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Relationship between motor function and psychotic symptomatology in young-adult patients with schizophrenia

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Compliance with ethical standards

Conflict of interest

All authors declare that they have no conflict of interest.

Abstract

Motor abnormalities have been indicated to be a core manifestation of schizophrenia and not just motor side-effects of antipsychotics. However, little is known about whether all of the complete motor function, including fine motor function, muscle strength, and balance is linked to psychotic symptoms. Therefore, this study was to investigate association between complete motor function and psychotic symptoms in young-adult schizophrenia patients who had no extrapyramidal motor symptoms, which were assessed using the Extrapyramidal Symptom Rating Scale. Seventy schizophrenia patients were recruited. Fine motor function, muscle strength, and balance were assessed using The McCarron Assessment of Neuromuscular Development. Psychotic symptoms were assessed using The Positive and Negative Syndrome Scale. Given gender differences in muscle power, the correlation between muscle strength and psychotic symptoms was analyzed by gender separately. Partial correlation controlling for effects of the chlorpromazine equivalent dosage of antipsychotics was conducted. Better fine motor function was correlated with less severe negative symptoms (r = -.49, p < .001) in the total sample. In men, better muscle strength was correlated with more severe positive symptoms and less severe negative symptoms (r = .41, p = .008; r = -.55, p < .001). The link between motor function and psychotic symptoms may support the cerebellar and basal ganglia hypotheses of schizophrenia, proposing that diverse schizophrenia symptoms may share the same neural deficiency, that is, dysfunction of cerebellum or basal ganglia. Considering the moderate-to-strong association between muscle strength and psychotic symptoms, muscle strength might be a powerful physical predictor of psychotic progression.

Keywords: Psychosis; Cerebellum; Basal ganglia; Muscle strength; Fine motor

Introduction

An increasing amount of evidence indicates that motor abnormalities are a core manifestation of schizophrenia [1,2]. In addition to reality distortion and cognitive deficits, motor disorders are also common in this population [3]. An amount of 66% of first-episode medication-free schizophrenia patients and 80% of chronic ones exhibit motor deficits [3]. Traditionally, motor impairments in schizophrenia have been mainly regarded as side-effects of antipsychotic treatment [4]. However, studies over the past decade [5-8] challenge this view by showing that antipsychotic-naïve patients and individuals at risk for psychotic onset have exhibited abnormal movements, indicating that motor abnormalities are an integral part of the illness itself, and antipsychotics are added afterwards to further affect motor performance in patients. Moreover, recent research [9-12] indicates that some motor performance, such as dyskinesia and postural sway, serves as early signs and physical markers of the disease development because it sensitively predicts the progression of psychotic symptoms at follow-up or later transition to psychotic disorders in at-risk populations. Given the illness-based nature and clinical meaning of motor deficits in schizophrenia, more research is warranted to elaborate how motor abnormalities link to psychosis in the disease and their related neural mechanisms.

Although accumulating studies [8,12-17] have reported that some motor impairments parallel severity of psychotic symptoms in schizophrenia patients and at-risk individuals, so far no complete motor function, including fine motor and gross motor function (balance and muscle strength) [18], has been assessed to provide a big picture of association between motor function and psychosis. Earlier research exclusively focused on specific motor assessments, such as balance [12,13], dyskinesia [8], and parkinsonism [14,15], or assessed fine motor function as part of a battery of neuropsychological or neurological examinations [16,17]. Although batteries used to measure neurological soft signs in earlier research encompass fine motor tasks and balance testing [19,20], very few studies have involved muscle strength, an essential factor of gross motor performance [18], into the motor assessment batteries. Therefore, it remains uncertain if all of the complete motor performance is associated with psychotic symptoms in schizophrenia. Emerging studies [1,2,5,7,11,21-25] propose that dysfunctional basal ganglia or cerebellum may play crucial roles in explaining the existence of two disparate manifestations, that is, motor abnormalities and psychosis, in schizophrenia because the basal ganglia and the cerebellum modulate information from widespread cerebral cortices related to perception, thinking, emotion, and motor function [26-28]. The aberrant basal ganglia or cerebellum fails to mediate these diverse cerebral functions and thus causes psychotic symptoms

and motor impairments simultaneously in patients [1,2,5,7,11,21-25]. The role of the aberrant cerebellum in explaining diverse symptoms of schizophrenia has been discussed in Andreasen's hypothesis with respect to cognitive dysmetria, which means impaired coordination of mental processing [21-24]. According to the basal ganglia/cerebellar hypotheses of schizophrenia and the well-structured knowledge of the influences of these two brain regions on fine and gross motor performance [29,30], it is hypothesized that all of the complete motor performance would be associated with psychosis.

To sum up, this study was to fill up the knowledge gap by examining association of the complete motor function, including muscle strength, balance, and fine motor function, with psychotic symptoms in schizophrenia patients. We hypothesized that all motor performance was associated with psychosis in patients. In order to minimize influences of motor side-effects of antipsychotics on the examined association, we only recruited schizophrenia patients who had no extrapyramidal motor symptoms, which were assessed using the Extrapyramidal Symptom Rating Scale. This study may provide empirical evidence at a behavioral level for the basal ganglia/cerebellar hypotheses of schizophrenia. The results may also benefit future longitudinal research examining which types of motor performance sensitively predict the onset of schizophrenia and serve as physical risk factors.

Methods

Participants

Participants were recruited from psychiatric day care or chronic wards of hospitals. The inclusion criteria included: (1) a diagnosis of schizophrenia or schizoaffective disorder without other Axis I psychotic diseases according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition [31]; (2) 18 to 35 years old to exclude influences of aging on motor performance; (3) remaining the same antipsychotics for at least four weeks right before the start of the study to show symptom stability; medication adherence was checked routinely by nurses in the day care and chronic wards; (4) no extrapyramidal symptoms based on results of the Extrapyramidal Symptom Rating Scale [32]; (5) comprehension of instructions based on observation by research personnel; and (6) no substance abuse or other medical conditions that may affect movements. The Extrapyramidal Symptom Rating Scale was administered by the first author (SMW), who was supervised by an experienced and senior psychiatrist (the second author; WCO) and got intense training through video-watching and live administration of the scale. The interrater reliability of SMW and WCO was assessed (ICC = 0.83). This study was carried out in accordance with the Declaration of Helsinki. This

study was approved by the human research ethics committee (no. ER-95-141). Written informed consent was obtained from all participants before research activities.

Movement assessment

The McCarron Assessment of Neuromuscular Development (MAND) [18] was administered to measure participants' movement abilities. The MAND consists of 10 representative fine and gross motor tasks (Table 1) that can reliably detect neurological dysfunction and suit all ages (from young children to adult) and a wide range of disability populations, including schizophrenia patients [18]. *Fine motor* tasks, which involve the use of small muscles in hands and arms and are related to finger dexterity, are: beads in box, beads on rod, finger tapping, nut and bolt, and rod slide. *Gross motor* tasks involve large muscle systems, the capacity to integrate proprioceptive cues, and are related to muscle power and balance control. They are hand strength, finger-nose-finger, jumping, heel-toe-walk, and standing on one foot. In addition to fine motor and gross motor factors, the tasks can also be grouped into four factors: (1) *Bimanual dexterity* consists of beads on rod and nut and bolt, both of which demand precise *bimanual coordination*; (2) *Persistent control*, including rod slide and finger-nose-finger, requires continuous regulation of movements and reflects the capacity of *impulse control*; (3) *Kinesthetic integration*, consisting of heel-toe-walk and standing on one foot, reflects *balance control*; and (4) *Muscle power*, including hand strength and jumping, is related to hand and leg *muscle strength.* The tasks are scored based on speed and quality of movements. Higher scores mean better movements. The test-retest reliability of MAND for mentally disabled adults is excellent (r = .98 for fine motor; r = .96 for gross motor). The predictive validity of this movement battery for work performance after one year in mentally disabled adults is high (r = .70) [18].

