



## Gait and motor imagery of gait in early schizophrenia

Elise Lallart <sup>a</sup>, Roland Jouvent <sup>a</sup>, François R. Herrmann <sup>b</sup>, Olivier Beauchet <sup>c</sup>, Gilles Allali <sup>d,\*</sup>

<sup>a</sup> Emotion Center – CNRS USR 3246, Pitié-Salpêtrière Hospital, Paris, France

<sup>b</sup> Department of Rehabilitation and Geriatrics, Geneva University Hospitals and University of Geneva, Switzerland

<sup>c</sup> Department of Neuroscience, Division of Geriatric Medicine, Angers University Hospitals, UPRES EA 2646, University of Angers, UNAM, Angers, France

<sup>d</sup> Department of Clinical Neurosciences, Division of Neurology, Geneva University Hospitals and University of Geneva, Switzerland

### ARTICLE INFO

#### Article history:

Received 1 October 2010

Received in revised form 5 October 2011

Accepted 11 December 2011

#### Keywords:

Schizophrenia

Gait disorders

Motor imagery

Executive function

Motor control

### ABSTRACT

Although gait disorders were described in schizophrenia, motor imagery of gait has not yet been studied in this pathology. We compared gait, motor imagery of gait and the difference between these two conditions in patients with schizophrenia and healthy age-matched controls. The mean  $\pm$  standard deviation (S.D.) of Timed Up and Go (TUG), imagined TUG (iTUG) and delta time (i.e.; difference between TUG and iTUG), was used as outcomes. Covariables include Mini Mental State Examination, the Frontal Assessment Battery (FAB), FAB's subitems, the Positive and Negative Syndrome Scale and the Unified Parkinson's Disease Rating Scale (UPDRS). Seventeen patients with early schizophrenia and 15 healthy age-matched controls were assessed. Schizophrenia patients performed the TUG and the iTUG slower than the controls. Multivariate linear regressions showed that iTUG and delta time were associated with the conflicting instruction of the FAB. The present study provides the first evidence that patients with schizophrenia performed gait and motor imagery of gait slower than healthy controls. These deficits could be in part explained by impaired executive function and specifically by a disturbance in the sensitivity to interference.

© 2012 Elsevier Ireland Ltd. All rights reserved.

### 1. Introduction

Before the advent of neuroleptics, gait disorders were described in patients with schizophrenia as a characteristic of the illness (Bleuler, 1911). Quantitative gait analysis confirmed these descriptions and showed a decrease of gait velocity due to a shorter stride length (Putzhammer et al., 2005). Ataxic gait in patients with schizophrenia seems also to be more frequent than in control subjects, and is related to old age and previous history of alcohol abuse, involving a dysfunction of the visuo-cerebellar circuit (Jeon et al., 2007). In addition, it was shown in patients with schizophrenia that infant motor developmental delay was associated with deficits in cognitive function involving executive function in adults (Murray et al., 2006). This last description suggests that executive function could contribute to motor disorders in schizophrenia (Brebion et al., 2000).

Motor imagery (MI) refers to the mental simulation of an action without its actual execution (Jeannerod, 1995). Previous reports on Parkinson's disease in particular suggested that MI shares common neural structures with motor execution (Jeannerod, 1994; Dominey et al., 1995) and the frontostriatal structures is one of these regions (Dominey et al., 1995). Furthermore, in the realization of motor representations into motor performances, the dopaminergic system

seems to play an important role (Yaguez et al., 1999). A recent study on MI of locomotion showed that practice of MI modulates brain networks including supplementary motor area, basal ganglia, bilateral thalamus and right cerebellum (Ionta et al., 2010). Concerning schizophrenia, a review on MI in this pathology suggested an important role of the posterior parietal cortex in attentional dysfunctions and impairments in MI (Danckert et al., 2004).

To assess gait and MI of gait, we recently adapted an imagined version of the Timed Up and Go (TUG) (Beauchet et al., 2010). TUG is a basic test for the evaluation of functional mobility, measuring time while standing up, walking, turning and sitting down and it has been used to evaluate gait and balance performance (Podsiadlo and Richardson, 1991). We showed a relationship between the discrepancy of the time to perform the TUG and the imagined time to perform the TUG (delta time) and Mini Mental State Examination (MMSE) (Folstein et al., 1975) in a sample of older adults (Beauchet et al., 2010). Due to the absence of study on MI of locomotion in schizophrenia, we used this adapted version of the TUG in this population. Because of the role of the dopaminergic system and the suspected relationship between, on the one hand, gait disorders and cognitive function and, on the other, deficits in MI and cognitive function in schizophrenia, we hypothesized that slower TUG and imagined TUG (iTUG) would be observed in patients with schizophrenia. The objective of this prospective cross-sectional study was 1) to measure and compare the time of TUG, iTUG and the difference of time between these two conditions of realization (i.e., delta time) in a sample of patients with schizophrenia and healthy matched controls and 2) to

\* Department of Clinical Neurosciences, Division of Neurology, Geneva University Hospitals and University of Geneva, 4 rue Gabrielle-Perret-Gentil, 1211 Geneva, Switzerland. Tel.: +41 22 372 8302; fax: +41 22 372 8333.

