Schizophrenia Bulletin vol. 51 no. 4 pp. 1162–1172, 2025
https://doi.org/10.1093/schbul/sbae153
Advance Access publication September 2, 2024

Testing a Motor Score Based on PANSS Ratings: A Proxy for Comprehensive Motor Assessment

Niluja Nadesalingam[*,1], Alexandra Kyrou[1], Victoria Chapellier[1], Lydia Maderthaner[1], Sofie von Känel[1,2], Florian Wüthrich[1], Melanie G. Nuoffer[1,2], Stephanie Lefebvre[1], Anastasia Pavlidou[1], Thomas Wobrock[3,4], Wolfgang Gaebel[5], Joachim Cordes[5,6], Berthold Langguth[7], Peter Falkai[8], Thomas Schneider-Axmann[8], Wolfgang Strube[9], Alkomiet Hasan[9,10], and Sebastian Walther[1,11]

[1]Translational Research Center, University Hospital of Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland; [2]Graduate School for Health Sciences, University of Bern, Bern, Switzerland; [3]Centre of Mental Health, County Hospitals Darmstadt-Dieburg, Groß-Umstadt, Germany; [4]Department of Psychiatry and Psychotherapy, Georg-August University Göttingen, Göttingen, Germany; [5]Department of Psychiatry and Psychotherapy, Medical Faculty, Heinrich-Heine University, Düsseldorf, Germany; [6]Department of Psychiatry and Psychotherapy, Kaiserswerther Diakonie, Florence Nightingale Hospital, Düsseldorf, Germany; [7]Department of Psychiatry and Psychotherapy, University of Regensburg, Regensburg, Germany; [8]Department of Psychiatry and Psychotherapy, Klinikum der Universität München, Ludwig Maximilian University Munich, München, Germany; [9]Department of Psychiatry, Psychotherapy and Psychosomatics, Medical Faculty, University of Augsburg, Augsburg, Germany; [10]DZPG (German Center of Mental Health), Partner Site, Munich/Augsburg, Augsburg, Germany; [11]Department of Psychiatry, Psychosomatics, and Psychotherapy, Center of Mental Health, University Hospital of Würzburg, Würzburg, Germany

[*]To whom correspondence should be addressed; Translational Research Center, University Hospital of Psychiatry and Psychotherapy, Bolligenstrasse 111, 3000 Bern 60, Switzerland; tel: +41 31 930 9755, fax: +41 31 632 8950, e-mail: niluja.nadesalingam@unibe.ch

***Background and Hypothesis*: Abnormal psychomotor behavior is a core schizophrenia symptom. However, assessment of motor abnormalities with expert rating scales is challenging. The Positive and Negative Syndrome Scale (PANSS) includes 3 items broadly related to hypokinetic motor behavior. Here, we tested whether a sum score of the PANSS items mannerisms and posturing (G5), motor retardation (G7), and disturbance of volition (G13) corresponds to expert ratings, potentially qualifying as a proxy-marker of motor abnormalities. *Study Design*: Combining baseline datasets ($n = 196$) of 2 clinical trials (OCoPS-P, BrAGG-SoS), we correlated PANSS motor score ($PANSS_{mot}$) and 5 motor rating scales. In addition, we tested whether the cutoff set at ≥3 on each PANSS motor item, ie, "mild" on G05, G07, and G13 (in total ≥9 on $PANSS_{mot}$) would differentiate the patients into groups with high vs low scores in motor scales. We further sought for replication in an independent trial (RESIS, $n = 102$), tested the longitudinal stability using week 3 data of OCoPS-P ($n = 75$), and evaluated the validity of $PANSS_{mot}$ with instrumental measures of physical activity ($n = 113$). *Study Results*: $PANSS_{mot}$ correlated with all motor scales (Spearman-Rho-range 0.19–0.52, all $P \leq .007$). Furthermore, the cutoff set at ≥3 on each PANSS motor item was able to distinguish patients with high vs low motor scores in all motor scales except using Abnormal Involuntary Movement Scale (Mann-Whitney-U-Tests: all $U \geq 580$, $P \leq .017$). *Conclusions*: Our findings suggest that $PANSS_{mot}$ could be a proxy measure for hypokinetic motor abnormalities. This might help to combine large datasets from clinical trials to explore whether some interventions may hold promise to alleviate hypokinetic motor abnormalities in psychosis.**

Key words: schizophrenia/psychosis/motor abnormalities/hypokinetic motor disorders/psychopathology/clinical research

Introduction

Schizophrenia affects approximately 1% of the general population.[1] It is characterized by 8 symptom dimensions, including (1) hallucinations, (2) delusions, (3) negative symptoms, (4) disorganized speech, (5) cognition, (6) depression, (7) mania, and (8) abnormal psychomotor behaviors.[2]

Motor abnormalities have been reported across all stages of schizophrenia spectrum disorders.[3–5] At least

1 motor symptom was observed in drug-naïve first episode psychosis (66%), at hospital admission (59%), and in chronic patients (80%).[3,6,7] Abnormal psychomotor behaviors are associated with lower subjective well-being, poor social functioning, and lower quality of life.[8] Importantly, studies demonstrate that motor abnormalities have predictive value for clinical and functional outcomes.[9–12] Furthermore, hand gestures that are crucial for social interaction are affected by motor abnormalities contributing to stigmatization.[13–15] In sum, motor abnormalities are important sources of information on the course of schizophrenia and might become valuable treatment targets.

Nevertheless, in large-scale studies on the longitudinal course of schizophrenia or in treatment studies, little attention is paid to the assessment of motor symptoms. In prospective trials, motor assessment is often limited to single constructs, such as neurological soft signs, dyskinesia, parkinsonism, or akathisia,[10,16,17] whereas dystonia, catatonia, or psychomotor slowing are not investigated. Comprehensive clinical assessment of multiple motor constructs is time-consuming. Given the interest in motor signs and the longitudinal changes of motor symptoms, it would be most effective to analyze large datasets with a proxy measure of motor abnormalities. Ideally, one would be able to calculate a motor score from existing longitudinal ratings of psychopathology, such as the Positive and Negative Syndrome Scale (PANSS).[18]

The PANSS has been frequently used in schizophrenia treatment trials and observational studies. Single PANSS items cover some hypokinetic motor abnormalities, ie, G5 "mannerisms and posturing," G7 "motor retardation," and G13 "disturbance of volition." Item G5 mannerisms and posturing assesses unnatural, awkward, stilted, disorganized, or bizarre body movements or posture, which tap into catatonia symptoms.[19] Item G7 "motor retardation" summarizes reduced motor activity expressed in slow or low-amplitude movements as well as slowed speech, decreased response to stimuli, and poor body tone. This item references to psychomotor slowing.[20] Item G13 "disturbance of volition" involves disruptions in deliberate initiation, maintenance, and regulation of one's thoughts, behavior, movements, and speech. G13 also taps into core catatonia signs, such as verbigeration, perseveration, or ambitendency. Albeit these items span multiple symptom domains such as disorganization or abnormal psychomotor behavior, they tap predominantly into hypokinetic motor abnormalities, ie, catatonia and psychomotor slowing.[19–21] Studies probing the external validity of single PANSS items to characterize psychomotor abnormalities demonstrated insufficient validity with instrumental measures or brain imaging.[22,23] Alternatively, we sought to test the sum of 3 PANSS motor items creating a PANSS motor score ($PANSS_{mot}$) for hypokinetic motor abnormalities, which may provide better external validity than single items. Similarly, PANSS items P04 "excitement" and G14 "poor impulse control" potentially capture hyperkinetic motor abnormalities, such as dyskinesia, catatonia, or akathisia.[24] Thus, the 2 items could be summarized to a hyperkinetic $PANSS_{mot}$.

