Journal of Neural Transmission (2019) 126:531–558
https://doi.org/10.1007/s00702-019-01993-2

PSYCHIATRY AND PRECLINICAL PSYCHIATRIC STUDIES - REVIEW ARTICLE

Actigraphy studies and clinical and biobehavioural correlates in schizophrenia: a systematic review

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Received: 1 November 2018 / Accepted: 12 March 2019 / Published online: 19 March 2019

Abstract

Actigraphy is a non-invasive method of monitoring circadian rhythms and motor activity. We systematically reviewed extant evidence until September 2018 pertaining to actigraphy use in schizophrenia, its clinical/biological correlates and posit future research directions. Within 38 included studies involving 2700 subjects, patients with schizophrenia generally have lower motor activity levels, poorer sleep quality and efficiency, increased sleep fragmentation and duration compared with healthy controls. Lowered motor activity and longer sleep duration in patients were associated with greater severity of negative symptoms. Less structured motor activity and decreased sleep quality were associated with greater severity of positive symptoms, worse cognitive functioning involving attention and processing speed, illness chronicity, higher antipsychotic dose, and poorer quality of life. Correlations of actigraphic measures with biological factors are sparse with inconclusive results. Future studies with larger sample sets may adopt a multimodal, longitudinal approach which examines both motor and sleep activity, triangulates clinical, actigraphic and biological measures to clarify their inter-relationships and inform risk prediction of illness onset, course, and treatment response over time.

Keywords Actigraphy · Motor · Sleep · Schizophrenia

Introduction

Schizophrenia is a major psychiatric disorder which affects not only the thoughts and cognition, but also the emotions, behaviour, daily functioning, and quality of life of those afflicted (Costa et al. 2018; García et al. 2018; Strassnig et al. 2018). Sleep disturbance is a common symptom associated with the disorder (Chouinard et al. 2004) and can be a significant predisposing, precipitating or perpetuating factor affecting the non-remission or relapse of the illness (Afonso et al. 2014; Reeve et al. 2015; Van Kammen et al. 1986). In addition, positive and negative symptoms experienced in schizophrenia have been associated with motor and sleep activity in schizophrenia (Baandrup and Jennum 2015; Kurebayashi and Otaki 2017; Mulligan et al. 2016; Shin et al. 2016). Hence, there has been continuous interest in better evaluating sleep patterns and motor activity of patients as clinical markers of treatment outcomes and illness course over time (Birkhofer et al. 2013; Walther et al. 2015a, b).

Actigraphy is a non-invasive method of monitoring human rest and activity cycles including circadian rhythms and motor activity trends (Teicher 1995). It can measure a range of sleep-related parameters (for example, total sleep duration, sleep onset latency, wake after sleep onset, sleep efficiency, fragmentation) as well as motor activity variables (for example, activity counts, duration of activity, periods of inactivity, movement index). This facilitates assessment of these different parameters and their relationships with other clinical factors such as phenomenology, personal

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functioning, treatment response, illness trajectory and even biobehavioural markers such as serum and imaging parameters (Docx et al. 2017; Kluge et al. 2018). While most actigraphy monitors are watch-like devices worn on the wrist, some are worn as patches or electrodes on the chest, hip or limbs (Brown et al. 1990).

Since the accelerated use of clinical actigraphy in the 1990s (Brown et al. 1990; Sadeh et al. 1991), its application has been extended to neuropsychiatric disorders including affective disorders, attention deficit hyperactivity disorder (De Crescenzo et al. 2016; Scott et al. 2017; Teicher et al. 1997) and dementia (Khan et al. 2018). Initially, actigraphy has been relatively less applied to the examination of activity patterns in psychotic disorders, as seen in an earlier systematic review of 14 studies (Tahmasian et al. 2013). Since then, there has been increasing efforts to assess these actigraphic measures in the context of schizophrenia, and combining them with other biological and clinical parameters, including treatment.

In view of the clinical importance of better evaluating activity patterns and biobehavioural correlates in schizophrenia, as well as recent advances in this field since the last review of published studies until 2011 (Tahmasian et al. 2013), we conducted a systematic review to synthesise the extant evidence pertaining to the utility of actigraphy in schizophrenia and their clinical and biological correlates. In addition, we posited current limitations and future research implications and directions.

Methods

Literature search

We searched the National Centre of Biotechnology Information (NCBI), Pubmed/Medline and Cochrane databases for empirical studies related to the use of actigraphy in schizophrenia subjects, reported until September 2018. Potentially useful reports were screened as abstracts based on the inclusion criteria listed below. We reviewed promising studies as full reports and screened their bibliographies for additional references. Keywords for the literature search included "schizophrenia", "psychotic", "actigraphy", "actimetry", "activity sensors", either alone or as a combination of terms.

Inclusion/exclusion criteria

Reports were selected for inclusion if: (a) they involved empirical studies adopting actigraphy assessment and involved subjects diagnosed with schizophrenia by standard international criteria such as DSM or ICD; and (b) were in English.

Data extraction

For each individual study, we extracted variables including the number and type of subjects, socio-demographic characteristics, methods of actigraphy evaluation, other clinical or biological measures employed and salient findings.

Data synthesis

The preceding data were organised in digitalised spreadsheets and then summarised in tables to guide preparation of critical assessments included in this study as well as independent consideration by readers. We considered essential findings with respect to assessment of motor and/or sleep activity patterns using actigraphy and clinical and biobehavioural correlates in human subjects diagnosed with schizophrenia.

Results

Retrieved studies

A total of 65 studies were identified in the search of the databases, of which 16 were excluded as they did not meet inclusion criteria. Out of the remaining 49 full-text articles that were eventually assessed for eligibility, 11 were excluded due to reasons as follows: one was an earlier systematic review (Tahmasian et al. 2011), two were case studies (Haug et al. 2000; Wulff et al. 2006), seven did not include relevant patients (Cosgrave et al. 2018; Gonçalves et al. 2016; Kiang et al. 2003; Lunsford-Avery et al. 2015, 2017; Mittal et al. 2013; Reeve et al. 2017), and one did not perform subgroup analyses of schizophrenia patients from among patients with diagnoses of other mental disorders (Baandrup et al. 2016). This resulted in an overall total of 38 empirical studies being included for our synthesis. Figure 1 displays the PRISMA flowchart detailing the selection of relevant publications for inclusion in this review.

The summaries of main findings of the included studies are found in Table 1. Of these included studies, the majority (31 out of 38 studies) were conducted in Europe and USA. Overall, the total number of subjects was 2700, out of which 1803 (66.7%) were patients with schizophrenia, 341 (12.6%) were patients with other psychiatric disorders and 556 (20.6%) were healthy controls. The number of subjects in each study ranged from 11 to 199, with 52.6% ($N = 20$) of the included studies having 50 subjects and below. With the exclusion of two studies which did not provide gender data, 53.8% ($N = 1452$) of the overall subjects were male. The overall mean age of the subjects was 38.4 years, ranging

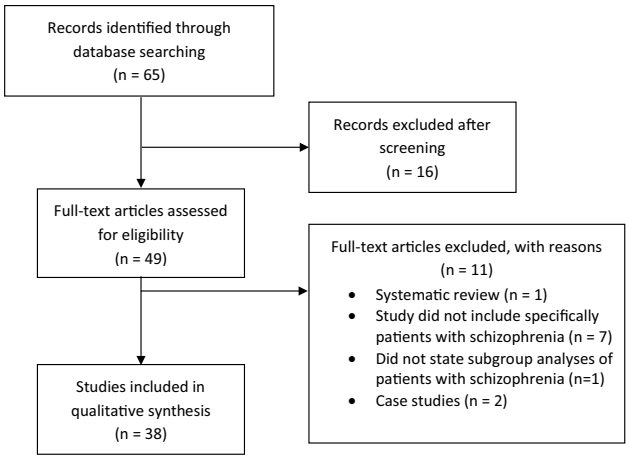

Fig. 1 PRISMA flowchart detailing the process by which empirical studies were included in the systematic review

between 22.5 and 58.3 years. Of the included studies, 24 (63.2%) assessed motor activity, 12 (31.6%) assessed sleep and two (5.3%) assessed both.