E-mail address: [gilles.allali@hcuge.ch](mailto:gilles.allali@hcuge.ch) (G. Allali).

examine whether there was an association between the performances of TUG, iTUG and delta time and the cognitive status.

## 2. Method

### 2.1. Participants

A total of 32 participants were enrolled in the study: 17 patients with schizophrenia (mean age  $30 \pm 9$  years, 50% women) and 15 healthy age and gender-matched controls (Table 1a). Patients with schizophrenia were recruited in the 10th unit of the Ville Evrard Hospital and control subjects in the campus of the Pitié-Salpêtrière Hospital.

The patients group met DSM-IV criteria for schizophrenia according to the Structured Clinical Interview for DSM-IV Axis I disorders (SCID) (eight paranoid, one disorganized and eight undifferentiated types). Positive and negative symptoms were also evaluated with the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987) by a psychiatrist of the unit of the Ville Evrard Hospital on the day of the experiment. Neuropsychological assessment, included Folstein's MMSE (Folstein et al., 1975), Stroop Test (Stroop, 1935), Trail Making Test (TMT) (U.S. War Department, 1944; Reitan, 1955) and the Frontal Assessment Battery (FAB) (Dubois et al., 2000). The FAB is a short bedside cognitive and behavioral battery assessing frontal lobe function. It consists of six subtests exploring conceptualization, mental flexibility, motor programming, sensitivity to interference, inhibitory control and environmental autonomy. The global scores of the FAB (/18) and its six subscores (/3) are presented in Table 1a. Extraparallel rigidity was evaluated with Unified Parkinson's Disease Rating Scale (UPDRS): the total UPDRS score refers to part III of the UPDRS (motor examination, item 18–31 assessing speech, facial expression, tremor, tonus, finger tapping, hand movements, leg agility, posture, gait and body bradykinesia); and the gait score refers to the item 29 of the UPDRS assessing specifically gait function. All tests were performed on the day of the experiment for both schizophrenic patients and healthy controls. All schizophrenic patients were on neuroleptic drugs (three typical, 14 atypical) without any modification in the previous 3 months. They were stable and were taking the same treatment for at least 4 weeks and for not more than 12 weeks. Schizophrenic patients treated with antidepressants, benzodiazepines, anticholinergics, or lithium for a time period superior to 1 month were excluded from the study. Exclusion criteria included other physical illness involving the central nervous system, current substance and/or alcohol abuse, and clinical evidence of mental retardation or any pathology interfering with gait. The mean illness-duration was 5 years (S.D. 3). Exclusion criteria for healthy controls were neurological and psychiatric disorders, substance abuse, or any pathology interfering with gait. Clinical and demographic characteristics of the participants are displayed in Tables 1a and 1b. After a complete description of the study to the participants, written informed consent was obtained. The study was conducted in accordance with the ethical standards set forth in the Declaration of Helsinki (1983). The local ethics committee approved the project.

**Table 1a**  
Clinical characteristics of participants ( $n = 32$ ).

	Normal ( $n = 15$ )	Schizophrenia ( $n = 17$ )	P-value <sup>a</sup>
Age, mean $\pm$ S.D. (years)	29 $\pm$ 5	30 $\pm$ 9	0.309
Female, $n$ (%)	7 (46.7)	9 (52.9)	1
Education (/3)	3 $\pm$ 0	2.5 $\pm$ 1	0.017
Neuropsychology			
Mini-mental state	30 $\pm$ 0	28 $\pm$ 2	<0.001
FAB (total score)	18 $\pm$ 0	14 $\pm$ 4	<0.001
Similarities (conceptualization)	3 $\pm$ 0	3 $\pm$ 1	0.007
Lexical fluency (mental flexibility)	3 $\pm$ 0	2 $\pm$ 1	<0.001
Prehension behavior (environmental autonomy)	3 $\pm$ 0	3 $\pm$ 0	1
Motor series (programming)	3 $\pm$ 0	2 $\pm$ 1	0.001
Conflicting instructions (sensitivity to interference)	3 $\pm$ 0	3 $\pm$ 2	0.029
Go-No Go (inhibitory control)	3 $\pm$ 0	3 $\pm$ 1	0.001
TMT-A	22 $\pm$ 6.8	51 $\pm$ 53	<0.001
TMT-B	42 $\pm$ 14	166 $\pm$ 178	<0.001
Stroop (word)	136 $\pm$ 38	102 $\pm$ 22	<0.001
Stroop (color)	98 $\pm$ 27	71 $\pm$ 14	<0.001
Stroop (interference)	71 $\pm$ 16	33 $\pm$ 12	<0.001
Similitude test	26 $\pm$ 4	14 $\pm$ 10	<0.001
Letter-number sequence	11 $\pm$ 7	7 $\pm$ 5	0.007
UPDRS			
Total score	0 $\pm$ 0	5.0 $\pm$ 1.6	<0.001
Gait score (1/4) $n$ (%)	0 (0)	9 (53)	<0.001

UPDRS: Unified Parkinson's Disease Rating Scale (Total score refers to part III of the UPDRS; Gait score refers to the item 29 of the UPDRS).

