Motor fluency deficits in the sequencing of actions in Schizophrenia

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SUMMARY

**Objective** – Many everyday activities depend on the capacity to organize and smoothly execute motor sequences. The present study tested the hypothesis that a sequencing deficit is associated with schizophrenia. A new method is used to distinguish between low and high order mechanisms for the impairment. **Methods and results** – The first task involved triggered sequences in which sensory information from one movement was the cue for initiation of the following movement. Results showed that the motor sequences were performed as fluently in patients as in controls. The second and third tasks involved sequences in which the entire movement sequence could be pre-planned. It was found that patients executed the sequences less fluently than controls but only under the condition where action-sequences were required. Furthermore, the patients’ fluency deficit increased with sequence complexity. **Conclusions** – The high discrimination power of task 3 gave us the means to control for a potential psychometric confound involving differential discriminating power and to argue in favor of a specific high-order motor fluency deficit in patients with schizophrenia. We suggest that basic low-order mechanisms that integrate sensory information with outgoing motor commands are preserved in schizophrenia whereas higher-order integrative mechanisms that are required for the smooth coordination of motor sequences are impaired.

**Key Words** Schizophrenia · Motor sequencing · Grip force · Planning · Reaction time
INTRODUCTION

The act of lifting and manipulating an object is a commonly performed motor action that is nevertheless a complex process involving close temporal coordination of activity both in the proximal arm muscles responsible for lifting, and in the finger muscles used to grip the object (Flanagan and Wing 1997). In normal controls, grip force is tightly scaled both to the mass and to the texture of manipulated objects (Johansson and Westling 1984). In patients with schizophrenia, even if finger forces are scaled both to texture and mass (Delevoye-Turrell et al. 2003), excessive and unnecessarily high force levels are developed (Vrtunski et al. 1989; Neumann and Walker 1999; Caligiuri and Lohr 1994). Recent work suggests however that this problem of force efficiency may arise only when action sequencing is required (Delevoye-Turrell et al. 2003). For example, in a reach-and-lift task patients with schizophrenia exhibited a significant delay between the onset of grip closure and the start of the upward lift movement; such an uncoordinated force pattern may have led to the development of excessive force levels in the patients compared to the comparison subjects. This abnormal behavior is consistent with the hypothesis that schizophrenia involves a fundamental cognitive abnormality, or dismetria (Andreasen 1999), which would be characterized by a deficit in the fluent coordination of sequences of action and thought (Wiser et al. 1998; Crespo Facorro et al. 1999).

The aim of the present study was to test directly the hypothesis that schizophrenia is characterized by a problem in the fluent coordination of motor sequences, and to discriminate between a low-order deficit i.e. the integration of afferent sensory input with efferent motor output, and a higher-order deficit i.e. the programming of motor sequences. Furthermore, we sought to distinguish between those processes involved in planning and execution, and those involved in coordinating multiple motor-elements within a single sequence.
In a task where a single effector is used to perform a sequence, each successive sub-movement – or motor element – is dependent on completion of the preceding one. It takes an appreciable amount of time for peripheral sensory information to reach the central nervous system (CNS) and in the presence of such delays, it is generally suggested that motor sequences may be organized in two fundamentally different ways depending on whether or not they require sensory information (for review, see Delevoye-Turrell and Wing 2004). First, sequencing may be based on concurrent processing of sensory information (Macefield and Johansson 1994). In this case, each element in the sequence will be initiated only after the arrival of the sensory feedback signaling the end of the preceding element. This mechanism will result in significant time intervals – approximately 90 ms (Johansson et al. 1992a) – between the completion of one element and the initiation of the next element of the sequence. In the following, we refer to motor actions organized in this fashion as triggered sequences. An alternative approach to sequencing involves pre-planning the entire sequence before its initiation as a whole (Billon et al. 1996). In this case, the sequence is represented as a single entity and performed without reference to feedback from events within the sequence. These motor sequences will be referred to in the following as planned sequences. The correct outcome of these planned sequences relies on well-defined predictive processes developed through previous experience, as well as the ability to organize through time and to coordinate information from multiple sources (e.g. context or memory based information). Over a series of trials, optimization of motor fluency for both triggered and planned sequences is reached by minimizing the time delays between successive elements.

In order to gain a better understanding of the nature of the motor sequencing deficits that may underlie schizophrenia (e.g. Sullivan et al. 2001), we evaluated motor fluency for both
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triggered and planned sequences in twenty-four patients with schizophrenia by means of three contrasting motor tasks.

