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Abstract Dysexecutive functioning, which is described as an enduring core feature of schizophrenia, has been associated with gait disorders. However, few studies have reported gait disorders in schizophrenia patients. The objective of this study was to examine the association between executive dysfunction and gait performance in recent-onset schizophrenia patients using the dual task paradigm. Thirty-two subjects participated to the study: 17 with recent-onset schizophrenia and 15 healthy age-matched controls. Executive functions were evaluated using the Frontal Assessment Battery, Stroop and Trail-Making tests. Mean values and coefficients of variation (CV) of the temporal gait parameters while single tasking (just walking) and while dual tasking (walking and forward counting, walking and backward counting, walking and verbal fluency) were measured using the SMTEC®-footswitch system. We focused on the CV of stride time as this measure has been shown to be the most representative parameter of higher gait control. A strong effect of the stride time was found in the group factor for the verbal fluency dual-task when compared to controls (Cohen's d mean = 1.28 and CV = 1.05). The effect was lower in the other dual tasks, and insignificant in the single task of walking. This study shows that patients exhibit higher stride-to-stride variability while dual tasking than controls. It also shows a stronger impact of verbal fluency on gait regularity compared to the other dual tasks revealing a relationship between the executive dysfunction and gait modification. Those results are in line with the idea that schizophrenia implies not only cognitive but also motor functioning and coordination impairment.

Keywords Gait control · Schizophrenia · Executive function · Dual task

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Introduction

Deficits of executive functioning have been described as an enduring core feature of schizophrenia. These deficits are apparent early in the illness (Saykin et al. 1994) and are a central feature of the broader intellectual decline. Behavioral studies in first-episode schizophrenia indicate a reduced performance on specific tasks involving frontal executive functioning (attention allocation and planning) (Townsend et al. 2001; Chan et al. 2006). Furthermore, functional imaging studies have demonstrated some extensive differences in regional brain activity during an executive task among patients with first-episode psychosis when compared to controls (Royer et al. 2009).

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An extensive body of the literature on the motor dysfunctions and the neurological soft signs has highlighted the observable gait and posture abnormalities in antipsychotic-naive schizophrenia patients (Bleuler 1911; Gupta et al. 1995; Chan et al. 2009), as well as in early schizophrenia patients (less than 10 years of illness) (Lallart et al. 2012). However, only one quantitative study on gait demonstrates that schizophrenia causes a decrease of gait velocity due to a shorter stride length (Putzhammer et al. 2004). Moreover, abnormal functional connectivity between the motor cortex and the cerebellum during the execution of a motor task was shown in schizophrenia (Kasparek et al. 2012) as well as the presence of neurological soft signs, which have been associated with corpus callosum structural abnormalities in schizophrenia (Bersani et al. 2011). A recent meta-analysis estimating the extent of neurological soft signs and morphological brain correlates showed that neurological soft signs in patients with schizophrenia were associated with reduced gray matter at the precentral gyrus, the cerebellum, the inferior frontal gyrus and the thalamus (Zhao et al. 2013). Interestingly, brainstem morphometric alterations are also associated with the severity of neurological soft signs in patients with schizophrenia (Hirjak et al. 2013).

Recently, several studies have shown evidence of a cognitive interference on gait control using the dual-task paradigm. This paradigm measures the ability to accurately allocate attention between two tasks performed simultaneously (a motor and cognitive one). More precisely, in those previous studies, an increase in stride-to-stride variability while dual tasking has been associated with executive dysfunction (Sheridan et al. 2003; Allali et al. 2010). Thus, the dual task related increase in gait variability has been considered as a marker of executive dysfunction in populations with cognitive impairment, such as healthy older adults (Hausdorff et al. 2005), patients with Alzheimer's disease and mixed dementia (Allali et al. 2005, Beauchet et al. 2008a, b; Allali et al. 2007), Parkinson's disease (Yogev et al. 2005; Amboni et al. 2008), Huntington's disease (Delval et al. 2008) and depression (Lemke et al. 2000).

This study furthers the research into the relationship between cognitive impairment and gait control. To assess cognitive impact on gait, the present study aims to quantify and compare mean values and coefficients of variation (CV) of stride time under single and dual task conditions in schizophrenia patients and healthy control subjects. We hypothesized that, given the supposed executive dysfunction related to the disorder, schizophrenia patients would present more gait variability in the dual task than healthy control subjects.

