Psychomotor Slowing in Schizophrenia

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Psychomotor slowing (PS) is a cluster of symptoms that was already recognized in schizophrenia by its earliest investigators. Nevertheless, few studies have been dedicated to the clarification of the nature and the role of the phenomenon in this illness. Moreover, slowed psychomotor functioning is often not clearly delineated from reduced processing speed. The current, first review of all existing literature on the subject discusses the key findings. Firstly, PS is a clinically observable feature that is most frequently established by neuropsychological measures assessing speed of fine movements such as writing or tasks that require rapid fingertip manipulations or the maintenance of maximal speed over brief periods of time in manual activities. Moreover, the slowed performance on the various psychomotor measures has been demonstrated independent of medication and has also been found to be associated with negative symptoms and, to a lesser extent, with positive and depressive symptoms. Importantly, performance on the psychomotor tasks proved related to the patients’ social, clinical, and functional outcomes. Several imaging studies showed slowed performance to coincide with dopaminergic striatal activity. Finally, conventional neuroleptics do not improve the patients’ PS symptoms, in contrast to the atypical agents that do seem to produce modestly improving effects.

Key words: finger tapping/pegboard tasks/processing speed/schizophrenia/slowing/writing

Introduction

Slowing of movements has been observed in schizophrenia since the beginning of the 20th century. Both Kraepelin and Bleuler already recognized and described the phenomenon of psychomotor slowing (PS) in schizophrenic patients as evidenced by the following observations:

Single movements are stiff, slow, forced, as if a certain resistance had to be overcome.1

The spontaneous movements are distinctly impaired; they are executed slowly and weakly. One often observes patients straining, for example, to open their lips when they wish to reply, but often only managing to utter soft low whispers (...). Others are still able to perform some activities; they are still able to get around, but even then, it is for the most part slowly, tremulously, feebly.2

Since these early descriptions of PS, prolonged reaction times (RTs) have consistently been reported in schizophrenic patients3 and have been referred to as “the closest thing to a north star in schizophrenic research.”4

However, with the introduction of neuroleptics in the 1950s, motor and cognitive symptoms in schizophrenia suffered from a major shift of attention toward positive symptoms, resulting in a relative, decades-long lack of research investigating the nature and impact of slowing of psychomotor functioning. When in the late 1980s it was suggested that the psychotic symptoms were perhaps not the core symptoms of the illness, this set off a new wave of research focusing on cognition and, in a much lesser extent, on psychomotor symptoms.5 The reappraisal of the role of PS and slowed information processing in schizophrenia is reflected in the recent delineation of processing speed as one of 7 affected independent cognitive domains in schizophrenia (measurement and treatment research to improve cognition in schizophrenia [MATRICS]).6

Almost a century has passed since the initial observations of PS in schizophrenia, and still little is known about the phenomenon. In contrast, in the literature, vast amounts of studies focused on PS in major depression, describing the various manifestations, characteristics, and significance of the symptoms in depressed patients.7 In schizophrenia, the symptoms are much less distinguished as separate, primary symptoms, and to the authors’ knowledge, to date, a review on this topic is still lacking.

With the present review we hence wished to achieve several goals: in the light of MATRICS, we sought to delineate PS from disturbances in processing speed. We wanted to evaluate all available literature on PS in schizophrenia and discuss its clinical presentation and
relationship to presented symptomatology, the applied methods to measure its manifestations, as well as its course, outcome, and treatment.

Methodology
The present review is based on a MEDLINE survey of the relevant literature published between 1970 and 2005. Terms (with number of entries) used in the search were as follows: “psychomotor slowing” (34), “motor slowing” (17), “cognitive slowing” (36), “slowing” (107), “motor speed” (196), “gross motor” (17), “processing speed” (136), “information processing” (678), “bradykinesia” (25), “hypokinesia” (20), “bradyphrenia” (6), “psycho-motor poverty” (67), “gait” (59), and “actometric” (2) all in combination with “schizophrenia.” All abstracts were read and potentially relevant articles were examined in full. Various other important cross-references were included. All randomized controlled studies in schizophrenia including cognitive variables were reviewed. Note that our search method may have excluded some articles that described data on PS when these were presented as cognitive data.

Defining “Psychomotor” in PS
We use the adjective psychomotor to describe all those activities and symptoms in which, rather than thinking or feeling, movement or action is the principal component, ie, in which the planning, programing, and execution of movements play a dominant role. Psychomotor tasks or tests focus on motor skills but involve more than just muscle contractions. We prefer the term psychomotor to stress this wider involvement of perceptual processes and cognitive control mechanisms. Yet, a strict distinction between motor activities and higher mental activities is impossible. We can only become aware of a cognitive activity through motor output, however small. Conversely, all motor actions need at least a few rudimentary higher order activities of goal selection and planning, and they are hardly possible without perception. As has been mentioned before, to qualify an activity, task, or symptom as psychomotor, the relative contribution of motor activity must be large, and its performance measurement must be predominantly determined by the speed and accuracy of the motor output.

Psychomotor activities may be either discrete, as in switching on a light, or continuous, like in walking, cycling, or swimming. They may require little variability, as in jotting down one’s signature, or demand considerable variation to suit the situation, as in returning a ball in tennis. They may consist of a single movement, like slamming the brake pedal, or of a sequence of movements like in writing or playing a musical instrument. All are cognitive activities, sometimes acquired after many months or years of practice. They express our knowledge and capabilities but are also essential even in our most humble daily care activities, eg, dressing, cleaning, cooking, or dishwashing. Hence, psychomotor activities are a key element in determining functional outcome in schizophrenia.

