Quantitative Motor Activity Differentiates Schizophrenia Subtypes

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Key Words
Actigraphy · Catatonia · Psychosis · Motor retardation · Negative syndrome · Antipsychotics

Abstract
Background: Motor symptoms are frequent in schizophrenia and relevant to the diagnosis of subtypes. However, the assessment has been limited to observations recorded in scales and experimental designs. The aim of this study was to use wrist actigraphy to obtain motor activity data in 3 schizophrenia subtypes. Methods: In total, 60 patients with schizophrenia (35 paranoid, 12 catatonic, 13 disorganized) were investigated using continuous wrist actigraphy over 24 h in an inpatient setting on average 38 days after admission. Data of the wakeful hours of the day were analyzed. Results: The activity level was predicted by schizophrenia subtype and by the type of antipsychotic medication. The movement index and mean duration of uninterrupted immobility were found to be predicted only by the schizophrenia subtype. Age, gender, duration of illness and chlorpromazine equivalents did not contribute to the variance of the activity data. A MANOVA demonstrated the significant differences in the 3 parameters between schizophrenia subtypes (p = 0.001). Patients with catatonic schizophrenia had lower activity levels, a lower movement index and a longer duration of immobility than those with paranoid schizophrenia. Conclusions: Schizophrenia subtypes can be differentiated using objective measures of quantitative motor activity. The increased duration of immobility appears to be the special feature of catatonic schizophrenia.

Introduction
The quality and frequency of motor symptoms in schizophrenia have been accorded importance in the diagnosis of subtypes and were described in detail in classical psychopathology [1, 2]. Today, their prevalence and thus the diagnosis of catatonia appears to be decreasing, and their clinical distinction from neuroleptic side effects is unreliable [3, 4].

Motor symptoms, however, occur frequently in schizophrenia. In fact, 50% of a schizophrenia group were found to present at least 1 motor symptom during the acute stage [5]. Further, motor symptoms are still part of the diagnostic criteria for schizophrenia in DSM-IV and ICD-10. They are necessary for the diagnosis of the catatonic subtype of schizophrenia even if the mere presence of motor symptoms is not sufficient in either classification system. Instead, a predominance of motor symptoms is required to allow the diagnosis of catatonia.

Research interest in motor symptoms of schizophrenia has increased within the past 2 decades, and several studies suggest an important role for the motor system in this disorder. The development of motor abilities has been re-
peatedly shown to be delayed in children who later suffer from schizophrenia [6–8]. A body of evidence supports impaired motor control and motor sequencing in schizophrenia [9–11]. Reduced volume in the cerebellum in schizophrenia was reported [8, 12] and thought to relate to disturbances of the motor system. Gait disturbances have been observed in patients with schizophrenia [13] as well as bradykinesia in 8–18% of the neuroleptic-naïve patients [14]. Parkinsonism and dyskinesia were demonstrated to be related to psychopathology in neuroleptic-naïve first-episode patients [15]. In addition, several studies on neurological soft signs have reported motor disturbances in both treated and untreated schizophrenia [16–19].

The assessment of motor symptoms, however, is challenging and often limited to clinical observation and specific rating scales. On the other hand, studies relying on quantitative measurements usually depended on laboratory settings [11, 20, 21]. To obtain information about the motor behavior of schizophrenic patients in naturalistic environments, objective quantitative measurements are needed.

Actigraphy is a validated tool in sleep medicine and has become important for motion analysis in psychiatric research [22]. However, only few studies on quantitative motor activity during wakefulness have been conducted in schizophrenia using actigraphy [23–25]. Farrow et al. [23, 24] reported a negative correlation of the cumulated activity counts with avolition. We have reported higher motor activity levels (AL) in cycloid psychoses as compared to paranoid schizophrenia [26] and poor correlation between objective motor activity and expert ratings [27]. In addition, disturbances of the sleep–wake cycle as measured by actigraphy were reported in schizophrenia [28–30].

We were interested whether DSM-IV schizophrenia subtypes would differ with regard to quantitative motor activity as measured by actigraphy. In particular, we hypothesized that specific motor features of catatonic schizophrenia could be identified compared to the other schizophrenic subtypes. Further, based on the fact that the clinical distinction between catatonic and drug-induced movement disorders is unreliable, we explored the possibility whether objective movement parameters would be more reliable to discriminate them.