Table 1 Demographic and cognitive characteristics of subjects ($n = 32$)

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

* Comparison based on Mann–Whitney test or Fisher exact test, as appropriate

Methods

Participants selection and clinical assessment

Thirty-two participants were included in the study: 17 stable patients with schizophrenia (9 females, 8 males) and 15 healthy controls (8 females, 7 males) matched by age and gender. The age ranges were between 18 and 45 (mean age 30 ± 9 years) (Table 1). The group of patients was recruited at the Ville-Evrard Psychiatric Hospital (10th unit) and met the DSM-IV (First et al. 1996) criteria for schizophrenia according to the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID). Psychiatrists of the Ville-Evrard Hospital determined the diagnosis of schizophrenia. Two experienced psychiatrists confirmed the diagnosis independently in face-to-face interviews

Table 2 Clinical characteristics of schizophrenia patient ($n = 17$)

	Schizophrenia ($n = 17$)
Years of illness ± SD (years)	5 ± 3
Type of schizophrenia	
Paranoid	8
Disorganized	1
Undifferentiated	8
Treatment	
Typical neuroleptic	3
Atypical neuroleptic	14
PANSS score	
Positive symptoms	21 ± 7
Negative symptoms	21 ± 15
Cognitive symptoms	47 ± 11

using the SCID (8 paranoid, 8 undifferentiated, 1 disorganized). Patients were included in the study sample only if both psychiatrists agreed on the diagnosis of schizophrenia. Only patients with less than 10 years of illness were included (years of illness = 4.5 ± 3 years). The presence and severity of psychotic symptoms was evaluated using the Positive and Negative Syndrome Scale (PANSS) (Kay et al. 1987): the scores for the positive and the negative symptoms were, respectively, 21 ± 10 and 22.5 ± 15, and 47 ± 11 for the cognitive symptoms (see Table 2). All patients were stable and had been taking their prescribed treatment for at least 4 weeks and for less than 12 weeks. Fourteen patients were on an atypical treatment, and three had a typical one. Four patients were on a combination of antipsychotic and antidepressant medications, one on a combination of antipsychotics and benzodiazepines, and 12 on antipsychotics exclusively (Haldol 10 mg, Risperidone 4 mg, or Olanzapine 15 mg). The mean of the chlorpromazine equivalents is 258.8 ± 61.8. In this study, patients treated with antidepressants, benzodiazepines, anticholinergics or lithium for a time period greater than 1 month were excluded from the study. In addition, all patients were rated on the Abnormal Involuntary Movement Scale (AIMS) and the Unified Parkinson's Disease Rating Scale (UPDRS). The total UPDRS score refers to the part III of the UPDRS (motor examination, items 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. Patients with dyskinesia, as defined by a score greater than one in at least one of the AIMS items, were excluded from the study.

Control participants were evaluated using the French version of the Mini International Neuropsychiatric Interview (MINI) questionnaire (Lecrubier et al. 1997) to ensure that they matched to the inclusion criteria. They had a mean age of 29 ± 5 years (clinical and demographic characteristics of the participants are displayed in Tables 1, 2). In addition, healthy controls were free of Axis I and II disorders and Axis I disorders in first-degree relatives.

The exclusion criteria for both groups included physical illness involving the central nervous system, substance and/or alcohol abuse, clinical evidence of mental retardation and any pathology interfering with gait. Subjects with a score of 25 or less on the Mini-Mental State Examination (MMSE) were also excluded from the study. Participants in the study were included after having given their written informed consent for research. The study was conducted in accordance with the ethical standards set forth in the Helsinki Declaration (1983).

Neurocognitive and behavioral assessment

Assessing executive functioning including mental flexibility, sensitivity to interference, inhibitory control, conceptualization, motor programming and environmental autonomy were performed the day of the experiment using the Trail-Making Test (TMT) A and B (US War Department 1944), the Stroop test (Stroop 1935) 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, and sensitivity to interference, inhibitory control and environmental autonomy. The global scores of the FAB are 18 and the maximum score on each subitem is 3. The global cognitive functioning was also assessed the same day using the MMSE (Folstein et al. 1975).