Here, we leverage existing well-characterized datasets to test whether a PANSS hypokinetic motor score summing G05, G07, and G13 was associated with expert ratings of motor abnormalities and could be established as a proxy-marker for motor abnormalities. We expect that subjects with high $PANSS_{mot}$ scores will have more severe hypokinetic movement disorders, such as catatonia, psychomotor retardation, and parkinsonism. Furthermore, we hypothesize that instrumentally assessed physical activity levels are correlating with $PANSS_{mot}$. Given that participants in these studies were predominantly presenting with hypokinetic motor abnormalities or negative symptoms, we primarily tested the $PANSS_{mot}$ on hypokinetic behaviors. In addition, we tested a hyperkinetic motor score from P04 and G14 but expected weak associations with motor rating scales within the existing datasets.

Methods

Participants

The current report consists of multiple datasets. The main analysis was based on the baseline data of $n = 196$ patients, who were recruited in the context of 2 randomized clinical trials, ie, OCoPS-P: *Overcoming Psychomotor Slowing in Psychosis* (ClinicalTrials.gov Identifier: NCT03921450)[11,25–31] and BrAGG-SoS: *Brain stimulation and Group therapy to improve Gesture and Social skills in Psychosis* (ClinicalTrials.gov Identifier: NCT04106427)[32–34] at the in- and outpatient departments of the University Hospital of Psychiatry and Psychotherapy, Bern, Switzerland (hereafter referred to as Bern-sample). All patients were diagnosed with schizophrenia spectrum disorders according to the Structured Clinical Interview for DSM-5 (SCID-5) and they provided written informed consent after receiving a complete description of the study. Both studies complied with the Declaration of Helsinki and were approved by the Bern Ethics Committee (OCoPS-P BASEC-Nr: 2018-02164; BrAGG-SoS BASEC-Nr: 2019-00798). General exclusion criteria included active substance dependence other than nicotine, neurological disorders compromising motor behavior, and traumatic brain injury. Most of the patients were on antipsychotic medication during data acquisition and the mean olanzapine equivalents were computed according to Leucht et al.[35] Assessments were performed by psychiatry residents in training with more than 2 years of experience. All raters were trained by the senior author with regular checks of interrater agreement. All assessments were performed in 1 baseline session including psychopathology and specific motor rating scales.

Furthermore, another dataset was used for independent validation. We included baseline data from the clinical trial RESIS: *Repetitive Transcranial Magnetic Stimulation for the Treatment of Negative Symptoms in Schizophrenia* (ClinicalTrials.gov Identifier: NCT00783120; approved by the Ethic Board of the University Medical Center Göttingen (approval number: 23/11/06)).[36] For this study a total of 175 patients were screened and 157 patients completed the baseline (day 0). Patients diagnosed with schizophrenia according to ICD-10 and Mini-International Neuropsychiatric Interview Plus interview[37] with predominant negative symptoms were enrolled in this trial. Additional inclusion criteria were stable antipsychotic medication for at least 2 weeks and a minimum illness duration of 1 year. Chlorpromazine equivalents according to Woods[38] are provided in table 1. Recruitment and data collection were conducted at 3 German university hospital centers, ie, Göttingen, Düsseldorf, and Regensburg (for further information, see Ref. 36). From this sample, we analyzed the data of $n = 102$ patients completing the PANSS and St. Hans Rating Scale (SHRS) assessments.[39] In this study, PANSS raters were trained by reviewing standardized videotaped interviews.

Measures

PANSS and PANSS$_{mot}$ Psychopathology was assessed with the PANSS.[18] We created a PANSS$_{mot}$ defined as the sum of the items mannerisms and posturing (G05), motor retardation (G07), and disturbance of volition (G13). The cutoff was set at ≥3 points ("mild") on each of the items: G05, G07, and G13. Every patient scoring ≥3 points on each of these 3 items (total ≥9 points) was categorized as presenting motor abnormalities. As these 3 items mainly describe hypokinetic motor abnormalities, we performed a second set of analyses on PANSS items describing hyperkinetic motor abnormalities, ie, (P04) excitement and (G14) poor impulse control.

Motor Abnormalities and Expert Rating Scales We assessed a range of motor abnormalities using expert rating scales, ie, (1) catatonia using Bush-Francis Catatonia Rating Scale (BFCRS) and Northoff Catatonia Rating Scale (NCRS), (2) parkinsonism using Unified Parkinson's Disease Rating Scale Part III (UPDRS), (3) psychomotor slowing using Salpêtrière Retardation Rating Scale (SRRS), (4) neurological soft signs using Neurological Evaluation Scale (NES), and (5) dyskinesia using Abnormal Involuntary Movement Scale (AIMS).[40–45]

In RESIS, motor abnormalities were assessed using the SHRS, which provides 9 subscores, ie, objective akathisia, subjective akathisia, dystonia, parkinsonism total, parkinsonism global, active dyskinesia total, active dyskinesia global, passive dyskinesia total, and passive dyskinesia global.[39]

Longitudinal Stability in OCoPS-P Study We investigated the longitudinal stability of correlations between PANSS$_{mot}$ and motor abnormalities using week 3 data ($n = 75$) of OCoPS-P.[25] In this randomized, placebo-controlled, double-blinded, 4-arm study, we investigated the effect of add-on repetitive transcranial magnetic stimulation on psychomotor slowing. After 3 weeks of daily treatment, patients completed a series of assessments, including psychopathology assessments comprising PANSS and different motor rating scales (BFCRS, UPDRS, SRRS, and AIMS).

External Validity with Actigraphy Gross motor behavior was captured by wearing the tri-axial-accelerometer Move4 (movisens GmbH, Karlsruhe, Germany) on the non-dominant hand. Physical activity levels of waking hours were used for the current analysis by including the baseline data of $n = 113$ patients from OCoPS-P. For further information, see Refs. 22,31.

Analysis

All analyses were computed using IBM SPSS Statistics (v29.0.0.0). First, we conducted the main analysis in the Bern-sample. We created 2 groups, ie, high vs low PANSS$_{mot}$, by setting the cutoff at total ≥9 points, with at least ≥3 points ("mild") on each of the following items: G05 mannerisms and posturing, G07 motor retardation, and G13 disturbance of volition. Employing Mann-Whitney-U-Tests, we tested for group differences in motor rating scales, ie, BFCRS, NCRS, UPDRS, SRRS, NES, and AIMS. In addition, we investigated the associations between PANSS$_{mot}$ and motor rating scales, including their subscores, ie, BFCRS, NCRS, NCRS affect, NCRS motor, NCRS behavior, UPDRS, SRRS, NES, and AIMS using Spearman correlations. The results of NES subscores are reported in supplementary tables S1 and S3.