Psychotic symptom assessment

The Positive and Negative Syndrome Scale (PANSS) [33,34] was used to evaluate severity of positive symptoms, negative symptoms, and general psychopathology in patients with schizophrenia. Higher scores mean more severe symptoms. The interrater reliability is high (agreement for subscales: .76 - .78). This scale has been demonstrated to have strong construct validity [33,34]. Psychotic symptoms and motor function were assessed within one week.

Data analysis

Six factor scores of MAND (fine motor, gross motor, bimanual dexterity, persistent control, muscle power, and kinesthetic integration) were created by averaging standardized task scores comprising each factor. Three domain

scores of PANSS (positive symptoms, negative symptoms, and general psychopathology) were obtained by calculating the sum of item scores for each domain. Considering this study did not limit antipsychotics taken by participants to a specific one, we calculated the chlorpromazine equivalent dosage of antipsychotics [35,36] to reflect different influences of heterogeneous antipsychotics. In order to detect the unique relationship between factor scores of MAND and domain scores of PANSS after controlling for effects of heterogeneous medications, we used partial correlation analysis to examine correlation coefficients between factor scores of MAND and domain scores of PANSS when the chlorpromazine equivalent dosage of antipsychotics was partialled out. The alpha level was set at .05 (two-tailed). Given gender differences in muscle power, the correlations of muscle power and thus gross motor to PANSS scores were analyzed by gender separately. The correlations of the other MAND factors to PANSS scores were analyzed by gender for additional information. Gender differences in PANSS domain scores and MAND factor scores were also examined for extra information. In order to correct inflated Type I errors of multiple testing and keep statistical power, we used the false discovery rate procedure [37], in which the q-value threshold was .05.

Results

Demographic data of participants

Seventy schizophrenia patients (28 women and 42 men) who met the inclusion criteria were recruited (Table 2 and Online Resource 1, 2, and 3). Eighteen patients (25.7%) were on clozapine, 15 patients (21.4%) on risperidone, nine patients (12.9%) on sulpiride, eight patients (11.4%) on olanzapine, eight patients (11.4%) on amisulpride, two patients (2.9%) zotepine, two patients (2.9%) on quetiapine, and one patient (1.4%) on ziprasidone. Two patients (2.9%) were on the combination of clozapine and sulpiride, and one patient (1.4%) was on each of the following combinations: amisulpride/sulpiride, aripiprazole/risperidone, amisulpride/clozapine, zotepine/olanzapine, and sulpiride/olanzapine.

Associations between movements and psychotic symptoms after controlling for effects of the chlorpromazine equivalent dosage of antipsychotics

Fine motor and gross motor

Better fine motor function was correlated with less severe negative symptoms (Table 3 and Online Resource 4). In men, better gross motor function was correlated with less severe negative symptoms (Table 4 and Online Resource 5). Both correlations were at a moderate-to-strong magnitude.

Bimanual dexterity, persistent control, muscle power, and kinesthetic integration

Better bimanual dexterity was correlated with less severe negative symptoms (Table 3 and Online Resource 4). Better persistent control was correlated with less severe positive and negative symptoms. Better kinesthetic integration was correlated with less severe negative symptoms and positive symptoms, although the latter became non-significant after multiple testing correction.

In men, better muscle power was correlated with more severe positive symptoms and less severe negative symptoms at a moderate-to-strong magnitude (Table 4 and Online Resource 5). In women, no correlations between muscle power and symptoms were found (Table 5 and Online Resource 6).

Discussion

This study adds evidence to the existing literature [8,12-17] suggesting that changes in motor performance are closely linked to changes in positive and negative symptoms in schizophrenia patients. Moreover, this study extends earlier findings by showing that the complete motor function, including muscle strength, was associated with positive and negative symptoms. The results of extensive linkages between motor function and positive/negative symptoms are consistent with the basal ganglia/cerebellar hypotheses of schizophrenia [1,2,5,7,11,21-25], proposing that diverse symptoms in schizophrenia may share the same underlying neural deficiency (i.e., the aberrant function of the basal ganglia or the cerebellum) and thus be intercorrelated. The result of moderate-to-strong association between motor function and psychotic symptoms suggests that motor function might be a valuable physical marker to indicate psychotic progression.

Muscle power was closely associated with the severity of positive symptoms and negative symptoms in men with schizophrenia. It has been consistently indicated that muscle strength correlates to the activity in the primary motor cortex (M1) [38-40], which projects to and receives output from the basal ganglia [28,30] and the cerebellum [26,27]. In addition, it has been known that the basal ganglia dysfunction, related to dopaminergic dysregulation, plays a pivotal role in the formation of positive symptoms [41,42]. Recent studies [13,43] have also shown that the aberrant cerebello-cortical connectivity is linked to positive and negative symptoms in the population at high risk for psychosis. Taken together, the basal ganglia or the cerebellum may link up motor function and psychotic symptoms. Indeed, abnormalities in the basal ganglia and the cerebellum have been reported in schizophrenia [44-47] and at-risk populations [13,48,49].

In line with previous reports [50], muscle power positively correlated with positive symptoms, which indicates the coexistence of increased muscle force and deteriorated positive symptoms in schizophrenia. Earlier research [51] has found the association between the smaller volume of the basal ganglia and more severe positive symptoms in schizophrenia. Recent research [43] has also found that aberrant cerebello-cortical hyperconnectivity is associated with deterioration of positive symptom after one year in people at high risk for psychosis. Although little is known about the influence of the basal ganglia and the cerebellum on muscle strength in schizophrenia, studies on patients with cerebellar disorders [29] have provided the evidence that patients demonstrate excessive force during hand gripping, which may be used to compensate for impaired motor control. Indeed, it has been reported that schizophrenia patients show aberrant force controlling [52,53]. More research is warranted to validate the impacts of the abnormal basal ganglia and cerebellum on muscle force processing and M1, which correlates to muscle force [38-40], in schizophrenia.

It is noteworthy that positive and negative symptoms were associated with muscle power reversely in this study. Earlier studies [22,54] reporting cortical deficits in schizophrenia have indicated the connection of positive symptoms to temporal lobe activity, and the connection of negative symptoms to frontal lobe activity. Taken together, in future research, it is of value to test whether and how aberrant function of the basal ganglia or the cerebellum separately and differently affects the cortical regions, such as M1, the other areas of the frontal lobe, and the temporal lobe. Regardless, considering the results showing moderate-to-strong association of muscle power to positive and negative symptoms, it is suggested to examine the neural connectivity between the basal ganglia/cerebellum and M1 in schizophrenia, which may be a unique window into more understanding of the neural mechanisms of psychotic symptomatology.

Fine motor performance correlated to the severity of negative symptoms in a moderate-to-strong magnitude. According to the definition of the MAND battery [18], fine motor performance involves finger tapping, finger dexterity, and bimanual coordination. Our results accord with earlier literature consistently showing that more severe negative symptoms occur with reduced performance of finger tapping [16,55,56], finger dexterity assessed by pegboard tests or drawing tests [16,55,57], and bimanual coordination [55] in schizophrenia patients. The involvement of the basal ganglia and the cerebellum in fine motor skills or coordination of limb movements has been well established [29,58,59]. Neuroimaging findings also indicate that more severe negative symptoms are associated with hyperactivated globus pallidus in the basal ganglia in schizophrenia patients [60] and stronger

cerebello-cortical connectivity in at-risk individuals [13]. Taken together, in accordance with the basal ganglia/cerebellar hypotheses of schizophrenia [1,2,5,7,11,21-25], abnormalities of the basal ganglia or the cerebellum may link up negative symptoms and fine motor function in patients.