The subject’s behavior during psychomotor tasks is governed by a number of neurocognitive processes or mechanisms that are listed in table 1, which is mainly based on an highly influential neuropsychological theory of motor-skill learning presented by Willingham and enriched by ideas on the cognitive control of action of Rushworth et al. It must be emphasized that Willingham listed these processes to characterize simple motor tasks like grasping and moving a cup. Even though the list is by no means exhaustive or final, we present it here to underline that motor control involves more than an adjustment of timing and forcing of muscle innervations. Higher order executive control processes implicated in the planning of movement sequences, task switching, inhibition of inadequate responses, performance monitoring, and error detection

<table>
<thead>
<tr>
<th>Process</th>
<th>Function in Motor Control</th>
<th>Anatomic Locus</th>
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<tbody>
<tr>
<td>Strategic</td>
<td>Goal or action selection</td>
<td>Various regions in frontal cortex</td>
</tr>
<tr>
<td></td>
<td>Switching to more optimal actions</td>
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<td></td>
<td>Inhibition of unwanted tendencies</td>
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<td>Perceptual motor integration</td>
<td>Selection of spatial targets</td>
<td>Parietal cortex</td>
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<td>Transfer to egocentric space</td>
<td>Premotor cortex</td>
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<tr>
<td>Sequencing</td>
<td>Ordering of movements in the correct sequence</td>
<td>Basal ganglia and supplementary motor cortex</td>
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<tr>
<td>Timing and force control</td>
<td>Adjustment of time and force of movements or muscle commands</td>
<td>Cerebellum</td>
</tr>
<tr>
<td>Dynamic Monitoring</td>
<td>Innervating muscles</td>
<td>Motor cortex</td>
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<tr>
<td></td>
<td>Evaluating outcome</td>
<td>Medial frontal cortex</td>
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</table>

*aModified from Willingham.*
<table>
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<tr>
<th>Study</th>
<th>Sample (n)</th>
<th>Mean Age</th>
<th>Inpatient/Outpatient</th>
<th>Medication</th>
<th>Psychomotor Task</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caligiuri et al\textsuperscript{120}</td>
<td>Neuroleptic-naive schizophrenic patients (24)</td>
<td>42.2</td>
<td>14 inpatients and 10 outpatients</td>
<td>/</td>
<td>Wrist rotation</td>
<td>12% of neuroleptic-naive schizophrenic patients had bradykinesia compared with none of the healthy controls.</td>
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<td></td>
<td>Healthy controls (24)</td>
<td>42.2</td>
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<tr>
<td>Carnahan et al\textsuperscript{121}</td>
<td>Schizophrenics (12)</td>
<td>29.3</td>
<td>?</td>
<td>Antipsychotics</td>
<td>Fitts’ task with mouse on graphics tablet</td>
<td>Relative to the healthy controls, the patients exhibited a movement-planning deficit without a decrement in movement execution. The patients still performed according to Fitts’ law, which states that in aiming movement time decreases as target distance decreases and target size increases.</td>
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<tr>
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<td>Healthy controls (12)</td>
<td>26.1</td>
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<tr>
<td>Fuller and Jahanshahi\textsuperscript{33}</td>
<td>Schizophrenics (11)</td>
<td>38.5</td>
<td>Outpatients</td>
<td>Antipsychotics</td>
<td>Purdue pegboard task and FTT</td>
<td>Patients were slower than the controls in both tasks in the unimanual but not in the bimanual condition. Peg placing was less slowed when performing a secondary task with the other hand. Pegboard and FTT performance significantly correlated with negative symptoms.</td>
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<td></td>
<td>Controls (13)</td>
<td>38.15</td>
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<tr>
<td>Gallucci et al\textsuperscript{122}</td>
<td>Schizophrenics (20)</td>
<td>31.1</td>
<td>?</td>
<td>2 unmedicated, 12 AAP, 6 CNL, and 4 anticholinergics</td>
<td>Handwriting movements recorded with graphics tablet</td>
<td>Handwriting in patients was not slowed but less efficient and consistent with a trend toward macrographic strokes.</td>
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<td>Matched controls</td>
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<tr>
<td>Henkel et al\textsuperscript{35}</td>
<td>Schizophrenics (16)</td>
<td>35.1</td>
<td>Inpatients</td>
<td>Test-retest: drug-free vs haloperidol (mean dose: 10.4 mg) and anticholinergics (n = 6)</td>
<td>Drawing of circles and writing of sentences on writing tablet</td>
<td>Performance of neuroleptic-free patients was slower. Slowing was associated with negative symptoms. Amelioration of negative symptoms under haloperidol treatment was significantly associated with speeding-up of handwriting.</td>
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<td></td>
<td>Healthy controls (16)</td>
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<tr>
<td>Holthausen et al\textsuperscript{34}</td>
<td>Schizophrenics (32)</td>
<td>24.8</td>
<td>?</td>
<td>Average dose: 6.1 mg haloperidol equivalents, 7 drug-free patients, and 15 on anticholinergics</td>
<td>FTT</td>
<td>FTT correlated with the depressive and the negative symptom dimension.</td>
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<td>Schizophreniform (10)</td>
<td>23.7</td>
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<td></td>
<td>Delusional disorder (2)</td>
<td>28.5</td>
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<td></td>
<td>Brief psychotic disorder (2)</td>
<td>18.0</td>
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<td></td>
<td>Psychotic disorder NOS (4)</td>
<td>31.8</td>
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<td>Study</td>
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<td>Jogems-Kosterman et al(^{38})</td>
<td>Schizophrenia (19)</td>
<td>37.0</td>
<td>14 outpatients</td>
<td>Antipsychotics (mean dosage 7.6 mg haloperidol equivalents)</td>
<td>Line-copying task, complex-figure copying task recorded on writing tablet</td>
<td>Patients’ movement initiation and execution was slowed. Overall, patients were one-third slower than the controls. Initiation time latencies with increasing complexity were significantly higher in the subgroup with higher negative symptoms. Increased reinspection times demonstrated affected planning strategy.</td>
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<tr>
<td></td>
<td>Controls (19)</td>
<td>37.5</td>
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<tr>
<td>Malla et al(^{16})</td>
<td>Schizophrenics (21)</td>
<td>29.0</td>
<td>?</td>
<td>Antipsychotics</td>
<td>Fitts’ task with mouse on graphics tablet</td>
<td>Weak correlations between psychomotor poverty and RTs and no correlations with movement times. Strong associations between RT and disorganization syndrome.</td>
</tr>
<tr>
<td>Mohamed et al(^{23})</td>
<td>First-episode schizophrenics (94)</td>
<td>26.1</td>
<td>Inclusion after admission</td>
<td>73 neuroleptic-naive patients, 14 receiving antipsychotics for less than a week, 7 for less than 2 wk</td>
<td>FTT</td>
<td>Impairments in speeded cognitive tasks with (SDST, and TMT) and without (Stroop) motor component. Patients performed relatively better on the FTT, leading the authors to conclude that poor performance on speeded tasks reflects bradyphrenia rather than bradykinesia.</td>
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<td></td>
<td>Normal controls (305)</td>
<td>25.5</td>
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<tr>
<td>Morrens et al(^{39})</td>
<td>Schizophrenics (30)</td>
<td>27.5</td>
<td>Inpatients</td>
<td>Atypical antipsychotics (22), conventional neuroleptics (7), and other psychotropics</td>
<td>SDST on graphics tablet</td>
<td>Both matching time (initiation) and writing time (execution) on SDST were slowed but unassociated. Matching time, reflecting slowing in higher order cognitive processes, but not writing time, reflecting PS, proved associated with other neuropsychological measures.</td>
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<tr>
<td></td>
<td>Controls (30)</td>
<td>33.0</td>
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<tr>
<td>Putzhammer et al(^{41})</td>
<td>Drug-naive schizophrenic patients (25)</td>
<td>/</td>
<td>?</td>
<td>In addition: 14 patients lorazepam and 12 patients biperiden</td>
<td>Movement analysis of gait</td>
<td>Relative to the healthy controls, all patients exhibited decreased gait velocity due to shorter stride length while cadence (steps per minute) was not affected. Conventional antipsychotics intensified the problem, whereas atypicals did not cause additional gait disturbances.</td>
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<td></td>
<td>Schizophrenic patients treated with CNL (16)</td>
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<td>Schizophrenic patients treated with AAP (25)</td>
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<tr>
<td></td>
<td>Healthy controls (25)</td>
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Table 2. Continued