Gait recordings

Gait analysis included the following tasks that were randomized to minimize any practice effect: walking only; forward counting (from 1 to 50) while walking; backward counting (from 50 to 1) while walking; and categorical verbal fluency (animal names) while walking. The verbal fluency task refers to a task that requires spontaneous word production under pre-specified search conditions, which have recently been used to examine executive functions (Strauss et al. 2006). Before testing, a trained evaluator gave standardized verbal instructions on the test procedure along with a visual demonstration of the walking test. For dual tasking, the participants were asked to walk while performing the cognitive task aloud at the best of their capacity. A practice trial preceded the measure task. The time needed to achieve the 10 meters walking distance was recorded using SMTEC® system (SMTEC®, Sport &

Medical Technologies SA, Nyon Switzerland), which consists of two footswitches providing a continuous measurement of temporal step parameters (Beauchet et al. 2008a, b). This system is a pair of innersoles fitted inside the subject's shoes. Each innersole contains two independent footswitches placed at the heel and the toe, which are linked to a portable data logger worn at the waist. The time was calculated using the first contact, which is defined by the activation of the heel sensors and the last contact, which corresponds to the time when the toe sensor goes off the walkway. Each subject completed one trial for each walking condition. The participants wore their own footwear. Mean values and CV (CV = [standard deviation/mean] × 100) of step, time, stride time, swing time and stance time for all walking conditions were determined during steady-state walking using the SMTEC® system (Beauchet et al. 2008a, b). In the present study, we focused on the CV measurements more than the mean values, since it has been shown to be the most representative and reliable dual-task measure of gait variability (Allali et al. 2007).

Statistical analysis

The characteristics of all the participants were described using mean and standard deviations. The normality of the distribution of all the parameters was checked with skewness and kurtosis tests before and after applying usual transformations to normalize non-Gaussian variables. First, comparisons between groups were performed using either the independent samples *t* test or the Mann–Whitney test or Fisher exact test as appropriate.

Second, we compared the two groups (schizophrenia and controls) for each condition (walking only, forward counting, backward counting, and verbal fluency) with the non-parametric test of Wilcoxon for two samples.

Cohen's d established the effect size of the means and the CV of stride time between the groups of subjects in each condition. Third, adjusted bivariate regression models evaluated the association between mean and CV values of stride time (dependent variable) and motor score deficit measured by the UPDRS (independent variables) in the schizophrenia group. Fourth, univariate linear regressions examined the interactions between the mean values and the CV of stride time (dependant variables) and the demographic and the clinical characteristics. We did a multiple comparison using the Bonferroni correction. Among the schizophrenia subjects, one participant was excluded from this analysis since his performance of gait was an outlier in the analysis. *P* values under 0.05 were considered statistically significant. All statistics were performed using the Stata Statistical Software, version 10.1.

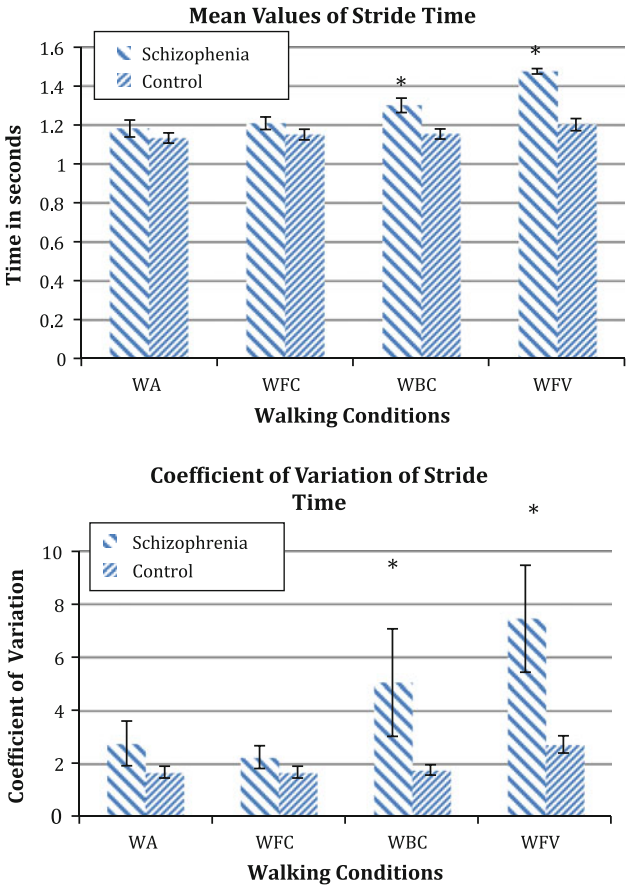

Fig. 1 Mean values and CV of stride according to the different conditions of gait (*WA* walk alone, *FC* forward counting while walking, *BC* backward counting while walking, *VF* verbal fluency while walking) between the groups of schizophrenia patients and controls

Results

Demographic and clinical characteristics

The clinical and demographic characteristics are presented in Tables 1 and 2. The global cognitive score assessed by MMSE was statistically different between the two groups (30 ± 0 for the control group; 28 ± 2 for the patient group; $P < 0.001$). The schizophrenia group performed worse on tests assessing executive functioning ($P < 0.05$) with the exception of the subtest of the FAB assessing programming ($P = 1$). Motor performance assessed by the UPDRS and its gait subscore presented significant deficits in the patients group ($P < 0.001$). No interaction between the symptoms, the subtype of schizophrenia, the type of treatment and the executive functions were found in the present study.