<sup>a</sup> Comparison based on Mann-Whitney test or Fisher-exact test, as appropriate.

**Table 1b**  
Clinical characteristics of schizophrenia patients ( $n = 17$ ).

	Schizophrenia ( $n = 17$ )
Years of illness $\pm$ S.D. (years)	5 $\pm$ 3
Type of schizophrenia	
Paranoid	8
Disorganized	1
Undifferentiated	8
Treatment	
Typical neuroleptic	1
Atypical neuroleptic	14
Phenothiazine	2
Antidepressant	4
Benzodiazepine	1
PANSS score	
Positive (/49)	21 $\pm$ 7
Negative (/49)	21 $\pm$ 15
General psycho	47 $\pm$ 11

### 2.2. Procedures

This study used the TUG test described by Podsiadlo and Richardson (1991). The participants were asked to perform the TUG at their self-selected speed in a well-lit environment. They all completed one trial for both the TUG and the iTUG in the following order: performing then imagining the TUG test while sitting on a chair. The time of each walking and imagined conditions was recorded with a stopwatch to the nearest 0.01 s. Before testing, the same trained evaluator (EL) gave standardized verbal instructions regarding the test procedure: For the TUG, the participants were seated, allowed to use the armchairs to help them to stand up. They were asked to walk 3 m, turn around, walk back to the chair and sit down. The stopwatch was started on the word "go" and stopped as the participant sat down. For the imagined condition (iTUG), the test was performed like in the study of test validation (Beauchet et al., 2010): the participants were sitting on the armchair and asked to imagine performing the TUG-test, meaning to imagine to stand up, to walk 3 m turn around, walk back to the chair and sit down. They chose to perform iTUG eyes opened or closed. The stopwatch was started on the order "go" and stopped when the participant pronounced the word "stop". The participants were free to use motor or visual imagery while performing iTUG. We did not control for the choice of the mental imagery strategy.

### 2.3. Outcomes

The outcomes were as follows: 1) the mean  $\pm$  S.D. time to execute and to imagine the TUG test (respectively, TUG and iTUG), 2) the mean  $\pm$  S.D. difference of time (i.e. delta time) between both TUG conditions calculated following the formula:  $(TUG - iTUG) / [(TUG + iTUG) / 2] \times 100$ ; and 3) the cognitive function with scores of MMSE, FAB, TMT-A and B, Stroop Test.

### 2.4. Statistical analysis

The participants' characteristics were summarized using means and standard deviations or frequencies and percentages, as appropriate. The normality of the parameters' distribution was verified with skewness and kurtosis tests before and after applying usual transformations to normalize non-Gaussian variables (TUG was normalized using an inverse transform, iTUG with an inverse square transform and no transformation for delta time) (Kleinbaum et al., 1987). Comparisons between groups of participants were performed using the independent samples *t*-test and  $\chi^2$  test as appropriate. Simple and bivariate linear regression analyses were performed to specify the association between TUG, iTUG, delta time and covariates. A stepwise forward procedure was also applied to reduce the number of variables in the regression models. A repeated measure analysis of variance (ANOVA) model was used to explain performance time and check for the effects of group (patients versus controls), the effect of task (performed and imagined TUG) along with their interaction, with task being the repeated factor. *P*-values less than 0.05 were considered as statistically significant. All the statistics were performed using the Stata Statistical Software, version 10.1.

## 3. Results

### 3.1. Clinical characteristics

The global cognitive score assessed by MMSE was statistically different between both groups ( $30 \pm 0$  for the control group;  $28 \pm 2$  for patients with schizophrenia;  $P < 0.001$ ). All the tests assessing the performance of executive functioning was worse in the schizophrenic group compared to the control group ( $P < 0.050$ ) with the exception

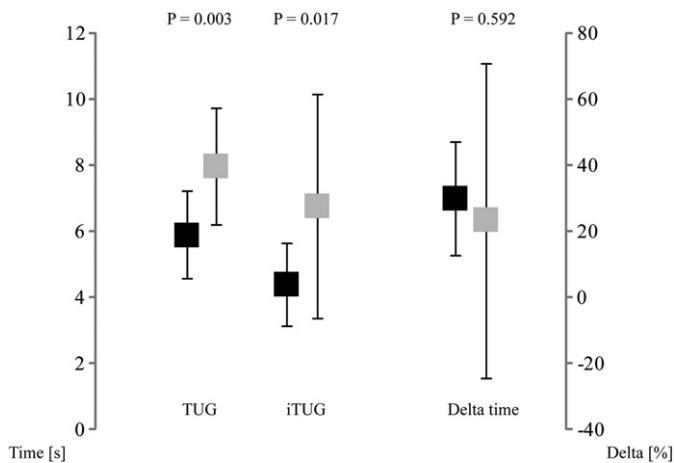
of the subtest of the FAB assessing programming ( $P=1.000$ ). Motor performance assessed by the UPDRS and its gait subscore presented significant deficits in the patients' group with schizophrenia compared to the control group ( $P<0.001$ ) (Table 1a). The PANSS scores for the positive and the negative symptoms were respectively  $21 \pm 7$  and  $21 \pm 15$  and the general score was  $47 \pm 11$  in schizophrenic patients (Table 1b).