<table>
<thead>
<tr>
<th>Study</th>
<th>Sample (n)</th>
<th>Mean Age</th>
<th>Inpatient/Outpatient</th>
<th>Medication</th>
<th>Psychomotor Task</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Putzhammer et al44</td>
<td>Drug-naive schizophrenic patients (14) 36</td>
<td>Inpatients</td>
<td>Inpatients</td>
<td>In addition: 8 patients in total lorazepam and 5 patients in total biperiden</td>
<td>Movement analysis of gait</td>
<td>Compared with the healthy controls, all patients had decreased gait velocity due to shorter stride length. The most striking difference was observed between the patients on CNL and the controls. Impaired gait parameters can be normalized in schizophrenic patients by external stimulation via treadmill walking.</td>
</tr>
<tr>
<td>Schroder et al124</td>
<td>Schizophrenics (12) 28 9 clozapine, 2 conventionals+ biperiden, and 1 drug free</td>
<td>?</td>
<td>27</td>
<td>Pronation/supination device during fMRI</td>
<td></td>
<td>No differences in measures of motor retardation (repetition rate and amplitude) between patients and controls. Variability was significantly increased in the patients and activation of sensorimotor and SMA cortices was significantly decreased.</td>
</tr>
<tr>
<td>Tigges et al125</td>
<td>Schizophrenics (27) 31.0 Inpatients 13 drug free and 14 CPZ-eq: 507 mg</td>
<td></td>
<td>Handwriting on writing tablet</td>
<td></td>
<td></td>
<td>Patients had longer stroke durations and decreased automatization. Stroke length and velocity were less regular in the treated patients. Stroke-length irregularity was higher in patients treated with atypicals and not with typicals. Positive and negative symptoms had little relation to the handwriting measures.</td>
</tr>
<tr>
<td>Van Hoof et al137</td>
<td>Schizophrenics (20) 39.9 Inpatients CPZ-eq = 710</td>
<td></td>
<td>SDST on a writing tablet</td>
<td></td>
<td></td>
<td>The depressed patients demonstrated an overall slowing in matching and writing times, whereas the schizophrenic patients only displayed prolonged matching times in comparison with both the depressed patients and the healthy controls.</td>
</tr>
<tr>
<td>Yang et al81</td>
<td>Schizophrenics (28) 29.3 19 outpatients and 9 other (?)</td>
<td></td>
<td>FTT</td>
<td></td>
<td></td>
<td>The FTT showed the strongest correlation with D2 receptor binding, while the WCST and attention test had no correlation with D2 receptor binding.</td>
</tr>
</tbody>
</table>

Note: AAP = atypical antipsychotics, CNL = conventional neuroleptics, CPZ-eq = chlorpromazine equivalents, FTT = finger-tapping test, SDST = Symbol Digit Substitution test, SMA = supplementary motor area, TMT = Trailmaking Test, WCST = Wisconsin Card Sorting Test, RT = reaction time, PS = psychomotor slowing, and NOS = not otherwise specified.
are highly important in psychomotor activity, greatly affect psychomotor speed, and frequently are disturbed in schizophrenia.

