Quantitative measurement of handwriting in the assessment of drug-induced parkinsonism

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Abstract

Monitoring drug-induced side effects is especially important for patients who undergo treatment with antipsychotic medications, as these drugs often produce extrapyramidal side effects (EPS) resulting in movement abnormalities similar to parkinsonism. Scientists have developed several objective laboratory tests to measure and research drug-induced movement disorders, but equipment and tests are complex and costly and have not become accepted in large-scale, multi-site clinical trials. The goals of this study were to test whether a simple handwriting measure can discriminate between individuals with psychotropic-induced parkinsonism, Parkinson's disease, and healthy individuals, and to examine some of the psychometric properties of the measure. We examined pen movement kinematics during cursive writing of a standard word in 13 patients with idiopathic Parkinson's disease (PD), 10 schizophrenia patients with drug-induced parkinsonism (SZ), and 12 normal healthy control participants (NC). Participants were instructed to write the word "hello" in cursive twice, at three vertical height scales. Software was used for data acquisition and analysis of vertical stroke velocities, velocity scaling, and smoothness. There were four important results from this study: (1) both SZ patients with drug-induced EPS and PD participants exhibited impaired movement velocities and velocity scaling; (2) performance on the velocity scaling measure distinguished drug-induced EPS from normal with 90% accuracy; (3) SZ, but not PD participants displayed abnormalities in movement smoothness; and (4) there was a positive correlation between age and magnitude of the velocity scaling deficit in PD participants. This study demonstrates that kinematic analyses of pen movements during handwriting may be useful in

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detecting and monitoring subtle changes in motor control related to the adverse effects of psychotropic medications.

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1. Introduction

While the pharmaceutical industry still strives to develop psychotropic medications with minimal side-effect liability, motor side effects continue to limit the effectiveness of treatment. Preventing, monitoring, and treating these drug-induced motor side effects are important concerns to most clinicians as the use of psychotropic medications continues to rise (Leucht, Wahlbeck, Hamann, & Kissling, 2003). Monitoring drug-induced side effects is especially important for patients who undergo treatment with antipsychotics (for schizophrenia) and antidepressants, as these drugs often produce extrapyramidal side effects (EPS) resulting in movement abnormalities, especially in the elderly patients (Caligiuri, Jeste, & Lacro, 2000). Drug-induced EPS are characterized by features of parkinsonism such as bradykinesia and dyskinetic movements both of which significantly impact mobility and daily functions.

There is an increasing need for objective measurement of the severity of drug-induced movement abnormalities in patients treated with antipsychotic medications. Currently, both industry- and government-sponsored clinical trials of new medications commonly rely on subjective, observer-based ratings of these movement side effects to evaluate patient safety and tolerance to medication. Scientists have developed several objective laboratory tests to measure and research various movement disorders, but equipment and tests are complex and costly and have not become accepted in large-scale, multi-site clinical trials. To fill this gap, we developed an easy-to-use and cost-effective system to reliably assess drug-induced EPS. This system is based on analyses of pen movement kinematics during handwriting.

The study of handwriting has a long history of use in neuropsychiatry, particularly for understanding neuroleptic-induced extrapyramidal side effects. Haase (1961) was the first to demonstrate a relationship between clinical effectiveness of neuroleptic medication and EPS using handwriting analysis. He noted that as neuroleptic dosage increased, patients showed parkinsonism. Patients' handwriting slowed (bradykinesia) and decreased in size (micrographia). When decreasing the dosage, the handwriting disturbances disappeared but also the beneficial effects of the medication diminished. This relationship was referred to as the "neuroleptic threshold": the minimum dose a patient needs to obtain clinical efficacy while minimizing any of these sedating side effects. Since then, clinicians have considered the extrapyramidal motor system as a reliable window into neuroleptic actions on the nervous system.

The use of handwriting to assess EPS has been the focus of research primarily in Europe (Gerken, Wetzel, & Benkert, 1991; Haase, 1961, 1978; Kuenstler, Hohdorf, Regenthal, Seese, & Gertz, 2000; Kuenstler, Juhnhold, Knapp, & Gertz, 1999). Gerken et al. (1991) studied movement size (i.e., area encompassed by handwriting) in schizophrenic patients

for predicting treatment response. Treatment with antipsychotics caused a reduction in the overall size of the handwriting samples in 33% of the treatment responders and 75% of the treatment non-responders. These results suggest that risk of developing intolerance to a neuroleptic medication can be detected prior to treatment in a majority of patients. The authors concluded that use of handwriting parameters could improve the evaluation of neurological side effects of neuroleptic medication beyond evaluation using observer-based rating scales alone.