**Task 1: Triggered Sequences**

The fluent execution of an action might be impaired in schizophrenia because sensory information is not well integrated with outgoing motor commands (Gordon and Soechting 1995) due to dysfunctional low-order integrative processes of a sub-cortical (cerebellar) nature (Müller and Dichgans 1994). We tested this hypothesis by means of a triggered sequencing task, during which subjects were required to let an object slip within grasp and then, quickly augment grip force in order to arrest object-slip. Here, grip augmentation (second element) could be initiated only after the arrival of sensory afferences from the digits signaling object-slip (first element). Thus, a successful trial required the fluent integration of afferent and efferent information about hand function.

Previously used in micro-neurographic studies, this task has provided the means to assess the role of the mechanoreceptors of the glabrous skin for rapid and accurate afferences about discrete mechanical events, e.g. changes in shear force or slip on the skin (Johansson and Weslting 1987). These studies have shown that triggered responses are abolished both in deafferented patients (Rothwell et al. 1982) and during anesthetic block (Johansson et al. 1992b; Nowak et al. 2002), stressing the importance of afferent information for triggered actions. In addition, as the time course for triggered actions is of the order of 100 ms, the underlying neural mechanisms are very probably reflexive, possibly involving cortical and subcortical pathways (Johansson et al. 1994; Macefield and Johansson 1994; Harrison et al. 2000), because the latencies are too short to involve controlled, voluntary intervention (Johansson and Westling 1984). Consequently, we propose that this task can provide a simple
method for the quantitative study of low-order integrative processes required for the fluent integration of incoming sensory information regarding slip with the outgoing motor program about grip.

**Task 2: Planned sequences**

To test the possibility that motor sequencing deficits previously described in patients with schizophrenia might be due to a problem in higher-order integrative processes, a sequential pointing task was used for which the timing of all elements of the sequence was self-initiated as well as self-paced. Consequently, the entire sequence could be pre-planned as a single movement (Sternberg et al. 1989). Here, a single 2-element tapping motion (finger *down*; finger *up*) was incorporated within a set of motor sequences whose complexity was increased. The critical variable measured was the duration of the brief contact between the index finger and the top surface of a target-object. This paradigm was specifically designed to reproduce the problem in prolonged contact duration described above in patients with schizophrenia during the reach-to-lift task (Delevoye-Turrell et al. 2003).

Here, both low-order and high-order integrative processes are required for normal performance. Indeed, low-order mechanisms are needed to minimize the duration of the brief contact (through the fluent integration of afferent and efferent information). In addition, higher-order processes are needed to integrate the tapping motion within sequences of increasing complexity.

**Task 3: Context effect**

Finally, to distinguish a problem in motor coordination from a more general deficit in motor planning, we used a simple visuo-motor pointing task; through instruction, the emphasis was
set either on minimizing execution-time, or on minimizing both initiation- and execution-
time. Under the first condition, emphasis was set upon the end point of the reach only, 
encouraging subjects to consider the task as a single movement of one element (point). Under 
the second condition, subjects were encouraged to first focus on removing the hand from a 
touch pad as fast as possible and then, to quickly continue through with the pointing task. 
Because the task required subjects to divide their attention between starting and executing the 
action, we suggest that the instruction created an arbitrary segmentation of the reach into two 
elements (lift and point).

In order to be fast, motor planning was necessary under both conditions. Thus, if 
schizophrenia affects motor planning, then patients should reveal abnormal patterns of 
response under both conditions. However, if the deficit lies within the integrative mechanisms 
required for the coordination through time of multiple sub-elements of a sequence, then 
patients should be specifically impaired under the condition where the arbitrary segmentation 
of the motor action was introduced.

In summary, our approach was to measure the time delay between successive motor elements 
both in triggered (Task 1) and in planned motor sequences (Tasks 2 & 3) in order to examine 
the possibility that schizophrenia affects higher order mechanisms, those required for the 
fluent execution of planned sequences. Task 3 was designed specifically to distinguish 
between a deficit affecting integration and a more general problem in motor planning.
Methods

Participants
Twenty-four outpatients with schizophrenia [14 males; mean age 36.0 ± 7.5 years; mean educational level 10.1 ± 3.3 years] and twenty-four healthy control subjects [14 males; mean age 35.4 ± 11.9 years; mean educational level 13.7 ± 4.6 years] participated in a single experimental session that lasted 60 minutes. It was comprised of three different motor tasks. Subjects and patients were paid for their participation. Written informed consent was obtained in accordance with the recommendations of the Declaration of Helsinki. The experimental protocol was approved by the local ethics committee.