**PS at a Clinical Level**

**Clinical Presentation of Slowed Psychomotor Functioning**

In clinical practice, patients diagnosed with schizophrenia can be observed to have longer thinking latencies and to be slow in their responses or in their movements. In more severely affected patients, movements can be extremely slow and psychomotor activity is sometimes reduced to the bare minimum, hindering their social-communicative interactions and daily-life activities. Both gross and fine motor performances have been reported to be affected.

In addition to slowed actions, a reduction in the quantity of psychomotor activity is also observed, sometimes recognized as negative symptoms. Liddle labeled this diminished psychomotor activity as the psychomotor poverty syndrome, encompassing poverty of speech, decreased spontaneous movements, and blunting of affect.

The importance of these observable symptoms or signs is reflected in the most often-used clinical assessment scales. The general psychopathology section of the Positive and Negative Symptom Scale comprises the item “motor retardation.” Similarly, the Scale for Assessment of Negative Symptoms uses the terms “decreased spontaneous movements,” “poverty of speech,” and “increased latency of response” to reflect reduced psychomotor functioning. The Scale for the Assessment of Positive Symptoms, which exclusively assesses positive symptoms, accordingly does not include items reflecting PS. Finally, the Signs and Symptoms of Psychotic Illness features the aspects “underactivity,” probing the amount of motor activity and poverty of speech.

**Categorizing Psychomotor Symptoms**

In schizophrenia, the various observable psychomotor symptoms can be classified into 3 groups. Apart from PS, patients may exhibit catatonic symptoms and neurological soft signs (NSS). Catatonic symptoms are specific motor abnormalities, such as stereotypy, stupor, or mutism, that are also associated with other psychiatric disorders. Bleuler described PS as a mild form of catatony, thus classifying this slowing as a catatonic symptom or symptom cluster. Although PS is generally no longer classified as such in modern classification systems like the DSM-IV-TR or in Taylor and Fink’s criteria for catatonia and can thus be seen as a separate psychomotor symptom cluster in schizophrenia, it can be argued that PS might indeed be an intermediate state toward stupor or catalepsy.

Also NSS, which include deficits in motor coordination, motor sequencing, and sensory integration, have been receiving increasing attention. These signs already appear to be present in first-episode patients or never-treated patients and seem to deteriorate progressively in chronic patients.

Few researchers have addressed the question whether there is a relationship between these various domains of psychomotor symptoms. Flashman and colleagues found NSS, as assessed by the Neurological Evaluation Scale (NES), to be correlated with decreases in motor speed on finger-tapping and pegboard tasks. However, their findings need to be interpreted with caution because besides other neuropsychological and neurological tests the NES itself also includes a tapping test.

**PS and Reduced Processing Speed**

The recent National Institute of Mental Health initiative MATRICS aimed to identify the separable, independently impaired cognitive domains by evaluating the available factor analytic studies. Processing speed was recognized as the first affected cognitive domain when ordering these cognitive domains from “relatively basic to high level” and was generally represented by the impaired performance on tasks such as the Symbol Digit Substitution Test (SDST) and the Trailmaking Test (TMT). Only a restricted number of the factor analytic studies included psychomotor tasks like the Grooved Pegboard or a token motor test, which loaded on the factor of processing speed. Brebion and his team had earlier defined processing speed as the speed in both mental and motor functions. However, one may ask whether reduced speed of information processing on the one hand and slowed initiation and execution of movements or PS on the other hand reflect the same impairment.

Two recent factor analytic studies indeed found a fine motor-speed factor in addition to a processing-speed factor. Bilder’s group performed a factor analysis on 101 patients and defined 4 factors of neurocognitive functioning. Besides “general executive and perceptual organization” and “declarative verbal learning and memory,” they found a “processing speed and attention factor” mainly represented by performance on the TMT and the SDST and a “simple motor functioning” factor reflected by performance on the finger-tapping test. Another factor analysis that included 150 patients similarly found a “motor” factor represented by a finger-tapping and a pegboard task in addition to an “attention” factor represented by the Stroop and the TMT. Consistent with these studies, in their recent meta-analysis on the cognitive effects of the atypical agents in schizophrenia, Woodward and colleagues also defined a “motor skill” domain, separate from a “processing speed” domain.

In one of our recent studies, we had 75 schizophrenic patients perform the SDST to assess their processing
speed, as well as a series of simple copying tasks to measure their psychomotor speed, both on a digitizing tablet (M. Morrens et al, unpublished data). A subsequent factor analysis of the 2 measures revealed 2 distinguishable factors, ie, a psychomotor and a more higher order cognitive, memory-related factor. Moreover, when classical neuropsychological measures for memory, attention, and executive functioning were entered as covariates, the patients’ SDST performance did not significantly differ from that of the controls, whereas the patient group was still highly impaired in the copying tasks. Based on these results, it may be concluded that in schizophrenic patients, performance on the SDST tends to reflect cognitive functions more than it does psychomotor speed.

Taken together, recent findings indicate that PS and reduced processing speed reflect 2 different symptom domains in schizophrenia.

Research on PS in Schizophrenia

Assessing Psychomotor Speed

In most studies, neuropsychological tasks are used to assess PS in schizophrenic patients (see table 2). Typically, these tests address psychomotor and other cognitive functions in time-limit conditions, and they are either more focused on processing speed or on psychomotor speed.

Tasks More Sensitive to Psychomotor Speed.