**Subjects and Methods**

**Subjects**

Study participants were recruited during the first 3 weeks after admission to the inpatient department of the University Hospital of Psychiatry Bern, Switzerland. The inclusion criterion was a DSM-IV diagnosis of schizophrenia based upon clinical interviews and review of all records available, taking into account the longitudinal course of the disorder. The exclusion criteria were a history of or concomitant neurological or medical disorder, or substance abuse (except for nicotine). Participation was unpaid. Sixty-three patients were included in the study with an overlap with the sample reported earlier [27]. Three of the patients received anticholinergic drugs which may influence motor activity and were excluded from the final analyses.

Chlorpromazine equivalents were calculated according to Rey et al. [31] and Woods [32]. In addition, 14 patients were also treated with antidepressants for the negative syndrome in schizophrenia. Seven received a selective serotonin reuptake inhibitor, 1 a selective noradrenaline reuptake inhibitor, 3 a selective serotonin and noradrenaline reuptake inhibitor, and 3 patients were on tricyclic antidepressants. No difference in antidepressant prescription was detected between the schizophrenia subgroups ($\chi^2 = 5.515; \text{d.f.} = 8; p = 0.773$). The demographic and clinical variables are displayed in table 1. After a complete explanation of the aims and procedures of the study, the patients provided written informed consent. The procedures are in accordance with the declaration of Helsinki and had been approved by the local ethics committee (KEK No. 208/06).

**Measures**

The patients were interviewed and assessed using the Positive and Negative Syndrome Scale (PANSS) [33]. In addition, they wore an actigraph (Actiwatch®; Cambridge Neurotechnology Inc., UK) on the wrist of the nondominant arm for 24 consecutive hours for the continuous recording of motor activity. Handedness was determined by asking the patients about the preferred hand when writing, brushing teeth and eating with a spoon.

**Motor Activity Parameters**

Movement counts of the actigraph were stored in 2-second intervals, allowing continuous recording for a maximum of 36 h on the 64-kB memory. We chose the smallest possible interval to achieve maximum temporal resolution. The nondominant arm was chosen because it reflects average movement during day- and nighttime, while actigraphy in the dominant arm represents maximum movements that are strongly related to manual work or activities [34]. The start of measurement varied between 10:00 and 15:00, but for the analyses we included the whole 24-hour cycle, so each hour of the day was covered. In 3 participants (1 of each subtype), however, we failed to record complete 24-hour datasets as these patients removed their actigraphs during sleep.

Motor activity is subject to circadian rhythms. By investigating inpatients of 1 large psychiatric university hospital we had the chance to normalize external and social rhythms. The patients on all wards get up around 7:00, have breakfast at 07:30, lunch at 11:30 and dinner at around 18:00. Also, they are engaged in several group activities during the day and have social contact until 22:00, when the lights are usually turned off. Measurements were performed exclusively during weekdays to assure that there was an equal impact of group therapies across the participants. At the end of the recording, the patients were asked to provide sleep log information and to fill in the Pittsburgh Sleep Quality Index [35].

**Data Analysis**

The data were analyzed using Sleep Analysis $5^\circledR$ (Cambridge Neurotechnology) and EXCEL$^\circledR$ templates for further analyses.
Using the sleep log information, we removed data collected during sleep. We chose to extract 3 parameters from the data that had previously been described [34] and used in schizophrenia [26, 27]. AL is the mean number of activity counts per hour. The movement index (MI) is the percentage of periods with an activity count >0, reflecting the proportion of 2-second periods with activity or immobility. The mean duration of uninterrupted immobility periods (MIP) provides a global measure of the distribution and number of immobility periods. Further analyses were performed using SPSS 15.0.

General linear models (GLM) were computed for AL, MI and MIP as dependent variables using Wald $\chi^2$. The main effects of the following predictors were compared: schizophrenia subtype, age, gender, type of antipsychotic medication, chlorpromazine equivalents, number of episodes and duration of illness. Afterwards, a MANOVA using Wilks’ $\lambda$ with AL, MI and MIP as dependent variables and schizophrenia subtype as between-subject variable was performed. Bonferroni correction was applied for multiple comparisons. Differences between groups in the descriptive statistics were tested using 1-way ANOVAs or $\chi^2$ tests when appropriate. Correlations of activity parameters were performed using Pearson’s correlation. All levels of significance are 2-tailed.

### Results

**Motor Activity during Wakefulness**

For each of the motor activity parameters a GLM was computed with the predictors schizophrenia subtype, chlorpromazine equivalents, type of antipsychotic drugs used (none, atypical, typical or both), age, gender, number of episodes and duration of illness. The GLM of AL demonstrated a significant main effect for schizophrenia subtype ($\chi^2 = 6.055, p = 0.014$) and type of antipsychotic treatment ($\chi^2 = 3.861, p = 0.049$). However, an ANOVA for AL with schizophrenia subtype and type of antipsychotic failed to detect an interaction of both factors ($F_{5, 60} = 0.984, p = 0.437$).

