Schizophrenia Research 168 (2015) 50–55

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

Circadian rest–activity rhythm in individuals at risk for psychosis and bipolar disorder

Juliana Castro [a,*], Marcio Zanini [b], Bruno da Silva Brandão Gonçalves [c], Fernando Morgadinho Santos Coelho [a,d], Rodrigo Bressan [b], Lia Bittencourt [a], Ary Gadelha [b], Elisa Brietzke [b], Sergio Tufik [a]

[a] Departamento de Psicobiologia, Universidade Federal de Sao Paulo, Sao Paulo, Brazil
[b] PRISMA/PROESQ — Departamento de Psiquiatria, Universidade Federal de Sao Paulo, Sao Paulo, Brazil
[c] Instituto Federal Sudeste de Minas Gerais, Campus Barbacena, Barbacena, Brazil
[d] Departamento de Neurologia e Neurocirurgia, Universidade Federal de Sao Paulo, Sao Paulo, Brazil

ARTICLE INFO

Article history:
Received 31 March 2015
Received in revised form 11 July 2015
Accepted 14 July 2015
Available online 26 July 2015

Keywords:
At-risk mental states
Ultra-high risk
Psychosis
Bipolar disorder
Circadian rhythm
Actigraphy

ABSTRACT

Background: At-risk mental states (ARMS) are clinical syndromes that are associated with higher risk, compared with the general population, for developing psychosis and bipolar disorder. Circadian rhythm misalignments have been proposed to be part of this early phase of the clinical course.
Objective: To compare circadian rhythm of activity and rest changes between ARMS individuals and a healthy control group.
Methods: Forty volunteers of both genders, aged between 13 and 27 years old, participated in this study (n = 20 ARMS group, and n = 20 healthy controls). The ARMS individuals were classified as ultra-high risk for psychosis according to the CAARMS (*Comprehensive Assessment of At-risk Mental State*) or at high risk for bipolar disorder according to criteria proposed by Bechdolf and colleagues. Participants used an actigraph for fifteen days, kept a sleep diary, and completed the Epworth Sleepiness Scale, the Pittsburgh Sleep Quality Index, and a Morningness–Eveningness Questionnaire.
Results: Compared with healthy volunteers, the ARMS group presented worse sleep quality (P = 0.010); longer nap durations (P = 0.038), shorter wake times (P = 0.001), higher total sleep times (P = 0.011), and shorter activity duration (P = 0.021), sleep rhythms were more fragmented, the circadian rest–activity rhythms were less synchronized with the dark–light cycle and had lower amplitudes of motor activity.
Conclusion: The results suggest alterations in the circadian rest–activity rhythms (and likely in sleep–wake cycle patterns) in ARMS individuals compared with healthy controls. It is possible that circadian rhythms of activity and rest changes are one of the prodromal clinical and behavioral expressions of the brain changes that underlie ARMS individuals.

1. Introduction

Schizophrenia and bipolar disorder are psychiatric disorders that together occur in 3% of the population (Kessler et al., 2005; Perala et al., 2007). The putative prodrome and first onset of these disorders occur during adolescence or early adulthood. These periods are critical for normal development characterized by significant neurodevelopment and emotional and cognitive maturation. In parallel, social and educational/vocational achievements and independence are emerging (Rice and Barone, 2000; Steinberg, 2005). Also, the courses of these diseases are often chronic and debilitating (Mathers et al., 2006). Treating these disorders requires the continuous use of psychotropic drugs and complex psychosocial strategies. Moreover, even with the best available treatment, most patients with these conditions remain seriously functionally impaired (Larson et al., 2010).

The recent psychiatric literature has focused, therefore, on studying preventive strategies for these disorders, which could minimize their clinical, family, economic and social impacts (Saraceno, 2002). However, the primary prevention of any disease necessarily implies knowledge of the transition process from a healthy to a disease state so that strategies can be adopted to prevent this change. In the case of major mental disorders, a large body of evidence that began with the classic descriptions by Kraepelin in the nineteenth century indicates the presence of a period lasting from days to years. During these periods, the symptoms of psychosis or mood disorders begin and gradually increase in frequency, intensity and duration until they acquire sufficient functional impact to be considered well-established mental disorders (Angst, 2002). Furthermore, in the prodromal phases, definitive predictions of the clinical expression of the syndromal stage are not possible (Yung et al., 2008). Attenuated positive symptoms occur in the prodromal phases of

* Corresponding author at: Rua Napoleao de Barros, 925 — Vila Clementino, São Paulo, SP 04024-002, Brazil.
E-mail address: juvilela.castro@gmail.com (J. Castro).

http://dx.doi.org/10.1016/j.schres.2015.07.024
0920-9964/

both schizophrenia and bipolar disorder (Angst, 2002; Bechdolf et al., 2010; Yung and McGorry, 1996; Yung and Nelson, 2011), and mood symptoms can also occur in both conditions (Tohen et al., 2003). Such attenuated positive symptoms are compatible with data that support a considerable degree of overlap in the neurobiology and genetic susceptibility for both disorders (Ivleva et al., 2008).