Kuenstler et al. (1999) used positron emission tomography to examine the relationship between reduction in handwriting size (expressed by area) and dopamine D_2 receptor occupancy in schizophrenic patients before and after treatment with antipsychotics (haloperidol, clozapine, or risperidone). Two important findings emerged from their work. First, they found reductions in handwriting size in all participants following treatment, regardless of the medication type. This confirms a fundamental link between the actions of neuroleptic medications and disturbances of motor control. Second, there was a highly significant linear relationship between D_2 receptor occupancy and reduction in handwriting area. The authors concluded that analysis of handwriting size might be well suited for evaluating neurological side effects of neuroleptic medications. Findings from the few published studies of handwriting analysis are consistent in demonstrating that antipsychotics induce observable changes in handwriting. Moreover, these changes are not limited to conventional antipsychotics but are likely present in atypical antipsychotics as well.

Traditionally, decisions regarding EPS were based on subjective observer-based ratings. Alternative approaches to quantify EPS are gaining acceptance. For example, using a measure of wrist rotation, we reported that a measure of velocity scaling (VS) is sensitive to the presence of parkinsonian movement disorder (Caligiuri, Lohr, & Ruck, 1998). Other transduction systems such as load cells are useful for quantifying force variability that accompanies involuntary movements such as tremor and dyskinesia (Caligiuri, 1997). Despite the success with laboratory-based measures of drug-induced movement disorders, they still have not attained widespread use in the clinical setting. Quantitative, unbiased measurement systems based on common everyday motor behaviors, such as handwriting have not been validated for the purpose of assessing drug-induced motor side effects.

Based on the literature showing a relationship between handwriting disturbances and antipsychotic treatment, we reasoned that handwriting movement analysis might be a viable tool in the early detection and management of medication-induced extrapyramidal side effects, such as parkinsonism. The goals of this study were to test whether an everyday handwriting task can discriminate between individuals with psychotropic-induced parkinsonism, Parkinson's disease, and healthy individuals and to examine some of the psychometric properties of the measure. Based on our previous work with velocity scaling and handwriting movements in PD, we hypothesize that kinematic measures of velocity scaling and dysfluency during handwriting will discriminate PD and SZ participants with drug-induced EPS from healthy participants.

2. Methods

2.1. Participants

Participants consisted of 13 (9 males and 4 females) individuals diagnosed with idiopathic Parkinson's disease (PD), 10 individuals (9 males and 1 female) meeting DSM-IV

(American Psychiatric Association, 1994) criteria for schizophrenia (SZ) and having clinically observable drug-induced parkinsonism, and 12 (10 males and 2 females) normal healthy comparison participants (NC). We have found no reason to suspect that our measures would be affected by gender. PD participants were included in this study to evaluate the construct validity of handwriting measure as an index of parkinsonian bradykinesia. The mean (±SD) duration since their initial diagnosis of PD was 8.9 (5.5) years. The mean ages for the three participant groups were 66.7 (9.6), 48.7 (10.5), and 53.0 (12.9) years for the PD, SZ, and NC participants, respectively. As PD is typically a disease associated with aging, the PD participants were significantly older than SZ ($p \leqslant .005$) and the NC ($p \leqslant .05$) participants. All PD participants were treated with some form of levodopa-replacement therapy at the time of study, typically sustained release form of Sinemet. All SZ participants were treated with antipsychotic medications at the time of study.

2.2. Conventional neurological assessment

Assessments included the Unified Parkinson's Disease Rating Scale (UPDRS, Fahn & Elton, 1987) and the Simpson–Angus EPS scale (SAEPS, Simpson & Angus, 1970) to rate the severity of parkinsonism for the PD and SZ participants, respectively. PD participants were administered the UPDRS within four hours of taking their first morning dose of medication. This coincided with the time when motor symptoms were optimally managed. Based on the motor exam portion of the UPDRS (Part 3), six of the 13 PD patients were considered to have moderate motor impairment; while seven were rated a mild or minimal at the time of study. The means (SD) on UPDRS Part 3 subscale score for the 6 PD patients with moderate and 7 with mild motor impairment were 28.3 (3.8) and 13.4 (3.1), respectively. Three of the 10 SZ patients were rated as having moderate parkinsonism; while seven had mild parkinsonism. Eight SZ participants had co-morbid tardive dyskinesia.