Furthermore, we explored how well PANSS$_{mot}$ was able to predict the catatonia caseness based on DSM-5 as well as BFCRS criteria using logistic regressions, while controlling for age and current daily dosage of antipsychotic medication. For the DSM-5 diagnosis of catatonia, the presence of 3 or more of the following items is required, ie, catalepsy, waxy flexibility, stupor, agitation, mutism, negativism, posturing, mannerisms, stereotypies, grimacing, echolalia, and echopraxia.[46] BFCRS, on the other hand, requires only the presence of 2 items of the first 14 items of BFCRS for catatonia case definition.[41] Moreover, we analyzed the effectiveness of PANSS$_{mot}$ in predicting the catatonia categorization using ROC-curves. We chose to do this analysis only for the motor abnormality catatonia, since there are clear and validated criteria for the diagnosis of catatonia.[19,21]

Table 1. Demographic and Clinical Data of the Different Studies

Study	Bern-sample		OCoPS-P		BrAGG-SoS		RESIS		Comparability OCoPS-P, BrAGG-SoS, and RESIS	
N	196		125		71		102			
	N	%	*N*	%	*N*	%	*N*	%	Test	*P*
Number of females (%)	91	46.4	61	48.8	30	42.3	25	24.5	$X^2_{(2, N = 298)} = 14.4$	.001
Number of inpatients	123	62.8	114	92.8	9	12.7				
No information about antipsychotics	0	0	0	0	0	0	4	3.9	$X^2_{(2, N = 298)} = 7.8$	.020
Patients with no antipsychotics (*n*)	10	5.1	3	2.4	7	9.9	1	1.0	$X^2_{(2, N = 294)} = 10.0$	.007
Monotherapy (*n*)	90	45.9	61	48.8	29	40.8	23	22.5	$X^2_{(2, N = 294)} = 15.1$	<.001
Combination therapy with other antipsychotics (*n*)	34	17.3	29	23.2	5	7.0	22	21.6	$X^2_{(2, N = 294)} = 8.8$	.012
Combination therapy with other medication[a] (*n*)	42	21.4	19	15.2	23	32.4	18	17.6	$X^2_{(2, N = 294)} = 8.6$	.013
Combination therapy with other antipsychotics and medication[a] (*n*)	20	10.2	13	10.4	7	9.9	34	33.3	$X^2_{(2, N = 294)} = 26.1$	<.001
Patients with Clozapine-intake (*n*)	45	23.0	25	20.0	20	28.2	17	16.7	$X^2_{(2, N = 294)} = 3.1$	.217
Patients with antiparkinsonian medication-intake (*n*)	1	0.5	0	0	1	1.4	12	11.8	$X^2_{(2, N = 294)} = 21.5$	<.001
FGA (*n*)	10	5.1	8	6.4	2	2.8	0	0	$X^2_{(2, N = 294)} = 6.9$	.031
SGA (*n*)	155	79.1	98	78.4	57	80.2	74	72.5	$X^2_{(2, N = 294)} = 0.6$	.749
FGA and SGA (*n*)	21	10.7	16	12.8	5	7.0	23	22.5	$X^2_{(2, N = 294)} = 9.5$	.009
	Mean	SD	Mean	SD	Mean	SD	Mean	SD		
Olanzapine equivalents. in mg	14.6	11.2	16.0	11.3	12.2	10.7	14.5	11.5	$F_{(2, 291)} = 2.6$	.079
Chlorpromazine equivalents. in mg							565	446		
Age in years	37.7	12.5	36.2	12.6	40.3	12.0	34.9	9.3	$F_{(2, 295)} = 5.0$	.008
BMI in kg/m^2	26.0	5.3	25.1	5.0	27.6	5.6	28.8	6.8	$F_{(2, 269)} = 11.1$	<.001
Duration of illness in years	12.4	11.8	10.3	10.8	16.0	12.5	9.8	9.1	$F_{(2, 271)} = 7.8$	<.001
Number of episodes	5.9	7.2	5.0	6.6	7.5	7.9	5.3[b]	5.5[b]	$F_{(2, 262)} = 3.2$	.042
PANSS total	73.0	20.6	77.6	17.9	64.7	22.6	78.9	15.0	$F_{(2, 295)} = 14.9$	<.001
PANSS positive	15.3	5.7	16.2	5.3	13.7	6.0	13.7	4.2	$F_{(2, 295)} = 8.2,$	<.001
PANSS negative	20.7	7.4	22.1	6.7	18.2	7.9	25.8	4.4	$F_{(2, 295)} = 30.1$	<.001
PANSS motor score (G5 + G7 + G13)	7.2	3.1	7.8	3.1	6.2	2.8	7.2	2.3	$F_{(2, 295)} = 7.9$	<.001
BFCRS total	4.4	4.6	5.0	4.4	3.5	4.8			$t(194) = -2.2$	.028
NCRS total	8.8	5.2	8.8	5.2						
UPDRS total	16.5	11.1	18.6	11.5	12.8	9.1			$t(174) = -3.9$	<.001
SRRS total	19.4	9.0	20.6	8.5	17.0	9.6			$t(125) = -2.6$	.010
NES total	14.6	9.5	14.4	9.6	15.1	9.2			$t(187) = 0.5$	.622
AIMS total	1.1	2.7	0.8	2.1	1.6	3.5			$t(99) = 1.7$	.101
SHRS Akathisia subjective							0.7	1.3		
SHRS Akathisia objective							0.5	1.0		
SHRS Dystonia							0.1	0.4		
SHRS Parkinsonism total							3.0	4.7		
SHRS Parkinsonism global							0.5	0.8		
SHRS passive Dyskinesia total							0.6	1.7		
SHRS passive Dyskinesia global							0.1	0.4		
SHRS active Dyskinesia total							0.5	1.6		
SHRS active Dyskinesia global							0.1	0.3		

Note: BMI, body mass index; FGA, first-generation antipsychotics; SGA, second-generation antipsychotics; PANSS, Positive and Negative Syndrome Scale; BFCRS, Bush-Francis Catatonia Rating Scale; NCRS, Northoff Catatonia Rating Scale; UPDRS, Unified Parkinson's Disease Rating Scale Part III; SRRS, Salpêtrière Retardation Rating Scale; NES, Neurological Evaluation Scale; AIMS, Abnormal Involuntary Movement Scale; SHRS, St. Hans Rating Scale.
[a]Other medication such as benzodiazepines, antidepressants, and antiepileptics.
[b]Number of inpatient treatments.

Next, we tested these associations in an independent dataset (RESIS), by correlating $PANSS_{mot}$ with the 9 subscores of SHRS using Spearman correlations.

In addition, we tested the longitudinal stability of the associations between $PANSS_{mot}$ and the motor scales BFCRS, UPDRS, SRRS, and AIMS using week 3 behavioral data of OCoPS-P. Finally, we verified the external validity by computing Spearman correlations between $PANSS_{mot}$ and actigraphic physical activity levels using OCoPS-P baseline data.

As sensitivity analyses, we checked for possible differences in $PANSS_{mot}$ between patients receiving first generation vs second generation antipsychotics with Mann-Whitney-U-Tests in the Bern-sample. Moreover, we tested the correlation of olanzapine equivalents on $PANSS_{mot}$. Furthermore, we conducted further sensitivity analysis by correlating $PANSS_{mot}$ with the PANSS subscores, ie, PANSS total, PANSS positive, PANSS negative, and additionally PANSS general excluding the 3 PANSS motor items. Finally, we tested whether a score of 2 items (P04 and G14) would reflect hyperkinetic motor abnormalities by applying the same Spearman correlations with motor rating scales and actigraphy. These results are reported in supplements. All analyses were corrected for multiple comparisons using FDR-correction, except for the logistic regressions and ROC-curves.

Results

Demographic and Clinical Information

The Bern-sample consisted of patients with moderate to severe psychopathology, including pronounced motor symptoms. Mean age was 37.7 ± 12.5 years and mean duration of illness was 12.4 ± 11.8 years. All but 10 subjects were on antipsychotics. Table 1 gives more information.

High vs Low $PANSS_{mot}$ in the Bern-Sample

Mann-Whitney-U-tests revealed that the cutoff set at 3 points on each PANSS motor item was able to distinguish between low and high motor scores in all motor rating scales (all $U \geq 580$, $P \leq .017$, $P_{(FDR)} \leq .021$) excluding AIMS (see figure 1, supplementary tables S1 and S2).