Psychiatric diagnoses of patients [9 disorganized, 7 positive and 8 characterized with negative symptoms] were established by a senior psychiatrist (FK) in agreement with the patients’ therapist through a semi-structured interview (MINI+, Lecrubier, 1997); patients were included in the study only if they fulfilled the DSM-IV criteria for schizophrenia. Once included, FK collected the demographic information and ran the series of clinical tests for all subjects. The average age at symptom onset was 24.6 ± 8.4 years, the average disease duration was 12.8 ± 8.0, and the number of hospitalization periods was 6.1 ± 6.6. None of the patients had received any changes in their treatment regimens over the preceding three months suggesting that they were clinically stable. Mean symptom severity, as measured by the Brief Psychiatric Rating Scale (BPRS) total score, was 37.0 ± 12.8. With the Scale for the Assessment of Positive (SAPS) and Negative Symptoms (SANS), the group mean scores were 20.0 ± 18.2 and 34.6 ± 24.6, respectively. Twenty-one of the twenty-four patients were receiving atypical neuroleptic treatment, administered in a standard dose (mean dose = 181.0 ± 90.1 mg/day of chlopromazine or equivalent). Eight were also receiving an antiparkinsonian
treatment (mean dose = 13.7 mg/day; range: 5-30 mg/day of lepticur equivalent). Three of the patients were not receiving any treatment.

Control subjects were recruited through local advertising and pair-matched with the patients with schizophrenia. There were no significant differences between controls and patients for Age, Sex or level of Education (p > .40). Exclusion criteria for both groups were visual and auditory disorders, history of neurological illness or trauma, alcohol and substance abuse, age older than 55 years or younger than 18 years. Subjects were all right-handed as determined through the Edinburgh Handedness Inventory.

**Apparatus**

A 6-axis load cell (ATI – Novatech Gamma SI-130-10) was used to measure force (in N) and torque (in N.mm⁻¹) changes in X-, Y-, and Z-axes. In tasks 2 and 3, an accelerometer (Entran EGA-F-25) was taped to the top of the subjects’ hand and recorded hand-acceleration (in m.s⁻²) during hand movement. Data was sampled at a 1000 Hz.

**Tasks.** Three motor tasks were used to determine the nature of the motor sequencing problems in schizophrenia.

**Task 1: Triggered Sequences**

Subjects were seated in front of a table and used the right dominant hand to grip the load cell in precision grip with thumb on one side and index, middle and ring fingers on the other. The load cell was held with: the X-axis aligned vertically; the Y-axis aligned horizontally parallel with the grip axis; the Z-axis aligned horizontally perpendicular to the grip axis. The subjects held this object approximately 10 cm above the tabletop. Their task was to release their grip on the manipulated object in order to allow it to slip under the effects of gravity. As soon as
the load cell began to slip, their task was to arrest the fall of the object by increasing the grip force applied through the fingers – for more details about the procedure and apparatus, see Turrell et al. (2001). In order for a trial to be accepted, slips were required to occur within 3 s from the start of the trial, which was signaled by an auditory signal. A block of 10 trials was recorded for each individual.

Task 2: Planned Sequences

The load cell was placed flat upon the table 20 cm in front of the subjects’ right-dominant shoulder. The accelerometer was used to record hand-acceleration during movement. Two series of trials were run in an identical set order for all subjects. The first series was intended to measure the tap duration in a “natural” situation i.e. without subjects paying attention to the dynamic characteristics of the tap; the second series explicitly put pressure on the subjects to minimize contact duration.

1- Natural condition: Subjects produced series of 5 taps on the top of the load cell. They were required to produce these taps with the index finger and without moving the wrist, so that the palm of the hand remained in contact with the table. From one series to the next, they were encouraged to change the rhythm of execution of the sequence. At the end of each series, subjects were asked to reproduce verbally the rhythm they had just executed (e.g. dit dah dah dit dit). This procedure was followed to encourage subjects to pay attention to the entire sequence and not to the way in which they executed each tap. Subjects performed 10 trials. The contact duration of the first tap of each sequence only was analyzed and was considered to comprise two elements (2-elm; finger down, finger up).

2- Pressure condition: In this condition, subjects were explicitly instructed to produce the
shortest tap possible on the top of the load cell. Twenty trials were performed for each type of sequence, in a blocked semi-randomized order. In the two-element sequence (2-elm), subjects tapped the top of the load cell with the index finger without moving the wrist so that the palm of the hand remained in contact with the table. In the three-element sequence (3-elm), subjects started each trial with the hand resting on a touch pad that was at the edge of the table aligned with their right shoulder. The subjects’ task was to reach towards and tap the top of the load cell. Finally, in the four-element sequence (4-elm), subjects started with the wrist resting on the touch pad and their task consisted in reaching towards the load cell, tap the top of it, before lifting the hand up to stabilize it precisely 30 cm above the tabletop. Visual indication was provided beyond the object to indicate the target zone for the end of the movement. For all three sequences, the subjects were reminded every 5 trials that the goal of the tapping action was to produce the shortest contact duration possible on the load cell.