When we performed an independent t test on AL, we found a nonsignificant trend towards higher AL in the patients treated with atypical antipsychotic drugs only ($T_{40} = –1.853, d.f. = 38, p = 0.072$). However, the type of antipsychotic drug used was comparable between the schizophrenia subtypes (see table 1).

The GLM of MI found a significant main effect only for schizophrenia subtype ($\chi^2 = 5.968, p = 0.015$). Similarly, the GLM of MIP showed a significant main effect only for the predictor schizophrenia subtype ($\chi^2 = 11.563, p < 0.001$). None of the other predictors had a significant effect on any of the activity parameters.

As the GLMs revealed schizophrenia subtype to have a main effect on motor activity parameters, these 3 parameters were entered as dependent variables into a MANOVA with schizophrenia subtype as between-subject factor. Schizophrenia subtype demonstrated a significant overall effect (Wilks’ $\lambda$: $F_{5, 60} = 4.320, p = 0.001$). Significant differences between schizophrenia subtypes

### Table 1. Characteristics of the schizophrenia subtypes

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Schizophrenia subtype</th>
<th>Comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>paranoid (n = 35)</td>
<td>catatonic (n = 12)</td>
</tr>
<tr>
<td>Male gender</td>
<td>18/51.4</td>
<td>6/50.0</td>
</tr>
<tr>
<td>Antipsychotic treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>2/5.3</td>
<td>0/0</td>
</tr>
<tr>
<td>Typical</td>
<td>2/5.7</td>
<td>2/16.7</td>
</tr>
<tr>
<td>Atypical</td>
<td>24/68.6</td>
<td>5/41.7</td>
</tr>
<tr>
<td>Both</td>
<td>7/20.0</td>
<td>5/41.7</td>
</tr>
<tr>
<td>Age, years</td>
<td>39.60/9.64</td>
<td>45.50/12.19</td>
</tr>
<tr>
<td>Duration of illness, years</td>
<td>10.97/8.84</td>
<td>6.34/5.70</td>
</tr>
<tr>
<td>Episodes</td>
<td>7.31/6.21</td>
<td>4.25/2.96</td>
</tr>
<tr>
<td>Chlorpromazine equivalents</td>
<td>488.45/350.35</td>
<td>566.13/537.62</td>
</tr>
<tr>
<td>PANSS positive score</td>
<td>17.60/5.53</td>
<td>14.92/4.03</td>
</tr>
<tr>
<td>PANSS negative score</td>
<td>17.06/5.43</td>
<td>20.00/7.66</td>
</tr>
<tr>
<td>PANSS total score</td>
<td>75.51/15.51</td>
<td>79.92/17.60</td>
</tr>
</tbody>
</table>
were detected in each of the dependent variables: AL (F2, 60 = 4.629, p = 0.014), MI (F2, 60 = 3.615, p = 0.033) and MIP (F2, 60 = 10.397, p < 0.001). The post hoc t-tests revealed differences between patients with catatonic and paranoid schizophrenia (see fig. 1a–c). Indeed, in paranoid schizophrenia the highest AL and MI were found, while patients with catatonic schizophrenia displayed the longest duration of immobility.

AL correlated negatively with the PANSS negative subscore. On the other hand, the PANSS positive subscore correlated positively with MI and negatively with MIP (see table 2). Therefore, stronger negative syndrome severity was associated with less activity, while stronger positive syndrome scores indicated shorter immobility and a higher proportion of active periods.

The PANSS item score for motor retardation was highest among catatonia patients (χ2 = 19.337, d.f. = 10, p = 0.008). However, motor retardation to some extent was rated frequently in each subtype (paranoid 37%, catatonic 91%, disorganized 47%). As expected, specific symptoms such as mannerism were most frequent among patients with catatonic schizophrenia (92%; χ2 = 28.880, d.f. = 12, p < 0.001), while other items of the negative syndrome were equally rated between the groups (social avoidance: p = 0.237; lack of spontaneity: p = 0.427; blunted affect: p = 0.499). Likewise, the PANSS items disturbance of volition and depression were not rated differently between the groups (p = 0.147 and p = 0.518).

**Sleep**

The actual sleep time differed between the groups (see table 3). No variations were identified in terms of sleep quality and motor activity during sleep.