Actigraphy in relation to motor activity and sleep parameters

In terms of motor activity, studies using actigraphic motor parameters have generally observed that patients with schizophrenia have a lower total motor activity level compared to healthy controls (Bracht et al. 2012; Fasmer et al. 2016) and patients with depression (Berle et al. 2010). In a study performed by Berle et al. (2010) comparing the motor activity of 23 schizophrenia patients, 23 major depressive patients and 32 healthy controls, the schizophrenia group was found to have higher inter-daily stability and lower intra-daily variability than controls, especially in patients treated with clozapine. This suggests that schizophrenia patients have a more structured and monotonous motor behavioural pattern.

In terms of sleep parameters, patients with schizophrenia tended to have poorer sleep quality and efficiency as well as increased sleep fragmentation and sleep duration compared with healthy controls (Hofstetter et al. 2005; Mulligan et al. 2016; Robillard et al. 2015). A study performed by Robillard et al. (2015) compared measures of sleep–wake and activity–rest patterns among five groups of participants, namely healthy controls and patients with anxiety disorders, unipolar depression, bipolar disorder and psychotic disorders, using actigraphy and sleep diaries. Patients with psychotic disorders were found to have more prolonged sleep and irregular circadian rhythms compared to healthy controls, as well as the most unstable sleep schedules amongst all groups (Robillard et al. 2015).

Afonso et al. (2014) compared the sleep patterns of 34 schizophrenia patients with that of 34 healthy controls. An actimetry sensor was worn for 7 consecutive days while participants carried out their usual activities. Bedtime, wake time, night awakenings and day naps were recorded in a diary to aid researchers in distinguishing sleep from sedentary activities on the sensor-recorded patterns. They found that schizophrenia patients had higher sleep latency, more night awakenings and poorer sleep efficiency. In addition, three patients were found to have advanced sleep-phase syndrome and another three had irregular sleep–wake rhythms.

Actigraphy in relation to clinical correlates (psychopathology, cognition, clinical course, functioning, treatment)

In terms of psychopathology, lower motor activity and longer total sleep time have been associated with greater severity of negative symptoms (Docx et al. 2012, 2013, 2017; Shin et al. 2016; Walther et al. 2009b, 2014; Wichniak et al. 2011) including apathy (Kluge et al. 2018) and avolition (Docx et al. 2013) (see Fig. 2). Conversely, increased (Shin et al. 2016) but less structured motor activity (Walther et al. 2014), and decreased sleep quality (Afonso et al. 2011a, 2014) were associated with greater severity of positive symptoms (see Fig. 3). Walther et al. (2014) used actigraphy to measure mean activity level in counts/min and the Positive and Negative Syndrome Scale (PANSS) to assess symptom severity in 100 subjects with schizophrenia. They analysed the time series of movement counts over 60 min to establish if the amount of movement at one time point would be associated with that of subsequent time points. Reduced number of lags, indicating less structured movement patterns, was found to be associated with higher positive syndrome scores, while higher negative syndrome scores was associated with lower mean motor activity.

Afonso et al. (2014) divided 23 schizophrenia patients into predominantly positive and negative groups and along with actigraphy, used the Pittsburgh Sleep Quality Index to assess sleep patterns. They found that 11 out of the 23 patients studied had irregular sleep–wake cycles with daytime napping and night-time fragmentation. In addition, patients with predominantly positive symptoms had more disrupted sleep–wake patterns compared to the predominant negative symptom group. Poor sleep quality is also predictive of positive psychotic symptoms the following day, such as delusions and hallucinations (Mulligan et al. 2016). Regarding illness subtypes, it has been suggested that lower motor activity differentiated patients with schizophrenia, especially the catatonic subtype (Walther et al. 2009b), from other psychotic spectrum conditions such as cycloid psychosis (Walther et al. 2009a).

Furthermore, decreased motor activity and sleep quality were associated with poorer cognitive functioning involving attention and processing speed (Chen et al. 2016), reduced

Table 1 Summary of main findings of studies employing actigraphy in schizophrenia

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
1	Kluge et al. (2018)	18 (mean age 32.6 ± 9.5, males 72.2%, mean duration of illness 9.8 ± 7.2, 14 schizophrenia patients, 4 patients with schizoaffective disorder)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Motor activity count	Functional magnetic resonance imaging Ecological momentary assessment Brief Negative Symptom Scale Positive and Negative Syndrome Scale Global Assessment of Functioning scale Personal and Social Performance Scale Calgary Depression Scale Modified Simpson–Angus Scale Barnes Akathisia Rating Scale Modified Rogers Scale	Motor activity is negatively associated with interview-based apathy. Interview-based apathy is associated with ventral striatum hypoactivation and decreased motor activity level is associated with inferior frontal gyrus hypoactivation	↓ Motor activity →↑ apathy/↓cortical activation	Only 1 group, no effect size
2	Docx et al. (2017)	20 schizophrenia patients (mean age 32.55 ± 8.21, M:F 18:2, mean duration of illness 9.23 ± 5.46) 16 healthy controls (mean age 30.56 ± 6.73, M:F 13:3)	Actiwatch AW7 (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level (average cumulated activity per hour)	Positive and Negative Syndrome Scale Diffusion kurtosis imaging	Motor activity level in patients was negatively correlated with negative symptoms, but positively correlated with mean kurtosis in the inferior, medial and superior longitudinal fasciculus, the corpus callosum, the posterior fronto-occipital fasciculus and the posterior cingulum, indicating possible altered white matter microstructure in posterior brain regions	↓Motor activity→↑ negative symptoms, diffusion-weighted imaging measures	Activity levels Hedges' $g = -0.909$

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
3	Walther et al. (2017)	46 schizophrenia patients (mean age 38.0 ± 11.5, males 63.0%) 44 healthy controls (mean age 38.8 ± 13.6, males 59.1%)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level (movement counts/h) for all non-sleep periods	Magnetic resonance imaging (3T scanner) to acquire resting state functional MRI Bush Francis Catatonia Rating Scale (BFCRS) Modified Rogers Scale (MRS) Unified Parkinson's disease rating scale (UPDRS) motor part and MRS Abnormal involuntary movement scale (AIMS) Neurological evaluation scale (NES) Finger tapping task	Patients had increased functional connectivity in associations between left M1 with thalamus and cerebellum as compared to controls Altered resting state functional connectively was associated with motor abnormalities at the behavioural level	↑ Functional connectivity abnormalities→↑motor abnormalities	Activity levels Cohen's $d = -0.804$
4	Chen et al. (2016)	199 schizophrenia patients (mean age 44.0 ± 9.9, males 61.3%, duration of illness 23.8 ± 6.5) 60 healthy controls (mean age 41.1 ± 9.6, males 56.7%)	wActiSleep-BT ActiGraph (Pensacola, FL, USA)	Light physical activity, min/day (LPA), moderate–vigorous physical activity, min/day (MVPA)	Vienna Test System Cognitrone test (attention and concentration) Grooved Pegboard Test (manual dexterity, upper-limb motor speed, hand–eye coordination, processing speed) Positive and Negative Syndrome Scale (PANSS)	Patient group was less physically active and had poorer attention/concentration and processing speed. Patients who recorded higher levels of light physical activity had better improved cognition than those with more moderate–vigorous physical activity	↓Motor activity→↑ cognition	LPA Cohen's $d = -4.15$ MVPA Cohen's $d = -0.933$