### 3.2. Timed Up and Go and imagined Timed Up and Go

All participants were able to complete the TUG test in both conditions. As shown in Fig. 1, performed TUG was slower in schizophrenic patients compared to controls ( $8.0 \pm 1.8$  s versus  $5.9 \pm 1.3$  s with  $P=0.003$ ). Schizophrenic patients imagined also TUG more slowly compared to control participants ( $6.8 \pm 3.4$  s versus  $4.4 \pm 1.3$  s with  $P=0.010$ ). Finally, there were no significant differences for the delta time performance ( $23.3 \pm 47.6$  for the controls versus  $30.1 \pm 17.1$  for the patients with  $P=0.592$ ).

### 3.3. Correlations between Timed Up and Go and clinical characteristics

Univariate regression showed that schizophrenia ( $P=0.001$ ), UPDRS gait score ( $P=0.005$ ), UPDRS total score ( $P=0.001$ ), MMSE ( $P=0.016$ ), FAB total score ( $P=0.038$ ), PANSS positive symptoms ( $P=0.030$ ), PANSS negative symptoms ( $P=0.045$ ), and PANSS general score ( $P=0.020$ ) were associated with the performed TUG. In the bivariate model, after adjustment for schizophrenia, no previous parameter remained significantly associated with the performed TUG. Univariate regression showed that schizophrenia ( $P=0.016$ ), FAB total score ( $P=0.021$ ), the conflicting instructions of the FAB ( $P<0.001$ ), PANSS negative symptoms ( $P=0.045$ ), and PANSS general score ( $P=0.041$ ) were separately associated with the iTUG. In bivariate model, after adjustment for schizophrenia, only the conflicting instructions of the FAB ( $P=0.001$ ) were associated with iTUG. The forward stepwise regression showed that the conflicting instructions of the FAB ( $P<0.001$ ) were associated with iTUG. Univariate regression showed that only the conflicting instructions of the FAB ( $P<0.001$ ) were separately associated with an increase of delta time. In bivariate model, after adjustment for schizophrenia, the conflicting instructions of the FAB ( $P=0.001$ ) and the UPDRS total score ( $P=0.001$ ) were associated with the delta time. The forward stepwise regression showed that the conflicting instructions of the FAB ( $P<0.001$ ), schizophrenia ( $P=0.001$ ) and the UPDRS total score ( $P=0.028$ ) were also associated with the delta time (Table 2).



**Fig. 1.** Performance of healthy controls and schizophrenia patients. Mean values and standard deviation of Timed Up and Go (TUG), iTUG and delta time assessed by the formula:  $(TUG - iTUG) / [(TUG + iTUG) / 2] \times 100$  in healthy controls (in black) and in schizophrenia patients (in gray). Comparisons between groups are based on *t*-test.

### 3.4. ANOVA on TUG and groups of participants

An ANOVA with a repeated design (performed and imagined TUG) showed a strong group effect ( $F(1,30)=14.02$ ;  $P<0.001$ ) with the schizophrenia group taking more time to perform both TUG and iTUG and a task effect with a shorter time for iTUG ( $F(1,30)=5.14$ ;  $P=0.031$ ) but no group by task interaction ( $F(1,30)=0.06$ ;  $P=0.080$ ) (for exact values see Section 3.2).

## 4. Discussion

Mental imagery has already been studied in schizophrenia. Danckert et al. (2002) suggested that imagined movements showed no reliable relationship to target size. In addition, enhanced vividness of mental imagery in schizophrenia has been shown in previous studies (Sack et al., 2005). However, to the best of our knowledge, the present study provides the first evidence that motor imagery of gait is slower in schizophrenia. Brain networks activated during the mental imagery of gait have been previously studied mainly in healthy subjects. Imaging studies of the cortical involvement in gait control suggest that the prefrontal regions are activated during MI of gait. Using positron emission tomography, Malouin et al. (2003) showed that the involvement of multiple cerebral regions involving supplementary motor area was required during the imagination of gait. Recently, brain networks activated during mental imagery of gait were studied using functional magnetic resonance imaging (fMRI). Converging results showed that networks involving bilateral primary motor cortex, supplemental motor area, prefrontal regions and cerebellum are recruited during mental imagery of gait (Bakker et al., 2008; Iseki et al., 2008; Wang et al., 2009; la Fougere et al., 2010). In a recent fMRI study assessing the effect of aging on motor imagery of gait, the elderly subjects presented a prominent activation in the supplementary motor area (Zwergal et al., 2010). Other functional imagery techniques, such as near-infrared spectroscopy, were also used to highlight the role of the prefrontal regions in the preparation and execution of walking (Suzuki et al., 2008). Brain atrophy reported in schizophrenia involves specifically the prefrontal region, particularly the left one, as shown in a meta-analysis on brain volume in schizophrenia (Honea et al., 2005).