Decreased kinesthetic integration, or so-called balance control, was associated with more severe positive and negative symptoms. Because it has been known that the basal ganglia and the cerebellum are implicated in equilibrium and postural control [21,45,61], dysfunction of the basal ganglia or the cerebellum is likely to give rise to deterioration of balance as well as psychotic symptoms simultaneously in schizophrenia and thus cause the association between balance and psychotic symptoms. The association of the basal ganglia/cerebellum with positive and negative symptoms [13,41-43,60] has been discussed in the earlier paragraphs.

This study has some limitations. First, the sample size of women in this study is relatively small, which may reduce variation of data regarding muscle power and severity of psychotic symptoms and thus lead to weak correlations between motor power and psychosis in women. This study needs to be replicated in a new schizophrenia sample with a larger sample size of women to ascertain if linkage between muscle power and psychotic symptoms exists in women with schizophrenia. Second, although medication effects on motor function were minimized through recruiting patients having no extrapyramidal motor symptoms, and were statistically controlled through conducting partial correlation controlling for effects of the chlorpromazine equivalent dosage of antipsychotics, these did not eliminate all possible influences of antipsychotics on motor function in patients. For example, influences of antipsychotics on the serotonergic system, which is involved in motor function [62], failed to be partialled out in partial correlation because the chlorpromazine equivalent dosage used in the analysis only reflected influences of antipsychotics on the dopaminergic system [63]. Because influences of antipsychotics on motor performance still potentially existed in the patients of this study, it is impossible to eliminate the explanation that the association between motor performance and positive/negative symptoms observed in this study might derive from effects of antipsychotics, in addition to aberrant function of basal ganglia/cerebellum. Therefore, this study is exploratory in nature. Future research may further test if the identified association in this study remains robust in drug-naïve first-episode patients or at-risk populations so as to provide advanced behavioral evidence for the basal ganglia/cerebellar hypotheses of schizophrenia. Third, no healthy controls were involved in this study, so that the results were unable to provide information of whether schizophrenia participants in this study showed motor deficits in the motor tasks compared with healthy people. Although literature [16,17,55-57] has consistently indicated motor

impairments in schizophrenia patients, future studies comparing motor performance in the MAND tasks between patients and healthy controls will help address this concern. It is also worth for future research to not only have a healthy control group but also have a clinical control group with a level of psychotic severity different from that in the targeted patient group to examine both influences of the illness and the severity of psychotic symptoms on motor function.

Fourth, this study is unable to test association of brain abnormalities in the basal ganglia and the cerebellum with psychotic symptoms and the complete motor function in schizophrenia due to the lack of neuroimaging data. In addition, this study did not assess if cognitive function, which is commonly known to be impaired in schizophrenia patients and is also linked to the basal ganglia [64,65] and the cerebellum [21,22], is associated with psychotic symptoms, the complete motor function, and brain abnormalities in patients. Future research needs to detect brain activities and conduct a wide spectrum of assessments, including psychotic, the complete motor, and cognitive assessments, in a schizophrenia sample, and examine associations among these varying symptoms and brain abnormalities to underpin the basal ganglia/cerebellar hypotheses. Last, this study assessed the complete motor function, including fine motor and gross motor function (muscle strength and balance), in schizophrenia patients. However, earlier literature [66] also provided another classification of motor assessments: catatonic signs, extrapyramidal signs, and neurological soft signs. The different grouping strategies of motor tests/tasks between literature (three domains) and MAND (fine motor, gross motor, bimanual dexterity, persistent control, muscle power, and kinaesthetic integration) cause somewhat different tasks included in the two assessment batteries. Future research combining these two assessment batteries will contribute to comprehensive understanding of motor function in schizophrenia. In addition, it is worthy of exploring detailed muscle properties, such as muscle tone, which can be objectively measured using myotonometers [67,68], in schizophrenia and examining their association with psychotic symptoms in future studies.

Our results may benefit future studies examining risk factors of psychotic onset in at-risk individuals. Considering the moderate-to-strong link of muscle strength and fine motor function to psychotic symptoms shown in this study, it is of value to examine in future research if muscle strength and fine motor function could be significant physical predictors of transition to psychotic disorders in people at high risk for psychosis. In conclusion, the results of extensive linkages between motor function and positive/negative symptoms may support the basal ganglia/cerebellar hypotheses of schizophrenia [1,2,5,7,11,21-25].

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Table 1 Ten tasks of the McCarron Assessment of Neuromuscular Development.

Tasks	Content	Two-factor category	Four-factor category
Beads in box	Take beads from the far box and move them to the near box as quickly as possible within 30 seconds by using one hand. Scoring: The total number of beads moved by the dominant hand and non-dominant hand.	Fine motor	N/A
Beads on rod	Take beads by the dominant hand and place beads on the metal rod held in the non-dominant hand as quickly as possible within 30 seconds when eyes are open and closed individually. Scoring: The total number of beads on the rod with eye open and eye closed.	Fine motor	Bimanual dexterity
Finger tapping	Tap the index finger of one hand to touch the suspended rubber band and the board on the table as quickly as possible with 10 seconds. Scoring: The sum of qualitative and quantitative measurements, based on the listed criteria in the scoring sheet [18], for both hands.	Fine motor	N/A
Nut and bolt	Hold the nut with the non-dominant hand, and hold the bolt with dominant hand. Turn the bolt into the nut by using the dominant hand as quickly as possible. Scoring: 100 minus the time required. The large nut and bolt and the small set are used. The total score is the sum of performances for the two sets.	Fine motor	Bimanual dexterity
Rod slide	Hold and slide the rod, which is suspended over the platform board, horizontally from the ipsilateral to contralateral side as slowly as possible (a maximal score is 30 seconds) by using one hand. Scoring: The sum of qualitative and quantitative measurements, based on the listed criteria in the scoring sheet [18], for both hands.	Fine motor	Persistent control

Hand strength	Grip power measured by a hand dynamometer when the shoulder is forwardly flexed and the elbow is extended under a standing position. Scoring: The sum of the best of two trials for each hand.	Gross motor	Muscle power
Finger-nose-finger	Touch the tip of the nose and the tip of the extended index finger of one hand by the index finger of the other hand for five consecutive rounds at a comfortable pace. Scoring: The sum of qualitative measurements, based on the listed criteria in the scoring sheet [18], for both hands when eyes are open and closed.	Gross motor	Persistent control
Jumping	Jump with both feet. Scoring: The sum of qualitative and quantitative measurements, based on the listed criteria in the scoring sheet [18], for the best one of three trials.	Gross motor	Muscle power
Heel-toe-walk	Forward (three meters) and then backward (three meters) tandem walk as carefully as possible with both hands on hips. Scoring: The sum of qualitative measurements, based on the listed criteria in the scoring sheet [18], for the forward and backward trials.	Gross motor	Kinesthetic integration
Standing on one foot	Stand on one foot with the unused foot off the floor (a maximal score is 30 seconds). Scoring: The sum of performances for both legs when eyes are open and closed.	Gross motor	Kinesthetic integration

Table 2 Demographic data, scores of psychotic symptoms and motor function in participants with schizophrenia.