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
5	Fang et al. (2016)	199 schizophrenia patients (mean age: 44.0 ± 9.9, mean duration of illness 23.8 ± 6.5) 60 healthy controls (mean age 41.1 ± 9.6, males 56.7%)	wActiSleep-BT ActiGraph (Pensacola, FL, USA)	Total sleep time Sleep efficiency Sleep onset latency Total activity counts Wake after sleep onset Number of awakenings Average length of awakening	Venous blood sampling: white blood cell concentration, neutrophil concentration, neutrophil–lymphocyte ratio (NLR), platelet–lymphocyte ratio (PLR) Positive and Negative Syndrome Scales Sleep log	Sleep quality is negatively associated with inflammatory marker counts	↓Sleep quality→↑ inflammatory state	Physical activity Cohen's $d = 0.362$ Sleep quality/efficiency Cohen's $d = 0.510$
6	Fasmer et al. (2016)	24 schizophrenia patients (mean age 46.77 ± 10.9, males 87.5%) 23 patients with mood disorders (mean age 42.87 ± 11.0, males 56.5%) 29 healthy controls (mean age 37.87 ± 13.3, males 37.9%)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity count, proportional to intensity of movement Mean activity count Mean duration for active and inactive periods Longest active and inactive period	Montgomery–Asberg Depression Rating Scale	Patient group had highest duration of inactive periods, but had less disturbed distribution of active and inactive periods compared to depression group	Motor inactivity: SZ > depression	Motor inactivity (SZ vs. depression) Cohen's $d = 1.02$

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
7	Mulligan et al. (2016)	22 schizophrenia/schizophreniform disorder/schizoaffective disorder/delusional disorder/psychotic disorder not otherwise specified/nonaffective psychosis (mean age 37.4 ± 10.4, males 59.1%, mean duration of illness 12 ± 6.2)	PRO-Diary (CamNtech Ltd., Cambridge, UK)	Sleep efficiency (%) Sleep fragmentation: index of time spent mobile during sleep period Total sleep time	Consensus Sleep Diary Experience Sampling Methodology Measures Positive and Negative Syndrome Scale Psychotic Symptom Rating Scale Calgary Depression Scale Drug Abuse Screening Test Alcohol Use Disorders Identification Test Personal and Social Performance Scale Insomnia Severity Index Brief Screen for Sleep Disorders	Increased sleep fragmentation and reduced subjective and objective sleep efficiency predicted greater next-day auditory hallucinations. Increased objective sleep fragmentation and reduced subjective sleep quality predicted greater paranoia and delusions of control. Sleep discontinuity and perceptions of sleep quality are more important than sleep duration in prediction of next-day symptoms	↓Sleep quality→↑ positive symptoms	NA
8	Shin et al. (2016)	61 chronic schizophrenia patients (mean age 46.59, males 57.4%, duration of illness 21.75 ± 7.91)	Mobile health device Fitbit flex® (Fitbit, San Francisco, USA)	Quantitative physical activity (steps/day)	Positive and Negative Syndrome ScaleSimpson–Angus Scale	Amount of physical activity was positively associated with severity of both positive and negative symptoms of schizophrenia	↑Motor activity→↑ psychotic symptoms	Only 1 group, no effect size
9	Baandrup and Jennum, (2015)	42 (mean age 46.17 ± 9.5, males 59.5%, mean duration of schizophrenia 21.07 ± 10.7, 37 schizophrenia/schizoaffective disorder, 5 bipolar disorder)	Actiwatch Spectrum (Philips Respironics, Murrysville, PA, USA)	Total sleep duration (mins) Sleep efficiency (%) Sleep latency (mins) Number of awakenings Duration of wakefulness after sleep onset (mins)	Polysomnography Sleep log	Actigraphy is a reliable measure of total sleep time in patients with severe mental illness which can also be measured by polysomnography		NA

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
10	Janney et al. (2015)	46 schizophrenia/schizoaffective patients (mean age 45.6 ± 9.8, males 37%)	ActiGraph AM-7164 (Florida)	Total activity level (min/day) Total daily sedentary behaviour	Modifiable Activity Questionnaire	Patients who are overweight or obese are sedentary for an average of 13 h a day and carry out low-intensity, intermittent and unstructured motor activity	↓Motor activity →↑ BMI	Sedentary min/day (patients vs. non-users of mental health services) Cohen's $d = 1.59$ Total activity level (patients vs. non-users of mental health services) Cohen's $d = -2.17$
11	Osipov et al. (2015)	16 schizophrenia patients (mean age 45.17 ± 12.3, males 58%, mean duration of illness 6.47 ± 3.4) 19 healthy controls (mean age 51.77 ± 8.8, males 75%)	Adhesive patch (Proteus Biomedical, CA)	ECG-derived mean heart rate Motor activity (mean acceleration on 15 s interval)		Low locomotor activity and high mean heart rate predictive for patient group	SZ: ↓motor activity/↑heart rate	Locomotor activity Hedges' $g = -1.27$ Heart rate Hedges' $g = 0.686$
12	Robillard et al. (2015)	30 psychotic disorders (mean age 22.5 ± 5.1, males 66.7%) 56 anxiety disorders (mean age 20.4 ± 5.1, males 51.8%) 135 unipolar depression (mean age 20.0 ± 4.4, males 34.8%) 80 bipolar disorder group (mean age 23.1 ± 5.3, males 25.0%) 41 healthy controls (mean age 25.3 ± 5.8, males 46.3%)	Actiwatch-64/L/2 (Philips Respironics, Murrysville, PA, USA)	Sleep onset/offset (time points when participants fell asleep and woke up, mean timing of onset/offset episode) Sleep period (total length of the sleep episode, time btw onset and offset) Total sleep time Wake after sleep onset (WASO) Sleep efficiency	Sleep diary	Psychosis group was associated with prolonged sleep duration and unstable sleep schedules, while anxiety, depression and bipolar groups were associated with sleep initiation difficulties and poor/unstable sleep consolidation	↑ Sleep duration predictive of psychosis	Total sleep time (psychosis vs. controls) Cohen's d = 0.608

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
13	Walther et al. (2015a)	43 schizophrenia patients in within-episodes sample/"acute/stabilisation phase" (mean age 36.9 ± 9.5, M:F 28:15, mean duration of illness 11.1 ± 10.7) 18 schizophrenia patients in between-episodes sample/"stable phase" (mean age 34.7 ± 10.5, M:F 13:5, mean duration of illness 8.7 ± 8.0)	Actiwatch AW7 (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level (counts/h)	Positive and Negative Syndrome Scale	Within-episode motor activity decreases with increasing negative syndrome scores and hence constitutes a "state characteristic" of spontaneous motor activity in schizophrenia. Between-episode motor activity remains stable and hence constitutes a "trait characteristic"	Illness course: trait (stable motor activity) versus state feature (↓motor activity→↑negative symptoms)	Activity level (within episodes; pre- vs. post-stabilisation) Hedges' *g* average: 0.0243 Activity level (between episodes; index vs. later episode) Hedges' *g* average: 0.202
14	Walther et al. (2015b)	33 first episode schizophrenia patients (mean age 31.9 ± 12.5, males 61%, duration of illness 1.7 ± 3.2) 115 multiple episode schizophrenia patients (mean age 39.6 ± 11.2, males 57%, duration of illness 12.7 ± 10.2)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level (counts/h)	Positive and Negative Syndrome Scale	Illness chronicity is negatively associated with physical activity levels in patients. Activity level is negatively associated with antipsychotic medication dose for first episode patients, does not differ with antipsychotic type	↓Motor activity→↑illness chronicity and ↑antipsychotic dose	Activity level (multiple episodes vs. first episode patients) Cohen's $d = -0.550$

