

Clinical Application of Actigraphy in Psychotic Disorders: A Systematic Review

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Abstract Actigraphy has become increasingly recognized as a useful method to study sleep/wake patterns and activity monitoring. It is a reliable tool for confirming a diagnosis and evaluating the effect of treatments for sleep problems in patients with primary psychiatric diagnoses such as schizophrenia. In addition, actigraphy is an objective measure that circumvents the lack of insight and often unreliable self-reporting of mental health related problems. However, the literature regarding the use of actigraphy in research and clinical applications related to severe psychiatric populations is scarce. Amalgamation of the evidence is needed to advance the use of actigraphy in psychiatry. We summarized the literature to date related to the use of actigraphy in patients with psychotic disorders, specifically schizophrenia. We conducted a systematic review of journal databases. Sixty-six studies emerged from the search of the electronic search engines, 14 were RCTs/case-control studies and 14 were review/guideline papers and others were case studies. Results of the RCT/case-control studies comparing

the use of actigraphy with patients versus control were summarized. Actigraphy not only allows for the objective evaluation of sleep habits and circadian rhythm disorders, but also helps to clarify and compare sleep and activity patterns among severe psychiatric disorders such as schizophrenia. Additionally, actigraphy data can be used as an outcome measure for changes in sleep patterns either when primary psychotic disorders are treated and/or when the sleep disturbance associated with the psychotic disorder is treated. Finally, actigraphy serves as a supplementary tool to study neuropathology of movement-related psychiatric disorders including schizophrenia.

Keywords Actigraphy · Assessment · Diagnosis · Psychosis · Schizophrenia · Sleep · Circadian rhythms · Motor activity · Movement · Neuropathology · Measurement · Pharmacological interventions · Systematic review · Psychiatry

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Introduction

In the past few decades, actigraphy has been recognized as a useful method to monitor sleep disorders and to study sleep/wake patterns. Although nocturnal polysomnography (NPSG) remains the gold standard in sleep medicine, actigraphy offers several advantages to NPSG. Actigraphy allows a long term ambulatory recording of sleep patterns over a period of several nights, while NPSG usually offers a short term assessment. Also, actigraphy seems more cost effective tool than NPSG. Although actigraphy does not measure actual sleep stages, actigraphy data provide a good estimate of the overall timing of sleep quality, sleep quantity, and activity/restlessness [1, 2].

Initially, actigraphy presented with problematic issues such as lack of validity and reliability. However, research in the past decades has addressed methodological flaws and has allowed for a wide variety of the applications and utility of actigraphy in both research and clinical areas [1, 2, 3].

Although methodological issues differ across devices and study populations, studies have demonstrated that actigraphy is sensitive in detecting unique sleep patterns in specific primary sleep disorders, some medical or neurobehavioral disorders and in pharmacologic and non-pharmacologic interventions [2, 3]. In addition, actigraphy is a reliable tool for evaluating efficacy of treatment in a number of sleep disorders. Actigraphy may also be used to evaluate sleep patterns in individuals who are unable to tolerate PSG, such as infants and demented elderly [3–5]. Thus, in their reviews of the methodology, both Sadeh and Ancoli-Israel have proposed that actigraphy has reached the maturity level for application in the clinical setting [2, 3].

Although actigraphy has been widely used in research and clinical application, it has only recently emerged as a beneficial tool in investigating the relationship between sleep patterns and severe psychiatric disorders. To date, severe mental health disorders have been largely understudied with actigraphy (Fig. 1). The present paper summarizes the current knowledge in the application of actigraphy related to the sleep and movement problems only related to psychotic disorders. Specifically, we review the clinical application of actigraphy in schizophrenia, brief psychosis, schizophreniform, schizoaffective disorder, delusional disorder and psychotic disorders related to mood disorders based on diagnostic and statistical manual of mental disorders (DSM-IV-TR) [6]. Moreover, this review focuses on important theoretical and practical questions including how severe psychotic disorders influence the sleep/wake pattern and circadian rhythm, how the changes of the sleep/wake patterns able to alter psychotic symptoms, how clinicians can measure the efficacy of treatments on sleep patterns in practice and the advantage of using

actigraphy as a complementary tool to study neuropathology of movement related psychiatric disorders such as schizophrenia.

First, we outline evidence for the application of actigraphy and the utility to patients with psychotic disorders. The empirical studies providing evidence for the use of actigraphy in identifying sleep habits and circadian rhythm is described. Also, we examine the usage of actigraphy in clarifying or comparing diagnoses. In addition, we assess the application of actigraphy as an accessory tool to investigate the relationship between motor functioning and neuropathology of disorders. Finally, we provide an overview of research incorporating actigraphy to evaluate treatment of sleep problems in patients and evaluating the treatment efficacy and its impact on sleep pattern.

Methods

We searched the medical electronic search engines (PubMed and EMBASE) for studies using actigraphy with human subjects suffering from psychotic disorders (June 2011). Key terms were psychotic disorder [MeSH], schizophrenia [MeSH] and (actigraphy [MeSH] OR actigraphy OR actometry OR actimetry).