	Total sample (N = 70)	Gender		Gender difference: Mann-Whitney *U* test	
		Men (*n* = 42)	Women (*n* = 28)		
	Mean (SD)	Mean (SD)	Mean (SD)	Z	*p*
Age (years)	29.64 (4.50)	30.02 (4.27)	29.07 (4.84)	-0.69	.492
Illness duration after diagnosis (years)[a]	9.28 (4.23)	9.74 (3.98)	8.56 (4.59)	-1.50	.135
Education (years)	11.10 (2.76)	11.45 (2.43)	10.57 (3.16)	-1.41	.159
Chlorpromazine equivalents (mg/day)[b]	506.38 (264.19)	541.03 (286.56)	453.77 (220.79)	-1.16	.248
PANSS scores					
Positive symptoms	13.07 (4.03)	12.14 (3.65)	14.46 (4.24)	-2.53	**.011**[d]
Negative symptoms	13.60 (4.17)	13.57 (4.37)	13.64 (3.94)	-0.35	.723
General psychopathology	28.63 (5.06)	28.17 (4.10)	29.32 (6.25)	-0.37	.714
MAND factor scores[c]					
Fine motor	-8.931E-16 (0.634)	0.001 (0.671)	-0.001 (0.586)	-0.34	.737
Gross motor	-2.901E-16 (0.672)	0.229 (0.648)	-0.343 (0.559)	-3.57	**<.001**[e]
Bimanual dexterity	-1.848E-15 (0.847)	-0.005 (0.874)	0.008 (0.822)	-0.21	.834
Persistent control	8.697E-16 (0.862)	0.119 (0.873)	-0.179 (0.830)	-2.00	.046
Muscle power	-2.541E-16 (0.929)	0.497 (0.792)	-0.745 (0.543)	-5.65	**<.001**[f]

Kinesthetic integration	-8.721E-16 (0.891)	0.008 (0.910)	-0.012 (0.877)	-0.04	.971
MAND task scores (raw scores)					
Beads in box	40.53 (7.06)	38.67 (6.91)	43.32 (6.45)	-2.76	**.006**[d]
Beads on rod	16.84 (3.28)	16.45 (3.37)	17.43 (3.12)	-0.99	.323
Finger tapping	92.16 (19.21)	95.50 (18.47)	87.14 (19.54)	-1.71	.086
Nut and bolt	161.44 (9.10)	162.43 (8.87)	159.96 (9.40)	-1.40	.162
Rod slide	79.47 (10.93)	80.62 (10.70)	77.75 (11.25)	-1.52	.128
Hand strength	59.14 (17.12)	68.19 (15.16)	45.57 (9.04)	-5.72	**<.001**[f]
Finger-nose-finger	61.06 (9.38)	62.31 (9.72)	59.18 (8.68)	-1.67	.094
Jumping	63.90 (17.22)	71.90 (15.44)	51.89 (12.10)	-4.94	**<.001**[f]
Heel-toe-walk	26.50 (6.06)	26.71 (6.09)	26.18 (6.12)	-0.26	.796
Standing on one foot	72.86 (29.95)	72.29 (30.76)	73.71 (29.22)	-0.35	.728

PANSS The Positive and Negative Syndrome Scale, *MAND* The McCarron Assessment of Neuromuscular Development.

[a]N = 69 due to missing data in one woman's medical chart

[b]N = 68 due to missing drug data of one men and one women in the database

[c]Factor scores were created by averaging standardized task scores comprising each factor. Descriptive data of the factor scores are given to three decimal places for clear information

[d]$q < .05$, [e]$q < .01$, [f]$q < .001$ (after the multiple testing correction of the false discovery rate procedure)

Table 3 Partial correlation between motor function and psychotic symptoms in the total sample with schizophrenia (N = 70)[a] after controlling for the chlorpromazine equivalent dosage of antipsychotics.

Motor function	Positive symptoms		Negative symptoms		General psychopathology	
	r	*p*	*r*	*p*	*r*	*p*
Two-factor category						
Fine motor	-.25	.040	-.49	**<.001**[c]	-.19	.126
Gross motor	NA	NA	NA	NA	NA	NA
Four-factor category						
Bimanual dexterity	-.16	.186	-.36	**.003**[b]	-.14	.260
Persistent control	-.34	**.005**[b]	-.33	**.007**[b]	-.22	.074
Muscle power	NA	NA	NA	NA	NA	NA
Kinesthetic integration	-.27	.026	-.29	**.017**[b]	-.16	.197

[a]Because of missing data of the medication dosage in one men and one women in the database, a total of 68 patients were analyzed

[b]$q < .05$, [c]$q < .001$ (after the multiple testing correction of the false discovery rate procedure)

Table 4 Partial correlation between motor function and psychotic symptoms in men with schizophrenia (n = 42)[a] after controlling for the chlorpromazine equivalent dosage of antipsychotics.

Motor function	Positive symptoms		Negative symptoms		General psychopathology	
	r	*p*	*r*	*p*	*r*	*p*
Two-factor category						
Fine motor	-.07	.676	-.53	**<.001**[c]	-.24	.130
Gross motor	.15	.370	-.51	**<.001**[c]	-.12	.453
Four-factor category						
Bimanual dexterity	-.05	.763	-.39	**.012**[b]	-.09	.581
Persistent control	-.25	.123	-.29	.073	-.28	.079
Muscle power	.41	**.008**[b]	-.55	**<.001**[c]	.01	.952
Kinesthetic integration	.01	.945	-.33	.038	-.15	.363

[a]Because of missing data of the medication dosage in one men, 41 men with schizophrenia were analyzed

[b]$q < .05$, [c]$q < .01$ (after the multiple testing correction of the false discovery rate procedure)

Table 5 Partial correlation between motor function and psychotic symptoms in women with schizophrenia (n = 28)[a] after controlling for the chlorpromazine equivalent dosage of antipsychotics.

Motor function	Positive symptoms		Negative symptoms		General psychopathology	
	r	*p*	*r*	*p*	*r*	*p*
Two-factor category						
Fine motor	-.55	**.004**[b]	-.42	.035	-.11	.586
Gross motor	-.49	.012	-.30	.132	-.15	.454
Four-factor category						
Bimanual dexterity	-.32	.109	-.26	.193	-.19	.355
Persistent control	-.42	.033	-.49	.011	-.16	.450
Muscle power	-.10	.623	-.07	.730	-.06	.775
Kinesthetic integration	-.62	**<.001**[b]	-.24	.232	-.17	.405

[a]Because of missing data of the medication dosage in one women, 27 women with schizophrenia were analyzed

[b]q <.05 (after the multiple testing correction of the false discovery rate procedure)

Supplementary material

Online Resource 1- Figure. The severity of (a) positive symptoms, (b) negative symptoms, and (c) general psychopathology in men (n = 42) and women (n = 28)

Online Resource 2- Figure. Motor function of (a) fine motor, (b) gross motor, (c) bimanual dexterity, (d) persistent control, (e) muscle power, and (f) kinesthetic integration in men (n = 42) and women (n = 28)

Online Resource 3- Figure. Detailed task performance on (a) beads in box, (b) beads on rod, (c) finger tapping, (d) nut and bolt, (e) rod slide, (f) hand strength, (g) finger-nose-finger, (h) jumping, (i) heel-toe-walk, and (j) standing on one foot in men (n = 42) and women (n = 28)

Online Resource 4- Figure. Partial correlation between (a) persistent control and positive symptoms, (b) fine motor function and negative symptoms, (c) bimanual dexterity and negative symptoms, (d) persistent control and negative symptoms, and (e) kinesthetic integration and negative symptoms in the total sample after controlling for the chlorpromazine equivalent dosage of antipsychotics