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
15	Afonso et al. (2014)	34 schizophrenia patients (mean age 33.82 ± 8.30, males 64.7%, duration of illness 11.85 ± 8.52) 34 healthy controls (mean age 34.74 ± 8.60, males 55.9%)	SOMNOwatch	Sleep latency Sleep onset	Positive and Negative Syndrome Scale Pittsburgh Sleep Quality Index WHO Quality of Life Measure (Abbreviated, Portuguese version)	Patients have poorer objective sleep quality (lower sleep efficiency, higher sleep latency and more night-time awakenings), subjective sleep quality, more disturbed sleep–wake patterns (advanced sleep-phase syndrome and irregular sleep–wake rhythm) and reduced quality of life vs. healthy controls	↓Sleep quality→↓quality of life	Sleep efficiency Cohen's $d = -0.737$ Sleep latency Cohen's $d = 1.06$ Night-time awakenings Cohen's $d = 0.876$
16	Walther et al. (2014)	100 schizophrenia patients (mean age 39.2 ± 11.1, males 57%, duration of illness 10.5 ± 9.9)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Mean activity level (counts per 2 s)	Positive and Negative Syndrome Scale	PANSS positive syndrome scores can be predicted by fewer number of lags (i.e. less structured movement patterns) while PANSS negative syndrome scores can be predicted by low mean motor activity	↓Motor activity→↑positive and negative symptoms	Only 1 group, no effect size

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
17	Bracht et al. (2013)	21 schizophrenia patients (mean age 34.2 ± 8.2, males 61.9%, duration of illness 8.07 ± 9.6) 21 healthy controls (mean age 34.6 ± 8.2, males 61.9%)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level during wake (cumulated counts/h)	Magnetic resonance imaging (3T-MR scanner) with diffusion tensor imaging (fractional anisotropy, mean-mean diffusivity) Probabilistic fibre tracking was adopted to investigate pathways connecting the dorsolateral prefrontal cortex (dlPFC), the rostral anterior cingulate cortex (rACC), the pre-supplementary motor area (pre-SMA), the supplementary motor area proper (SMA-proper), the primary motor cortex (M1) and subcortical foci Positive and Negative Syndrome Scale Sleep log (sleep timing, duration)	Patients had lower activity levels than controls. Higher probability indices in pathways connecting rACC, pre-SMA and SMA-proper as well as in pathways connecting M1 and pre-SMA with caudate nucleus, putamen, pallidum and thalamus and a reduced spatial extension of motor pathways in schizophrenia	Diffusion imaging measures	Activity level Cohen's $d = -1.11$
18	Docx et al. (2013)	27 schizophrenia (mean age 32.48 ± 7.94, M:F 24:3) 22 healthy controls (mean age 30.04 ± 5.88, M:F 19:3)	Actiwatch AW7 (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level (average cumulated activity per hour)	Positive and Negative Syndrome Scale St. Hans Rating Scale Salpêtrière Retardation Rating Scale Neurological Evaluation Scale Finger Tapping Test Purdue Pegboard Test Line Copying Task (LCT)	Low activity levels in schizophrenia are associated with negative symptom severity including avolition and clinically assessed psychomotor slowing	↓Motor activity →↑ negative symptoms	Activity level Cohen's $d = -0.941$

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
19	Bracht et al. (2012)	106 schizophrenia/schizophreniform disorder patients (mean age 37.72 ± 11.00, males 52.8%, mean duration of illness 9.08 ± 9.19)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level (mean counts/hr) Movement index Mean duration of uninterrupted immobility periods	Bern Psychopathology Scale Sleep log	Compared with objective actigraphic measures of motor activity, Bern Psychopathology Scale's global scale motor behaviour score, motor behaviour domain's quantitative and subjective ratings have shown good external validity for assessment of motor behaviour in schizophrenia patients		Only 1 group, no effect size
20	Le Seac'h et al. (2012)	27 schizophrenia patients (mean age 30.1 ± 6.9, mean duration of illness 7.1 ± 5.2) 15 healthy controls (mean age 28.2 ± 5.9)	Inertia sensors (Xsens sensors MTx)	Movement at 50 Hz of: 3D linear accelerations] Rate of turn in roll, pitch and yaw	Neurological Soft Signs Examination (Romberg, standing heel-to-toe balance, alternative movements of foot and hand) Diagnostic Interview for Genetic Studies Positive and Negative Syndrome Scale Simpson–Angus Scale Abnormal Involuntary Movement Scale Abnormal Involuntary Movement Scale Edinburgh Inventory and Handedness score Mini-Mental State Examination	Patients had higher Neurological Soft Signs Examination scores, with significant difference in balance task outcomes using inertia sensors vs. healthy controls. Inertial sensors can potentially quantify motor impairments in patients with schizophrenia, especially for subtle dysfunction in early-onset or high-risk cases	Neurological Soft Signs	NA

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
21	Sano et al. (2012)	19 schizophrenia (mean age 38.5 ± 8.4, males 47.4%) 11 healthy controls (mean age 36.4 ± 12.7, males 45.5%)	Mini-Motionlogger (Ambulatory Monitoring, Inc., Ardsley, NY)	Activity level (counts/min)	Positive and Negative Syndrome Scale Five-factor Model for PANSS items Drug-Induced Extrapyramidal Symptoms Scale	Patients had intermittent bursts in activity counts with more episodes of slowing down/cessation of movement, and enhanced persistency of locomotor activity once initiated vs. controls		Activity level Hedges' $g = -0.085$
22	Afonso et al. (2011a)	11 Schizophrenia patients with predominant positive symptoms (mean age 37.2 ± 10.2, males 81.8%, duration of illness 13.4 ± 8.7) 12 Schizophrenia patients with predominant negative symptoms (mean age 39.8 ± 9.7, males 83.3%, duration of illness 15.6 ± 9.4)	SOMNOwatch	Movement index Activity level (counts/hour) Mean duration(s) of uninterrupted immobility Sleep latency Sleep onset (by light sensor and 5-min immobility criterion)	Positive and Negative Syndrome Scale Pittsburgh Sleep Quality Index WHO Quality of Life Measure (Abbreviated, Portuguese version) Sleep diary (sleep and wake timings, night-time awakenings, day naps)	Half of the patients had sleep–wake cycle irregularity (day napping, night fragmentation). Positive symptom group had more disrupted sleep–wake patterns, poorer subjective sleep quality and quality of life than negative symptom group. Worse self-reported quality of life was associated with poorer sleep quality	↓Sleep quality →↑ positive vs. negative symptoms, ↓ quality of life	NA

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
23	Afonso et al. (2011b)	34 schizophrenia: patients (mean age 33.82 ± 8.30, males 64.7%) 34 healthy controls (mean age 34.74 ± 8.60, males 55.9%)	SOMNOwatch	Sleep latency Sleep onset (by light sensor and 5-min immobility criterion)	Salivary Melatonin Assays (nocturnal melatonin levels) Positive and Negative Syndrome Scale Pittsburgh Sleep Quality Index Sleep diary (sleep and wake timings, night-time awakenings, day naps)	Sleep latency and night-time awakenings were significantly higher in patients. Melatonin levels were negatively correlated with sleep latency, total sleep time and positively correlated with sleep efficiency in controls but not in patients, suggesting that melatonin sleep-promoting action seems to be compromised in schizophrenia	Melatonin levels	Sleep latency Cohen's $d = 1.06$ Night-time awakenings Cohen's $d = 0.876$
24	Birkhofer et al. 2013	20 unmedicated schizophrenia patients (mean age 38 ± 11.1, males 55%, duration of illness 3 median 5.5) 20 medicated schizophrenia patients (mean age 33 ± 9.3, males 55%, duration of illness 3.2 median 5.0)	Actometer (Gefatec, Berlin, Germany)	4 h daytime ECG 4 h night-time ECG	ECG 24-h Holter monitors (Reynolds Medical, Hertford UK) Brief Psychiatric Rating Scale Eppendorf Schizophrenia Inventory Beck Depression Inventory State-Trait Anxiety Inventory Clinical Global Impression Scale	Significantly reduced deceleration capacity at night in medicated vs. non-medicated schizophrenia patients	Medication treatment	NA