Results

A total of 66 studies emerged from the systematic literature review search of the electronic search engines. From which, there were 14 RCTs/case–control studies and 14 review/

Fig. 1 The literature on actigraphy based on the Medline database, not including meeting abstracts. These keywords plus “actigraphy” were searched, and results were limited to keywords specifically found in the title and/or abstract

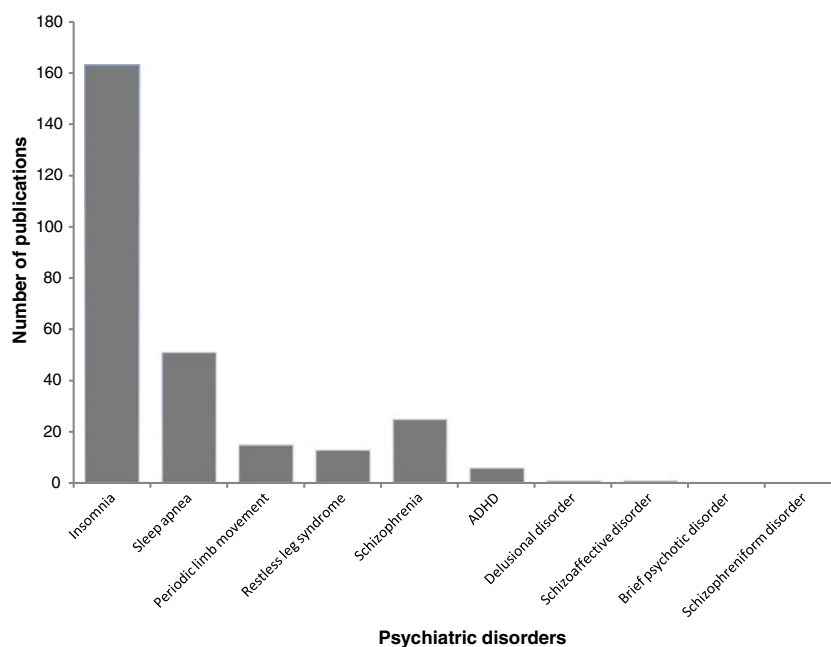


Table 1 Summary of 14 RCTs/case-control studies using actigraphy with human subjects suffering from psychotic disorders

Studies (year)	Psychiatric diagnoses (DSM IV)	Demographic characteristics	Sleep assessment tools/version of actigraphy	Placement of device	Other assessment tools	Duration of actigraphy recording	Actigraphic assessed parameters
Afonso P et al. 2011	Patients with schizophrenia	68 (34 patients, mean age 33.8±8.6 and 34 controls, mean age 34.7±8.3)	Actimeters (SOMNO watch, Actigraphy System)	Non-dominant wrists	Pittsburgh Sleep Quality Index (PSQI), Positive And Negative Syndrome Scale (PANSS), Salivary melatonin concentrations were determined by Radio-immunoassay with a I-labeled tracer (Bühlmann Laboratories, Basel, Switzerland)	Seven consecutive days	Sleep Quality, Sleep latency, Total sleep Time, Sleep efficiency, Night time awakenings
Walther S et al. 2011	Patients with schizophrenia	25 (11 patients, mean age 35.6±12.5 and 14 controls, mean age 31.71±6)	Actiwatch (Cambridge Neurotechnology, Inc, Cambridge, UK)	Non-dominant Wrist	Brain MRI (Siemens Mgneto), Positive And Negative Syndrome Scale (PANSS), Simpson-Angus Scale (SAS), Modified Rogers Scale (MRS), Northhoff Catantonia Scale (NCS)	24 h	Activity level (AL)
Walther S et al. 2011	Patients with schizophrenia	43 (19 patients, mean age 33.2±11.1 and 24 controls, mean age 33.7±10.6)	Actiwatch (Cambridge Neurotechnology Inc, UK)	Left wrist (non-dominant)	Positive And Negative Syndrome Scale (PANSS), Simpson-Angus-Scale, MRI Acquisition Diffusion Tensor Imaging (DTI)	24 consecutive hours	Activity level (AL)
Wichniak A et al. 2011	patients with schizophrenia and patients with schizophreniform disorder	73 (64 patients with schizophrenia, and 9 patients with schizophreniform disorder, mean age 29.2±10.2 and 36 controls, mean age 30.1±10.4)	Actigraph (actiwatch AW4, Cambridge Neurotechnology Inc., UK)	Wrist of the non-dominant arm	Clinical Global Impressions Scale (CGI), Positive And Negative Symtomes Scale (PANSS), Calgary Depression Rating Scale for Schizophrenia (CDSS), Udvalg for Kliniske Undersogelser, (UKU), Side Effect Rating Scale, Barnes Akathisia Rating Scale (BARS)	Seven consecutive days	Sleep latency Total sleep time Sleep efficiency
Waters et al. 2011	Patients with schizophrenia	13 (6 patients with schizophrenia, mean age 44.33±4.96 and 7 Controls mean age 42.71 ±7.52)	ActiWatch 2 actigraph (Respironics, Murrysville, PA)	Wrist	Athens Insomnia Scale (AIS), Epworth Sleepiness Scale (ESS)	28 consecutive days	Total sleep time, Sleep efficiency, Sleep latency,

Table 1 (continued)