At-risk mental states (ARMS) are clinical syndromes that are associated with higher risk, compared with the general population, for developing psychosis and bipolar disorder. The transition rates from ARMS to full psychosis, in one-year follow-up, range from 15 to 54% (Gee and Cannon, 2011). For bipolar disorder, rates are approximately 24% (Bechdolf et al., 2010). Sampling from different populations may be contributing to the drop in transition rate (McGorry and H.J., 2009). Recently, attempts to prevent the conversion have been made using interventions such as antipsychotics, dietary supplementation with omega-3 and cognitive–behavioral therapy. These interventions have shown promising but still limited and seldom-replicated results (McGorry et al., 2002; Morrison et al., 2004; Ruhrmann et al., 2010). One of the major limitations to improve preventive interventions is the limited knowledge on the biological processes underlying transition to psychosis.

Misaligned circadian patterns are one of the most prominent symptoms of schizophrenia and bipolar disorder (Ancoli-Israel and Roth, 1999; Harvey, 2008; Mansour et al., 2005a, 2005b). Circadian rhythms are regulated by the suprachiasmatic nucleus (SCN), and this regulation is influenced by the light information received by the retina (Moore, 1973; Moore and Eichler, 1972). The SCN also coordinates scheduled release of multiple peptides and hormones (such as melatonin from the pineal gland) (Son et al., 2011). Disturbances in circadian patterns have been reported at initial phases of a psychotic episode or anticipating a manic episode (Brietzke et al., 2012; Ritter et al., 2012; Roybal et al., 2007). Also, they were related to disease neuroprogression (Harvey, 2008). Thus, disruption of circadian rhythms can signal and/or contribute to disease conversion.

Nevertheless, there are few studies that have investigated circadian rhythms in the mental states of risk. In this sense, the objective of this study was to compare the rest–activity rhythms of individuals in mental states of risk for developing psychosis and bipolar disorder with healthy controls.

2. Methods

This study was approved by the Ethics Committee of the Universidade Federal Sao Paulo (CEP 0834/11). Participants and their legal guardians (when required) read and provided written informed consent.

2.1. Participants

Forty volunteers were selected for this study, aged 13 to 27 years, of both genders. Twenty individuals in at-risk mental states risk (ARMS group), and 20 healthy individuals (control group) were matched for gender and age with the ARMS group. The selected age range is that, at least, 85% of psychosis and bipolar disorder cases initiate (Nelson et al., 2013).

2.1.1. At-risk mental state individuals

Subjects were selected among those who were referred to the Program for Recognition and Intervention in Individuals in At-risk Mental States (PRISMA), from the Department of Psychiatry, Universidade Federal de Sao Paulo. PRISMA is a specialized service for assessing and treating individuals in at-risk states. After their diagnoses, the volunteers were referred to the Department of Psychobiology of the Universidade Federal de São Paulo for the study procedures.

- Inclusion criteria for the ARMS group:
  The ARMS individuals comprised two input possibilities: meeting the criteria for ultra-high risk for psychosis as suggested by Yung et al. (2005) or meeting the diagnostic criteria for high risk for

Table 1
At-risk mental state criteria.

Ultra-high risk for psychosis	
Attenuated positive symptoms	Presence of positive symptoms of moderate severity but not clearly psychotic; present more than one time per month, more than 1 h per week in recent years, associated with reduced social and occupational functioning.
Brief intermittent psychotic symptoms	Presence of brief episodes of a full psychotic illness, might involve all of the symptoms of a psychosis (especially delusions and hallucinations).
Trait and state risk factors	Vulnerable family history of psychosis in a 1st-degree relative or a diagnosis of Personality Disorder Schizotypal, associated with a decline in social and occupational functioning.
Bipolar risk	
Sub-threshold mania	At least two consecutive days, not to exceed four days: humor abnormally elevated; expansive or irritable mood accompanied by at least two of the following criteria: (1) inflated self-esteem or grandiosity, (2) decreased need for sleep, (3) more talkative than usual or pressured speech, (4) flights of ideas or subjective experience of quick thinking, (5) distractibility, (6) increase in goal-directed activities or psychomotor agitation.
Depression + cyclothymic features	For at least one week: depressed mood or loss of interest or pleasure, accompanied by at least two of the following criteria: (1) significant weight loss (2) insomnia or hypersomnia nearly every day, (3) psychomotor retardation or agitation, (4) fatigue or loss of energy, (5) feelings of worthlessness or excessive or inappropriate guilt, (6) diminished ability to think or concentrate, (7) recurrent thoughts of death or suicide.
Depression + genetic risk	For at least one week: depressed mood or loss of interest or pleasure accompanied by at least two of the following criteria: (1) significant weight loss (2) insomnia or hypersomnia nearly every day, (3) psychomotor retardation or agitation, (4) fatigue or loss of energy, (5) feelings of worthlessness or excessive or inappropriate guilt, (6) diminished ability to think or concentrate, (7) recurrent thoughts of death or suicide, (8) First-degree relative with BD.