Task 3: context effect

As in the previous task, the load cell was placed flat upon the table 20 cm in front of the subjects’ right-dominant shoulder. For all trials, subjects rested the wrist of the right dominant hand on the initial touch pad, which was fixed at the edge of the table. At the auditory signal, the subjects’ task was to move the hand to tap the top surface of the load cell with the index finger. There were two experimental conditions. In the first, subjects were instructed to tap the load cell as fast as possible at the auditory signal (global sequences, 1-elm). In the second, subjects were required to lift the hand off the touch pad as fast as possible at the auditory signal. This instruction was intended to encourage subjects to be both fast in initiating and fast in executing the movement (segmented sequences, 2-elm).
RESULTS

**Task 1: triggered sequences**

Baseline levels were measured during the first 250 ms of each trial. The start of object vertical slip along the X-axis produced a change in torque about the Y-axis. Slip onset was identified as the time at which the torque about this Y-axis first showed a change greater than 5 times the variability of the baseline. The start of grip force increase was taken as the first moment in time when the rate of change of grip force was 5 times greater than the standard deviation of the baseline. A t-test\(^1\) was run to assess the effect of Group (controls; patients) on mean grip force baseline, mean force stability and mean time delays between the start of object vertical slip and the start of grip force increase.

The slip task requires the use of sensory feedback about slip onset to arrest object fall by increasing grip force. All subjects required practice in order to succeed in letting the object slip within 3 s from the start of the trial. On average, patients required more practice trials than controls (8 vs. 2 trials). Nevertheless, the general pattern of slip/grip force modulation was similar for all subjects (figure 1). The object was dropped only 5 times in total across the 48 subjects. It was not dropped more often by patients than by controls.

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*Insert Figure 1 approximately here*

The analysis of the experimental trials revealed that patients used higher grip force levels (5.6 N) and revealed greater force instability (SD=1.2 N) than matched controls (5.3 N SD 0.8 N) but these differences did not reach significance. For the mean time delays, the Group effect did not reach significance, \(F(1,46) = -0.015; \) ns. The time between object slip and the start of grip force increase was 94 ms SD 18 ms and 95 ms SD 21 ms for controls and patients,

\(^1\) All statistical analyses were two-sided and interpreted in relation to a significance level set at \(\alpha=0.05.\)
respectively (figure 2 – left). These results suggest that the fluent integration of afferent and efferent information for hand function is preserved in schizophrenia. Mean time intervals were similar for the non-treated (98 ms SD 29 ms) and the treated (93 ms SD 20 ms) patients with schizophrenia, suggesting no secondary effect of treatment on low-order motor processes.

**Task 2: Planned sequences**

For each subject and experimental condition, the force and contact duration of the taps were measured. Overall, patients applied higher force levels (7.2 N; range=1.1-28.0 N) than the controls (3.8 N; range=1.5-8.3 N), $F(1,46) = -5.103; p<.05$. For both groups, contact durations were constant across the force range: the force-duration correlation coefficients were not significantly different from zero for either the patients or the controls, which suggested that the tapping duration was not dependent on the finger-force exerted at contact. Finally, the force levels were equivalent across the four types of sequences for both patients and controls. Consequently, in the following, only the contact duration of the taps are reported.

A two-way repeated measures ANOVA with Group (controls; patients) and Condition (natural:2-elm; pressure:2-elm) as factors, was first carried out to assess the effect of emphasizing the importance of a short contact duration. Second, a two-way repeated measures ANOVA was carried out on the results from the Pressure condition only in order to test the effect of sequence complexity with Group (controls; patients) and Complexity (2-elm; 3-elm; 4-elm) as factors. Finally, the magnitudes of peak acceleration and peak deceleration were subjected to a two-way repeated measure ANOVA with Group (controls; patients) and Complexity (3-elm; 4-elm) as factors.
Patients and controls performed all sequences without apparent difficulty. The first ANOVA (natural vs. pressure) revealed a significant main effect of Group, $F(1,46) = 42.561; p<.001$: the contact duration between finger and object was shorter for controls (44 ms SD 18 ms) than for patients (116 ms SD 63 ms). The Condition main effect was also significant, $F(1,46) = 11.993; p<.01$, indicating that when emphasis was set on minimizing the contact duration, the contact durations were shortened significantly for both patients (from 134 ms SD 67 ms to 98 ms SD 59 ms) and controls (from 50 ms SD 15 ms to 39 ms SD 22 ms). The interaction Group $\times$ Condition was not significant, $F(1,46) = 3.365; ns$.