Online Resource 5- Figure. Partial correlation between (a) muscle power and positive symptoms, (b) fine motor function and negative symptoms, (c) gross motor function and negative symptoms, (d) bimanual dexterity and negative symptoms, and (e) muscle power and negative symptoms in men with schizophrenia after controlling for the chlorpromazine equivalent dosage of antipsychotics

Online Resource 6- Figure. Partial correlation between (a) fine motor function and positive symptoms, and (b) kinesthetic integration and positive symptoms in women with schizophrenia after controlling for the chlorpromazine equivalent dosage of antipsychotics

Online Resource 1- Figure. The severity of (a) positive symptoms, (b) negative symptoms, and (c) general psychopathology in men (n = 42) and women (n = 28)

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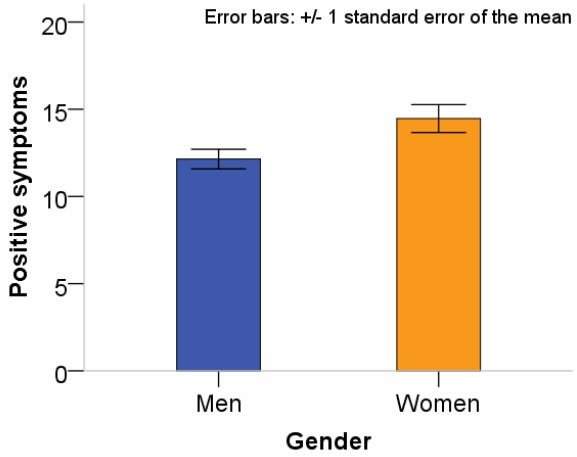

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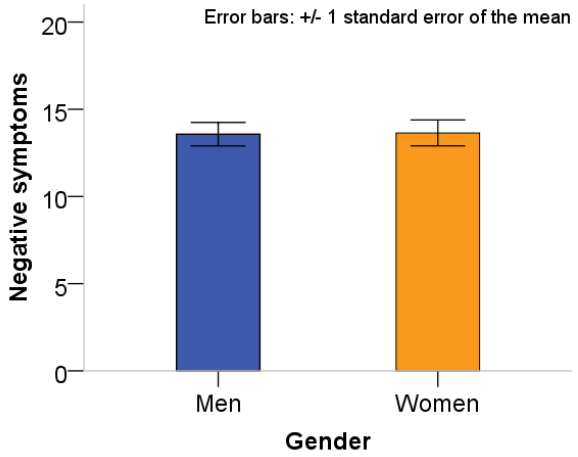

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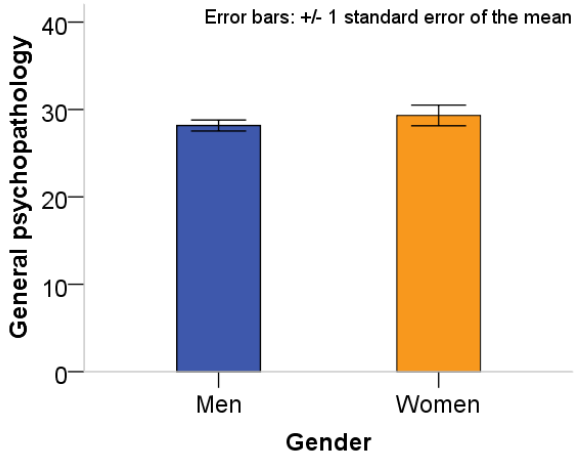
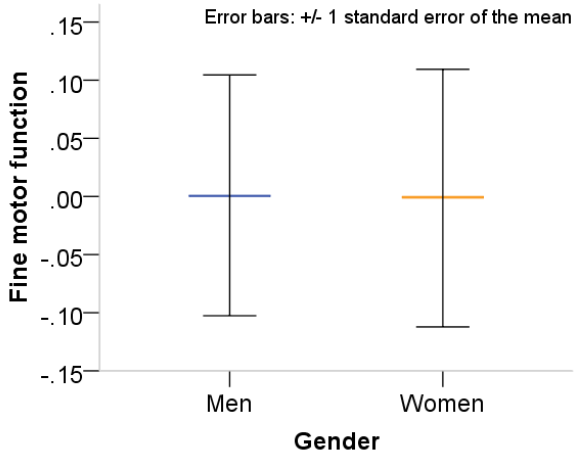
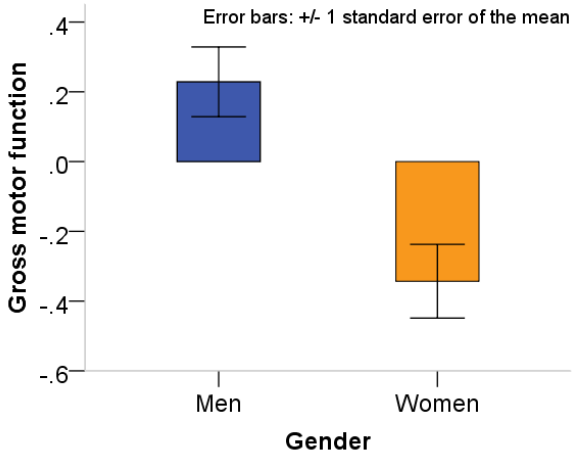


Online Resource 2- Figure. Motor function of (a) fine motor, (b) gross motor, (c) bimanual dexterity, (d) persistent control, (e) muscle power, and (f) kinesthetic integration in men (n = 42) and women (n = 28)

(a)



(b)



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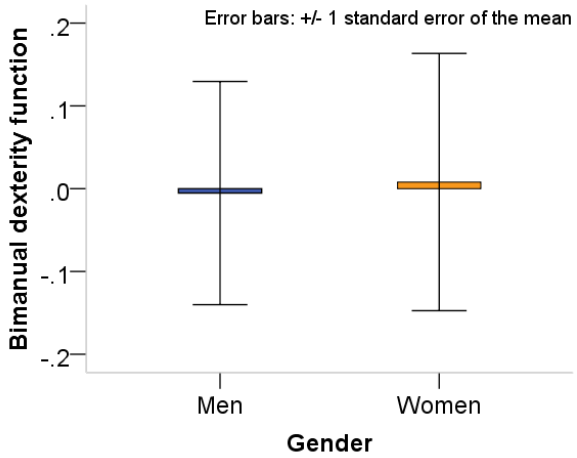

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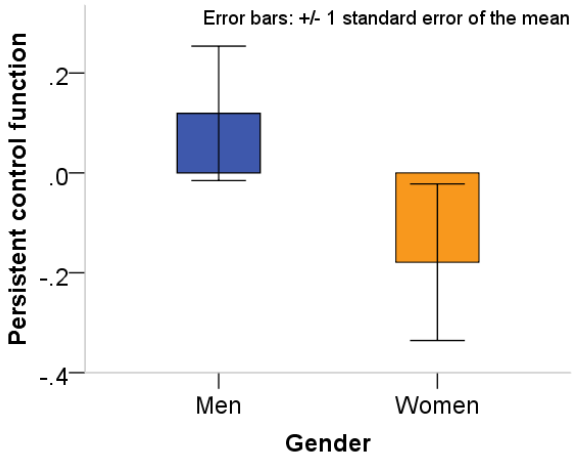