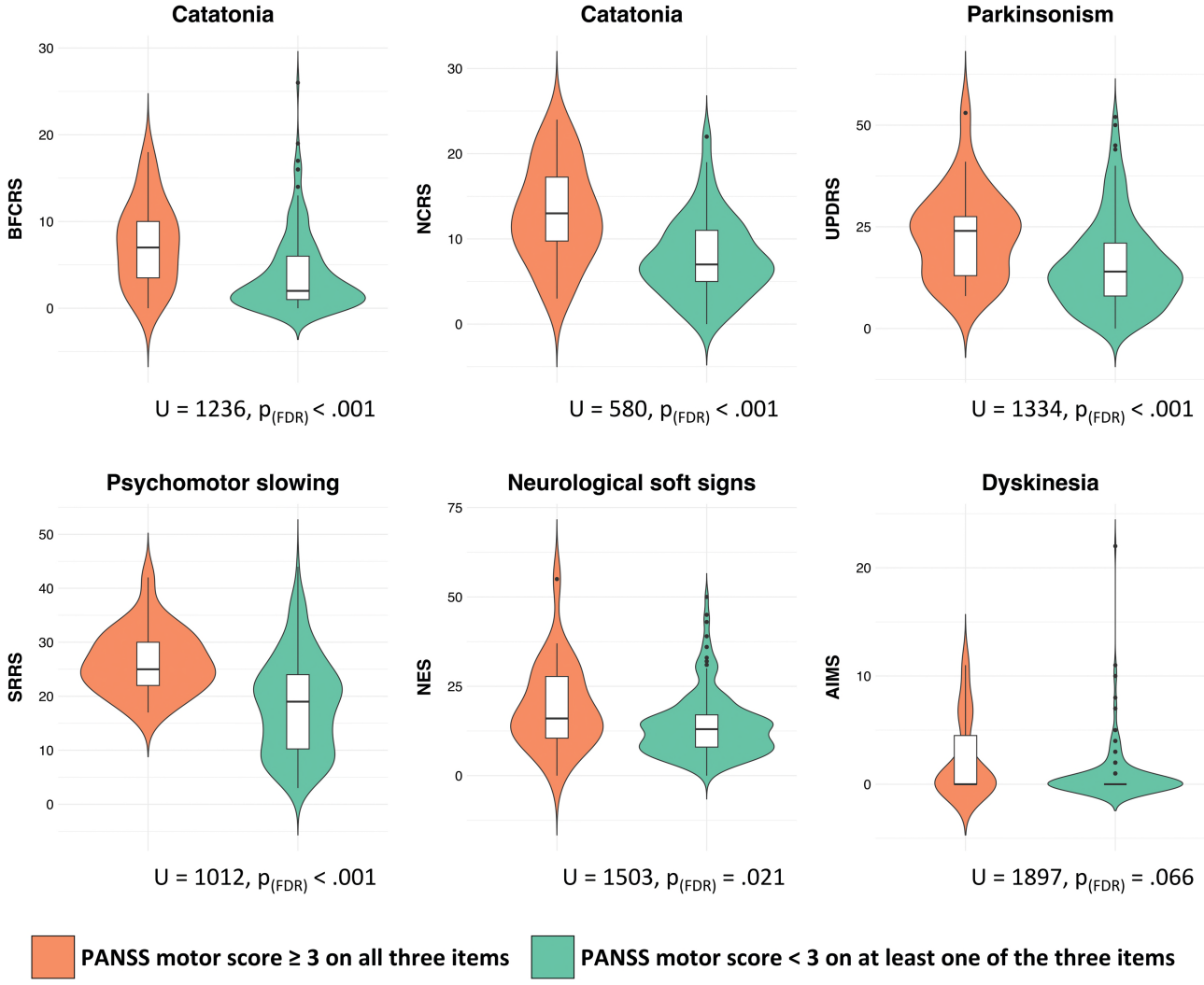

Fig. 1. Difference in motor rating scales based on PANSS motor score in the Bern-sample.

Note: The categorization of patients into high and low PANSS motor score resulted in differences especially in hypokinetic motor abnormalities catatonia, parkinsonism, and psychomotor slowing. Within the boxplots, the lower and upper whiskers represent the minimum/lowest value and the maximum/highest value, respectively. Dots are outliers. The box displays the interquartile range between 1 and 3 quartile. The middle line inside the box is the median.

Table 2. Correlations Between PANSS Motor Score and Motor Rating Scales in the Bern-Sample

		BFCRS	NCRS	NCRSm	NCRSb	NCRSa	UPDRS	SRRS	NES	AIMS
$PANSS_{mot}$	Rho	0.52	0.67	0.57	0.47	0.57	0.48	0.69	0.34	0.19
	$P_{(FDR)}$	<.001	<.001	<.001	<.001	<.001	<.001	<.001	<.001	.007

Note: Displayed are Spearman-Rho-values. PANSS, Positive and Negative Syndrome Scale; PANSSmot, PANSS motor score; BFCRS, Bush-Francis Catatonia Rating Scale; NCRS, Northoff Catatonia Rating Scale; NCRSm, NCRS motor; NCRSb, NCRS behavior; NCRSa, NCRS affect; UPDRS, Unified Parkinson's Disease Rating Scale Part III; SRRS, Salpêtrière Retardation Rating Scale; NES, Neurological Evaluation Scale; AIMS, Abnormal Involuntary Movement Scale.

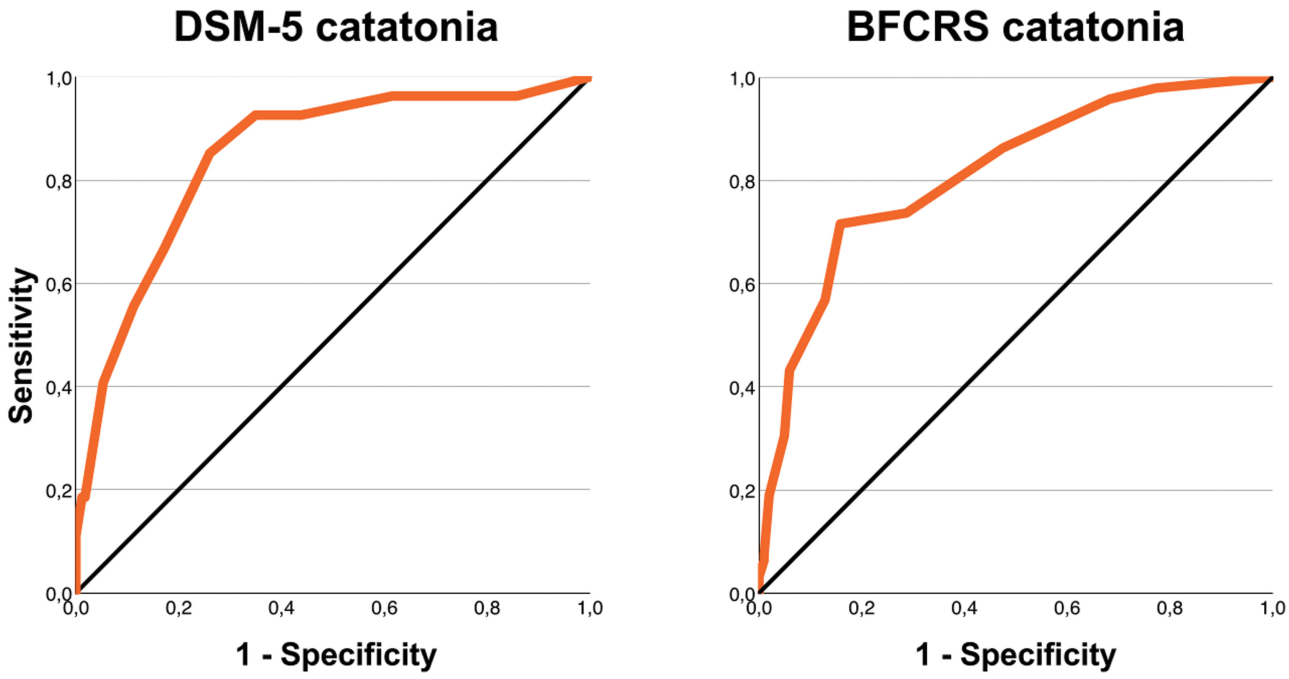

Fig. 2. ROC-curves catatonia.