Fine Motor Tests. A first group of tests gauges speeded motor actions without addressing more higher order cognitive processes. It includes tasks that require the maintenance of maximal speed over brief periods of time (eg, finger tapping, pronation-supination test) or rapid fingertip manipulations (eg, pin test, pegboard tasks). It should be noted that tasks that prescribe rapid fine and repetitive movements also address functions such as motor coordination and visuospatial monitoring, functions also known to be affected in schizophrenic patients.

Drawing and Writing Tasks. Handwriting has been demonstrated to be slowed in schizophrenic patients. To investigate slowing of fine motor movements in patients, some researchers used graphics tablets to record performance on drawing and writing tasks. Subjects draw or copy the presented stimuli on a digitizer that is connected to a PC so that several reaction- and movement-time measures are computed allowing the investigator to assess the various stages involved in the completion of the movements. Indeed, movement control is the result of strategic and perceptual-motor integration, sequencing, and muscular dynamic processes. Thus, even the simplest movement depends on the activation of several different processes. Through its accurate recordings of movements, the writing tablet facilitates a rudimentary subdivision of the processes involved. It also allows the manipulation of the cognitive load involved in the initiation and execution of movements, which is of interest for the delineation of potential deficits in planning strategies. Schizophrenic patients are significantly slowed compared with healthy controls, even when copying a simple line or simple, familiar figures (M. Morrens et al, unpublished data; J. Van Hecke et al, unpublished data).

Interestingly, the digitized psychomotor performance of schizophrenic patients suggests that a slowed initiation of movements might be systematically present in all patients, whereas an additional slowed execution of writing movements might manifest itself in more severely affected (in)patients and thus might be associated with their poor functioning.

Gross Motor Tasks. An ultrasonic movement analysis system found evidence for decreased gait velocity in neuroleptic-naive schizophrenics, which resulted from reduced stride length rather than from step frequency. In addition, the gait disturbances worsened as a cause of conventional but not atypical antipsychotic treatment. Two studies using standardized actometric recordings merely applied the technique to validate scales addressing neuroleptic-induced movement disorders.

Tasks More Sensitive to Speed of Information Processing.

Classical “Processing-Speed” Tests. Tests assessing speed of information processing are widely used in cognitive studies of schizophrenia. Typical examples are the SDST, the TMT, or even the Stroop color-word test.

The tests are all sensitive to PS although they primarily address a wide range of other cognitive functions that are also known to be affected in schizophrenic patients, such as working memory, attention, or visuospatial scanning. For this reason, they are not the most appropriate tools for the assessment of speed of psychomotor functioning.

Reaction-Time Paradigms. Reaction-time paradigms have been used since the early days of neuropsychological research in schizophrenia, and they have systematically shown responses in patients to be impaired.

In contrast to the above-mentioned, more internally driven processing-speed tests, reaction-time trials involve the rapid initiation of responses that are elicited by external cues. Although they also have a psychomotor, executive component, reaction-time paradigms are mainly sensitive to deficits in vigilance and processing speed.

Relationships Between PS and Other Symptoms

Slowing and Positive Symptoms. An association between PS and positive symptoms is often lacking. However, Fuller and Jahanshahi did demonstrate a correlation between pegboard placement and positive symptoms in a small patient sample. Similarly, our group found the initiation and execution of the copying movement of
Psychomotor Slowing in Schizophrenia

Table 3. Tasks Assessing Processing Speed and Psychomotor Performance Showing Associations with Negative Symptoms or Liddle’s Psychomotor Poverty in Cross-Sectional and Longitudinal Studies

<table>
<thead>
<tr>
<th>Neuropsychological Tasks and Studies</th>
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<td><strong>Cross-sectional studies</strong></td>
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<td>Processing-speed tasks</td>
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<td>Trailmaking test</td>
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<td>SDST</td>
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<td>Slower responses on 2-choice guessing task</td>
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<td>Prolonged critical interstimulus interval in the backward masking task</td>
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<td>Reaction-time paradigms</td>
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<td>Psychomotor tasks</td>
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<td>Pegboard task, finger tapping</td>
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<td>Drawing tasks (M. Morrens et al, unpublished data)</td>
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<td><strong>Longitudinal studies</strong></td>
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<tr>
<td>Processing-speed tasks</td>
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<tr>
<td>SDST and verbal fluency</td>
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<td>Psychomotor tasks</td>
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<tr>
<td>Drawing tasks</td>
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</table>

**Note:** SDST = Symbol Digit Substitution Test.

However, studies employing processing-speed and reaction-time paradigms were not consistent in reporting associations between negative symptoms and deteriorated performance.

**Slowing and Depressive Symptoms.** In research into depressive illnesses, PS has been investigated as an important cluster of symptoms. Few studies investigated the neurobiological correlates of slowing in schizophrenic patients. Heinz et al. already suggested that the relationship between PS and striatal D2 receptor occupancy in schizophrenia needed to be clarified. However, more than 10 years later, still very limited data are available. In an fMRI study, Müller et al. demonstrated an overactivation of the basal ganglia in schizophrenia patients with PS.

**The Course of PS**

Evidence of PS as measured by a pegboard task has been found in adolescents with schizophrenia spectrum disorders as well as in unmedicated patients early in the course of the illness. Performance on this task has also been linked to familial risk of schizophrenia, suggesting that PS may be familialistically transmitted. Only one longitudinal study explored the evolution of PS in schizophrenia. A group of first-episode or recent-onset patients was administered a series of cognitive tasks at index hospitalization and again after 5 years. They exhibited stable or improved performance on all cognitive tasks, except on the finger-tapping test, the performance of which was highly significantly worsened at the 5-year follow-up.