Studies (year)	Psychiatric diagnoses (DSM IV)	Demographic characteristics	Sleep assessment tools/ version of actigraphy	Placement of device	Other assessment tools	Duration of actigraphy recording	Actigraphic assessed parameters
Hauge ER et al. 2011	Patients with schizophrenia and major depression	49 (24 chronic patients with schizophrenia, mean age 47.4±11.1; 25 patients with major depression, mean age 42.9±10.7) 32 controls, average age 38.2±13.0 years	Actiwatch, (Cambridge Neurotechnology Ltd, England)	Right wrist	Fourier Analysis, Sample Entropy	300 min, containing not more than 4 consecutive minutes without activity	mean activity [SD & root mean square successive differences (RMSSD)]
Manoach et al. 2010	Patients with schizophrenia	29 (14 patients with schizophrenia, mean age 41±7 and 15 controls, mean age 42±6)	Mini-Mitter Actiwatch®-64 actigraph (Mini-Mitter Company, Inc., Bend OR), Polysomnography	Wrist	Finger Tapping Motor Sequence Test (MST), Stanford Sleepiness Scale (SSS) for subjective alertness	Three nights	total sleep time, sleep onset latency, sleep efficiency
Berle et al. 2010	Patients with schizophrenia and major depression	78 (23 patients with Schizophrenia, mean age 46.7±10; 23 patients with major depression, mean age 42.8±11.0 and 20 controls, mean age 38.2±13.0)	Actiwatch, (Cambridge Neurotechnology Ltd, England)	Right wrist	Montgomery-Asberg Depression Rating Scale (MADRS), Brief Psychiatric Rating Scale (BPRS)	2 weeks	Total and night time activity,
Apiquian R et al. 2008	Patients with schizophrenia	40 (20 patients, mean age 28.5±7.2 and 20 controls, mean age 30.3±5.8)	Actiwatch-16 (Mini Mitter Company, Bend, OR)	Non-dominant wrist	Positive And Negative Syndrome Scale (PANSS), Calgary Depression Scale for schizophrenia (CDSS), Barnes Akathisia Scale, Simpson Angus Scale	6 days before the onset of antipsychotic treatment and 28 days after treatment onset	Mean activity, total sleep time
Birkhofer A et al. 2007	Patients with schizophrenia	56 (28 medicated patients, mean age 34±8.3 and 28 controls, mean age 36±13.4)	Actometer (Gefutec, Berlin)	Wrist of non-dominant	24-hours electrocardiogram recordings, Deceleration Capacity (DC) Eppendorfer Schizophrenie Inventar (ESI), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI)	24 hours	—
Martin J et al. 2005	Patients with schizophrenia	56 (28 patients, mean age 58.3±9.8 and 28 controls)/ mean age 57.3±9.2	Actillum wrist actigraph (Ambulatory Monitoring Inc Ardsley New York	wrist	—	72 Consecutive hours	Bedtime, Time in bed, Total sleep time, Minutes awake during the night, Percent of time in bed asleep,

Table 1 (continued)

Studies (year)	Psychiatric diagnoses (DSM IV)	Demographic characteristics	Sleep assessment tools/ version of actigraphy	Placement of device	Other assessment tools	Duration of actigraphy recording	Actigraphic assessed parameters
Shamir E et al. 2000	patients with schizophrenia	19 patients, mean age 42±5	actigraphy (semintor murism pharmaceutical Tel Aviv, Israel)	wrist	urinary melatonin measurement	3 consecutive nights of the end of each period	Number of awakenings, Average awakening length Final awakening time, Time out of bed, Total time awake, Percent of time out of bed spent awake, Total daytime sleep time, Number of daytime sleep episodes, Sleep efficacy, Sleep latency, Total sleep time, Wake after sleep onset duration
Dursun et al. 1999	patients with schizophrenia	24 (16 patients, mean age 36.1±9.2 and 8 controls, mean age 33.8±11.6)	Actigraphy (Switzerland)	Right wrist	visual analogue scale,	5 consecutive days	Fragmentation index, Number of awaking movement index
Lauerma H et al. 1994	patients with schizophrenia	30 (13 patients, mean age 18.9±8.7 and 17 controls, mean age 29.5±8)	Actometer (Gruhwiler Electronics, Switzerland)	Both wrists	Continuous infrared video recording and the static charge sensitive bed method during the movement recording nights	Two nights	Motor activity during waking and sleep
Studies (year)	Medication for underlying disease	Duration of medication for underlying disease	Neuroleptic induced movement disorders	Other side effect of medication	Conclusion	Reference	
Afonso P et al. 2011	Atypical antipsychotic				sleep-promoting action of endogenous melatonin was compromised in schizophrenia. Also, increased sleep latency in schizophrenia are not related to the diminished output of melatonin.	[7]	

Table 1 (continued)

Studies (year)	Medication for underlying disease	Duration of medication for underlying disease	Neuroleptic induced movement disorders	Other side effect of medication	Conclusion	Reference
Walther S et al. 2011	Risperidone (n=5), clozapine (n=3), olanzapine (n=2), Quetiapine (n=1)	—	—	—	Basal ganglia dysfunction may lead motor retardation in schizophrenia, resulting in a predominance of cortical motor control	[8•]
Walther S et al. 2011	Atypical antipsychotics	—	Patients experienced mild extrapyramidal Symptoms according to the Simpson-angus scale	—	Structural disconnectivity like changes of white matter integrity lead to disturbed motor behavior in schizophrenia	[9•]
Wichniak A et al. 2011	54 patients were treated with olanzapine was administered in monotherapy in 18 patients. The Treatment with olanzapine was combined with other drugs including antidepressants (n=13), Mood (stabilizers n=5), Anxiolytics (n=3), Other anti-Psychotics (n=3) or an Anticholinergic (n=1)	—	—	—	Treatment with olanzapin or risperidone among patients with schizophrenia exhibit low physical activity and altered sleep pattern which promote metabolic side effects. These alternations are linked to negative and depressive symptoms.	[10•]
Waters et al. 2011	19 patients Were treated With Risperidone, 9 of them were treated in monotherapy and 10 in Combination With antidepressants (n=4), or an Anxiolytic (n=1)	—	—	—	Patients showed significant delays in the initiation of sleep and greater diurnal variations in sleep characteristics as compared to controls and change in sleep/wake pattern is followed by a change in symptom severity.	[11]
Hauge ER et al. 2011	for schizophrenia: (Traditional antipsychotics, Atypical antipsychotics except clozapine, Clozapine, Mood stabilizers) for MDD: (Antidepressants, Lithium, Mood stabilizers except lithium, Antipsychotics Anxiolytics, Hypnotics)	—	—	—	Patients with schizophrenia and depression showed distinctly different profiles of motor activity	[12]