Note: The effectiveness of $PANSS_{mot}$ in predicting patients with catatonia vs without catatonia.

Association Between $PANSS_{mot}$ and Motor Rating Scales in the Bern-Sample

Spearman correlations revealed that the $PANSS_{mot}$ was associated most strongly with hypokinetic motor abnormalities (all Rho ≥ 0.48, $P < .001$, $P_{(FDR)} < .001$, see supplementary figures S1–S5). In contrast, hyperkinetic motor abnormalities and coordination had lower correlation values (see table 2 AIMS and NES, supplementary table S3 NES subscores). Sensitivity analyses indicated no significant association between $PANSS_{mot}$ and current daily dosage of antipsychotics or class of antipsychotics (see supplementary material). Furthermore, $PANSS_{mot}$ had higher correlation coefficients with motor rating scales than the PANSS positive or general subscore (see supplementary table S4). Finally, $PANSS_{mot}$ correlated with PANSS negative (Rho = 0.65, $P_{(FDR)} < .001$) and PANSS general (Rho = 0.50, $P_{(FDR)} < .001$) (see supplementary tables S5–S6).

Logistic Regressions and ROC-Curves for Catatonia in the Bern-Sample

$PANSS_{mot}$ predicted catatonia according to DMS-5 and BFCRS criteria with an accuracy of 87.8% (Wald-Chi^2 = 26.3, df = 1, $P < .001$) and 76.0% (Wald-Chi^2 = 42.8, df = 1, $P < .001$), respectively, while controlling for age and current daily dosage of antipsychotic medication. The analysis on the effectiveness of $PANSS_{mot}$ in predicting the categorization into patients with catatonia vs without catatonia according to DSM-5 as well as BFCRS indicated an AUC of 0.847 and 0.811, respectively (see figure 2).

Replication: $PANSS_{mot}$ in RESIS

This analysis is based on the baseline data of patients (n = 102) who completed PANSS and SHRS assessments at day 0. Demographic and clinical information is depicted in table 1. In this sample, $PANSS_{mot}$ correlated only

Table 3. Correlations Between PANSS Motor Score and Subscores of the St. Hans Rating Scale in RESIS

		AKA s	AKA o	DYT	PAR t	PAR g	DYK ta	DYK ga	DYK tp	DYK gp
$PANSS_{mot}$	Rho	0.05	0.04	0.02	0.22	0.28	0.05	0.04	0.03	0.07
	P-value	.619	.684	.822	.024	.005	.625	.670	.727	.473
	$P_{(FDR)}$	.818	.818	.822	.107	.042	.818	.818	.818	.818

Note: Displayed are Spearman-Rho-values. PANSS, Positive and Negative Syndrome Scale; PANSSmot, PANSS motor score; AKA s, Akathisia subjective; AKA o, Akathisia objective; DYT, Dystonia; PAR t, Parkinsonism total; PAR g, Parkinsonism global; DYK ta, Dyskinesia total active; DYK ga, Dyskinesia global active; DYK tp, Dyskinesia total passive; DYK gp, Dyskinesia global passive.

with the SHRS subscores parkinsonism total and parkinsonism global (see table 3).

Longitudinal Stability: $PANSS_{mot}$ in OCoPS-P at Week 3

A total of 75 patients of OCoPS-P completed PANSS and motor assessments at week 3. Descriptives are given in supplementary table S7. Analyses at week 3 revealed strong correlations between $PANSS_{mot}$ and catatonia, parkinsonism, and psychomotor slowing (Spearman-Rho range 0.31–0.65, $P \leq .007$, $P_{(FDR)} \leq .009$). The correlation between $PANSS_{mot}$ and dyskinesia was the weakest (Rho = 0.26, $P = .023$, $P_{(FDR)} = .023$).

External Validity: $PANSS_{mot}$ and Physical Activity Levels in OCoPS-P

A total of 113 patients of OCoPS-P wore wrist-actigraphs during baseline assessments. Higher $PANSS_{mot}$ was associated with lower physical activity levels (Rho = −0.44, $P < .001$, $P_{(FDR)} < .001$). Moreover, Mann-Whitney-U-tests indicated that patients with high vs low $PANSS_{mot}$ differed in physical activity levels, $U = 539$, $P = .007$. Activity levels were inversely correlated with PANSS negative (Rho = −0.54, $P < .001$, $P_{(FDR)} < .001$) and PANSS total (Rho = −0.31, $P < .001$, $P_{(FDR)} = .002$), but not with PANSS positive or general score omitting the 3 PANSS motor items G5, G7, and G13 (see supplementary table S8).

Sensitivity Analyses: PANSS Hyperkinetic Score and Motor Ratings

Addition of either P04 or G14 to the $PANSS_{mot}$ failed to increase the correlation values with motor rating scales or actigraphy (see supplementary tables S9 and S10) When a separate hyperkinetic $PANSS_{mot}$ was computed summing P04 and G14, correlations were low and insignificant, except for the BFCRS ($r = 0.21$) and NCRS affect ($r = 0.26$) (see supplementary table S11 and figure S6). Including all 5 PANSS items into the motor score had no additional benefit for the correlations with motor rating scales (supplementary table S12).

Discussion

With our study, we wish to introduce a new PANSS motor subscore based on the PANSS items G5 mannerisms and posturing, G7 motor retardation, and G13 disturbance of volition as a proxy of expert rating scales for specific motor abnormalities in schizophrenia. Our analysis revealed that the $PANSS_{mot}$ correlated with all motor rating scales. Moreover, schizophrenia patients categorized into high and low $PANSS_{mot}$ groups differed substantially in all hypokinetic motor rating scales, ie, BFCRS, NCRS, UPDRS, and SRRS. Additionally, $PANSS_{mot}$ proved to be an effective predictor of catatonia case definition based on DMS-5 as well as BFCRS with moderate accuracy. Further, we replicated the correlation between $PANSS_{mot}$ and parkinsonism in the RESIS dataset. In addition, the associations between $PANSS_{mot}$ and motor rating scales remained stable over a period of 3 weeks in the OCoPS-P sample. Finally, $PANSS_{mot}$ correlated with instrumental measures of physical activity. Thus, the $PANSS_{mot}$ holds promise in capturing broad hypokinetic psychomotor abnormalities with little information from a standard rating scale.

Proxy for Motor Abnormalities?