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
25	Bromundt et al. (2011)	14 schizophrenia patients (mean age 39.9 ± 9.6, males 92.9%, mean duration of illness 14.2 ± 10.9)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Total daily activity level (counts/hour) Rest–activity cycles (relative amplitude, inter-daily stability index, intra-daily variability)	Neuropsychological tests Trail Making Test Stroop colour–word interference task Supermarket-test Structured Clinical Interview for Positive and Negative Syndrome Scale Brief Psychiatric Rating Scale Clinical Global Impression Scale Simpson–Angus Scale Sleep–wake log Salivary Melatonin Assays (nocturnal melatonin levels)	Normal rest–activity cycles correlated with significantly better frontal lobe function and prefrontal cortex function is significantly affected by lack of sleep. Positive and negative symptoms were not significantly associated with circadian rhythm quality or cognitive performance	↓ Circadian rhythm quality →↓ frontal lobe function	Only 1 group, no effect size
26	Walther et al. (2011a)	11 schizophrenia patients (mean age 35.36 ± 12.54, males 74%, mean duration of illness 8.93 ± 13.29) 14 healthy controls (mean age 31.71 ± 6.08, males 57%)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Average amount of movement per hour	Positive and Negative Syndrome Scale Simpson–Angus Scale Modified Rogers Scale Northoff Catatonia Scale Structural magnetic resonance imaging, arterial spin labelling	Patients had reduced activity levels and perfusion of the left parahippocampal gyrus, left middle temporal gyrus, right thalamus, and right prefrontal cortex. Positive correlations of cerebral blood flow and motor activity were found in bilateral prefrontal areas and in the right rostral cingulate motor area (rCMA) in patients	↓ Motor activity →↓ cerebral perfusion of temporal, thalamic, frontal regions	Activity level Hedges' $g = -0.978$

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
27	Walther et al. (2011b)	19 schizophrenia patients (mean age 33.2 ± 11.1, males 63.2%, mean duration of illness 7.5 ± 10.4) 24 healthy Controls (mean age 33.7 ± 10.6, males 45.8%)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Cumulated activity counts during wake divided by net of recording time in hours	Sleep log Positive and Negative Syndrome Scale Simpson–Angus Scale Diffusion tensor imaging	Schizophrenia patients had lower activity levels and lower fractional anisotropy (FA) values in prefrontal and left temporal clusters. Linear negative associations found between FA and activity level underneath right supplementary motor area, right precentral gyrus and posterior cingulum in patients but not controls	Diffusion tensor imaging measures	Activity levels Hedges' $g = -1.01$

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
28	Wichniak et al. (2011)	73 schizophrenia/schizophreniform disorder (mean age 29.2 ± 10.2, males 63%, mean age of onset 23.5 ± 5.1) 36 healthy Controls (mean age 30.1 ± 10.4, males 58.3%)	Actiwatch AW4 (Cambridge Neurotechnology, Inc., Cambridge, UK)	Total sleep duration (mins) Sleep latency (mins) Sleep efficiency (%)	Positive and Negative Syndrome Scale Calgary Depression Rating Scale for Schizophrenia Udvalg for Kliniske Undersogelser Side Effect Rating Scale Barnes Akathisia Scale Athens Insomnia Scale Epworth Sleepiness Scale	Patients had lower mean 24-h activity, mean 10-h daytime activity and longer time in bed and total sleep time than healthy controls. Higher Positive and Negative Syndrome Scale scores (especially negative symptoms) related to lower activity. Higher depressive symptoms related to lower mean 24-h activity, longer time in bed, higher Athens Insomnia Scale score and higher Epworth Sleepiness Scale score	↓ Motor activity → ↑ negative and depressive symptoms	NA

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
29	Berle et al. (2010)	23 schizophrenia patients (mean age 46.7 ± 10.9, males 87%, mean age of first hospitalisation 24.4 ± 9.3) 23 major depressive disorder patients (mean age 42.8 ± 11.0, males 57%) 32 healthy controls (mean age 38.2 ± 13.0, males 37.5%)	Actiwatch AW7 (Cambridge Neurotechnology, Inc., Cambridge, UK)	Total activity counts Night-time activity counts	Brief Psychiatric Rating Scale Montgomery–Asberg Depression Rating Scale	Lower total motor activity in schizophrenia and depression group. More pronounced reduction in night-time activity in schizophrenia vs. depression. Schizophrenia group (especially clozapine-treated patients) had higher inter-daily stability and lower intra-daily variability than controls reflecting more structured/monotonous behavioural patterns	↓ Motor activity: SZ > depressed	Activity level (SZ vs. dep) Cohen's $d = -0.463$ Night-time activity (SZ vs. dep) Cohen's $d = -0.708$
30	Manoach et al. (2010)	15 schizophrenia patients (mean age 41 ± 7, M:F 11:3, mean duration of illness 16 ± 8) 15 healthy controls (mean age 42 ± 6, M:F 11:4)	Mini-Mitter Actiwatch-64 (Mini-Mitter Company, Inc., Bend, OR)	Wrist movement in 15-s epochs Sleep and nap time (based on wrist immobility)	Finger tapping motor sequence test (MST) Stanford Sleepiness Scale (SSS) Polysomnography (Embla A10 ambulatory monitor)	Patients showed significant reductions in fast sigma frequency power and in spindle density during S2q4 sleep at the electrode proximal to the motor cortex controlling the hand that performed the MST		Spindle density S2q4 Hedges' $g = -0.750$

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
31	Walther et al. (2009a)	16 paranoid schizophrenia (mean age 31.63 ± 9.05, males 50%, mean duration of illness 7.31 ± 6.12) 16 cycloid psychosis (mean age 31.00 ± 9.67, males 43.8%, mean duration of illness 1.62 ± 2.75)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level (mean no. of activity counts/h) Movement Index (% epochs with activity count > 0, i.e. true activity) Mean Duration of Uninterrupted Immobility Periods (global measure of immobility epochs)	Sleep log Positive and Negative Syndrome Scale	Cycloid psychosis group had higher motor activity levels than paranoid schizophrenia group. Female gender was also associated with fewer active periods	↓ Motor activity → clinical subtype (schizophrenia) and Gender (female)	Motor activity (cycloid vs. paranoid SZ) Hedges' $g = 0.810$
32	Walther et al. (2009b)	35 paranoid schizophrenia (mean age 39.60 ± 9.64, males 51.4%, mean duration of illness 10.97 ± 8.84) 12 catatonic schizophrenia (mean age 45.50 ± 12.19, males 50.0%, mean duration of illness 6.34 ± 5.70) 13 disorganised schizophrenia (mean age 36.23 ± 10.26, males 69.2%, mean duration of illness 14.85 ± 10.50)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level (mean no. of activity counts/h) Movement Index (% epochs with activity count > 0, i.e. true activity) Mean Duration of Uninterrupted Immobility Periods (global measure of immobility epochs)	Positive and Negative Syndrome Scale	Catatonic schizophrenia had lower activity levels, lower movement index and a longer duration of immobility than those with paranoid schizophrenia	↓ Motor activity → clinical subtype (catatonic SZ)	NA

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
33	Walther et al. (2009c)	55 schizophrenia patients (mean age 38.82 ± 11.05, males 60%, mean duration of illness 10.86 ± 9.01)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Activity level (mean no. of activity counts/h) Movement Index (% epochs with activity count > 0, i.e. true activity) Mean Duration of Uninterrupted Immobility Periods (global measure of immobility epochs) Maximum activity in 2 s Maximum immobility duration	Positive and Negative Syndrome Scale	High PANSS negative syndrome subscale scores predicted low activity levels	↓Motor activity → ↑ negative symptoms	Only 1 group, no effect size
34	Farrow et al. (2005)	16 schizophrenia patients (mean age 36 ± 8, males 100%, mean duration of illness 14 ± 8)	Actiwatch (Cambridge Neurotechnology, Inc., Cambridge, UK)	Actiwatch reading over 24 h	Structural magnetic resonance imaging (1.5 T System, Eclipse, Philips Medical Systems, Ohio, USA)	Total activity was positively correlated with volume of left anterior cingulate cortex	Volume of left anterior cingulate cortex	Only 1 group, no effect size
35	Hofstetter et al. 2005	29 schizophrenia patients (mean age 48+/-7, M:F 27:2, mean age at first hospitalisation 25 ± 9)	Model # 24.000 (Ambulatory Monitoring, Inc., Ardsley, NY)	Sleep duration Sleep proportion Number of long awake episodes Mean sleep episode Longest sleep episode	Pittsburgh Sleep Quality Index (PSQI) Ways of Coping Questionnaire Quality of Life Scale (QLS) Positive and Negative Syndrome Scale	Poor sleep quality predicted low quality of life and reduced preference for employing positive reappraisal when facing a stressor	↓Sleep quality → ↓ quality of life, ↓ positive cognitive appraisal	Only 1 group, no effect size