Similarly, impaired performance on processing-speed tasks has been observed in high-risk subjects (SDST), in adolescents with schizophrenia (SDST, Stroop, and TMT), and in stabilized first-episode psychosis patients (SDST, TMT, and Stroop). Ueland and Townsend found performance on the SDST and/or TMT to be the most impaired of all cognitive measures in adolescents and first-episode patients, respectively. Interestingly, a meta-analysis demonstrated impaired TMT performance in relatives of schizophrenic patients as well.

Again, only one longitudinal study investigated the evolution of reaction-time outcomes in preschizophrenic patients and found intact performance following a 12-month test-retest interval.

**The Neurobiological and Anatomical Substrates of PS**

Few studies investigated the neurobiological correlates of slowing in schizophrenic patients. The relationship between PS and striatal D2 receptor occupancy in schizophrenia needed to be clarified. However, more than 10 years later, still very limited data are available. In an fMRI study, Müller et al. demonstrated an overactivation of the basal ganglia in schizophrenia patients with PS.
ganglia during finger tapping in untreated patients. In another fMRI study, comparing 6 akinetic schizophrenics to healthy controls during finger-to-thumb manipulations and clench-and-open-the-fist tasks, the patients revealed hypoactivity in the supplementary motor area, the left primary sensorimotor cortex, bilateral lateral premotor and inferior parietal cortices, and hyperactivity in the right primary sensorimotor cortex and bilaterally in a mesial frontal oculomotor area.\(^{80}\) Yang et al\(^{81}\) found an association between striatal D2 densities and finger tapping in schizophrenic patients using single photon emission computed tomography.

Hokama’s team\(^{82}\) related increased volumes of basal ganglia in their patients, especially of the caudate, to poorer performance on finger tapping. Finally, other neuroimaging studies have also implicated the parietal cortex in motor-plan generation in schizophrenia.\(^{83}\)

It is interesting to look into other conditions associated with PS, such as aging or Parkinson’s disease (PD), in order to identify the neurobiological substrates underlying this symptom cluster. Consistent with the findings in schizophrenia, age-related PS and slowing in PD have been associated with hypoactivity of the subcortical regions. In PD, slowed movements or impaired finger-tapping performance has been associated with hypoactivation of the basal ganglia circuitry, the supplementary motor area, and premotor area.\(^{84-86}\) It was suggested that the hypoactivation of the supplementary motor area is secondary to insufficient thalamocortical facilitation in these patients.\(^{85}\) Deep brain stimulation of the internal global pallidus and the subthalamic nucleus in 8 PD patients resulted in improved finger-tapping performance.\(^{87}\) Similarly, in elderly subjects, slower finger tapping has been associated with increased echogenicity of the substantia nigra.\(^{88}\)

**PS and Outcome**

There is evidence for an association between speed of psychomotor functioning and social, clinical, and functional outcomes, which in the past 30 years has been replicated in several studies.\(^{89,90}\)

In their prospective study, Pogue-Geile and Harrow\(^{91}\) found clinically observable psychomotor retardation in schizophrenic patients to be the strongest predictor of rehospitalization. Rapid fingertip movements and speeded manual manipulations have been shown to predict the patients selected for rehabilitation programs,\(^{92}\) as well as vocational functioning,\(^ {93}\) quality of life,\(^ {94}\) and subjective quality of family contact.\(^ {95}\) Perlick et al\(^ {96}\) demonstrated pegboard placing to be the strongest discriminator of long-term in- and outpatients. Lehoux and colleagues\(^ {97}\) similarly demonstrated that various neuropsychological measures correlated to social functioning but that performance on a pegboard task was the best predictor. Finally, using drawing tasks, Jogems-Kosterman\(^ {90}\) found that both schizophrenic in- and outpatients exhibited slowed movement initiation but that only inpatients, and not outpatients, showed slowed movement execution as well. She suggested that the severity of motor dysfunction could predict prognosis,\(^ {98}\) with greater motor impairment indicating a more severe course of the illness\(^ {99}\) and poorer treatment outcome.\(^ {100}\)

Unsurprisingly, more research focused on the predictive value of processing speed and RTs on outcome in schizophrenia.\(^ {90,101}\) Zahn and Carpenter\(^ {51}\) found that acute schizophrenic patients who had faster RTs at admission had a moderately significant tendency for showing greater clinical improvement over the course of a brief hospital stay (3–4 months) than patients with slower RTs. This was in line with earlier findings of Cancro et al\(^ {4}\) who used a longer follow-up period and found RTs to be predictive of clinical outcome 3 years later. It was speculated that the overall level of RT reflects an individual’s “environmental responsivity,” which may be a critical factor in the recovery process that potentiates the effects of treatment.\(^ {102}\) Processing-speed tasks such as the SDST, TMT, and the Stroop have been associated with better employment outcomes,\(^ {103}\) quality of life,\(^ {57}\) and to better results in a shopping task.\(^ {104}\) They were also shown to be predictive of hospital inpatient status.\(^ {105}\)

**PS and Antipsychotic Medication**

**Antipsychotics and Slowing**

It has been suggested that rather than an intrinsic feature of schizophrenia, slowing is merely a side effect of neuroleptic treatment. Although several early studies found treatment with neuroleptics, especially chlorpromazine, to cause an impairment in psychomotor functioning,\(^ {106}\) later reports yielded less consistent findings for other conventional neuroleptics.\(^ {106}\) More recent studies even demonstrated improvement of psychomotor functioning after both atypical and conventional antipsychotic treatment.\(^ {30,102,107,108}\) It has been suggested that the superior performance following atypical antipsychotics compared with the performance after conventional in tests assessing psychomotor speed may merely be attributable to the absence of side effects in the samples taking atypical antipsychotics.\(^ {109}\)

Yet, although many studies have tried to implicate antipsychotic treatment in the generation of PS,\(^ {106,110-112}\) the symptom has been demonstrated independent of medication\(^ {68}\) (see also chapter ‘The Course of PS’). Conventional neuroleptics do not seem to further slow motor speed, although they do appear to produce an impairment in fine motor coordination due to extrapyramidal symptoms (EPS).\(^ {113}\) It should be noted that Henkel et al\(^ {15}\) indeed demonstrated a correlation between EPS and increases in the variability of peak velocity based on handwriting performance recorded on a graphics tablet.