Gait data

The comparison of the performances is shown in Fig. 1 and Tables 3 and 4. It shows a strong effect between

Table 3 Stride time mean: mean, standard deviation, Student's *t* test, non-parametric Wilcoxon test & Cohen's d effect size

Stride time mean	Group				Student's *t* test				Wicoxon		Cohen's *d*
	Schizophrenia		Control								
Condition	Mean	SD	Mean	SD	Type	*t*	*df*	Pr > |t|	Z	Pr > |Z|	
Normal walking	1.182	0.174	1.133	0.109	Equal	0.96	31	0.343	0.900	0.374	0.34
Forward counting	1.209	0.130	1.151	0.113	Equal	1.35	31	0.185	1.063	0.287	0.47
Backward counting	1.301	0.145	1.154	0.107	Equal	3.278	30	0.003	2.870	0.007	1.15
Verbal fluency	1.476	0.305	1.202	0.129	Unequal	3.14	16.81	0.006	2.561	0.016	1.28

Table 4 Stride time coefficient of variation (%): mean, standard deviation, Student's *t* test, non-parametric Wilcoxon test & Cohen's d effect size

Stride time mean	Group				Student's *t* test				Wicoxon		Cohen's *d*
	Schizophrenia		Control								
Condition	Mean	SD	Mean	SD	Type	*t*	*df*	Pr > |t|	Z	Pr > |Z|	
Normal walking	2.744	3.385	1.659	0.915	Unequal	1.24	17.06	0.232	1.481	0.139	0.49
Forward counting	2.225	1.717	1.659	0.917	Unequal	1.17	22.60	0.254	0.776	0.444	0.42
Backward counting	5.040	7.863	1.741	0.810	Unequal	1.62	14.26	0.128	2.971	0.003	0.72
Verbal fluency	7.462	7.285	2.706	1.337	Unequal	2.32	12.62	0.038	2.241	0.033	1.05

groups in the dual task of backward counting and verbal fluency. In the control group, the mean of CV is 2.706 ± 1.337 % for the verbal fluency task, whereas it is 1.659 ± 0.915 % for the walking alone condition, 1.659 ± 0.917 % for the forward condition, and 1.741 ± 0.810 % for the backward counting condition. Comparatively, in the group of patients, the difference of mean between the single and the dual tasks was particularly striking: 2.744 ± 3.385 % for the walking alone condition, 2.225 ± 1.717 % for the forward counting condition, 5.040 ± 7.863 % for the backward counting condition, and 7.462 ± 7.285 % for the verbal fluency condition. The Wilcoxon test also confirms the result that the difference between the two groups is in the backward and the verbal fluency conditions (Table 3). Table 2 also shows a very strong effect size of the mean between the two groups of subjects for the backward counting (1.15) and the verbal fluency (1.28) conditions, contrary to the walking only (0.34) and forward counting (0.47) conditions (Cohen's d). Concerning the CV of stride time, the effect size was particularly strong in the verbal fluency condition (1.05) when compared to the other conditions. This analysis exhibits that the more difficult the condition (verbal fluency), the higher the effect size of the CV of stride time between the groups.

Table 5 Adjusted bivariate regression models showing the association between coefficient of variation of stride time (dependent variable) and schizophrenia and motor score deficit (independent variables)

	Adjusted		
	β	95 % CI	*P* value
Walking alone			
Schizophrenia[a]	−0.17	(−3.14; 2.80)	0.907
UPDRS (total score)	−0.33	(−1.39; 0.74)	0.535
Walking and backward counting			
Schizophrenia[a]	−3.25	(−6.510; 0.012)	**0.051**
UPDRS (total score)[b]	0.27	(−0.89; 1.42)	0.640
Walking and forward counting			
Schizophrenia[a]	−2.66	(−5.83; 0.51)	0.097
UPDRS (total score)[b]	0.47	(−0.66; 1.60)	0.403
Walking and verbal fluency			
Schizophrenia[a]	−3.87	(−6.66; −1.09)	**0.008**
UPDRS (total score)[b]	0.79	(−0.18; 1.76)	0.108

β Coefficient of regression corresponding to an increase or a decrease of coefficient of variation of stride time

CI confident interval

[a] Group of schizophrenia patients

[b] *UPDRS* Unified Parkinson's Disease Rating Scale (total score) reflecting extrapyramidal signs

In addition, the bivariate regression models showed a strong association between the CV of stride time and schizophrenia for the verbal fluency condition ($P = 0.008$) (Table 5). Also, Table 5 shows that the CV of stride time was not dependent from the clinical evaluation of the UPDRS.