For the sequence complexity manipulation, ANOVA revealed again a main effect of Group, $F(1,46) = 141.989; p<.001$. The interaction Group $\times$ Complexity was also significant, $F(2,92) = 20.998; p<.001$. The Tukey HSD test indicated that for controls, contact durations were similar for all sequences. For the patients, the more complex the sequence, the longer were the contact times (figure 2-right). This effect of sequence complexity on the mean time of contact was present in both the non-treated (85, 112, 137 ms) and the treated (100, 129, 136 ms) patients with schizophrenia.

The kinematic profiles were similar in the 3-elm and the 4-elm sequences, for both patients and controls. However, the duration of the reaching movement was longer for patients (608 ms SD 141 ms) than for controls (521 ms SD 135 ms), $F(1,46) = 9.499; p<.01$. ANOVA revealed that controls (M=0.39 m.s$^{-2}$; range: 0.17-0.61 m.s$^{-2}$) accelerated significantly faster than patients (M=0.29 m.s$^{-2}$; range=0.11-0.48 m.s$^{-2}$), $F(1,46) = 3.201; p<.05$. However, both groups decelerated at a similar rate (M=0.42 m.s$^{-2}$; range=0.26-0.57 m.s$^{-2}$), $F(1,46) = 0.503$;
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ns. These results suggest that overall patients and controls used a similar visuomotor guidance strategy to precisely position the hand over the load cell before initiating the tap motion: for all subjects, the index finger contacted the object i.e. the downward motion of the finger was terminated, before complete immobilization of the hand.

Task 3: context effect

Figure 3 illustrates the mean reaction time obtained for the control group (black circles) and the patient group (white triangles) under the two experimental conditions (global sequences – 1elm; segmented sequences – 2elm). ANOVA revealed a significant interaction Group x Condition, $F(1,46) = 6.199; \ p<.01$. The Tukey HSD test showed that the reaction times for global sequences were similar for controls (282 ms SD 131 ms) and for patients (292 ms SD 63 ms), $p=.62$. However, for segmented sequences, reaction times were significantly faster in controls (250 ms SD 59 ms) than in patients (342 ms SD 121 ms), $p<.001$. Finally, controls reacted significantly faster for segmented than for global sequences (difference of 32 ms) whereas patients reacted slower for segmented than for global sequences (difference of 49 ms). Non-treated patients reacted faster than treated patients, but performance patterns were similar in both groups (295 vs. 254 ms in the non-treated patients and 350 vs. 297 ms in the treated patients, for the segmented and the global condition, respectively).

For movement times, the Group effect was significant, $F(1,46) = 24.77; \ p<.001$: patients moved overall slower (346 ms SD 7 ms) than controls (310 ms SD 8 ms). Both groups moved faster for global (259 ms SD 8 ms) than for segmented sequences (405 ms SD 8 ms), $F(1, 46) = 430.89; \ p<.001$, as encouraged through instruction. The interaction was significant, $F(1, 46) = 16.49; \ p<.001$, indicating that the increase in movement time between the global and the segmented sequences was greater for controls (from 221 ms SD 8 ms to 402 ms SD 8 ms).
than for patients (from 287 ms SD 7 ms to 408 ms SD 7 ms). Movement times were similar for the non-treated (329 ms SD 195 ms) and the neuroleptic treated patients (348 ms SD 133 ms).

**Evaluating a potential Psychometric Confound**

Experimental psychopathology struggles with the fact that patients’ behavioral impairments are difficult to interpret as specific cognitive deficits. This difficulty, referred to as the psychometric confound (MacDonald and Kang 2006), occurs because mental disorders such as schizophrenia usually result in impairments across many tasks, and some of these impairments may appear larger simply because a task has greater discriminating power (Chapman and Chapman 1973). Hence, in table 1, we present four indicators, which together provide the information needed to argue here in favour of a specific problem in the fluent coordination of planned sequences in patients with schizophrenia, and not simply a reflection of differential sensitivity in the tests used.