Table 1 (continued)

Studies (year)	Medication for underlying disease	Duration of medication for underlying disease	Neuroleptic induced movement disorders	Other side effect of medication	Conclusion	Reference
Manoach et al. 2010	12 patients on atypicals, one on typicals, and one on both antipsychotic medications	at least six weeks		deficits in sleep-dependent memory consolidation	Reduced sleep-dependent consolidation of motor procedural learning in schizophrenia was shown and this deficit is relevant to specific sleep stages suggesting that sleep is an important contributor to cognitive deficits in schizophrenia.	[13]
Berle et al. 2010	Clozapine (481 ±218 mg) Other antipsychotics antidepressants, some co-medicated with lithium, mood stabilizers, antipsychotics, anxiolytics or hypnotic	—	—	—	Motor activity was significantly reduced in both schizophrenic and depressed patients. Patients with schizophrenia showed less complexity and more structured behavior in their motor activity patterns.	[14]
Apiquian R et al. 2008	Risperidon, Haloperidol, Biperidin, Lorazepam, Sulpiride, Olanzapine, amisulpride	28 days	Extrapyramidal side-effects (EPS), Acute akathisia	—	Unmedicated schizophrenic patients exhibit low levels of motor activity. This finding persists after antipsychotic treatment even though symptoms improve.	[15]
Birkhofer A et al. 2007	Olanzapine (10-25 mg), Risperidone (2-12 mg), Clozapin (12.5-600 mg), Quetiapin (400-600 mg), Amisulprid(-), Chloprathixon(80-150 mg)	—	—	—	Schizophrenic patients treated with antipsychotics showed reduced heart rate deceleration capacity. This may be an indicator of increased cardiovascular mortality risk	[16]
Martin J et al. 2005	—	—	—	—	Older schizophrenia patients showed more disruption of sleep and circadian rhythm compare to controls suggesting patients sleep disruption was beyond what is attributable to advanced age alone	[17]
Shamir E et al. 2000	Neuroleptic , 19/19 Benzodiazepines , 9/19 SSRIs anti-depressants , 3/19	Two treatment periods of 3 weeks with one week washout between	—	—	Melatonin improves sleep efficiency in patients with schizophrenia with low quality sleep	[18]

Table 1 (continued)

Studies (year)	Medication for underlying disease	Duration of medication for underlying disease	Neuroleptic induced movement disorders	Other side effect of medication	Conclusion	Reference
	Other drugs , 5/19	treatment periods (7 weeks totally)				
Dursun et al. 1999	Risperidone, chlorpromazine, haloperidol, flupenthixol	Typical antipsychotics for 91.3±62.7 weeks and the risperidone having been treated with risperidone for 9.5±4.3 weeks.			Patients treated with risperidone had better sleep quantity, sleep quality, and general functioning compare to patients treated with typical antipsychotic drugs	[19]
Lauerma H et al. 1994	All patients received neuroleptic medication				Abnormal laterality of arousal, attention or movement system during sleep have been seen in schizophrenia due to abnormality in the sleep dependent modification of attentive behavior, or the lateralized effects of neuroleptic medication	[20]

guideline papers and the rest were case studies. Some of papers were excluded because they were not published in English. Results of the RCT/ case-control type studies are summarized in Table 1.

Actigraphy has been used to investigate movement and sleep disturbance in a wide range of psychiatric patients (Fig. 1) including: primary sleep disorders, Attention deficit hyperactive disorder (ADHD), schizophrenia, anorexia nervosa, affective disorders as well as chronobiology and psychopharmacology [3, 21]. Thus, actigraphy has become a useful tool to identify sleep and movement disturbances in psychiatry particularly in patients with primary psychotic disorders such as schizophrenia that often have lack of insight or difficulties in self-reporting health related information, such as sleep/wake patterns.

1. Actigraphy and Assessment of Sleep Patterns, Habits and Circadian Rhythms

1.1. Assessment of Sleep/Wake Patterns

In the clinical setting, sleep problems are recognized as a common complaint among patients with various psychotic disorders. Actigraphy, as a noninvasive and objective tool, allows clinicians and researchers to continuous measuring of sleep/wake patterns over a period of several days in psychotic disorders such as schizophrenia during psychosis and remission in both inpatient and outpatient setting [15, 22•]. Researchers and clinicians alike have applied this methodology in patients with schizophrenia. For example, Hofstetter and colleagues evaluated sleep quality, psychiatric symptoms, and quality of life in patients with schizophrenia or schizoaffective disorder during their post-acute phase. Participants completed several questionnaires including the Pittsburgh Sleep Quality Index (PSQI), the Positive and Negative Symptom Scale (PANSS), the Heinrichs Quality of Life Scale (HQLS) and the Ways of Coping Scale (WCS). Actigraphy was used to confirm subjective ratings of sleep disturbance in a subsample of seven of the 29 subjects for three weeks. Their results revealed that poor sleep plays an important role in sustaining poor quality of life and impaired coping strategies in schizophrenia [23]. In another study, Afonso and colleagues used actigraphy to investigate difference in sleep patterns in individuals with predominantly negative versus positive symptoms. Twenty-three patients with schizophrenia underwent continuous wrist-actigraphy for seven consecutive days and nights and completed the PSQI to evaluate sleep quality. Results indicated that patients with schizophrenia experienced sleep and circadian rhythm problems, and these disruptions may have negative effects on their rehabilitation strategies. Patients with predominant positive symptoms showed more disrupted sleep/wake patterns. Based on actigraphy data, authors could provide