Our analyses suggest that $PANSS_{mot}$ does qualify as a proxy for motor abnormalities in schizophrenia spectrum disorders. This is mainly true for hypokinetic motor abnormalities, including catatonia, psychomotor slowing, and parkinsonism.[47] The correlations were especially high between $PANSS_{mot}$ and all hypokinetic motor abnormalities, but less so with dyskinesia. This is in line with recent findings from imaging studies demonstrating different neuronal correlates for dyskinesia and parkinsonism, respectively.[48] In addition, the cutoff set at 3 on each PANSS motor item (G5, G7, and G13) identified a group of patients with higher levels of catatonia, psychomotor slowing, and parkinsonism, compared to patients below the cutoff. However, the cutoff was not able to differentiate between patients with more severe vs less severe dyskinesia or neurological soft signs, especially in the subscores sensory integration and motor coordination. The RESIS study used a different rating scale for

motor abnormalities but replicated our initial findings. $PANSS_{mot}$ was linked to parkinsonism but not to hyperkinetic motor abnormalities (akathisia, dystonia, and dyskinesia) in this sample. This is slightly different compared to the findings in the Bern samples, where dyskinesia was also correlated with $PANSS_{mot}$. Next to differences in the operationalization of the different motor rating scales we must consider that expert raters for OCoPS-P and BrAGG-SoS were specifically trained to detect motor abnormalities and are probably also more sensitive using the PANSS motor items. Furthermore, RESIS patients demonstrated pronounced negative symptoms at baseline and not all patients had the capacity to complete SHRS assessments.

The longitudinal data of OCoPS-P suggests that the associations between $PANSS_{mot}$ and ratings of motor abnormalities were stable over 3 weeks. In that regard, $PANSS_{mot}$ was linked to expert ratings of hypokinetic motor abnormalities in 2 samples from the baseline values of 3 different clinical trials as well as in the longitudinal follow-up of 1 trial. However, the quality of the ratings depends on the attention paid to motor signs during assessments. In situations where raters are less familiar with the assessment of psychomotor behavior, $PANSS_{mot}$ may also fail to detect individuals with motor abnormalities. Finally, $PANSS_{mot}$ alone will not allow distinguishing the type of hypokinetic motor abnormality, given the substantial covariance or conceptual overlap between catatonia, parkinsonism, or psychomotor slowing.[24,47,49] Thus, the score will indicate the severity of hypokinetic psychomotor behaviors, but not allow disentangling parkinsonism from catatonia.

We have also considered including 2 PANSS items potentially describing hyperkinetic motor abnormalities, such as agitation, akathisia, or dyskinesia. However, neither the addition of item P04, G14, nor the combination of both did increase the correlation coefficients between the $PANSS_{mot}$ and the expert rating scales. Thus, hyperkinetic movement disorders were less likely to be captured by PANSS ratings. Groups of subjects with high vs low scores on the hyperkinetic motor score failed to differ on any motor rating scale. Besides issues with the operationalization of hyperkinetic motor abnormalities in the PANSS one of the most likely reasons for the weak associations observed are probably the sample characteristics. The available datasets included mainly patients with prominent negative symptoms and hypokinetic motor abnormalities.

Instrumental measures of behavior such as wrist-actigraphy are considered the gold standard to capture motor abnormalities, especially hypokinetic motor abnormalities including catatonia, parkinsonism, and psychomotor slowing.[12,30,31,47] In schizophrenia, actigraphically assessed physical activity is related to altered white matter integrity,[50,51] resting-state functional connectivity,[52] negative symptoms,[53,54] positive symptoms,[55] and the course of schizophrenia episodes.[56] Similarly, higher $PANSS_{mot}$ also correlated with lower physical activity levels, corroborating its external validity. Interestingly, in a previous report, no associations were found between each of the single items G5, G7, and G13 and actigraphically determined activity levels in schizophrenia.[22] In contrast, the current study demonstrated associations when these single PANSS items are combined to the $PANSS_{mot}$ score.

According to sensitivity analyses, $PANSS_{mot}$ was not related to current daily dose and types of antipsychotic medication. Abnormal psychomotor behavior is associated with more severe symptoms of psychosis. Indeed, $PANSS_{mot}$ demonstrated strong correlations with negative symptoms or general symptoms of psychosis, less so with positive symptoms. Still, $PANSS_{mot}$ has stronger associations to the motor rating scales than PANSS general or PANSS total.

Recognition and assessment of motor abnormalities are critical because of their association with social and community functioning.[10,11] Antipsychotic drug trials involving hundreds of patients diagnosed with schizophrenia spectrum disorders typically assess symptom severity using the PANSS. The $PANSS_{mot}$ might prove helpful in detecting motor abnormalities in study participants but would also allow testing for secondary effects on hypokinetic motor abnormalities in these trials. The $PANSS_{mot}$ therefore holds promise in secondary analyses of large-scale existing datasets from randomized controlled trails. The utility may even extend to individual-patient meta-analyses. However, in prospective studies addressing abnormal psychomotor behavior specifically, we recommend using validated motor rating scales as well as instrumental measures such as actigraphy or gait analyses instead.[25,31] The choice of instrument will depend on the motor abnormality in question.

Limitations

Some limitations of these analyses should be considered. First, we combined datasets of clinical trials with heterogeneous patient groups, introducing some selection bias limiting generalizability. For OCoPS-P, patients with severe motor symptoms were recruited, whereas for RESIS, patients with predominantly negative symptoms prevailed. In BrAGG-SoS participants were stabilized outpatients with substantial chronicity. However, the main findings regarding hypokinetic motor abnormalities were similar across samples. We would expect similar associations in clinical trials with schizophrenia patients. Additionally, only few patients presented with severe dyskinesia. This may explain the lack of a group difference in AIMS scores due to low variability. Furthermore, data was mostly acquired in patients with chronic schizophrenia and long-term exposure to antipsychotics.

Thus, we cannot completely rule out medication effect, although $PANSS_{mot}$ was unrelated to the current daily dose and type of antipsychotics. Similarly, the $PANSS_{mot}$ should also be tested in the early course of psychosis. Finally, the current analyses should be replicated in larger datasets.

Conclusion

A novel sum score of 3 PANSS motor items correlated with expert ratings of hypokinetic psychomotor abnormalities and instrumental measures of physical activity. Effects were replicable in different datasets and proved reliable over 3 weeks. Thus, the $PANSS_{mot}$ may qualify as a proxy measure of hypokinetic psychomotor abnormalities in psychosis in large trials that lack specific motor assessments.

Supplementary Material

Supplementary material is available at https://academic.oup.com/schizophreniabulletin/.

Acknowledgments

We would like to thank all the patients participating in our studies and especially Dr Danai Alexaki and Daniel Gama Baumann for clinical assessments. S.W. has received honoraria from Lundbeck, Mepha, and Neurolite. A.H. is editor of the German (DGPPN) schizophrenia treatment guidelines, first author of the WFSBP schizophrenia treatment guidelines; on advisory boards of and speaker fees from AbbVie (speaker fees only), Advanz (speaker fees only), Janssen Cilag, Lundbeck, Recordati, Rovi, and Otsuka. T.W. is or was a member of the steering group of the German (DGPPN) schizophrenia treatment guidelines, coauthor of the WFSBP schizophrenia treatment guidelines, advisory board member of Boehringer, Janssen Cilag, Otsuka/Lundbeck, and Rovi, received paid speakerships in the last 5 years from Boehringer, Janssen Cilag, Lundbeck/Otsuka, Recordati and Rovi. B.L. received honoraria for consultancy and speakers' fees from ANM, AstraZeneca, Autifony Therapeutics, Decibel Therapeutics, Desyncra, Gerson Lehmanns Group, Lundbeck, Merz, MagVenture, Medical Tribune, Neurolite, Neuromod, Novartis, Pfizer, Rovi, Schwabe, Sea Pharma, Servier, Sonova and Sound Therapeutics; research funding from the Tinnitus Research Initiative, Bayhost, the German Research Foundation, the German Bundesministerium für Bildung und Forschung, the American Tinnitus Association, AstraZeneca, cerbomed, Neuromod and the European Union; funding for equipment from MagVenture and Deymed Diagnostic; and travel and accommodation payments from Eli Lilly, Lundbeck, Servier, and Pfizer. BL owns shares of Sea Pharma. P.F. has received research support/honoraria for lectures or advisory activities from Boehringer-Ingelheim, Janssen, Lundbeck, Otsuka, Recordati, and Richter. W.G. was the leading editor of the DGPPN S3 Schizophrenia guideline (2019); Member of the Lundbeck Neurotorium (former Neuroscience Foundation). The other authors report no financial relationships with commercial interests.