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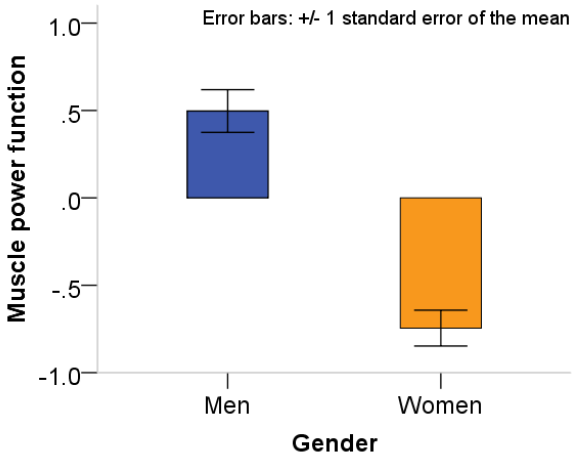
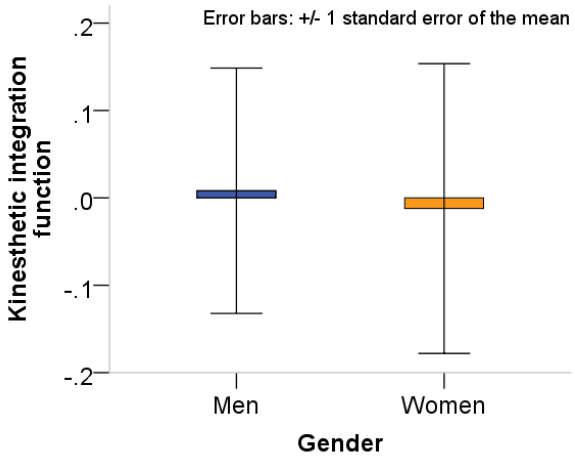
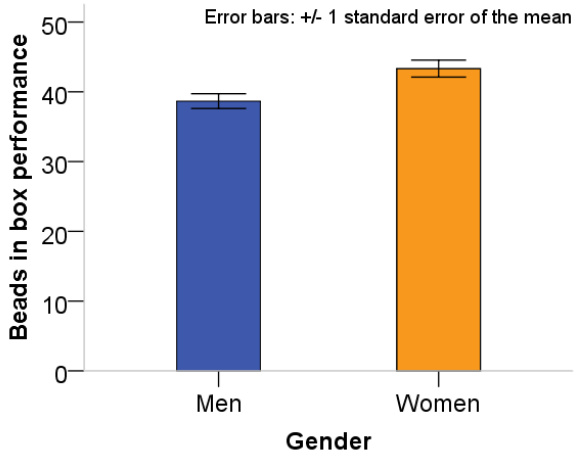

Error bars: +/- 1 standard error of the mean
Muscle power function
1.0
.5
.0
-.5
-1.0
Men
Women
Gender

(f)


Error bars: +/- 1 standard error of the mean
Kinesthetic integration function
.2
.1
.0
-.1
-.2
Men
Women
Gender

Online Resource 3- Figure. Detailed task performance on (a) beads in box, (b) beads on rod, (c) finger tapping, (d) nut and bolt, (e) rod slide, (f) hand strength, (g) finger-nose-finger, (h) jumping, (i) heel-toe-walk, and (j) standing on one foot in men (n = 42) and women (n = 28)

(a)



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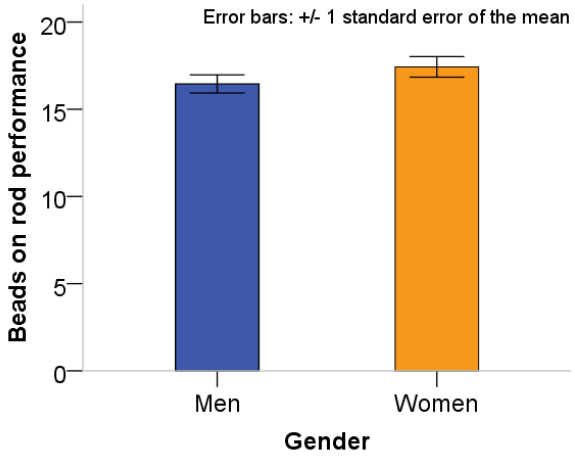

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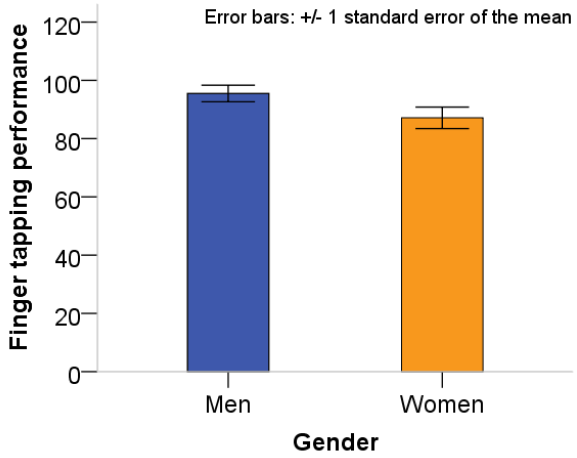

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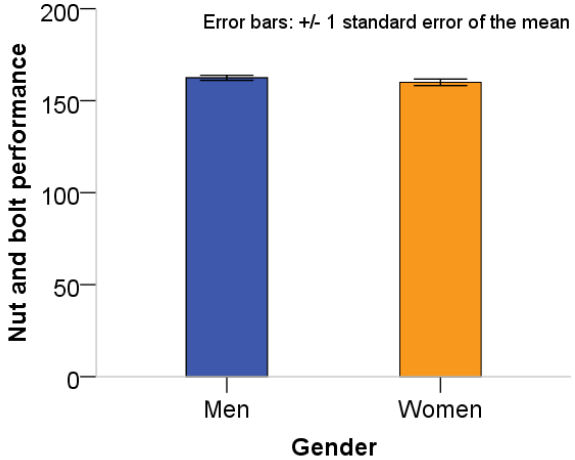

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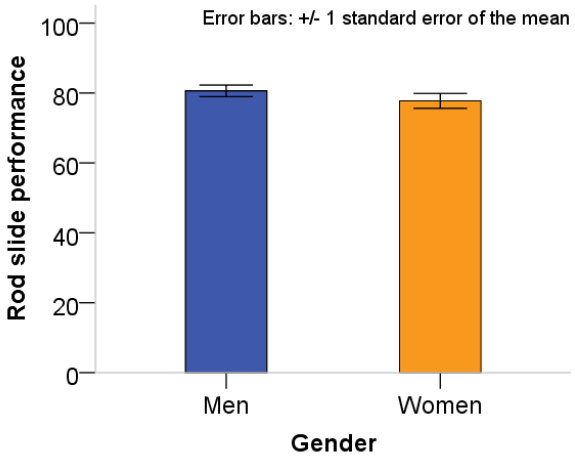
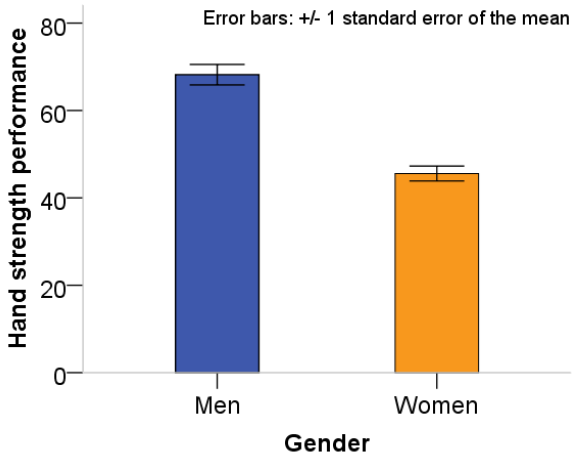
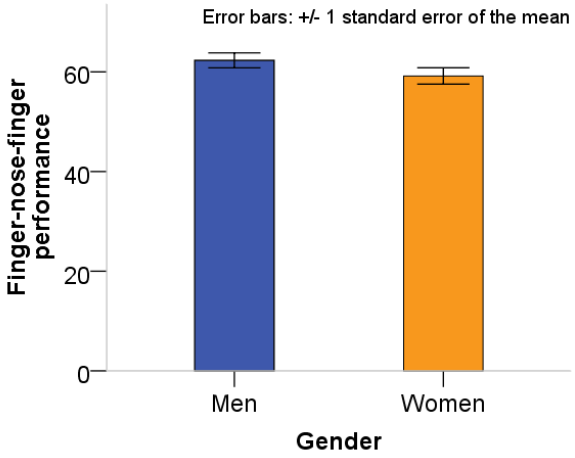