The motor performances and motor imagery of patients are slower than those of the healthy controls. This result is in accordance with the observation that motor imagery involves neural mechanism similar to those operating during the real action (Jeannerod, 1994). Previous studies on movement impairment in schizophrenia suggested that the phase of planning is already disturbed in schizophrenia in comparison with healthy controls (Carnahan et al., 1997). Furthermore, motor control in schizophrenia was also related to the prefrontal regions like in the Exner's study, in which 15 subjects with first-episode of schizophrenia present morphological abnormalities of the left pre-SMA. This region is specifically related to disturbances of higher motor control (Exner et al., 2006).

Interestingly, in the forward linear regression model, the delta time between the performed and the imagined TUG was strongly explained by the effect of schizophrenia (adjusted effect:  $-63.942$ ), meaning that the patients with schizophrenia from the present study are unaware of estimating their own gait capacity. Impairment in reality monitoring or difficulty in internally generated thoughts and action is affected by schizophrenia. Dysfunction of self-monitoring in schizophrenia is independent of attentional control (Turken et al., 2003), suggesting a specific deficit in the frontoparietal networks (Danckert et al., 2004). This conscious action monitoring has been specifically studied in healthy subjects in movement and it has been modulated experimentally (Kannape et al., 2010). In the field of motor imagery, a study of hand pointing task showed that patients with schizophrenia were unable to generate accurate internal images of their hand movement (Danckert et al., 2002). Such abnormality in the representation of the motor action timing has been

**Table 2**

Uni- and bivariate linear regressions (on schizophrenia) looking for an association between performed Timed “Up and Go”, imagined Timed “Up and Go” and delta time<sup>a</sup> (dependant variable) and baseline characteristics.

	Crude model			Bivariate (schizophrenia)			Stepwise forward model		
	Unadjusted effect <sup>b</sup>	95% CI <sup>c</sup>	P-value	Adjusted effect <sup>b</sup>	95% CI <sup>c</sup>	P-value	Adjusted effect <sup>b</sup>	95% CI <sup>c</sup>	P-value
<b>Timed “Up and Go”</b>									
<b>Performed</b>									
Schizophrenia	−2.078	[−3.23; −0.92]	<b>0.001</b>						
UPDRS (gait/4)	2.121	[0.795;3.447]	<b>0.003</b>	1.050	[−0.652; 2.752]	0.217			
UPDRS (total score)	0.356	[0.184;0.528]	< <b>0.001</b>	0.299	[−0.050;0.648]	0.090	0.356	[0.184;0.528]	< <b>0.001</b>
MMSE	−0.523	[−0.944; −0.102]	<b>0.016</b>	−0.066	[−0.620;0.488]	0.809			
FAB (total score)	−0.246	[−0.478; −0.014]	<b>0.038</b>	0.043	[−0.258;0.346]	0.769			
FAB (conflicting instructions)	0.02	[−1.475; 1.517]	0.977	1.018	[−0.294;2.33]	0.123			
PANSS positive/49	0.079	[0.008; 0.151]	<b>0.030</b>	−0.070	[−0.194;0.052]	0.250			
PANSS negative/49	0.067	[0.014; 0.132]	<b>0.045</b>	−0.048	[−0.146;0.049]	0.322			
PANSS general psycho	0.045	[0.007; 0.084]	<b>0.020</b>	−0.059	[−0.138; 0.020]	0.142			
<b>Imagined</b>									
Schizophrenia	−2.371	[−4.260; −0.481]	<b>0.016</b>				1.153	[−0.534;2.839]	0.173
UPDRS (gait/4)	1.825	[−0.389; 4.040]	0.103	0.131	[−2.732; 2.993]	0.926			
UPDRS (total score)	0.214	[−0.103; 0.530]	0.178	−0.428	[−1.006;0.151]	0.141			
MMSE	−0.360	[−1.043; 0.322]	0.290	0.397	[−0.497;1.293]	0.371			
FAB (total score)	−0.408	[−0.750; −0.065]	<b>0.021</b>	−0.211	[−0.701;0.278]	0.384			
FAB (conflicting instructions)	−3.925	[−5.628; −2.220]	< <b>0.001</b>	−3.453	[−5.268; −1.637]	<b>0.001</b>	−3.453	[−5.269; −1.637]	<b>0.001</b>
PANSS positive/49	0.075	[−0.036; 0.188]	0.180	−0.138	[−0.338;0.061]	0.168			
PANSS negative/49	0.100	[0.002; 0.199]	<b>0.045</b>	0.013	[−0.149;0.176]	0.866			
PANSS general psycho	0.061	[0.002; 0.119]	<b>0.041</b>	−0.017	[−0.153;0.117]	0.788			
<b>Delta time</b>									
Schizophrenia	6.726	[−19.816; 33.270]	0.609				−49.313	[−98.041; −0.586]	<b>0.047</b>
UPDRS (gait/4)	1.265	[−28.347; 30.877]	0.931	11.186	[−28.812;51.184]	0.572			
UPDRS (total score)	1.401	[−2.733; 5.536]	0.494	9.223	[1.543; 16.904]	<b>0.020</b>	8.061	[1.910;14.212]	<b>0.012</b>
MMSE	−1.051	[−9.943; 7.840]	0.811	−5.276	[−17.879; 7.327]	0.399	−6.875	[−16.055; 2.304]	0.136
FAB (total score)	2.275	[−2.438; 6.990]	0.332	2.901	[−3.981; 9.784]	0.396			
FAB (conflicting instructions)	48.020	[25.585; 70.455]	< <b>0.001</b>	52.906	[28.689; 77.123]	< <b>0.001</b>	47.072	[24.615; 69.528]	< <b>0.001</b>
PANSS positive/49	−0.078	[−1.562; 1.406]	0.915	0.902	[−1.982; 3.787]	0.527			
PANSS negative/49	−0.527	[−1.859; 0.805]	0.426	−0.714	[−2.987; 1.558]	0.525			
PANSS general psycho	−0.271	[−1.067; 0.524]	0.492	−0.485	[−2.384; 1.414]	0.605			