**Discussion**

The results demonstrate differences in motor activity during wakefulness in schizophrenia subtypes and support our hypothesis. In fact, they diverge in terms of the magnitude of activity (AL), the relative amount of active periods (MI) and the mean duration of immobility (MIP). Patients with catatonic schizophrenia had a lower overall AL, lower MI and longer immobility periods as compared to patients with paranoid schizophrenia. No post hoc differences were found between the disorganized and other subtypes. Even though the type of antipsychotic medication had some unspecific effect on AL, there was no interaction of antipsychotic and subtype associated with AL. All other factors presumably influencing motor activity, such as age, gender, chlorpromazine equivalents and duration of illness, had no effect on the parameters tested.
As in an earlier study [27], reduced magnitude of motor activity (AL) was associated with higher PANSS negative syndrome scores. In contrast, with higher PANSS positive syndrome scores we found a shorter duration of immobility (MIP) and a higher proportion of active periods (MI). Both correlations indicated less rest during marked positive syndromes. Some single PANSS items might be more relevant to motor activity than others. As expected, motor retardation and mannerisms were rated most frequently in catatonic schizophrenia. Depression, lack of spontaneity, disturbance of volition and social avoidance displayed no differences between the subtypes.

In the GLMs we found no impact of chlormpromazine equivalents on the motor activity parameters, nor could we observe an impact of the type of antipsychotic administered on MIP and MI. In AL, however, there was a difference between the types of antipsychotic administered. On the other hand, we failed to find specific differences in the post hoc tests. In addition, there was no interaction of the factors antipsychotic medication and subtype of schizophrenia. A nonsignificant trend towards higher activity was observed in AL when we compared atypical versus typical antipsychotics. This ambiguous result is in line with the finding that atypical antipsychotic drugs vary substantially in their ability to induce extrapyramidal side effects [36]. However, there were no differences between the groups in terms of the prescription of antipsychotic drugs.

The most prominent difference between the subtypes was found in the duration of immobility. Thus, our results suggest that the duration of immobility could reflect specific catatonic symptomatology, the intrinsic motor disturbances in schizophrenia [15] or both.

Catatonic patients exhibit an irregular pattern of activity with longer periods of immobility followed by active phases. This could also explain the low average AL because longer immobility would contribute to lower AL. Similarly, longer duration of immobility would decrease the proportion of active periods in favor of inactive periods and thereby lead to a lower MI. Our results suggest that motor activity in catatonic schizophrenia is characterized by intermittent inhibitions preventing the patients from regular, fluent movement patterns. These phenomena, interestingly, are usually not perceived by clinical observation and lack operationalization in standard psychopathological scales and diagnostic systems. In fact, no significant difference in the negative syndrome was detected between the subgroups. Motor retardation as a PANSS item was frequent in all subgroups, even though the scores in catatonia were higher. Therefore, the categorization of single patients as catatonic simply by the observation of reduced motor activity is imprecise. Employing actigraphic measures such as the duration of immobility could increase the quality of diagnosis, adding an objective parameter to the clinical observation of rather complex catatonic movement patterns like mannerisms, stereotypy, echophenomena, perseveration and automatic obedience.

Patients with catatonic schizophrenia were shown to have specific deficits in decision making and set shifting, neuropsychological measures associated with ventral prefrontal cortical function [37]. Indeed, the medial prefrontal cortex is critical to the evaluation of the relevance of cognitive goals and motor acts [38]. Findings from neuroimaging studies in catatonic schizophrenia reported a reduced cerebral blood flow in the parietal lobe [39].