Table 1 (continued)

	Studies (year)	Demographics (age, % males, diagnosis, duration of illness)	Actigraph model	Actigraphy-assessed parameters	Other assessment tools	Main findings	Clinical/biological correlates with actigraphy measures	Effect size (patients vs. controls unless otherwise stated)
36	Martin et al. (2005)	28 schizophrenia patients (mean age 58.3, males 50%) 28 healthy controls (mean age 57.3, males 50%)	Actillume (Ambulatory Monitoring, Inc., Ardsley, NY)	Total and percent sleep time at night Total and percent wake time at night Number of awakenings Average length of awakenings Total and percent sleep time during the day Total and percent wake time during the day Number of daytime sleep episodes Mean light exposure levels for day intervals Number of minutes of exposure to light over 1000 lx	Sleep Interview Questionnaire (Ancoli-Israel et al. 1991)	Patients spent longer in bed, had more disrupted nighttime sleep, slept more during the day, and had less robust circadian rhythms of activity and light exposure compared to controls. Within patients, working was associated with improved sleep and circadian rhythms	↓Sleep quality →↓ employment	Time in bed Cohen's $d = 1.44$ Number of awakenings Cohen's $d = 1.10$ Number of daytime sleep episodes Cohen's $d = 0.857$
37	Poyurovsky et al. (2000)	16 neuroleptic-induced akathisia (NIA) (mean age 36.4, males 50%, mean age of onset 23.7) 16 Non-NIA (mean age 29.6, males 62.5%, mean age of onset 22.6)	AMA-32 (Ambulatory Monitoring, Inc., Ardsley, NY)	Total motor activity over 24 h Total sleep duration (mins) Sleep latency (mins) Sleep continuity (duration of sleep w/o awakening) Sleep efficiency (%)	Self-rated sleep questionnaire Barnes Akathisia Scale Clinical Global Impression scale Positive and Negative Syndrome Scale	NIA group had higher overall motor activity and higher daytime motor activity in afternoon and evening than non-NIA group	Extrapyramidal side effects	Overall motor activity (NIA vs. no NIA) Hedges' $g = 1.56$ Afternoon motor activity (NIA vs. no NIA) Hedges' $g = 1.07$ Evening motor activity (NIA vs. no NIA) Hedges' $g = 0.902$
38	Shamir et al. (2000)	19 schizophrenia patients (mean age 42 ± 5, M:F 12:7)	Somnitor (Neurim Pharmaceuticals, Tel Aviv, Israel)	Sleep efficiency Sleep latency Total sleep time Wake after sleep onset duration Fragmentation index Number of awakenings	Urinary 6-SMT	All patients had low melatonin output. Melatonin replacement significantly improved rest-derived sleep efficiency especially in low-efficiency sleepers	↓ Sleep efficiency →↓ melatonin level	Only 1 group, no effect size

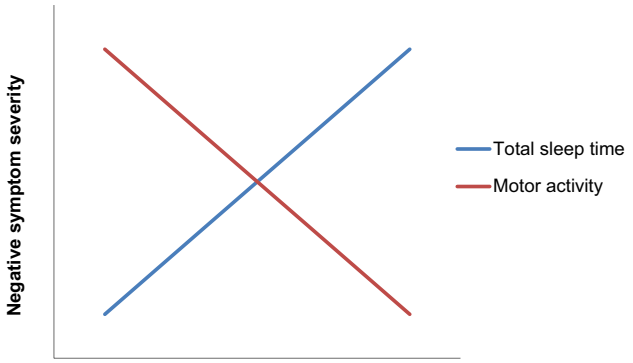

Fig. 2 Relationship between actigraphic measures and negative symptoms

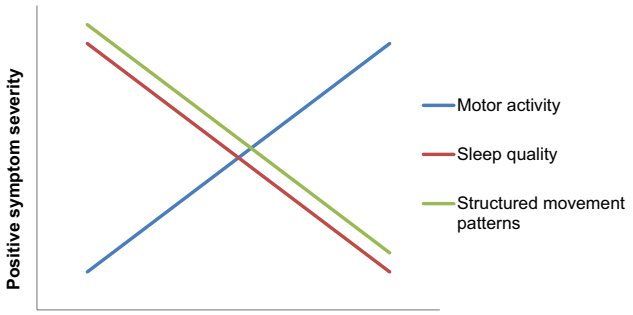

Fig. 3 Relationship between actigraphic measures and positive symptoms

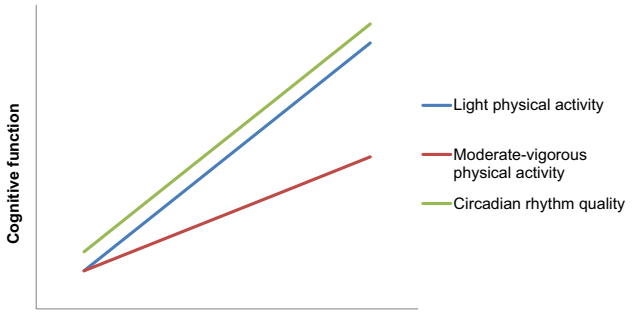

Fig. 4 Relationship between actigraphic measures and cognitive function

employment of positive reappraisal (Hofstetter et al. 2005) with implication of frontal lobe function (Bromundt et al. 2011). Chen et al. (2016) examined attention and concentration, and used the Grooved Pegboard Test to test for manual dexterity, upper-limb motor speed, hand–eye coordination and processing speed, in order to compare the cognitive functioning of 199 schizophrenia patients with 60 healthy controls. They found that the schizophrenia group was less engaged in light and moderate–vigorous activity and had poorer attention, concentration and processing speed than the control group. Participating in more light physical activity or moderate–vigorous activity was associated with better cognitive performance among patients with schizophrenia, with the influence of light activity being stronger than that of moderate–vigorous activity. Patients with schizophrenia who spent more time doing light activity had better performance on cognitive measures. Bromundt et al. (2011) evaluated frontal lobe functioning using Trail Making Test, Stroop and Supermarket Item Tests and observed that normal rest–activity circadian rhythm cycles correlated with significantly better cognitive functioning involving the frontal lobe (see Fig. 4).

In terms of illness trajectory, there is some evidence that lower motor activity is associated with chronicity of schizophrenia (Walther et al. 2015b) which needs validation in other samples. Actigraphy has shown potential in the precise detection of Neurological Soft Signs (NSS), known minor neurological signs more prevalent in individuals with schizophrenia than in a healthy population (Heinrichs and Buchanan 1988). This was observed in a study by Le Seac'h et al. (2012) using actigraphy paired with in-built inertial sensors capable of accurately calculating fine motor movements. They found that actigraphy detection of specific fine movements while performing neurological tasks assessing balance, alternative movements and extrapyramidal rigidity was positively correlated with the presence of NSS on clinical examination. Given that studies have demonstrated the increasing potential of NSS as both markers of early stages of schizophrenia and prognosticators of disease and treatment outcomes (Chan et al. 2016; Tamagni et al. 2013), the ability to objectively quantify and precisely detect them via actigraphy would be clinically valuable.