Distinct models for performed Timed “Up and Go”, imagined Timed “Up and Go” and delta time. In the crude model (first column), an univariate linear regression was performed to look for an association between performed TUG (i), iTUG (ii) and delta time (iii) and each parameter (schizophrenia, UPDRS gait score, UPDRS total score, MMSE, FAB total score, FAB conflicting instruction subscore, PANSS positive, PANSS negative and PANSS general). In the bivariate model on schizophrenia (second column), a bivariate linear regression on schizophrenia was performed to look for an association between performed TUG (i), iTUG (ii) and delta time (iii) and each parameter (schizophrenia, UPDRS gait score, UPDRS total score, MMSE, FAB total score, FAB conflicting instruction subscore, PANSS positive, PANSS negative and PANSS general). In the third column, a stepwise forward model was applied to reduce the number of variables in the regression models looking for an association between performed TUG (i), iTUG (ii) and delta time (iii) and each parameter (schizophrenia, UPDRS gait score, UPDRS total score, MMSE, FAB total score, FAB conflicting instruction subscore, PANSS positive, PANSS negative and PANSS general). UPDRS: Unified Parkinson's Disease Rating Scale (Total score refers to part III of the UPDRS; Gait score refers to the item 29 of the UPDRS).  $P < 0.05$  indicated in bold.

<sup>a</sup> Calculated from the following formula: [(Timed “Up and Go” performed unadjusted for height − Timed “Up and Go” imagined) / (Timed “Up and Go” performed unadjusted for height + Timed “Up and Go” imagined) / 2] × 100.

<sup>b</sup> Effect estimated from coefficient of regression beta and corresponding to an increase in mean value of imagined Timed “Up and Go”.

<sup>c</sup> Confidence interval.

associated with passivity phenomena in schizophrenia (Maruff et al., 2003). In addition, due to role of the dopaminergic system in mental imagery (Yaguez et al., 1999), neuroleptic treatment could also contribute to this strong effect of schizophrenia explaining the delta time.

Mental imagery has been broadly studied in schizophrenic patients. Conflicting results exist regarding the relationship between mental imagery vividness and hallucinations in schizophrenia. Some reports suggested that increased imagery vividness is related with hallucinations (Mintz and Alpert, 1972; Morrison et al., 2002a; Morrison et al., 2002b), whereas this observation was not supported by others studies (Brett and Starker, 1977; Oertel et al., 2009). Some authors suggested that vividness of mental imagery might be considered as a trait marker across the schizophrenia spectrum (Oertel et al., 2009). These conflicting results in the field of mental imagery vividness and hallucination in schizophrenia highlight that mental strategy during imagined behavior is not clearly understood. Furthermore in the present study, the fact that we did not control for eyes open versus eyes closed during the mental imagery task represents a limitation in the understanding of mental strategy during imagined movement.

iTUG and delta time scores were only associated with the same subtype of executive functions, the sensitivity to interference, assessed by the conflicting instructions of the FAB. This deficit in

behavioral self-regulation may be observed in tasks in which verbal commands conflict with the sensory information. Patients with schizophrenia exhibit some deficits in executive function related to the frontal lobe (Liddle and Morris, 1991). Another explanation of this relationship is that gait control seems to be related to the prefrontal regions, as shown by functional neuroimaging techniques in patients with gait disorders and prefrontal lesion (Della Sala et al., 2002). Functional neuroimaging techniques have greatly contributed to the understanding of this relationship between the prefrontal regions and the cerebral control of gait in humans. fMRI (Bakker et al., 2008; Wang et al., 2009; Ionta et al., 2010; la Fougere et al., 2010) and positron emission tomography (PET) (Malouin et al., 2003) have been employed to study gait control, through the use of motor imagery paradigms. Use of both techniques and different motor imagery paradigms highlighted the importance of the prefrontal region in the gait control.