possible evidence that the inadequate sleep may negatively impact quality of life in patients with schizophrenia especially in cases with predominant positive symptoms [22•]. Actigraphy also allows for the physiological measurement of sleep patterns in individuals with psychotic disorders in their natural environment during periods in which symptoms are adequately managed. For example, Waters and colleagues examined sleep/wake patterns in six patients with schizophrenia and seven healthy subjects in their home environment for 28 days. They investigated the relationship between severity of psychotic symptoms like hallucinations and delusions and diurnal variations in sleep/wake patterns. Patients showed significant delays in the initiation of

sleep and greater diurnal variations in sleep characteristics compared to controls. Overall, their findings suggest a negative relationship between sleep quality and symptom severity. Using actigraphy, the authors identified that sleep patterns in individuals with schizophrenia remain disturbed even when the disorder is treated adequately [11]. Lauerma and colleagues recorded the motor activity from 13 medicated patients with schizophrenia and 17 healthy controls using bilateral wrist actigraphy during the two consecutive days and nights. Their findings revealed that the dominant hand remained more active and this was not related to movement excess. Also, patients did not show lateralization to the non-dominant side during nocturnal low activity period or sleep. In schizophrenia, it appears that abnormal laterality of arousal and attention and movement during sleep may induce abnormality in the sleep-related behavior or due to the lateralized effects of neuroleptic medication. Therefore, actigraphic measurement helped to clarify the role of hemispheric asymmetry to understand the neuropathology of schizophrenia [20].

In addition, Robillard and colleagues used actigraphy to evaluate sleep/wake patterns of young adults with psychotic disorders and to investigate the potential relationship between sleep and mood disturbances in these patients. They found that the sleep/wake patterns in the natural environment were more disrupted and less consolidated in patients with psychotic disorders compared to healthy subjects. Patients also showed high night-to-night variability. In addition, sleep disturbances in the patients were associated with severe depressive and anxiety symptoms which may suggest common brain pathology [24]. Birkhofer and colleagues recorded 4-hour periods of sleep/wake profile with actigraphy as well as heart rate variability and the deceleration capacity in 24-hour electrocardiogram recordings. They recruited 28 medicated patients with

schizophrenia and 28 healthy controls to identify coherent sleep/wake phases and to ensure comparable levels of activity across subjects. Their findings demonstrated a reduction of heart rate deceleration capacity in patients treated with antipsychotics suggesting a reason for increased cardiovascular mortality risk. Thus, actigraphy may be a complementary aid to evaluate different aspects of schizophrenia pathogenesis [16].

In summary, actigraphy has improved the understanding of sleep habits in individuals with psychotic disorders in less intrusive, less acute environments than the sleep lab setting, and allows for the objective measurement of sleep in periods when the individual is a familiar and routine environment. It seems that actigraphy provide some objective information to assess subjective report of sleep problems in schizophrenia with and without other comorbidities.

1.2 Assessment of Circadian Activity Rhythms

Impairment of circadian rhythm is notable in patients with schizophrenia. For example, Wulff and colleagues reported a patient with schizophrenia who underwent long-term simultaneous wrist actigraphy (6 weeks) as well as other non-invasive techniques to quantify sleep/wake cycles such as typical light exposure and melatonin profiles. The findings revealed various rest-activity patterns such as delayed sleep phase and irregular rest-activity phases. Authors proposed that perhaps, these abnormalities induce the sleep/wake pattern disruption, precipitate cognitive dysfunction and the lack of social interactions all relative to schizophrenia [25]. Furthermore, Martin and colleagues evaluated 24 hours circadian rhythms as well as light-exposure levels of 28 geriatric patients with schizophrenia using actigraphy. They found disruption in circadian rhythms and sleep/wake patterns of patients. Patients who had better performance on neuropsychological tasks had less daytime sleep as well as greater consolidated nighttime sleep. It seems that there may be a strong association between sleep/wake patterns, circadian rhythms and cognitive functioning in schizophrenia [26]. In separate work, Martin and colleagues compared sleep/wake patterns or circadian activity rhythms of those 28 elderly patients with schizophrenia (mean age = 58.3 years) to 28 age-matched healthy controls using actigraphy. Their findings suggested that sleep and circadian rhythm of older schizophrenia patients was more disrupted than healthy controls. Thus, sleep disruption of schizophrenia was greater than what is attributable to sleep disturbance typically expected from ageing [17].

Bromundt and colleagues recruited 14 subjects with schizophrenia to investigate the relationship between

circadian rhythm patterns and cognitive performance in patients with schizophrenia. Continuous wrist actigraphy was monitored for 3 weeks. Saliva samples for endogenous melatonin secretion were collected as a circadian phase marker and neuropsychological tasks were performed. Patients showed a wide range of circadian sleep/wake cycle patterns from normal to highly disrupted patterns. Also, higher cognitive functioning in patients with schizophrenia was associated with more consolidated circadian rhythms and constant sleep patterns [27]. Afonso and colleagues compared the endogenous melatonin sleep-promoting effect in 34 patients with schizophrenic and 34 healthy controls. They provided support that melatonin levels may be negatively correlated with sleep latency, total sleep time and positively correlated with sleep efficiency in healthy subjects but not in patients with schizophrenia. Typical sleepiness effects of the usual nocturnal rise in endogenous melatonin may be compromised in patients with schizophrenia [7].