In terms of treatment and functioning, data are sparse. Decreased motor activity has been associated with higher antipsychotic dose, especially in early onset cases (Walther et al. 2015b), while increased motor activity has been associated with greater neuroleptic-induced extrapyramidal side effects (Poyurovsky et al. 2000). Poor sleep quality has been associated with poorer quality of life for patients with schizophrenia (Afonso et al. 2014) and working has been correlated with better sleep and circadian rhythms (Martin et al. 2005).

Actigraphy and biological and neuroimaging correlates

Based on extant data, poor sleep quality has been associated with various biological factors such as raised inflammatory marker counts like neutrophil concentration (Fang et al. 2016) and decreased melatonin (Afonso et al. 2011b). Decreased motor activity has been associated with reduced cerebral perfusion of cortical (frontal, temporal) and subcortical (thalamus, hippocampal) brain regions (Walther et al.

2011a), decreased frontal–striatal activation on functional magnetic resonance imaging and lower anterior cingulate volume (Farrow et al. 2005). Shamir et al. (2000) demonstrated that patients with chronic schizophrenia tended to have low melatonin output based on nocturnal urinary excretion of 6-sulfatoxymelatonin, a key melatonin metabolite. Hence, melatonin treatment could improve sleep quality in low-efficiency sleepers, including increase in sleep efficiency, duration and shortened latency (Shamir et al. 2000). Subsequently, Afonso et al. (2011b) demonstrated using actigraphy and nocturnal salivary melatonin radioimmunoassay that concentrations of endogenous nocturnal melatonin between schizophrenia patients and healthy controls were not statistically different. However, the sleep-promoting action of melatonin may be compromised in schizophrenia as the schizophrenia patient group had worse sleep quality with higher latency, lower efficiency and more night-time awakenings.

Docx et al. (2017) performed diffusion kurtosis imaging (DKI) on 20 schizophrenia patients and 16 controls and examined correlations and group differences with regard to fractional anisotropy (FA), mean diffusivity (MD), mean kurtosis (MK) and motor activity level. In the schizophrenia group, motor activity levels were positively correlated with MK in the inferior, medial and superior longitudinal fasciculus, corpus callosum, posterior fronto-occipital fasciculus and posterior cingulum. Walther et al. (2011b) found lower FA levels in the prefrontal and left temporal regions in schizophrenia patients. They also observed a negative correlation between motor activity levels and white matter integrity beneath the right supplementary motor area. Bracht et al. (2013) reported that increased probability index values, an indication that a voxel is part of the connecting fibre bundle of interest (PIBI), were correlated with motor activity in the left pre-SMA–SMA-proper connection for patients with schizophrenia. With regard to functional magnetic resonance imaging (fMRI), Kluge et al. (2018) study, which involved functional magnetic resonance imaging with reward anticipation tasks, found that lower motor activity level was associated with inferior frontal gyrus hypoactivation, while interview-based apathy was associated with ventral striatum hypoactivation. Additionally, resting state fMRI revealed that spontaneous motor activity was correlated with functional connectivity between left M1 and right cerebellum in patients (Walther et al. 2017).

Discussion

Clinical implications of findings

Our review reveals that most studies pertaining to the use of actigraphy in schizophrenia were conducted in Europe and the USA over the last two decades. While all have incorporated either motor activity or sleep trends, few have combined both major parameters or applied them to the comparison of different psychiatric conditions. In addition, there have been more studies correlating changes in motor activity or sleep quality with psychotic psychopathology as compared to cognitive functioning, illness trajectory, treatment factors, daily function or quality of life. Correlations of actigraphic measures with biological factors are yet sparser and have yielded less conclusive results.

Actigraphy studies have captured patterns that may distinguish schizophrenia patients from healthy controls, including monotonous motor activity patterns (Berle et al. 2010), lower mean levels of activity (Sano et al. 2012), as well as sleep irregularities and disturbances (Afonso et al. 2014; Robillard et al. 2015). Only two studies (Fasmer et al. 2016; Robillard et al. 2015) compared the actigraphic patterns between schizophrenia and non-psychotic disorders including affective and anxiety disorders, demonstrating a pattern of prolonged sleep duration, unstable sleep schedules and greater motor inactivity in the schizophrenia group. Another two studies by Walther et al. (2009a, b) examined subtypes of psychotic spectrum disorders (such as cycloid psychosis vs. paranoid/disorganised/catatonic schizophrenia) and attempted to delineate clinical presentations of these conditions based on motor activity. Several studies have also begun to explore the use of actigraphic measures in participants with at-risk mental state (ARMS). ARMS has been associated with the development of psychosis over a 10-year period (Fusar-Poli et al. 2012; Nelson et al. 2013; Yung et al. 1996). Similar to findings in schizophrenia patients, actigraphic measures showed less regular circadian rest–activity rhythms and more nap time in the day for ARMS individuals as compared to healthy controls (Castro et al. 2015). Further evaluation may proffer better clinical markers that can supplement extant clinical evaluation and corroborative information from family members, to distinguish between different psychiatric disorders and even subtypes of psychotic disorders.

Furthermore, actigraphic patterns hold promise as surrogate clinical markers of symptom status in patients with schizophrenia, given their close correlation with psychopathology. Increased positive symptoms are associated with less structured movement patterns (Walther et al. 2014) and disrupted sleep–wake patterns (Afonso et al. 2011a) whilst increased negative symptoms are associated with less motor activity (Kluge et al. 2017; Walther et al. 2014), prolonged sleep, more night-time awakenings and daytime sleepiness (Wichniak et al. 2011). These correlations with psychopathology are mirrored in studies involving ARMS individuals and healthy controls as well. Lunsford-Avery et al. (2015) noted that reduced sleep efficiency (SE), more wake upon sleep onset (WASO), and night-time movement correlated

with positive symptom severity in an ultra-high-risk population. They also found that reduced SE, increased WASO, and reduced total sleep time predicted greater positive symptom severity 1 year later. In a sample of healthy controls, participants were more likely to endorse a greater number of psychotic experiences when fewer hours of sleep as captured by actigraphy was coupled with poor perceived sleep quality (Cosgrave et al. 2018).

Next-day functioning has been found to be significantly affected by sleep disturbance and the presence of auditory hallucinations, while delusions of control can be predicted by different aspects of sleep disturbance (Mulligan et al. 2016). However, there are still comparatively fewer studies of correlations with cognitive and psychosocial functioning including quality of life (Afonso et al. 2011a, 2014; Bracht et al. 2012; Chen et al. 2016). Such studies would complement understanding of the inter-relationship between symptomatology, neuropsychological performance and impact on daily functioning in individuals with schizophrenia. Notwithstanding the fewer studies, available data from Afonso et al. (2011a, 2014) suggest that patients with schizophrenia, and in particular those with more positive symptoms, tend to report poorer sleep quality and lower quality of life and Hofstetter et al. (2005) also reported reduced preference for positive cognitive appraisal of circumstances around them and more avoidant coping compared to healthy controls. This behoves the need to better optimise the clinical management of these patients, especially positive symptomatology, by employing pharmacological and non-pharmacological interventions.

Early detection of schizophrenia is crucial for early intervention and educating patients on symptom management. One possible marker present in early stages of schizophrenia is Neurological Soft Signs, which can potentially be more reliably detected using actigraphy (Le Seac'h et al. 2012). Additionally, low level of motor activity has been correlated with the chronicity of the disorder as well as severity of avolition (Walther et al. 2015b). Hence, such objective measures could possibly be used to alert clinicians regarding possible onset of illness, deterioration of condition or to approximate the duration of illness. There are currently mixed findings regarding the effect of antipsychotic dosage on motor activity levels (Docx et al. 2017; Walther et al. 2009c, 2015b) and further research is required to tease apart the relative influence of medication and other disorder-related factors in contributing to lowered activity levels observed in schizophrenia patients. Antipsychotics have been associated with increased cardiovascular mortality (Birkhofer et al. 2013) and akathisia (Poyurovsky et al. 2000), highlighting the importance of close patient monitoring, which can be achieved through the use of actigraphic tools.