Relationships between performances in cognitive tasks, symptoms and gait

We did unilinear regressions to examine the interactions between the mean values and the CV of stride time (dependant variable) and the cognitive tests (predictive variables). The results showed a negative coefficient of regression between the CV of stride time in the backward counting and verbal fluency conditions (dependent variable) and the conflicting instructions of the FAB (independent variable) in the schizophrenia group (respectively $P = -0.002$ and -0.001 for the conditions). A positive correlation between the positive symptoms evaluated by the PANSS and the CV of stride time was also found.

Discussion

Our findings support the hypothesis that schizophrenia patients exhibit higher stride-to-stride variability while dual tasking than healthy controls and that this variability increases in dual task conditions. Indeed, in the schizophrenia group, the difference between the single and the dual tasks is significant and particularly striking, since the CV of the stride time increases considerably in the backward counting and the verbal fluency conditions. Likewise, the performances in the FAB decrease as the CV of stride time increases in the dual task (for the backward counting and the verbal fluency conditions) in the group of patients. This interference of dual-task inferring gait variability in those cognitive conditions supports Norman and Shallice's model of selection of an action as a competitive process (Shallice et al. 1989). In the literature, it has been shown that the verbal fluency test requires higher cognitive functions than the backward counting test as it includes short-term memory, verbal attention, semantic memory and executive processes such as initiation and strategic retrieval. The backward counting task only requires working memory (Ruff et al. 1997). Comparatively, the verbal fluency test has the specificity to involve the frontal and temporal lobes (Lepow et al. 2010). Furthermore, in schizophrenia, the categorical verbal fluency task is particularly impaired (Elvevag et al. 2001; Van Beilen et al. 2004; Bozikas et al. 2005).

In the verbal fluency condition, our analysis reveals a particularly strong effect size on the CV of stride time when compared to the other conditions for the patients group. Furthermore, the verbal fluency test provokes stronger gait variability in the dual task in patients with schizophrenia when compared to controls in dual tasks. Recent brain imaging studies support this idea and show that stride length is dependent on prefrontal cortex activation (Harada et al. 2009; Suzuki et al. 2004). Therefore, our results suggest that it is likely that cognitive tasks such as verbal fluency share complex neural networks connecting different regions (Gazzaley and D'Esposito 2006), which are interlinked with those of gait control. Converging results from functional MRI showed that networks implicated in gait control 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; van der Meulen et al. 2012; Wang et al. 2009) as well as verbal fluency (Birn et al. 2010). Interestingly, these brain regions were significantly associated with altered brain activations in studies assessing neurological soft signs in patients with schizophrenia (Zhao et al. 2013). Therefore, the demand placed by specific cognitive tasks may be enough to interfere with these networks and then disturb gait.

Concerning treatment, some studies have suggested that atypical medication improves executive functions (Harvey et al. 2004; Collie et al. 2006), while others have shown that conventional medication worsens the stride length regulation deficit (Putzhammer et al. 2004). In our study, the performances in gait and executive functions were not dependent on the type of antipsychotic taken.

The main limitation of this study is that the data displayed needs to be duplicated to a larger sample of patients with schizophrenia to confirm the results. Secondly, the SMTEC® system provides only the measurement of temporal step parameters contrary to electronic walkway; it could be interesting to include in a future study the spatial features of gait. Finally, although our study only includes patients recently diagnosed with schizophrenia without a long-term treatment with antipsychotic drugs, it would be interesting to assess the spatio-temporal gait parameters of antipsychotic-naive schizophrenia patients and to compare them with executive functions.

In summary, this study proposes a methodology to quantify the cognitive interference on gait in early schizophrenia using the dual-task paradigm. We have found a stronger increase in gait variability while performing a verbal fluency test, when compared to the other dual tasks. The results of our study support the idea that schizophrenia is characterized not only by cognitive dysfunctioning, but also by motor functions and coordination impairment. This can be explained by the fact that frontal lobe dysfunctions have implications on both bodily and cognitive abilities. This study contributes to the understanding of motor impairments and shows the importance

of executive dysfunction in the neurological soft signs of gait. Furthermore, quantitative measures of gait may provide a more sensitive means of detecting movement disturbances and cognition dysfunctions than do standard clinical observations alone, which could be easily implemented in clinical visits by timing patient's gait while they are performing a cognitive task.

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