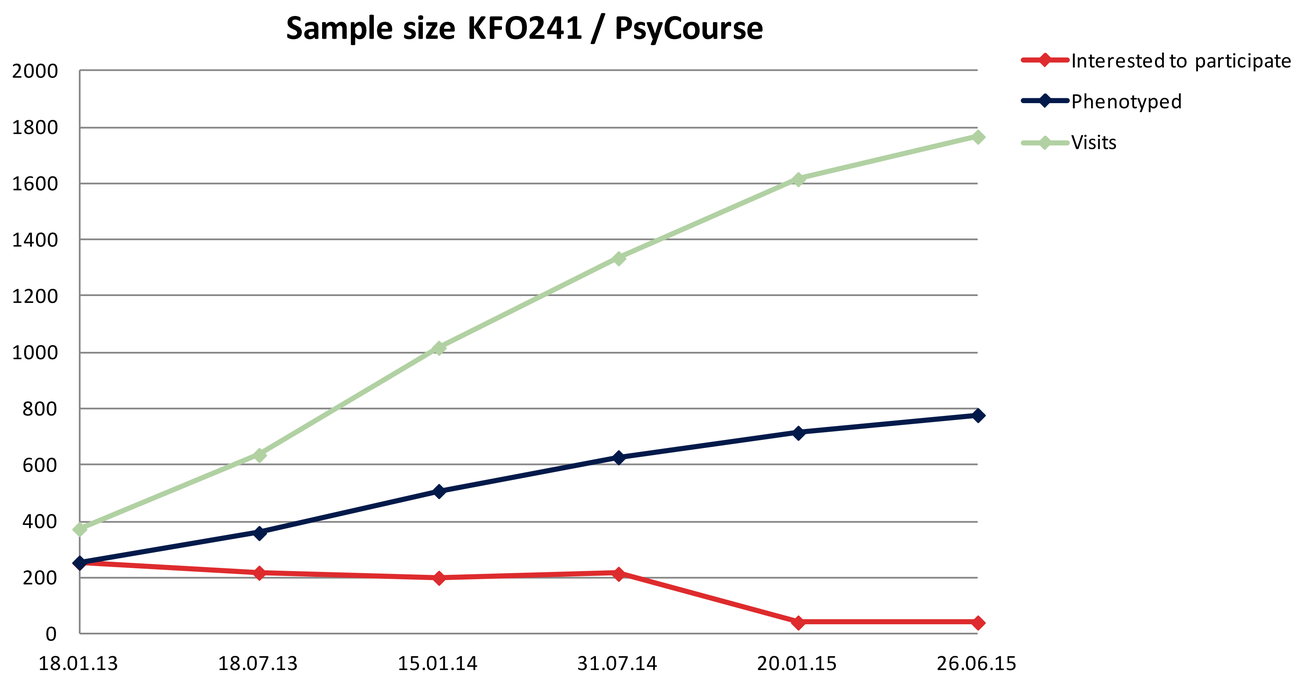
PsyCourse
www.psycourse.de

Available resources

The Institute of Psychiatric Phenomics and Genomics (IPPG) coordinates and participates in large-scale national and international research consortia studying the neurobiology of course and outcome of psychiatric disorder: KFO421 (www.kfo241.de), PsyCourse (www.psycourse.de), ConLiGen (www.conligen.org), and BipoLife (www.bipolife.org). Within KFO421 and PsyCourse, we have been establishing deeply phenotyped longitudinal cohorts of MDD, BD, and SCZ. The combined sample size will be nearing 1,500 patients by the end of 2016. Currently, an additional cohort of control individuals is being established. Within the context of ConLiGen, an international consortium involving expert centers from four continents, we have recruited the largest sample (n > 2,500) ever to study the genetics of lithium response in BD. Within the national network BipoLife, a multicenter project, focusing on improving recognition and care in BD, we are providing the phenotyping and biobanking platforms. This network allows not only for the molecular interrogation of course and outcome of BD but also of the biological underpinnings of response to innovative treatments such as targeted psychotherapeutic interventions or patient self-management via smart phones.

Proposed research

We are planning to investigate the impact of chronotype and circadian genes on course and outcome of major mental illness. We can tap into unique resources comprising comprehensive phenotyping (>2000 variables) and longitudinal biobanking (~20,000 biosamples in KFO and PsyCourse). The ConLiGen resource will in particular help us better understand the effects of lithium on chronobiological regulation. Analyes will include systematic chronotyping of individuals, targeted genetic sequencing of circadian genes, transcriptomic strategies as well as genomewide approaches.



Literature

1. Mansour HA, Wood J, Chowdari KV, Dayal M, Thase ME, Kupfer DJ, et al. Circadian phase variation in bipolar I disorder. Chronobiol Int. 2005;22(3):571-84.
2. McCarthy MJ, Welsh DK. Cellular circadian clocks in mood disorders. J Biol Rhythms. 2012 Oct;27(5):339-52.
3. McCarthy MJ, Nievergelt CM, Kelsoe JR, Welsh DK. A survey of genomic studies supports association of circadian clock genes with bipolar disorder spectrum illnesses and lithium response. PLoS One. 2012;7(2):e32091.
4. Mansour HA, Talkowski ME, Wood J, Chowdari KV, McClain L, Prasad K, et al. Association study of 21 circadian genes with bipolar I disorder, schizoaffective disorder, and schizophrenia. Bipolar Disord. 2009 Nov;11(7):701-10.