Studies correlating actigraphic measures with clinical and biological correlates have the potential to shed light on the underlying biological basis for clinical manifestations of schizophrenia. Poorer sleep quality in schizophrenia patients has been associated with increased inflammation (Fang et al. 2016), which could either reflect inherent biological state or further contribute to other comorbid health conditions experienced by patients with schizophrenia. Neuroimaging studies have observed decreased motor activity to be associated with decreased volume of anterior cingulate (Farrow et al. 2005) and reduced cerebral perfusion to cortical–subcortical brain regions (Walther et al. 2011a) which are implicated in schizophrenia. In addition, cerebral white matter changes (Bracht et al. 2013; Docx et al. 2017; Walther et al. 2011b) are associated with lower motor activity levels, which is consistent with earlier data linking deficit subtype of schizophrenia (with greater inactivity) with such brain white matter changes (Voineskos et al. 2013). Higher probability indices of cortical pathways involving supplementary motor areas may suggest possible compensatory mechanisms towards underlying basal ganglia dysfunction in patients (Bracht et al. 2013; Walther et al. 2011a).

Future directions

Several future directions can be posited. First, future studies may want to combine studies of motor with sleep activity to enable deeper phenotyping of the clinical features observed in patients with schizophrenia. Second, trans-diagnostic investigations involving different psychiatric conditions and subtypes of these conditions may allow better clinical understanding of underlying motor and circadian rhythm changes. Third, a multimodal approach allowing elucidation of interactive relationships between clinical, actigraphic and biological parameters (such as physiological, imaging measures) would enable more extensive correlations between these factors. Fourth, longitudinal studies are warranted to examine the utility of these actigraphic measures for prediction of relapse and prognostication. In the areas above, studies in this field could benefit from 'big data' approaches and cross-country collaborations which aggregate data from patients with various psychiatric conditions to examine clinical correlates of these actigraphic measures. Fifth, once better proven, actigraphy can be used as a potential objective monitor of treatment response, and feedback for different interventions including lifestyle changes. Patients can use actigraphy as a form of biofeedback to track their own activity and sleep, which in turn empower them to make further lifestyle changes (Shin et al. 2016). Correlations between actigraphic measures and symptoms can be charted over time using mobile applications or software which can be viewed by both the patient and clinician. Such monitoring techniques highlight specific areas which each patient could alter to bring about symptom alleviation and increased functionality. This can motivate patients to play

an active role in managing their illness. Clinicians can also harness this technology to track patients' progress or make individualised suggestions for lifestyle modification based on their baseline activity levels. Additionally, actigraphy is no longer limited to external wearables, with accelerometers and sleep tracking applications readily available on most mobile devices. Despite limitations in degree of accuracy, it may be an ideal option to introduce patients to the benefits of actigraphy even for those unable or unwilling to use wearables. Lastly, actigraphy also holds promise in the field of translational neuroscience, because motor activity alterations have trans-species value as demonstrated in studies such as that by Perry et al. (2009). They noted that mouse models with inhibited or lack of dopamine active transporter (DAT) function showed similar spatial patterns of locomotion as that observed in bipolar mania. This suggests potential neurobiological underpinnings and therapeutic targets for bipolar disorder, and such trans-species applications could be extended to schizophrenia as well.

Limitations of studies

There are several limitations of the studies reviewed. First, as a cross-sectional design was employed for most of the studies, causal relationships could not be established. Second, findings of studies with smaller sample sizes should be replicated in larger sample sets. Third, future studies may want to investigate the impact of different psychotropic medications on actigraphic patterns or include other confounders including gender, age, comorbid psychiatric disorders to better understand such actigraphic patterns in naturalistic real-life settings. Fourth, the presence of comorbid medical conditions such as sleep disorders can confound findings of poor sleep quality and daytime somnolence (Afonso et al. 2014) or increased inflammation (Fang et al. 2016). Germane to this, it has been noted that patients on antipsychotics have increased risk of developing metabolic syndrome and obstructive sleep apnoea (Lieberman 2004; Rishi et al. 2010). Fifth, inpatients had structured institutional schedules and ward routines, which may have affected actigraphically recorded inter-daily stability of motor activity (Manoach et al. 2010). The potential for these findings to be applied to outpatients who conversely, have greater independent control of their daily activities, is less certain.

Limitations of actigraphy

As a measure of sleep, sleep/wake timings are estimated by movement detected on actigraphy and not based on cortical activity levels (Robillard et al. 2015). Hence, sleep parameters provided by the device are only an approximate reflection of participants' sleep/wake states even with the use of sleep logs or diaries. This makes it liable to overestimating total sleep time and sleep efficiency. This is especially so in sedentary or bedbound patients who may be logged as being asleep during periods of akinesia (Manoach et al. 2010). Patients lying still in bed but remain vigilant may be logged as having shorter sleep onset latency than is the case (Manoach et al. 2010). Additionally, current actigraphy devices are not validated for measuring sleep stages (Martin and Hakim 2011). It is also not possible to log brief awakenings or periods of sleep, which can affect the accuracy of data collected in patients with severely disturbed sleep patterns. While devices with electroencephalographic sensors can be employed in tandem for these purposes (Ancoli-Israel et al. 2002), it may not be as conducive (Martin et al. 2005). Other modalities such as polysomnography, sleep diaries and sleep questionnaires can complement actigraphy to provide direct additional information regarding sleep duration, as well as derive subjective information on sleep quality.

As a measure of motor activity, the motion sensors employed within individual actigraph devices are currently not yet sufficiently adequate and precise for evaluating complex movements (Bracht et al. 2012). Examples of these include local movements of restricted muscle groups, coordination, movement sequence and symmetry. Similarly, only a limited number of Neurological Soft Signs can be picked up by current inertial sensors, limiting actigraphy's use in the identification of these clinical features (Krebs et al. 2000; Le Seac'h et al. 2012). Measurement accuracy may also be affected by movement sleep disorders like Periodic Limb Movement Disorder and REM Sleep Behaviour Disorder (Markkula and Lauerma 1997). It has been recommended that multiple devices be placed concurrently at different body parts or simultaneous video recording be done to overcome these limitations (Bracht et al. 2012; Le Seac'h et al. 2012; Poyurovsky et al. 2000). However, these methods will indubitably impact user's willingness for its wearability.

Evaluating the feasibility of actigraphy in the setting of long-term monitoring of schizophrenia patients with acute or residual active psychotic symptoms, patients may harbour persecutory and/or perceptual delusions about the wearable actigraphy devices. In one study, several participants believed that the device was making surveillance of their lives, tracking their location, or that they were being experimented upon (Shin et al. 2016). This has the potential to precipitate a psychotic relapse or worsen psychotic psychopathology. Patients may also discard these devices secondary to their psychotic experiences. Furthermore, disorganised thinking can potentiate unpredictable and erratic behaviour deviating from usual motor and sleep patterns and levels. For instance, as reported by Shin et al. (2016), some participants with known baseline of low motor activity displayed abnormally increased activity levels only during the recording period, leading to concerns about consistency of the data logged.

Conclusion

In conclusion, this review found lower motor activity and poorer sleep quality in patients with schizophrenia compared with healthy controls which are associated with clinical features (such as psychotic phenomenology, cognitive functioning, subtypes, quality of life, illness chronicity, medication dose) and less conclusively with biological features (inflammatory blood markers, structural and functional MRI features). Notwithstanding inherent limitations of studies reviewed and actigraphic tools, actigraphy holds promise as a surrogate objective monitor of clinical status, functioning, treatment response. It also shows potential to be a means of feedback for different interventions including lifestyle changes for patients with such a crippling psychiatric condition.

Compliance with ethical standards

Conflict of interest No authors or any close family members have any current financial conflicts of interest related to this paper. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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