Funding

This work was supported by the Swiss National Science Foundation (grant numbers #182469 and #184717 to S.W.). The Repetitive Transcranial Magnetic Stimulation (rTMS) for the Treatment of Negative Symptoms in Schizophrenia (RESIS) trial was supported by the Deutsche Forschungsgemeinschaft Grant no. FA-210/1. The funding sources had no further role in study design, in the collection, analysis, and interpretation of data as well as in the writing of the report and in the decision to submit the paper for publication.

References

1. Saha S, Chant D, Welham J, Mcgrath J, Hyman SE. A systematic review of the prevalence of schizophrenia. *PLoS Med*. 2005;2(5):e141. doi:10.1371/journal.pmed.0020141
2. Heckers S, Barch DM, Bustillo J, et al. Structure of the psychotic disorders classification in DSM-5. *Schizophr Res*. 2013;150(1):11–14. doi:10.1016/J.SCHRES.2013.04.039
3. Peralta V, Campos MS, De Jalón EG, Cuesta MJ. Motor behavior abnormalities in drug-naïve patients with schizophrenia spectrum disorders. *Mov Disord*. 2010;25(8):1068–1076. doi:10.1002/mds.23050
4. Mittal VA, Neumann C, Saczawa M, Walker EF. Longitudinal progression of movement abnormalities in relation to psychotic symptoms in adolescents at high risk of schizophrenia. *Arch Gen Psychiatry*. 2008;65(2):165–171. doi:10.1001/archgenpsychiatry.2007.23
5. Koning JP, Tenback DE, van Os J, Aleman A, Kahn RS, van Harten PN. Dyskinesia and parkinsonism in antipsychotic-naive patients with schizophrenia, first-degree relatives and healthy controls: a meta-analysis. *Schizophr Bull*. 2010;36(4):723–731. doi:10.1093/schbul/sbn146
6. Peralta V, Cuesta MJ. Motor features in psychotic disorders. I: factor structure and clinical correlates. *Schizophr Res*. 2001;47(2–3):107–116. doi:10.1016/S0920-9964(00)00013-X
7. Ungvari GS, Goggins W, Leung SK, Gerevich J. Schizophrenia with prominent catatonic features ("catatonic schizophrenia"). II. Factor analysis of the catatonic syndrome. *Prog Neuropsychopharmacol Biol Psychiatry*. 2007;31(2):462-468. doi:10.1016/j.pnpbp.2006.11.012
8. Kao YC, Liu YP, Chou MK, Cheng TH. Subjective quality of life in patients with chronic schizophrenia: relationships between psychosocial and clinical characteristics. *Compr Psychiatry*. 2011;52(2):171–180. doi:10.1016/j.comppsych.2010.05.008
9. Mittal VA. Cross-cutting advancements usher in a new era for motor research in psychosis. *Schizophr Bull*. 2016;42(6):1322–1325. doi:10.1093/schbul/sbw123

10. Pieters LE, Nadesalingam N, Walther S, van Harten PN. A systematic review of the prognostic value of motor abnormalities on clinical outcome in psychosis. *Neurosci Biobehav Rev.* 2022;132:691–705. doi:10.1016/j.neubiorev.2021.11.027
11. Nadesalingam N, Chapellier V, Lefebvre S, et al. Motor abnormalities are associated with poor social and functional outcomes in schizophrenia. *Compr Psychiatry.* 2022;115:152307. doi:10.1016/j.comppsych.2022.152307
12. van Harten PN, Walther S, Kent JS, Sponheim SR, Mittal VA. The clinical and prognostic value of motor abnormalities in psychosis, and the importance of instrumental assessment. *Neurosci Biobehav Rev.* 2017;80:476–487. doi:10.1016/j.neubiorev.2017.06.007
13. Walther S, Eisenhardt S, Bohlhalter S, et al. Gesture performance in schizophrenia predicts functional outcome after 6 months. *Schizophr Bull.* 2016;42(6):1326–1333. doi:10.1093/schbul/sbw124
14. Walther S, Stegmayer K, Sulzbacher J, et al. Nonverbal social communication and gesture control in schizophrenia. *Schizophr Bull.* 2015;41(2):338–345. doi:10.1093/schbul/sbu222
15. Galderisi S, Rossi A, Rocca P, et al.; Italian Network For Research on Psychoses. The influence of illness-related variables, personal resources and context-related factors on real-life functioning of people with schizophrenia. *World Psychiatry*. 2014;13(3):275–287. doi:10.1002/wps.20167
16. Miller DD, McEvoy JP, Davis SM, et al. Clinical correlates of tardive dyskinesia in schizophrenia: baseline data from the CATIE schizophrenia trial. *Schizophr Res.* 2005;80(1):33–43. doi:10.1016/J.SCHRES.2005.07.034
17. Schneider-Thoma J, Chalkou K, Dörries C, et al. Comparative efficacy and tolerability of 32 oral and long-acting injectable antipsychotics for the maintenance treatment of adults with schizophrenia: a systematic review and network meta-analysis. *Lancet (London, England)*. 2022;399(10327):824–836. doi:10.1016/S0140-6736(21)01997-8
18. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. *Schizophr Bull.* 1987;13(2):261–276. doi:10.1093/schbul/13.2.261
19. Heckers S, Walther S. Catatonia. *N Engl J Med.* 2023;389(19):1797–1802. doi:10.1056/NEJMra2116304
20. Osborne KJ, Walther S, Shankman SA, Mittal VA. Psychomotor slowing in Schizophrenia: implications for endophenotype and biomarker development. *Biomark Neuropsychiatry*. 2020;2:100016. doi:10.1016/j.bionps.2020.100016
21. Walther S, Stegmayer K, Wilson JE, Heckers S. Structure and neural mechanisms of catatonia. *Lancet Psychiatry*. 2019;6(7):610–619. doi:10.1016/S2215-0366(18)30474-7
22. Walther S, Koschorke P, Horn H, Strik W. Objectively measured motor activity in schizophrenia challenges the validity of expert ratings. *Psychiatry Res.* 2009;169(3):187–190. doi:10.1016/j.psychres.2008.06.020
23. Fritze S, Brandt GA, Benedyk A, et al. Psychomotor slowing in schizophrenia is associated with cortical thinning of primary motor cortex: a three cohort structural magnetic resonance imaging study. *Eur Neuropsychopharmacol*. 2023;77:53–66. doi:10.1016/j.euroneuro.2023.08.499
24. Walther S, Strik W. Motor symptoms and schizophrenia. *Neuropsychobiology.* 2012;66(2):77–92. doi:10.1159/000339456
25. Walther S, Alexaki D, Weiss F, et al. Psychomotor slowing in psychosis and inhibitory repetitive transcranial magnetic stimulation. *JAMA Psychiatry*. 2024;81(3):563–571. doi:10.1001/jamapsychiatry.2024.0026
26. Nuoffer MG, Lefebvre S, Nadesalingam N, et al. Psychomotor slowing alters gait velocity, cadence, and stride length and indicates negative symptom severity in psychosis. *Schizophrenia*. 2022;8(1):116. doi:10.1038/S41537-022-00324-X
27. Maderthaner L, Pavlidou A, Lefebvre S, et al. Neural correlates of formal thought disorder dimensions in psychosis. *Schizophr Bull.* 2023;49:S104–S114. doi:10.1093/schbul/sbac120
28. Lefebvre S, Gehrig G, Nadesalingam N, et al. The pathobiology of psychomotor slowing in psychosis: altered cortical excitability and connectivity. *Brain.* 2024;147(4):1423–1435. doi:10.1093/brain/awad395
29. Walther S, Nadesalingam N, Nuoffer M, Kyrou A, Wüthrich F, Lefebvre S. Structural alterations of the motor cortex and higher order cortical areas suggest early neurodevelopmental origin of catatonia in schizophrenia. *Schizophr Res.* 2022;263:131–138. doi:10.1016/J.SCHRES.2022.10.004
30. von Känel S, Nadesalingam N, Alexaki D, et al. Measuring catatonia motor behavior with objective instrumentation. *Front Psychiatry.* 2022;13:880747. doi:10.3389/fpsyt.2022.880747
31. Nadesalingam N, Lefebvre S, Alexaki D, et al. The behavioral mapping of psychomotor slowing in psychosis demonstrates heterogeneity among patients suggesting distinct pathobiology. *Schizophr Bull.* 2023;49(2):507–517. doi:10.1093/schbul/sbac170
32. Chapellier V, Pavlidou A, Mueller DR, Walther S. Brain stimulation and group therapy to improve gesture and social skills in schizophrenia—the study protocol of a randomized, sham-controlled, three-arm, double-blind trial. *Front Psychiatry.* 2022;13:909703. doi:10.3389/fpsyt.2022.909703
33. Chapellier V, Pavlidou A, Maderthaner L, von Känel S, Walther S. The impact of poor nonverbal social perception on functional capacity in schizophrenia. *Front Psychol.* 2022;13:804093. doi:10.3389/fpsyg.2022.804093
34. Pavlidou A, Chapellier V, Maderthaner L, von Känel S, Walther S. Using dynamic point light display stimuli to assess gesture deficits in schizophrenia. *Schizophr Res Cogn*. 2022;28:100240. doi:10.1016/J.SCOG.2022.100240
35. Leucht S, Samara M, Heres S, et al. Dose equivalents for second-generation antipsychotic drugs: the classical mean dose method. *Schizophr Bull.* 2015;41(6):1397–1402. doi:10.1093/schbul/sbv037
36. Wobrock T, Guse B, Cordes J, et al. Left prefrontal high-frequency repetitive transcranial magnetic stimulation for the treatment of schizophrenia with predominant negative symptoms: a sham-controlled, randomized multicenter trial. *Biol Psychiatry.* 2015;77(11):979–988. doi:10.1016/j.biopsych.2014.10.009
37. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry.* 1998;59(suppl 20):11980.
38. Woods SW. Chlorpromazine equivalent doses for the newer atypical antipsychotics. *J Clin Psychiatry.* 2003;64(6):663–667.
39. Gerlach J, Korsgaard S, Clemmesen P, et al. The St. Hans rating scale for extrapyramidal syndromes: reliability and validity. *Acta Psychiatr Scand.* 1993;87(4):244–252. doi:10.1111/J.1600-0447.1993.TB03366.X