Error bars: +/- 1 standard error of the mean
Rod slide performance
100
80
60
40
20
0
Men
Women
Gender

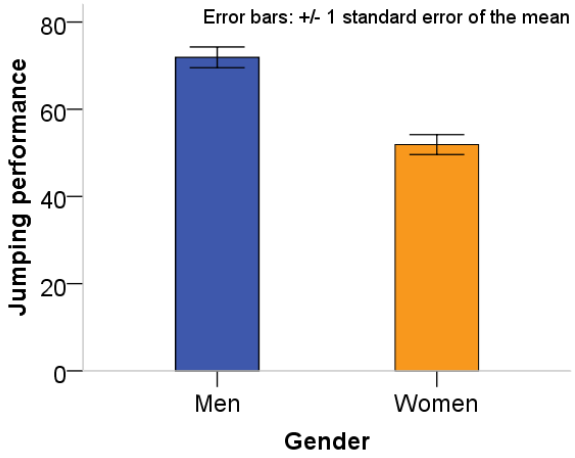
(f)


Error bars: +/- 1 standard error of the mean
Hand strength performance
80
60
40
20
0
Men
Women
Gender

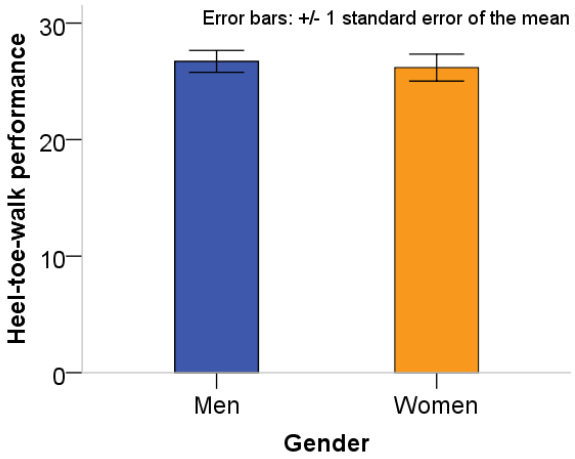
(g)


Error bars: +/- 1 standard error of the mean
Finger-nose-finger performance
60
40
20
0
Men
Women
Gender

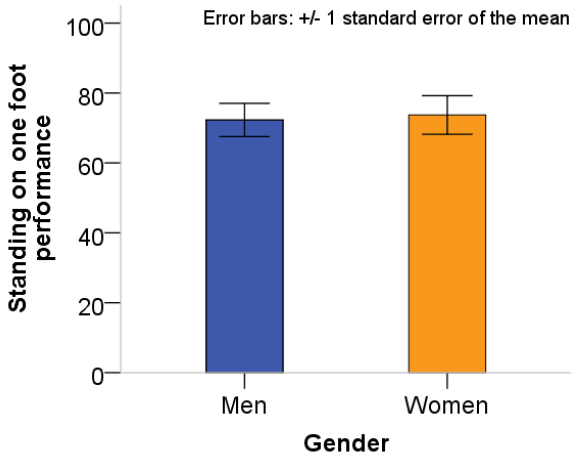
(h)


Error bars: +/- 1 standard error of the mean
Jumping performance
80
60
40
20
0
Men
Women
Gender

(i)


Error bars: +/- 1 standard error of the mean
Heel-toe-walk performance
30
20
10
0
Men
Women
Gender

(j)


Error bars: +/- 1 standard error of the mean
Standing on one foot performance
100
80
60
40
20
0
Men
Women
Gender

Online Resource 4- Figure. Partial correlation between (a) persistent control and positive symptoms, (b) fine motor function and negative symptoms, (c) bimanual dexterity and negative symptoms, (d) persistent control and negative symptoms, and (e) kinesthetic integration and negative symptoms in the total sample after controlling for the chlorpromazine equivalent dosage of antipsychotics

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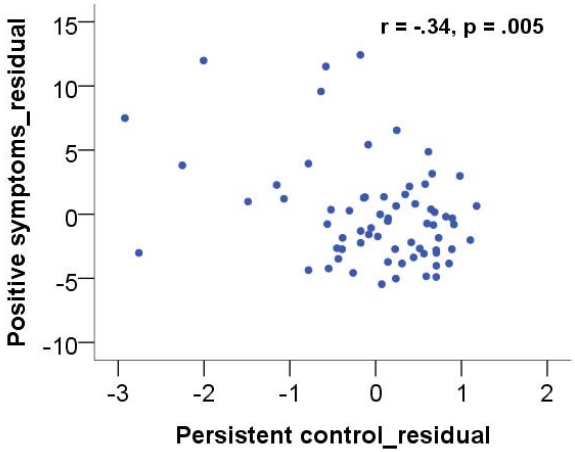

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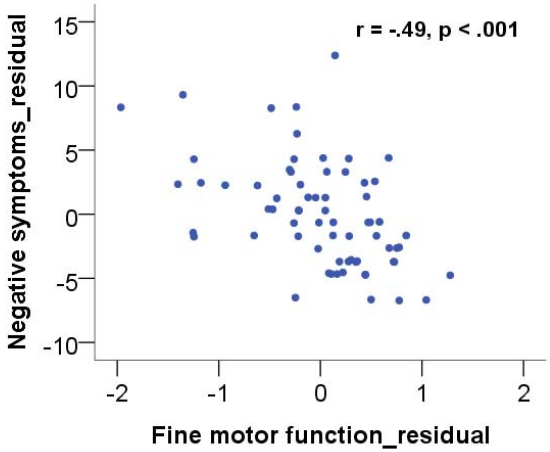

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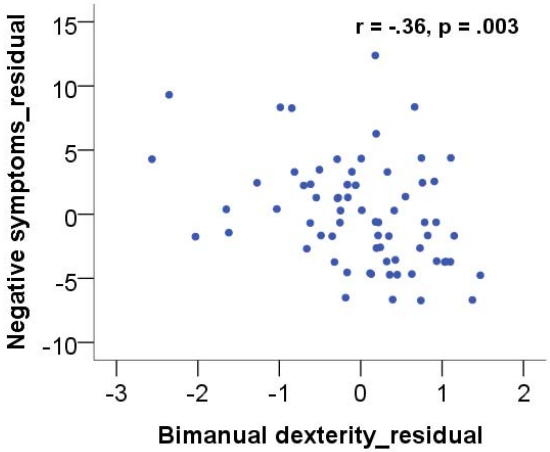