Thus, actigraphy has been a useful and objective tool for assessment of sleep/wake patterns and circadian rhythms of psychotic disorders particularly schizophrenia, and has allowed for improved understanding of the pathophysiology of these disorders in long-term patient care settings.

2. Actigraphy to Assess Potential Differential Diagnosis and Motor Activity

2.1 Actigraphy for Differentiating Between Disorders

Not only is actigraphy useful in measuring sleep pattern abnormality in individuals with specific psychiatric and neurological disorders, it allows clarification and comparison of sleep and activity patterns among different psychotic disorders. For example, Berle and colleagues used actigraphy to evaluate sleep patterns longitudinally within a group of schizophrenia and also in patients with major depression. Motor activity in both groups of patients was reduced but the schizophrenia group demonstrated less complex motor activity patterns and more structured behavior. Thus, it appears that that motor activity impairment may reflect different mechanisms in schizophrenia versus major depression [14]. Additionally, Haug and colleagues compared one patient with unipolar major depression disorder to one patient suffering from chronic schizophrenia using two weeks of actigraphy monitoring. The actigraphic measurement of the patient with schizophrenia presented active phases at nights, irregular activity levels during the day and delayed sleep phase syndrome compare to patient with depression. The conclusion was that actigraphy is a potentially beneficial tool in identifying circadian rest-activity phases in schizophrenia [28].

Haimov investigated the relationship between subjective sleep patterns and objective sleep measurement using actigraphy. They found that among subjects with schizophrenia and subjects with post-traumatic stress disorder (PTSD), there was no correlation between subjective and objective reports. Authors concluded that subjective reports in patients with each of these psychiatric conditions are not reliable. Thus, actigraphy appears to overcome that barrier by providing an objective means to evaluate sleep in this population, in which objective measurement of sleep disturbances is important for patients before prescribing hypnotic medications simply based on patient self-report [29].

Actigraphy also has the potential to differentiate among the three subtypes of schizophrenia. Walther and colleagues used actigraphy to compare motor activity in 3 subtypes (paranoid, catatonic, disorganized) of 60 patients with schizophrenia. Patients with catatonic schizophrenia had less activity levels, a lower movement index and a longer duration of immobility than subjects with paranoid schizophrenia. Therefore, increased duration of immobility as measured by actigraphy was identified as a significant feature of catatonic schizophrenia [30]. Actigraphy has also been used in the identification of different psychotic syndromes. For example, Walther and colleagues in another study used actigraphy during the daily waking hours during acute episodes of 16 patients with cycloid psychosis and 16 patients with paranoid schizophrenia. The level of motor activity and proportion of active versus inactive periods during waking hours were higher in cycloid psychosis. Their results confirmed general arousal in cycloid psychoses based on motor activity expression. Therefore, cycloid psychosis may be a syndrome with different symptoms and distinct pathophysiology [31].

Our team used actigraphy as part of our diagnostic evaluation in a case report of a 60-year-old woman with complaints of insomnia, agitation, and suicidal ideation. Her primary diagnosis was sleep state misperception (i.e., paradoxical insomnia). Primary treatment with trazodone and other hypnotic drugs was not successful. Then, careful psychiatric re-evaluation and wrist actigraphy resulted in a revised diagnosis of delusional disorder. It seems that paradoxical insomnia (i.e., sleep state misperception) might be considered as a sleep disorder and as a psychiatric disorder with psychotic symptoms in practice. Thus, actigraphy served as an objective tool to clarify the diagnosis [32].

Actigraphy has been used not only in schizophrenia, but also for other psychotic disorders such as postpartum psychosis. Clinicians can use it to identify possible markers of cycles or onset of diagnosis. Ross and colleagues evaluated changes in sleep patterns and behavior

during the perinatal period. They showed a robust interaction between sleep and perinatal psychiatric disorders. Thus, actigraphy could be used to evaluate sleep/wake patterns during pregnancy and may provide important information about the etiology, prevention and treatment of perinatal psychosis as well as postpartum mood disorders [33].

For additional severe psychiatric diagnosis, activity monitoring is a valid tool to help clinicians. Teicher, in a review, summarized the locomotor activity findings in several psychiatric disorders such as mood disorders and ADHD. He showed that activity levels are increased in mania, agitated depression, ADHD and Alzheimer's disease but it is decreased in the patients with bipolar depression and seasonal affective disorder. Circadian rhythm analysis may be helpful to discriminate between the activity patterns of some disorders like mania (dysregulated) and ADHD (intact or increased) [34].

Hauge and colleagues employs linear and non-linear mathematical methods including Fourier analysis and sample entropy to distinguish between schizophrenia and depression. They showed that motor activity was less in the schizophrenia and major depression, compared to healthy controls. The Fourier analysis of the activity counts that measured every minute of it showed that the relation between the variance in low and high frequency range in schizophrenia was less than what were recorded before during the controls. The sample entropy was higher in the patients with schizophrenia compared to the controls in the time series from the activity counts made every minute [12].

Taking together, actigraphy seems a valid method to clarify, compare and distinguish of sleep and activity patterns in different psychotic disorders and even it can differentiate the subtypes of schizophrenia. Also, it can be applied for other psychotic disorders such as postpartum psychosis.