Our study has some limitations. First, the small number of participants limited the number of variables of association in the multivariate linear model. Second, although we were able to control many characteristics, residual potential confounders may still remain. In particular, we did not control for the mental imagery strategy. Although mental imagery ability did not differ between schizophrenia

and healthy controls (Bocker et al., 2000), we can assume that schizophrenic patients and controls could differ in term of types of the mental imagery strategy. Furthermore, as mental imagery of schizophrenic patients is differentially affected by the condition of eyes opened or eyes closed (Danckert et al., 2004), it would be interesting in a following study to assess precisely this point for the iTUG. Finally, our normal control group differed from the patient group with schizophrenia in terms of the level of education.

In conclusion, these results provide, to the best of our knowledge, the first evidence that motor imagery of gait and gait performance are both slower in patients with schizophrenia. These deficits are explained by impaired executive function and specifically by a disturbance in the sensitivity to interference.

## Funding

Elise Lallart was supported by the Amory Sports Organization (ASO) and Gilles Allali was supported by a grant from the Swiss National Science Foundation (no. 33CM30-124115).

## Financial disclosures

None.

## Acknowledgment

The authors wish to thank the team of Ville-Evrard Hospital for their help in recruiting patients and evaluating their symptoms.

## References

- Bakker, M., De Lange, F.P., Helmich, R.C., Scheeringa, R., Bloem, B.R., Toni, I., 2008. Cerebral correlates of motor imagery of normal and precision gait. *Neuroimage* 41, 998–1010.
- Beauchet, O., Annweiler, C., Assal, F., Bridenbaugh, S., Herrmann, F.R., Kressig, R.W., Allali, G., 2010. Imagined Timed Up & Go test: a new tool to assess higher-level gait and balance disorders in older adults. *Journal of Neurological Sciences* 294, 102–106.
- Bleuler, E., 1911. *Dementia Praecox or the Group of Schizophrenias*.
- Bocker, K.B., Hijman, R., Kahn, R.S., De Haan, E.H., 2000. Perception, mental imagery and reality discrimination in hallucinating and non-hallucinating schizophrenic patients. *British Journal of Clinical Psychology* 39, 397–406.
- Brebion, G., Amador, X., David, A., Malaspina, D., Sharif, Z., Gorman, J.M., 2000. Positive symptomatology and source-monitoring failure in schizophrenia — an analysis of symptom-specific effects. *Psychiatry Research* 95, 119–131.
- Brett, E.A., Starker, S., 1977. Auditory imagery and hallucinations. *Journal of Nervous and Mental Disease* 164, 394–400.
- Carnahan, H., Aguilar, O., Malla, A., Norman, R., 1997. An investigation into movement planning and execution deficits in individuals with schizophrenia. *Schizophrenia Research* 23, 213–221.
- Danckert, J., Rossetti, Y., d'Amato, T., Dalery, J., Saoud, M., 2002. Exploring imagined movements in patients with schizophrenia. *Neuroreport* 13, 605–609.
- Danckert, J., Saoud, M., Maruff, P., 2004. Attention, motor control and motor imagery in schizophrenia: implications for the role of the parietal cortex. *Schizophrenia Research* 70, 241–261.
- Della Sala, S., Francescani, A., Spinnler, H., 2002. Gait apraxia after bilateral supplementary motor area lesion. *Journal of Neurology, Neurosurgery and Psychiatry* 72, 77–85.
- Dominey, P., Decety, J., Broussolle, E., Chazot, G., Jeannerod, M., 1995. Motor imagery of a lateralized sequential task is asymmetrically slowed in hemi-Parkinson's patients. *Neuropsychologia* 33, 727–741.
- Dubois, B., Slachevsky, A., Litvan, I., Pillon, B., 2000. The FAB: a Frontal Assessment Battery at bedside. *Neurology* 55, 1621–1626.
- Exner, C., Weniger, G., Schmidt-Samoa, C., Irle, E., 2006. Reduced size of the pre-supplementary motor cortex and impaired motor sequence learning in first-episode schizophrenia. *Schizophrenia Research* 84, 386–396.
- Folstein, M.F., Folstein, S.E., McHugh, P.R., 1975. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research* 12, 189–198.
- Honea, R., Crow, T.J., Passingham, D., Mackay, C.E., 2005. Regional deficits in brain volume in schizophrenia: a meta-analysis of voxel-based morphometry studies. *American Journal of Psychiatry* 162, 2233–2245.
- Ionta, S., Ferretti, A., Merla, A., Tartaro, A., Romani, G.L., 2010. Step-by-step: the effects of physical practice on the neural correlates of locomotion imagery revealed by fMRI. *Human Brain Mapping* 31, 694–702.