Overall, it can be concluded that slowing is an intrinsic feature of the disease, although it seems that neuroleptic
medication can influence some features of psychomotor functioning.

**Antipsychotics as a Treatment for PS**

Typical neuroleptics do not seem to improve patients’ psychomotor functioning, although it is not certain whether they impair it either. A recent meta-analysis of studies that investigated cognitive effects of typical agents compared with placebo or no medication in schizophrenic patients reported a negative effect size on motor functioning (effect size [ES] = -.11). The range of mean doses of chlorpromazine equivalents in the studies evaluated was 300–1581 mg daily. Recent double-blind studies comparing atypical agents with low doses of haloperidol (see table 4) generally did not find any impairing or improving effects of haloperidol.

A vast number of studies have addressed the therapeutic effects of atypical antipsychotics on cognitive functioning, although few included psychomotor measures. A 1999 meta-analysis investigated the effects of atypical agents on cognition. At the time, only 1 double-blind study and 3 open-label studies could be identified that comprised a task assessing psychomotor speed. Only one of the 3 open studies demonstrated improvement after correction for multiple comparisons.

A proper investigation of the effects of antipsychotics on psychomotor functioning in schizophrenia warrants several methodological considerations. In addition to the obvious preference for a randomized controlled double-blind study design, other possible confounders have to be minimized. Performance on psychomotor tasks should be controlled for age, duration of illness, and EPS. Given that EPS are generally more present after administration of conventional neuroleptics, this can be a major potential confounder when the effects of conventional and atypical agents on psychomotor task performance are compared. Moreover, most studies do not present adequate information on the nature of prestudy antipsychotic medication, relevant for a correct interpretation of the study outcome. Some studies may have high-dose conventional neuroleptics and start low-dose atypicals to demonstrate reduced psychomotor problems.

Recently, several randomized controlled double-blind studies that included at least one psychomotor measure have been published in which all studies that addressed the effects of clozapine, risperidone, olanzapine, and quetiapine on cognition were evaluated. Generally, on the motor skill domain (including the finger-tapping, pin, and Grooved Pegboard tests), an ES of .30 was found for these agents. Comparison of the various atypicals did not yield any differences in this domain.

Counter to psychomotor tasks, clinical trials assessing antipsychotics-induced cognitive improvement almost always include processing-speed tasks like the SDST or TMT. In their meta-analysis, Woodward and colleagues found the domain processing speed to improve significantly as a result of treatment with atypical antipsychotics (ES = .38). They found no significant differences in effect size between the antipsychotics, although between controlled and uncontrolled studies differences were significant.

**Discussion**

Although the earliest investigators of schizophrenia already recognized the cluster of symptoms referred to as PS in their patients, few studies have since been aimed at clarifying the nature and the role of slowed psychomotor functioning in the illness. Our review of the existing literature, the first on the subject, yielded several major findings. PS is a clinically observable feature that has been widely substantiated by neuropsychological measures assessing speed of fine movements such as writing or tasks that ask for rapid fingertip manipulations or maintenance of maximal speed over brief periods of time in manual activity. The few studies investigating gross motor disturbances also reported a slowing in gait. Slowed performance as examined with these psychomotor measures was observed independent of medication and has also been associated with negative symptoms and, to a lesser extent, with positive and depressive symptoms. Importantly, the patients’ performance on these psychomotor tasks proved to be related to their social, clinical, and functional outcomes. Several imaging studies showed the slowed performance to coincide with dopaminergic striatal activity. Finally, conventional neuroleptics do not improve the symptoms, in contrast to the atypical agents that do seem to generate modest, improving effects.

Next, we will try to account for the lack of research on slowed psychomotor functioning in schizophrenia and discuss the various PS classifications as well as its relationship to processing speed.

The relative lack of research looking into PS may have several reasons. First, the trend is not only restricted to schizophrenia research: motor control in general is often neglected in cognitive psychological research. This is perhaps best captured by Guthrie who was quoted to comment that “psychology leaves an organism stranded in thought, unable to engage in action.” Still, when
# Table 4. Double-Blind Controlled Trials Investigating Antipsychotic Effects on PS in Schizophrenia