2.2. Actigraphy for Assessment of Motor Activity in Psychotic Disorders

Movement problems are one of the most common symptoms of schizophrenia and they are part of the diagnostic criteria for schizophrenia in DSM-IV-TR. Walther and colleagues studied the relationship between the objective parameters of a motor activity measurement and the motor symptoms of the PANSS among 55 patients of schizophrenia using 24 hours continuous wrist actigraphy. They suggested that the reduced motor activity in measured quantity of movement is associated to the negative syndrome in schizophrenia. The motor specific items in the PANSS were less likely to show the quantity of motor activity in schizophrenia when compared to actigraphy.

Therefore, they concluded that actigraphy is a more valid tool to assess motor signs of psychopathology rather than observations in the PANSS [30, 35]. Also, Poyurovsky and colleagues used actigraphy to assess circadian locomotor activity of 16 patients with neuroleptic-induced akathisia (NIA) and 16 patients without NIA. Patients with NIA had persistent higher daytime motor activity than healthy participants. They concluded that ambulatory activity monitoring demonstrated a higher level of overall motor activity in patients with acute NIA compared to patients without NIA. Thus, actigraphy was a reliable method of measuring motor activity in patients with NIA [36].

Also, actigraphy was used to objectively evaluate some behavioral scores like Simpson-Angus Scale (SAS) which is an assessment of parkinsonian movement disorder related to psychiatric drug treatment. Janno and colleagues assessed 99 chronic institutionalized patients with schizophrenia with SAS against DSM-IV diagnostic criteria for neuroleptic-induced parkinsonism and objective motor assessment and concluded that SAS seems a reliable and valid instrument for neuroleptic-induced parkinsonism [37]. They also assessed Barnes Akathisia Rating Scale (BARS), a DSM-IV based screening method, and standardized lower limb actigraphy in order to quantifying NIA in 99 patients with schizophrenia. Their findings suggested that compared to quantitative actigraphy, BARS seems more practical for NIA. However, actigraphy may offer an objective additional option for evaluation of symptom severity [38]. In addition, they tried to analyze characteristic actometry patterns of neuroleptic-induced movement disorders (NIMDs) and pseudoakathisia (PsA) in schizophrenia. Their results showed that patients had different patterns in lower limb descriptive actigraphy than other patients in a non-selected sample. It seems that actigraphy is useful for measuring changes in the overall movement count or patterns after a change of risk factors such as dosage, antipsychotic type and time course. They suggested that further studies may show the ability of actigraphy to drive treatment decisions in a clinical practice [39].

In general, actigraphy may allow clinicians to identify potential psychotic syndromes as well as evaluation of standard method for motor measurement and add clarity to disorders that may have been previously misunderstood.

3. Actigraphy as an Accessory Tool to Investigate the Relationship Between Motor Functioning and Neuropathology of Psychotic Disorders

Several studies have used actigraphy to correlate motor functioning and neurophysiologic structure and

brain abnormalities in patients with psychotic disorders. For example, Farrow and colleagues recorded the spontaneous motor activity of 16 patients with schizophrenia (20 hours actigraphic measurement), as well as structural magnetic resonance imaging (MRI) to investigate whether such behavior was related to the volume of specific executive brain regions. They showed that total activity of patients was positively correlated with volume of left anterior cingulate cortex. Therefore, the volume of specific executive structures in the brain may be responsible for impairment of motor behavior [40]. Also, Walther and colleagues assessed resting state cerebral blood flow (CBF) to evaluate neurobiology of motor retardation in schizophrenia using MRI with arterial spin labeling and also wrist actigraphy. Their findings showed that motor activity was associated with CBF in motor cortical areas such as the dorsolateral prefrontal cortex and rostral cingulate motor area. This cortical association was not seen in controls that had higher overall motor activity. They concluded that basal ganglia dysfunction may be the reason of motor retardation in schizophrenia, resulting in a predominance of cortical motor control. On the other hand, CBF of cortical areas important for motor control was associated with voluntary motor behavior. It suggests a compensatory mechanism for dysfunction of basal ganglia [8•].

They also evaluated the objective motor activity and inters individual variance of white matter integrity and among 19 patients with schizophrenia and 24 healthy controls subjects using Diffusion Tensor Imaging (DTI) in MRI as well as wrist actigraphy on the same day. Patients showed lower activity levels (AL) as well as lower fractional anisotropy (FA) values in prefrontal and left temporal clusters. Also, they found linear negative associations of FA and AL underneath the right supplemental motor area (SMA), the right precentral gyrus and posterior cingulum in patients with schizophrenia. This effect within the SMA was not seen in healthy subjects. It may be possible that disturbed motor behavior in schizophrenia is due to the structural disconnections in the brain [9•].

Manoach recruited 14 patients with schizophrenia and 15 matched controls to see whether their failure to demonstrate normal sleep-dependent improvement during the motor procedural learning was related to the duration of Stage 2 sleep in the last quartile of the night and with spindle activity during this epoch. Participants performed finger tapping motor sequence test (MST), polysomnography and 3 nights of actigraphic monitoring. The findings showed that reduction of sleep-dependent consolidation of motor procedural learning in schizophrenia was associated with specific sleep stage. They suggested that sleep profile is contributing

to cognitive deficits in schizophrenia [13].

In summary, actigraphy can be considered as a useful tool in combination with advanced neuroimaging techniques to help to understand the pathophysiology and brain mechanism of psychotic disorders such as schizophrenia.