- Iseki, K., Hanakawa, T., Shinozaki, J., Nankaku, M., Fukuyama, H., 2008. Neural mechanisms involved in mental imagery and observation of gait. *Neuroimage* 41, 1021–1031.
- Jeannerod, M., 1994. The representation brain. Neural correlates of motor intention and imagery. *Behavioral Brain Sciences* 17, 187–245.
- Jeannerod, M., 1995. Mental imagery in the motor context. *Neuropsychologia* 33, 1419–1432.
- Jeon, H.J., Cho, M.J., Cho, S.J., Kim, S.U., Park, S.K., Kwon, J.S., Jeon, J.Y., Hahn, B.J., 2007. Quantitative analysis of ataxic gait in patients with schizophrenia: the influence of age and visual control. *Psychiatry Research* 152, 155–164.
- Kannape, O.A., Schwabe, L., Tadi, T., Blanke, O., 2010. The limits of agency in walking humans. *Neuropsychologia* 48, 1628–1636.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophrenia Bulletin* 13, 261–276.
- Kleinbaum, D.G., Kupper, L.L., Muller, K.E., 1987. *Applied Regression Analysis and Other Multivariable Methods*. PWS-KENT Publishing Company.
- la Fougere, C., Zwergal, A., Rominger, A., Forster, S., Fesl, G., Dieterich, M., Brandt, T., Strupp, M., Bartenstein, P., Jahn, K., 2010. Real versus imagined locomotion: a [18F]-FDG PET-fMRI comparison. *Neuroimage* 50, 1589–1598.
- Liddle, P.F., Morris, D.L., 1991. Schizophrenic syndromes and frontal lobe performance. *British Journal of Psychiatry* 158, 340–345.
- Malouin, F., Richards, C.L., Jackson, P.L., Dumas, F., Doyon, J., 2003. Brain activations during motor imagery of locomotor-related tasks: a PET study. *Human Brain Mapping* 19, 47–62.
- Maruff, P., Wilson, P., Currie, J., 2003. Abnormalities of motor imagery associated with somatic passivity phenomena in schizophrenia. *Schizophrenia Research* 60, 229–238.
- Mintz, S., Alpert, M., 1972. Imagery vividness, reality testing, and schizophrenic hallucinations. *Journal of Abnormal Psychology* 79, 310–316.
- Morrison, A.P., Wells, A., Nothard, S., 2002a. Cognitive and emotional predictors of predisposition to hallucinations in non-patients. *British Journal of Clinical Psychology* 41, 259–270.
- Morrison, A.P., Beck, A.T., Glentworth, D., Dunn, H., Reid, G.S., Larkin, W., Williams, S., 2002b. Imagery and psychotic symptoms: a preliminary investigation. *Behaviour Research and Therapy* 40, 1053–1062.
- Murray, G.K., Jones, P.B., Moilanen, K., Veijola, J., Miettunen, J., Cannon, T.D., Isohanni, M., 2006. Infant motor development and adult cognitive functions in schizophrenia. *Schizophrenia Research* 81, 65–74.
- Oertel, V., Rotarska-Jagiela, A., van de Ven, V., Haenschel, C., Grube, M., Stangier, U., Maurer, K., Linden, D.E., 2009. Mental imagery vividness as a trait marker across the schizophrenia spectrum. *Psychiatry Research* 167, 1–11.
- Podsiadlo, D., Richardson, S., 1991. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *Journal of American Geriatric Society* 39, 42–48.
- Putzhammer, A., Perfahl, M., Pfeiff, L., Hajak, G., 2005. Gait disturbances in patients with schizophrenia and adaptation to treadmill walking. *Psychiatry and Clinical Neurosciences* 59, 303–310.
- Reitan, R.M., 1955. The relation of the trail making test to organic brain damage. *Journal of Consulting and Clinical Psychology* 19, 393–394.
- Sack, A.T., van de Ven, V.G., Etschenberg, S., Schatz, D., Linden, D.E., 2005. Enhanced vividness of mental imagery as a trait marker of schizophrenia. *Schizophrenia Bulletin* 31, 97–104.
- Stroop, J.R., 1935. Studies of interference in serial verbal reactions. *Journal of Experimental Psychology* 18, 643–661.
- Suzuki, M., Miyai, I., Ono, T., Kubota, K., 2008. Activities in the frontal cortex and gait performance are modulated by preparation. An fNIRS study. *Neuroimage* 39, 600–607.
- Turkin, A.U., Vuilleumier, P., Mathalon, D.H., Swick, D., Ford, J.M., 2003. Are impairments of action monitoring and executive control true dissociative dysfunctions in patients with schizophrenia. *American Journal of Psychiatry* 160, 1881–1883.
- U.S. War Department, Adjutant General's Office, 1944. The new Army Individual Test of General Mental Ability. *Psychological Bulletin* 41, 532–538.
- Wang, J., Wai, Y., Weng, Y., Ng, K., Huang, Y.Z., Ying, L., Liu, H., Wang, C., 2009. Functional MRI in the assessment of cortical activation during gait-related imaginary tasks. *Journal of Neural Transmission* 116, 1087–1092.
- Yaguez, L., Canavan, A.G., Lange, H.W., Homborg, V., 1999. Motor learning by imagery is differentially affected in Parkinson's and Huntington's diseases. *Behavioural Brain Research* 102, 115–127.
- Zwergal, A., Linn, J., Xiong, G., Brandt, T., Strupp, M., Jahn, K., 2010. Aging of human supraspinal locomotor and postural control in fMRI. *Neurobiology of Aging*.