First, Cronbach's alpha ("the reliability coefficient"; Cronbach 1951) was computed for the control group only, in order to provide a measure of internal consistency for each task and condition (see Table 1). One can note that, except for the 2-elm condition of task 3, the alpha values are similar across and acceptable for all tasks and conditions as they are greater than 0.70 (Nunnaly 1978; Miller 1995). Second, the discriminating power, which is indexed by true score variance (TSV), was calculated for each task and condition as the product of the observed score variance and the reliability value (see Table 1). Here, results show that task 3 possesses the highest TSV whereas task 1 is where it is the lowest.
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The existence of a group effect in task 2 but not in task 1 could have been attributed to task differences in TSV coupled with a generalized deficit in patients. However, the inclusion of task 3 provides the means to discuss the specificity of the reported deficits. Indeed, our results reveal that the global (1-elm) condition of task 3 has greater TSV than any condition of task 1 or 2, but yields no group difference. Following e.g. Strauss (2001) and Knight & Silverstein (2001), the fact that the TSVs are ranked differently than the group differences suggests a specific fluency problem rather than a generalized deficit.

Finally, to evaluate the group effect size of the tasks where a group difference was found, Cohen’s d was computed. Results (table 1, line 8) show that task 1, task 3 and task 2 are increasingly powerful to discriminate between patients and controls. Following, Cohen (1992), the protocol used in task 2 provides a large effect size because $d > 0.8$, and condition 2-elm of task 3 would provide a medium effect size with $d > 0.5$.

**Discriminant validity**

In a final analysis, we computed the inter correlation values amongst tasks and conditions for the control group only in order to assess task-specificity. Results are presented in table 2 and reveal that the 3 conditions in task 2 are highly correlated with each other (gray zone). However, correlations are near zero between task 1 and task 2 suggesting that the triggered and the planned sequencing tasks very probably tap processes that are not related to each other, i.e. that are different. We suggest that task 1 (triggered sequences) and task 2 (planned sequences) reflect the working state of lower and higher order integrative processes, respectively, with only the later being impaired in patients with schizophrenia for the fluent sequencing of action sequences.
DISCUSSION

The aim of this study was to test the hypothesis that schizophrenia is characterized by a problem in the fluent coordination of motor sequences, and to discriminate between low and high-order mechanisms for the impairment. Our results confirm a fluency problem in schizophrenia but only for the execution of planned motor sequences i.e. those sequences requiring functional high-order processes. Similar observations were made in treated and non-treated patients, suggesting that the fluency deficits for planned sequences may be a core impairment in schizophrenia.

In our first task (triggered sequences), the incoming sensory information from the tips of the fingers (object-slip; first element of the sequence) had to be used to readjust the force level applied (grip increase; second element of the sequence). Hence, successful performance of the task was possible only through the fluent integration of afferent and efferent aspects of hand function, in order to readjust finger force to the changing forces at the finger/object contact. Here, the mean time delay between the two successive motor elements was around 95 ms, delay which suggests the intervention of long latency reflexes for the reactive control of precision grip (Johansson and Westling 1987; Johansson et al. 1994). Clinical studies have shown that these fast integrative mechanisms – which are too quick to permit voluntary-cognitive control – are very probably sub-cortical. Indeed, the somatosensory driven control of precision grip is not affected in their early stages by (1) TMS on the motor cortical regions (Macefield and Johansson 1994; Macefield et al. 1996), and (2) is normal in X-linked Kallmann patients who have neurological deficits to the fast conducting cortico-spinal system (Harrison et al. 2000). In the present study, we showed that the group mean time delays between two motor elements for triggered sequences were similar in patients with schizophrenia and in controls. These results support the hypothesis of preserved low-order (subcortical) integrative mechanisms in schizophrenia. In addition, a close examination of the
force patterns during the 250 ms baseline measures (figure 1), failed to show any evidence of
tardive dyskinesia in our patients with schizophrenia. Overall, our results argue against an
explanation of the sequencing deficits in schizophrenia in terms of dysfunctional low-order
sensorimotor processes.

In the second task (PLANNED SEQUENCES), subjects were required to execute a series of planned
motor sequences of increasing complexity. For the controls, the time delay between
successive elements was shorter for planned (40 ms) than for triggered (96 ms) sequences.
This suggests that both the order and the timing of the motor elements were pre-programmed,
and that sensory afferents were not used for the fluent execution of the planned sequences.
Furthermore, as the inter-element time delay did not increase with sequence complexity, one
can hypothesize that no further on-line processing of the sensory information took place
during the execution of the task (Sternberg et al. 1989). Overall, our results are in agreement
with those results reported in timing studies, which suggest that the role of sensory
information is not to initiate or execute motor sequences but rather to minimize
synchronization errors that may occur between self-produced actions and external pacing
signals (Billon et al. 1996).