Table 3. Sleep data

<table>
<thead>
<tr>
<th>Schizophrenia type</th>
<th>Paranoid mean</th>
<th>Paranoid SD</th>
<th>Catatonic mean</th>
<th>Catatonic SD</th>
<th>Disorganized mean</th>
<th>Disorganized SD</th>
<th>F</th>
<th>d.f.</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PSQI</td>
<td>6.50</td>
<td>3.57</td>
<td>8.00</td>
<td>2.66</td>
<td>5.83</td>
<td>3.10</td>
<td>1.393</td>
<td>2</td>
<td>0.257</td>
</tr>
<tr>
<td>Sleep efficiency, %</td>
<td>84.40</td>
<td>6.71</td>
<td>86.22</td>
<td>7.66</td>
<td>79.56</td>
<td>8.37</td>
<td>2.724</td>
<td>2</td>
<td>0.075</td>
</tr>
<tr>
<td>Sleep latency, hh:mm:ss</td>
<td>00:28:32</td>
<td>00:31:06</td>
<td>00:27:11</td>
<td>00:17:41</td>
<td>00:41:30</td>
<td>00:45:16</td>
<td>0.775</td>
<td>2</td>
<td>0.466</td>
</tr>
<tr>
<td>Actual sleep time, hh:mm:ss</td>
<td>07:41:38</td>
<td>01:36:42</td>
<td>08:55:05</td>
<td>01:28:16</td>
<td>06:09:45</td>
<td>03:21:06</td>
<td>5.008</td>
<td>2</td>
<td>0.010*</td>
</tr>
<tr>
<td>Immobile time percent, %</td>
<td>91.95</td>
<td>5.08</td>
<td>91.95</td>
<td>7.28</td>
<td>88.21</td>
<td>8.25</td>
<td>1.603</td>
<td>2</td>
<td>0.211</td>
</tr>
<tr>
<td>Sleep AL, counts/h</td>
<td>1,814.91</td>
<td>1,449.91</td>
<td>1,440.07</td>
<td>1,023.58</td>
<td>1,763.93</td>
<td>1,671.15</td>
<td>0.284</td>
<td>2</td>
<td>0.754</td>
</tr>
<tr>
<td>Sleep MI, %</td>
<td>4.65</td>
<td>3.26</td>
<td>4.52</td>
<td>3.31</td>
<td>5.46</td>
<td>4.34</td>
<td>0.285</td>
<td>2</td>
<td>0.753</td>
</tr>
<tr>
<td>Sleep MIP, s</td>
<td>78.55</td>
<td>60.05</td>
<td>79.33</td>
<td>54.24</td>
<td>53.23</td>
<td>33.75</td>
<td>1.034</td>
<td>2</td>
<td>0.363</td>
</tr>
</tbody>
</table>

*p = 0.008 (catatonic > disorganized; post hoc t test, Bonferroni correction).
40], structural alterations in frontoparietal areas [41] and functional deficits in the ventromedial prefrontal cortex [42]. Another explanation for reduced motor activity in catatonia stems from the association of negative symptoms and motor activity. In fact, negative symptoms correlate highly with catatonia [43] and some authors attribute this to a higher vulnerability of catatonic schizophrenia to neuroleptic-induced negative symptoms [44].

At the current state of research, it is not possible to attribute quantitative motor activity to a state or trait phenomenon in schizophrenia subtypes. From the historical view of schizophrenia subtypes we would conclude that disturbances of motor activity are stable over time and over different periods of the disorder [1, 2]. Neurological soft signs, however, seem to vary with the course of the disorder to some extent, while some symptoms remain stable after antipsychotic treatment [15, 19].

Slight differences between the groups were also documented for the actual sleep time, with disorganized schizophrenia displaying the shortest duration. However, our data on sleep measures are only of descriptive value. They must be interpreted with caution, since longer recording periods are recommended for actigraphic estimates of sleep [29, 45].

The strength of our study is the objective motor activity assessment during the wake period of a day in a patient group with comparable social and circadian rhythms. In addition, we ruled out the impact of age, gender, chlorpromazine equivalents and duration of illness on our activity data. Also, we excluded patients on anticholinergic medication. Limitations of the study are the small number of subjects with catatonic and disorganized subtypes, due to the lower prevalence. Since we did not control for the intrinsic parkinsonism and dyskinesia reported also in unmedicated schizophrenia [15], patients receiving anticholinergic drugs against extrapyramidal side effects were excluded. We did not, however, control for the smoking status, which might also influence motor behavior.

At entry, diagnoses were established according to DSM-IV after thorough clinical interview and review of the available records. However, no structured diagnostic interview was performed. Further, it cannot be excluded that ambidextrous patients, who use their nondominant arm more frequently than right-handed subjects, might have been included. Another problem is the correct interpretation of immobilization. In sleep research, strongly reduced activity or immobility during the day as measured by actigraphy is defined as daytime napping (i.e. sleep) [46, 47]. Higher activity scores in short-term actigraphy are associated with signs of arousal in EEG of healthy controls [48]. In psychiatric conditions, however, it is possible to be awake and akinetic. The participants were asked to report daytime napping in their sleep logs. Data during sleep periods were removed from the analysis of the main results on activity during wakefulness (see methods). However, we cannot rule out that some of the information provided by the patients was inaccurate.

To the best of our knowledge, this study is the first to report differences in schizophrenia subtypes regarding the quantitative motor activity by objective means. The major finding is the increased duration of immobility periods as a specific feature of catatonic schizophrenia. Still, further research should address the specific activity pattern in disorganized schizophrenia as well as the underlying pathophysiology of motor activity in schizophrenia subtypes. In addition, the duration of immobility and the MI were found to be independent of the type and dosage of antipsychotic drugs and therefore may reflect intrinsic motor features of schizophrenia. Actigraphy does not distress patients and may help better understand schizophrenia-specific movement disorders and evaluate the treatment outcome, as has been previously shown in dementia [49].

References

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