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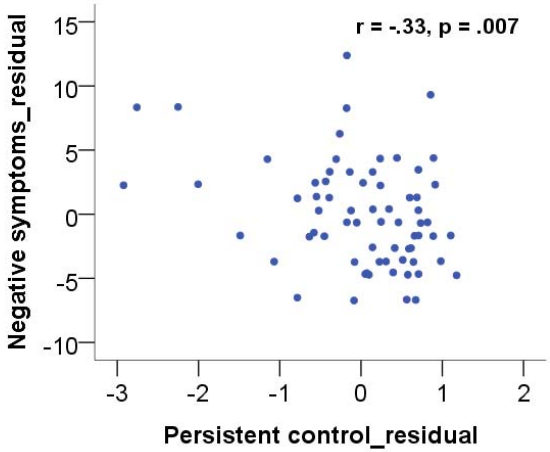
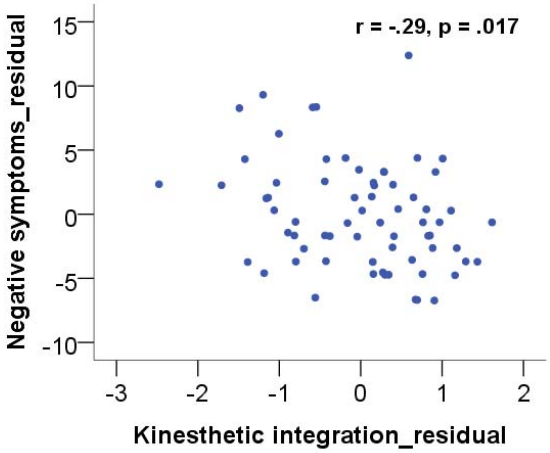
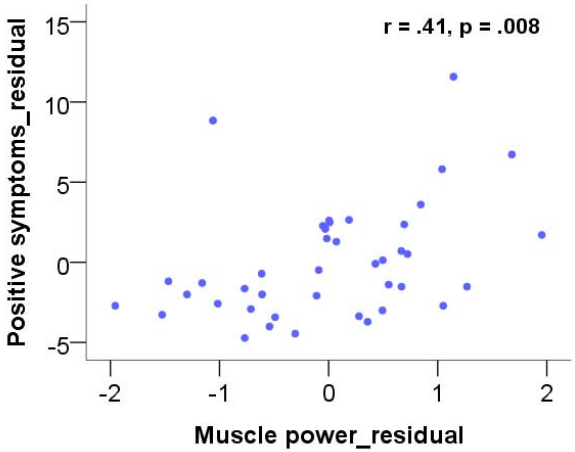


(e)

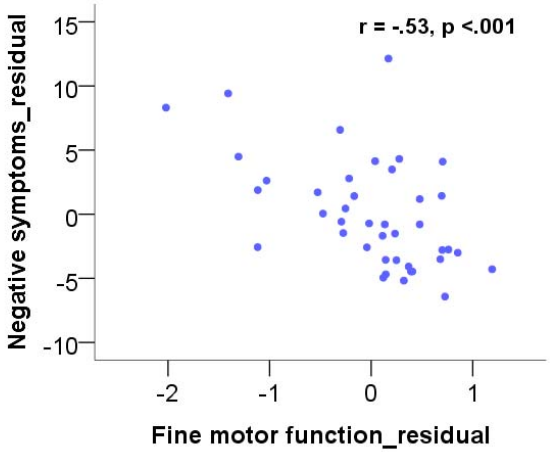

r = -.29, p = .017
Negative symptoms_residual
15
10
5
0
-5
-10
-3
-2
-1
0
1
2
Kinesthetic integration_residual

Online Resource 5- Figure. Partial correlation between (a) muscle power and positive symptoms, (b) fine motor function and negative symptoms, (c) gross motor function and negative symptoms, (d) bimanual dexterity and negative symptoms, and (e) muscle power and negative symptoms in men with schizophrenia after controlling for the chlorpromazine equivalent dosage of antipsychotics

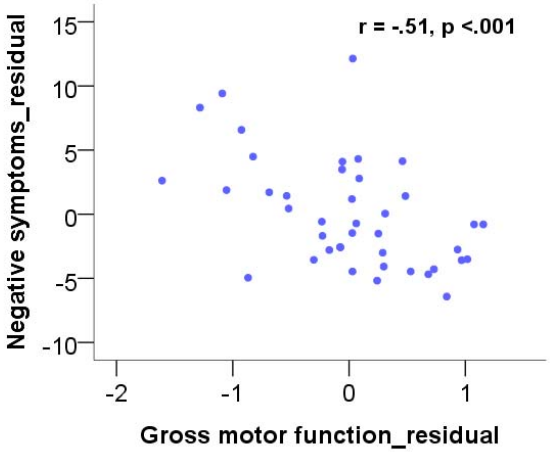
(a)



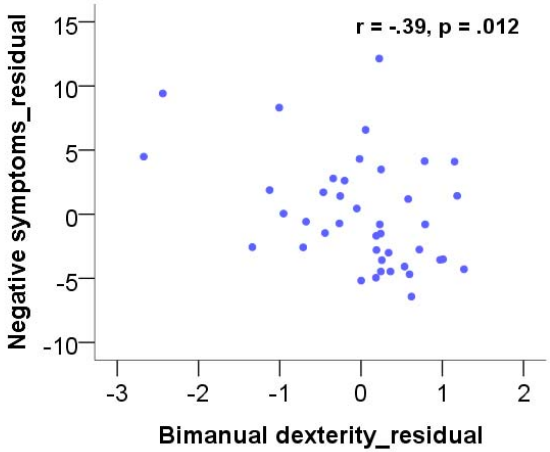
(b)



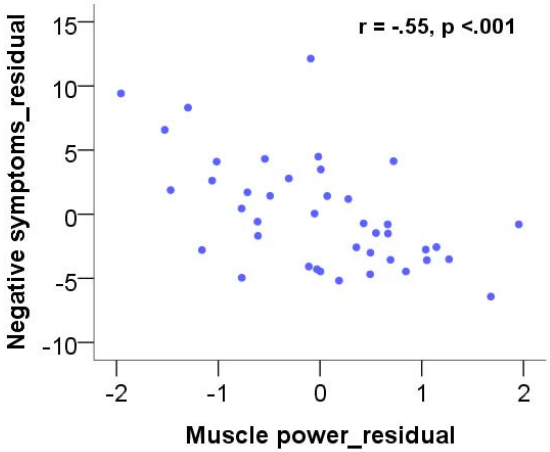
(c)



(d)

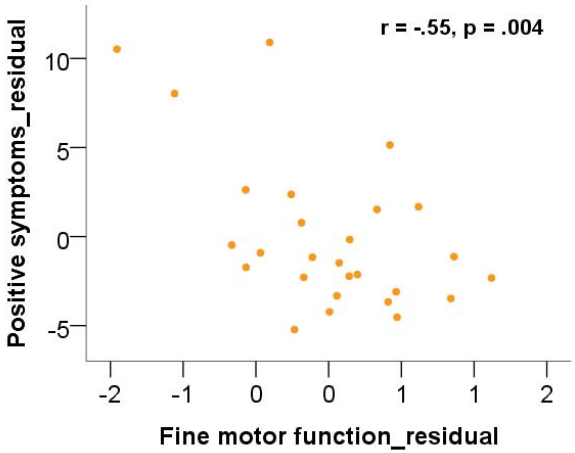


(e)


r = -.55, p <.001
Negative symptoms_residual
15
10
5
0
-5
-10
-2
-1
0
1
2
Muscle power_residual

Online Resource 6- Figure. Partial correlation between (a) fine motor function and positive symptoms, and (b) kinesthetic integration and positive symptoms in women with schizophrenia after controlling for the chlorpromazine equivalent dosage of antipsychotics

(a)



(b)