A different pattern of results was revealed in our patients with schizophrenia. Their
performance was characterized by inter-element delays that were (i) longer for planned than
for triggered sequences, (ii) abnormally long compared to the controls and (iii) exhibited time
delays that increased with sequence complexity. Overall, these data support the possibility
that schizophrenia is characterized by a lack of fluency in the execution of planned sequences
i.e. a high-order deficit in the temporal sequencing of multiple motor elements.
The fact that in patients the inter-element time delay increased with sequence complexity might have suggested a difficulty in pre-planning the entire sequence before its initiation and consequently, further processing might have been required during task execution. To further look into this possibility, a third task (context effect) was used for which subjects were required to perform a simple pointing act. Through instructions that emphasized either speed of starting or speed of completing the action, this movement was either considered as a single element (i.e. non-sequential) action or a two-element sequence action. In either case, it was considered that pre-programming was required to react fast to the auditory signal. Results revealed that when no sequencing was required, patients were as quick as controls in reacting to the auditory signal. When instruction indicated the need for sequencing, patients were significantly slower than controls (fig. 3). This argues against a general problem in motor planning but argues in favor of a specific problem in the fluent sequencing of action when planning is required. Interestingly, one may note that in the literature many studies suggest general slowness in schizophrenia for manual reaction times (Cohen and Servan-Schreiber 1992; Sereno and Holzman 1995; for a review Nuechterlein 1977) but the selected tasks often required sequencing, e.g. detect a white dot and then, detect a blue dot and then, press the switch as soon as the blue dot disappears (Zahn et al. 1998). Hence, it is possible that slowness is not characteristic of patients with schizophrenia but arises in these patients because sequencing is necessary. Little mention of this task-effect has been made in the literature and it will be important to confirm this finding with additional studies.

Losing the capacity to coordinate multiple elements of a motor sequence within a global action, the pre-planning phase is limited and consequently, might be expected to leave the central nervous system in need of sensory feedback about the end of each motor element in order to trigger each successive element of the sequence. This is consistent with the results
Motor fluency deficits in Schizophrenia reported in our patients with schizophrenia. Indeed, the inter-element time delays for planned sequences (109 ms) were at least as long and often longer that those observed for triggered sequences (95 ms). Hence, for planned sequences, patients may have relied on the preserved sensorimotor low-order functions to initiate subsequent elements in both triggered and planned motor sequences, rendering the execution of the latter rather fragmented and non-fluent in appearance.

The patterns of results in the three contrasting tasks allow us to eliminate three possible alternative explanations for the reported motor impairments. First, it might be argued that the sequencing deficits could have been due to a difficulty in maintaining the focus of attention throughout the series of trials. However, in this case, the variability of the reaction and movement times would have been significantly increased in patients compared to controls, and this was not the case. Second, it might have been suggested that the abnormal pattern of results in the schizophrenic group resulted from general slowness. Against this, we note that patients exhibited movement and reaction times similar to those measured in controls (tasks 1 and 3), yet still exhibited abnormal time delays in the planned sequences (task 2). Third, it might have been argued that the deficits could have arisen from the effects of neuroleptic medication. We suggest that this is unlikely as the sequencing deficits were observed in patients with (N=21) and without (N=3) neuroleptic treatment. Furthermore, force patterns in task 1 revealed an absence of Parkinson-like syndrome effect in all patients. However, given the small number of unmedicated patients we acknowledge the need for further replication studies with medication-free patients.

Lastly, it could have been that fluency deficits appeared in patients with schizophrenia in task 2 because of its greater discriminating power. Indeed, the comparison of tasks 1 and 2 is confounded with differential discriminating power (see TSVs and group differences in table
Motor fluency deficits in Schizophrenia

1). However, the inclusion of task 3, which was the task with the greatest discriminating power, gave us the means to show that patients performed as normal in a planned task that required no sequencing (1-elm, task 3) but were impaired when sequencing was required (2-elm, task 3; all conditions of task 2). Hence, we suggest that motor deficits in schizophrenia are not due to a generalized deficit, but may be associated specifically to a problem of planning action-sequences through time.