<table>
<thead>
<tr>
<th>Study</th>
<th>Diagnosis</th>
<th>Subjects</th>
<th>Mean Age (y)</th>
<th>Sample Size</th>
<th>Trial Duration (wk)</th>
<th>Medication Groups + Mean Dose Ranges</th>
<th>Psychomotor Measures</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kern et al&lt;sup&gt;102&lt;/sup&gt;</td>
<td>Schizophrenia Treatment resistant</td>
<td>40</td>
<td>56</td>
<td>8</td>
<td>Risperidone (6–7 mg/d) and haloperidol (15–19 mg/d)</td>
<td>Pin test and pursuit rotor</td>
<td>Patients on risperidone performed significantly better on pin test. No significances on pursuit-rotor task.</td>
<td></td>
</tr>
<tr>
<td>Purdon et al&lt;sup&gt;108&lt;/sup&gt;</td>
<td>Schizophrenia Within 5 y of first neuroleptic exposure</td>
<td>29</td>
<td>65</td>
<td>52</td>
<td>Olanzapine (5–20 mg), haloperidol (5–20 mg), and risperidone (4–10 mg)</td>
<td>Grooved Pegboard and FTT</td>
<td>Within group: improvement with olanzapine on pegboard. Between group: olanzapine &gt; haloperidol on both tasks, olanzapine &gt; risperidone on pegboard.</td>
<td></td>
</tr>
<tr>
<td>Purdon et al&lt;sup&gt;132&lt;/sup&gt;</td>
<td>Schizophrenia Chronic patients</td>
<td>34</td>
<td>25</td>
<td>26</td>
<td>Quetiapine (468.2 mg/d) and haloperidol (15.5 mg/d)</td>
<td>FTT and Grooved Pegboard</td>
<td>Only 11 patients completed the full study. No significant differences between and within groups on any of the psychomotor measures.</td>
<td></td>
</tr>
<tr>
<td>Bilder et al&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Schizophrenia and schizoaffective disorder Treatment resistant</td>
<td>41</td>
<td>101</td>
<td>14</td>
<td>Clozapine (452 mg/d), haloperidol (19.6 mg/d), olanzapine (20.2 mg/d), and risperidone (8.3 mg/d)</td>
<td>FTT</td>
<td>Significant improvement over time for clozapine for fine motor functioning factor. No group × time interactions.</td>
<td></td>
</tr>
<tr>
<td>Green et al&lt;sup&gt;133&lt;/sup&gt;</td>
<td>Schizophrenia and schizoaffective disorder Stable outpatients</td>
<td>43</td>
<td>62</td>
<td>104</td>
<td>Risperidone (6.1–5.7 mg/d) and haloperidol (5.2–4.5 mg/d)</td>
<td>Pin test</td>
<td>Pin test was part of memory and fluency factor in analysis. No between-group differences in any of the cognitive cluster scores.</td>
<td></td>
</tr>
<tr>
<td>Keefe et al&lt;sup&gt;134,135&lt;/sup&gt;</td>
<td>Schizophrenia, schizoaffective disorder, and schizophreniform disorder First-episode patients</td>
<td>24</td>
<td>167</td>
<td>52</td>
<td>Olanzapine (9.6–11.3 mg/d) and haloperidol (4.6–4.8 mg/d)</td>
<td>FTT</td>
<td>No improvement in either medication group after 12 or 52 wk.</td>
<td></td>
</tr>
<tr>
<td>Keefe et al&lt;sup&gt;136&lt;/sup&gt;</td>
<td>Schizophrenia and schizoaffective disorder Chronic in- and outpatients</td>
<td>39</td>
<td>414</td>
<td>52</td>
<td>Olanzapine (n = 159), risperidone (n = 158), and haloperidol (n = 97)</td>
<td>Grooved Pegboard</td>
<td>Significant improvement in the risperidone and olanzapine groups but not in the haloperidol group at 52 wk.</td>
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Note: FTT = finger-tapping test and PS = psychomotor slowing.
compared with other illnesses that are accompanied by PS like major depression, the symptom has been investigated even less in schizophrenia. An additional explanation may be that EPS related to antipsychotic treatment can mimic or worsen the motor slowing that was already present in these patients prior to treatment. The observed slowing of their psychomotor processes has hence often been solely attributed to the antipsychotic treatment, even though the same psychomotor symptoms had already been reported before the introduction of neuroleptics and were already known to occur in neuroleptic-naive patients and relatives of schizophrenic patients. Moreover, recent research even suggests that antipsychotic treatment may improve PS. Possibly, this may have obscured deviations in psychomotor symptoms like slowing in clinical practice, preventing their detection or recognition. Third, some authors have suggested that slowing is the result of depressive symptoms or of negative symptoms such as apathy or motivational problems. Effectively, correlations between negative and cognitive symptoms like PS have been demonstrated frequently although the associations were rather modest.

Bleuler described motor slowing as a catatonic symptom, but today, PS is no longer classified as such. Yet, it is indeed plausible to consider slowed psychomotor functioning as a mild catatonic feature and an intermediate state toward stupor. However, to date, no study has looked into the relationship between slowing and catatonic features, making it impossible to draw a distinction between the nature of slowing and other catatonic traits. It would be interesting to explore whether performance on a finger-tapping or drawing task might help to single out the catatonic features of the illness.

Although slowing of psychomotor functioning has mostly been investigated by use of tasks that assess the speed of cognitive processing, it should be noted that in schizophrenia, PS may exist alongside reduced processing speed and that such tasks therefore do not allow a proper assessment of the phenomenon (M. Morrens et al, unpublished data). Several factor analyses corroborated this notion by identifying a fine motor-speed factor in addition to a processing-speed factor in their respective patient samples (M. Morrens et al, unpublished data). This may have implications for future research, especially considering that within the framework of MATRICS only one domain, ie, processing speed, was identified as reflecting reduced speed of psychomotor functioning.

As PS is an array of symptoms comprising several processes, in PS-related schizophrenia research, priority should be given to the identification of the various individual processes that together result in slowed performance. It also warrants a further delineation of the role the separate processes fulfill in the pathophysiology of schizophrenia, their impact on patients’ social and functional outcomes, and their relationship to negative and depressive symptoms as well as to other cognitive impairments.

To date, our knowledge of the neurobiology of slowed functioning is rather limited because only very few studies have investigated the associations between performance on the tasks featuring in this field of research and the electrophysiological or radiological markers of brain functioning. We also still know little about the longitudinal course of psychomotor symptoms in the illness. Many of the findings on the speed of psychomotor functioning in schizophrenic patients and its relation to other symptoms and aspects of their illness were based on cross-sectional research or studies lasting between 1 and 5 years maximum. Clearly, the reported findings should be verified and extended in study designs covering much longer periods. Finally, the phenomenon of PS also merits more attention in research studying the effects of pharmacological treatment in schizophrenic patients.

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References