40. Buchanan RW, Heinrichs DW. The neurological evaluation scale (NES): a structured instrument for the assessment of neurological signs in schizophrenia. *Psychiatry Res.* 1989;27(3):335–350. doi:10.1016/0165-1781(89)90148-0
41. Bush G, Fink M, Petrides G, Dowling F, Francis A, Catatonia I. Rating scale and standardized examination. *Acta Psychiatr Scand.* 1996;93(2):129–136. doi:10.1111/j.1600-0447.1996.tb09814.x
42. Fahn S, Elton R, Members of the UPDRS development committee. the unified Parkinson's disease rating scale. In: Fahn S, Marsden CD, Calne DB, Goldstein M, eds. *Recent Developments in Parkinson's Disease*. Vol 2. Florham Park: Macmillan Healthcare Information; 1987:153–163.
43. Guy W. *ECDEU Assessment Manual for Psychopharmacology*. MD: US Department of Health, Education and Welfare; 1976.
44. Northoff G, Koch A, Wenke J, et al. Catatonia as a psychomotor syndrome: a rating scale and extrapyramidal motor symptoms. *Mov Disord*. 1999;14(3):404–416. doi:10.1002/1531-8257(199905)14:3<404::AID-MDS1004>3.0.CO;2-5
45. Widlöcher D, Ghozlan A. The measurement of retardation in depression. In: Hindmarch I, Stonier PD, eds. *Human Psychopharmacology: Measures and Methods*. Vol 2. New York: John Wiley and Sons; 1989.
46. Tandon R, Heckers S, Bustillo J, et al. Catatonia in DSM-5. *Schizophr Res.* 2013;150(1):26–30. doi:10.1016/J.SCHRES.2013.04.034
47. Walther S, Vladimirova I, Alexaki D, et al. Low physical activity is associated with two hypokinetic motor abnormalities in psychosis. *J Psychiatr Res.* 2022;146:258–263. doi:10.1016/j.jpsychires.2021.11.014
48. Sakreida K, Chiu WH, Dukart J, et al. Disentangling dyskinesia from parkinsonism in motor structures of patients with schizophrenia. *Brain Commun*. 2022;4(4):fcac190. doi:10.1093/BRAINCOMMS/FCAC190
49. Rogers D. The motor disorders of severe psychiatric illness: a conflict of paradigms. *Br J Psychiatry*. 1985;147(3):221–232. doi:10.1192/bjp.147.3.221
50. Walther S, Federspiel A, Horn H, et al. White matter integrity associated with volitional motor activity. *Neuroreport.* 2010;21(5):381–385. doi:10.1097/WNR.0b013e328337ca29
51. Walther S, Federspiel A, Horn H, et al. Alterations of white matter integrity related to motor activity in schizophrenia. *Neurobiol Dis.* 2011;42(3):276–283. doi:10.1016/j.nbd.2011.01.017
52. Walther S, Stegmayer K, Federspiel A, Bohlhalter S, Wiest R, Viher PV. Aberrant hyperconnectivity in the motor system at rest is linked to motor abnormalities in schizophrenia spectrum disorders. *Schizophr Bull.* 2017;43(5):982–992. doi:10.1093/schbul/sbx091
53. Walther S, Stegmayer K, Horn H, et al. The longitudinal course of gross motor activity in schizophrenia—within and between episodes. *Front Psychiatry.* 2015;6:10. doi:10.3389/fpsyt.2015.00010
54. Kluge A, Kirschner M, Hager OM, et al. Combining actigraphy, ecological momentary assessment and neuroimaging to study apathy in patients with schizophrenia. *Schizophr Res.* 2018;195:176–182. doi:10.1016/j.schres.2017.09.034
55. Walther S, Ramseyer F, Horn H, Strik W, Tschacher W. Less structured movement patterns predict severity of positive syndrome, excitement, and disorganization. *Schizophr Bull.* 2014;40(3):585–591. doi:10.1093/schbul/sbt038
56. Walther S, Stegmayer K, Horn H, Razavi N, Müller TJ, Strik W. Physical activity in schizophrenia is higher in the first episode than in subsequent ones. *Front Psychiatry.* 2015;5:191. doi:10.3389/fpsyt.2014.00191