4. Actigraphy and Pharmacological Interventions for Sleep and Movement Problems

Actigraphy has implications in the investigation of efficacy of pharmacological agents in treating secondary sleep impairment. Specifically, actigraphy has been used to provide outcome data when evaluating whether treating sleep problems in psychotic disorders improves the quality of life. In addition, actigraphy has been used to assess whether treatments for psychiatric patients subsequently improves sleep patterns during interventional conditions. Shamir investigated the use of melatonin replacement to improve insomnia complaints in patients suffering from schizophrenia. They used actigraphy to investigate sleep/wake pattern in patients with schizophrenia objectively and also evaluate the effects of melatonin on sleep quality in a randomized, double-blind, cross-over, clinically based trial that included 19 patients with schizophrenia. Participants were given melatonin or placebo for 2 treatment periods of 3 weeks each with a week of washout between treatment periods. Sleep parameters were measured continuously using actigraphy. Their findings showed that melatonin replacement improved sleep efficiency compared to placebo and this improvement was better in low-efficiency subjects. During melatonin therapy, low efficiency sleepers showed a greater tendency toward shortened sleep latency and increased sleep duration rather than high efficiency subjects. Overall, the authors concluded that melatonin improves both sleep quality and quantity in patients with schizophrenia [18]. Furthermore, actigraphy was also used in a double-blind, placebo-controlled study that evaluated adjunctive armodafinil therapy in patients with stable schizophrenia treated with atypical antipsychotics. Kane and colleagues used actigraphy to assess patients with stable schizophrenia who are being treated with oral risperidone, paliperidone, or olanzapine. They exhibited abnormal patterns of sleep and wakefulness, disturbances in sleep continuity and daytime sleepiness [41].

Apiquian and colleagues used actigraphy in an attempt to examine the effects of medication management on activity and sleep and wakefulness patterns of 20 unmedicated patients with schizophrenia during baseline and also when treated with either typical or atypical antipsychotics. They wore a wrist actigraph for five consecutive days. Patients were treated with low-dose haloperidol or risperidone. Compared to healthy controls, untreated patients showed reduced activity during morning, early

and late nights as measured by actigraphy. During treatment with haloperidol or risperidone, a significant effect on activity level, particularly with haloperidol was seen. Their results suggested that unmedicated patients exhibit abnormally low levels of motor activity. Although there is some symptoms' improvement after treatment with an antipsychotic, reduced activity remains [15]. Similarly, Dursun and colleagues compared the effects of risperidone with typical antipsychotic medications such as chlorpromazine, haloperidol, flupenthixol in patients with schizophrenia and a group of healthy controls. Sleep was evaluated using a sleep quality visual analogue scale as well as actigraphy record for 5 consecutive days. Patients with schizophrenia had more disturbed sleep than controls. Particularly, patients treated with risperidone had better sleep quantity, sleep quality, and general functioning compare to patients treated with typical antipsychotic drugs [19].

It has been suggested that atypical antipsychotics may differ in the probability of causing motor retardation in psychotic disorders. Walther and colleagues measured 24 hours continuous actigraphic measurement from 16 patients with schizophrenia treated with olanzapine and 23 patients with risperidone. They found olanzapine group had higher activity levels than risperidone group. The results indicate that patients on olanzapine are more active during the day than risperidone group [42]. Furthermore, Wichniak and colleagues investigated the activity and sleep patterns of 7 consecutive days of 73 patients with schizophrenia treated with olanzapine or risperidone. Their findings showed that patients who were treated with olanzapine or risperidone had lower physical activity and longer rest time in comparison to healthy subjects. These alternations may induce several metabolic side effects. Although, there was no differences in actigraphic measurements, scores of daytime sleepiness and sleep quality scales between patients treated with olanzapine and risperidone. These changes in activity and sleep pattern are related to clinical characteristics particularly the negative and depressive symptoms [10].

Taken together, actigraphic allows the researchers to assess the efficacy of different pharmacological interventions on sleep/wake patterns of specific disorder like schizophrenia, objectively.

Limitations

Actigraphy does have some disadvantages and it should be noted that it is not the gold standard to detect sleep disorders. Actigraphy cannot detect the sleep staging in individuals. Computer scoring programs are variable and may not control for potential artifacts. Also, validity of actigraphy

method in special subjects such as elderly people, patients with other major health problems, patients with long periods of immobility, and poor quality of sleep is more questionable. Furthermore, the results from our review, particular the outcome from the search engines, maybe different once the new DSM will be out, and thus this review may need further update. Additionally, our result may be interpreted differently in terms of the emerging DSM-V, given that psychotic disorders has been suggested to be replace by attenuated psychosis syndrome; and instead of schizophrenia, salience dysregulation syndrome could be substituted.

Conclusion

The recent literature suggests that actigraphy has wide applications in the field of psychiatry and it is a reliable tool for evaluating sleep patterns in patients with severe forms of psychopathology such as psychotic disorders. Actigraphy is suggested for evaluation of sleep/wake habits and circadian rhythms among psychotic disorders and to aid in the differentiation between vague diagnoses. It has potential to investigate the relationship between motor functioning and neuropathology of psychotic disorders as a supplementary method. In addition, actigraphy may be helpful in the assessment of sleep/wake patterns after pharmacological interventions. In summary, actigraphy has improved our understanding of motor function and sleep patterns in individuals with psychotic disorders in less acute environments than the laboratory setting, and allows for the objective measurement of sleep in periods when the individual is in a familiar and routine environment.

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