In conclusion, our results confirm that even simple motor actions are impaired in schizophrenia, as long as they require the sequencing of at least two elements. They furthermore indicate that this abnormality appears for higher-order integration and not for the basic sensorimotor mechanisms that require minimal controlled processing. Central to the control and execution of most commonly performed actions, a deficit in motor fluency can severely impact on everyday life function. Hence, it will be important in future studies to determine to what extent the impairment revealed here for planned sequences is related to higher-order cognitive functions (memory; attention) and clinical symptoms (Neumann and Walker 2003). Our previous results have suggested that the efference copy is preserved in schizophrenia when considering passive movements (Delevoye-Turrell et al. 2002; 2003). Abnormalities were observed only for active ones. These results are coherent with that reported by Knoblich et al. (2004), which suggested that abnormal motor control is revealed in schizophrenia as soon as the movement becomes voluntary, i.e. requires the subjects’ attention (Frith 2005). The data presented here in task 3 suggest however that in schizophrenia, movement execution can be as fast as that observed in healthy controls even when voluntarily performed by the subject (condition 1-elm, global). Abnormalities seem to be more specifically associated to the need to organize multiple sub-elements within a coherent and fluent motor plan (condition 2-elm, segmented). Hence, one may ask: What
occurs when multiple sub-elements are to be sequenced? Is the efference copy itself different for motor sequences than for unit-actions? Or is the planning-phase different due to the need to prepare for the smooth passage from one element of the sequence to the next? At the physiological level, this latter hypothesis would require good communication between brain areas concerned with initiating actions (frontal cortex) and sensory areas concerned with processing and integrating the consequences of actions (thalamus). There is some evidence in favor of abnormal connectivity between brain areas in schizophrenia (Fletcher et al. 1996; Fletcher et al. 1999). Hence, a fruitful line for future research in the cognitive neuropsychology of schizophrenia would be to explore whether abnormal connectivity between frontal and parietal regions via the thalamus is associated to fluency problems in the sequencing of planned (motor) actions.
TABLE AND FIGURE CAPTION

Figure 1. A typical trial from the triggered sequence task as seen in a typical medicated patient with schizophrenia. The subjects’ task was to slowly release grip on the object (top trace) in order to let the object slip by a few centimeters (bottom trace) without letting it drop. As soon as they detected the occurrence of a finger-slip (dotted line), subjects typically increased grip force (solid line) in order to arrest object fall. The force patterns were similar in patients and pair matched controls.

Figure 2. Mean contact durations (with standard deviations) for controls (black circles) and patients with schizophrenia (white triangles). This measure was an indicator of the programmed time interval between the end of the first element and the start of the second element of a sequence, in function of the nature (triggered sequences; planned sequences) and the complexity of the sequences (1-elm, 2-elm, 3-elm).

Figure 3. Mean group reaction times (with standard deviations) for controls (black circles) and patients with schizophrenia (white triangles) performing the pointing task under pressured-time conditions emphasizing the execution time (global condition: 1-elm), or both the start and the execution time (segmented condition: 2-elm) of the pointing movement.

Table 1. Group mean and standard deviations are reported for controls and patients. Then, in order to address the psychometric confound question, we provide the reliability scores (standardized Cronbach's alpha – Cronbach 1951) and the discrimination power² (true score variances – TSV) for the control group only, the group differences as well as the effect sizes³ (Cohen’s d) for each task and condition. One can clearly note that the pattern of group

²True score VAR = reliability * observed score VARcontrols
³ d_Cohen = (M_control-M_patient)/(SD_pooled) with SD_pooled = root((observed score VAR_control + observed score VAR_patient)/2)
difference is not in the same ranked order as that observed for the TSV. Namely, the global (1-elm) but not the segmented (2-elm) condition of task 3 has greater TSV than any condition in task 1 or 2, but yields no significant group difference. Hence, our results suggest that the motor deficits in schizophrenia is not due to a generalized deficit but may be associated to a specific problem of planning action-sequences through time.

Table 2. This table presents the inter correlation values for the various tasks and conditions in order to reveal discrimination amongst tasks that putatively measure different processes. The most significant correlations are found within task 2 (highlighted). One can note the close to null correlation values between tasks 1 and 2, suggesting that these tasks very probably tap different cognitive processes.
Figure 1
Figure 2
Figure 3

- Control subjects (N=24)
- Patients with schizophrenia (N=24)
## Table 1

<table>
<thead>
<tr>
<th></th>
<th>Task 1</th>
<th>Task 2</th>
<th>Task 3</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>2-elm</td>
<td>2-elm</td>
<td>3-elm</td>
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<tr>
<td><strong>Control Group mean</strong></td>
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<td><strong>Discrimination power - True score variance</strong></td>
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<td><strong>Group difference</strong></td>
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<td>70*</td>
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<td><strong>Effect size – d Cohen</strong></td>
<td>0.09</td>
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Motor fluency deficits in Schizophrenia

Table 2

<table>
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REFERENCES


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