2.3. Instrumentation

Handwriting samples were recorded using a non-inking pen on a Wacom UD 9×12 digitizing tablet (30 cm $\times$ 22.5 cm, sampling rate 100 Hz, RMS accuracy 0.01 cm) attached to a notebook computer running the MovAlyzeR software.

2.4. Procedures

Participants were instructed to write the word "hello" twice from left to right and to stay within the upper and lower boundary lines drawn on a piece of white paper with their dominant (right) hand. The dominant arm rested on a table and the participant was free to rotate the digitizing tablet to a comfortable angle. Instructions were to write in a comfortable speed. Participants did not receive feedback of the written samples. The experiment did not systematically control for writing speed, visual guidance, or other factors known to influence handwriting performance (Ondo, Wang, Thomas, & Vuong, 2005).

Three conditions were administered with boundary line heights of 1 cm, 2 cm, and 4 cm. We used the MovAlyzeR software to filter, estimate vertical velocity, segment each word into up and down strokes, and extract the kinematic and temporal features for each stroke. Data reduction consisted of determining vertical stroke sizes (in cm) and peak velocities
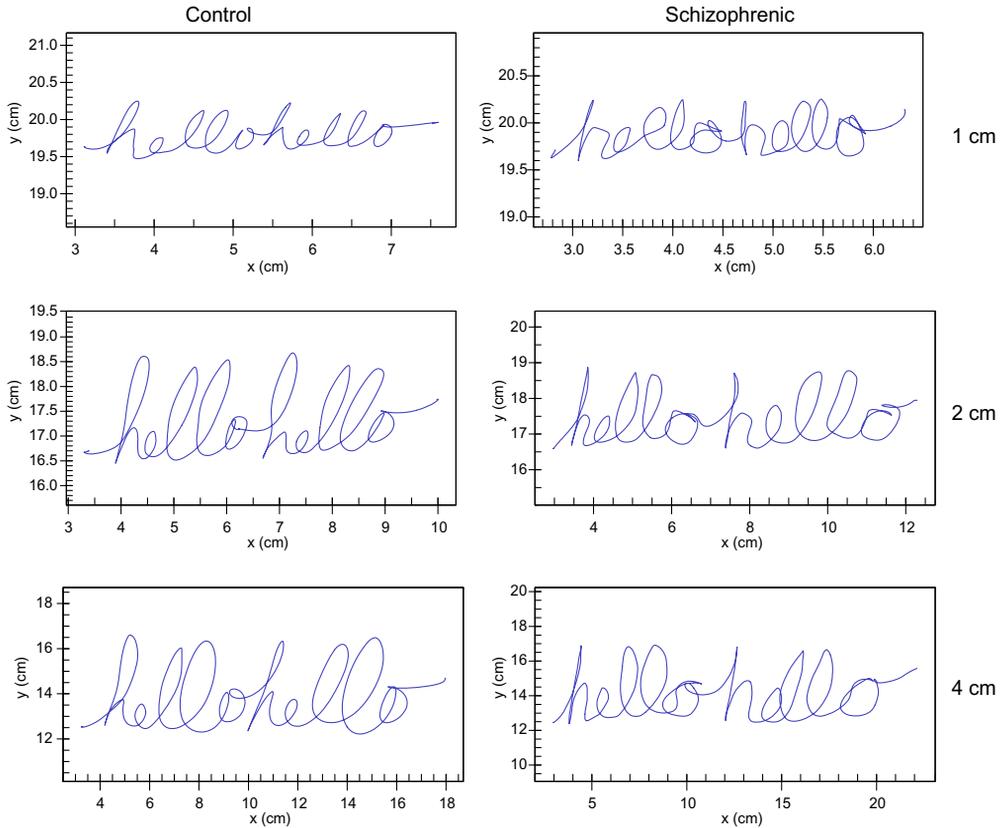
Fig. 1. Handwriting samples for a single healthy control participant (left column) and schizophrenia participant with drug-induced EPS (right column) for the 1 cm (top), 2 cm (middle), and 4 cm (bottom) stroke height conditions.

(in cm/s) for the medial "ll" segments in the cursive writing pattern "hello" for each amplitude condition. Handwriting patterns and vertical stroke velocity waveforms are shown in Figs. 1 and 2, respectively, for a healthy control participant and schizophrenia patient with drug-induced EPS. While the samples shown in Fig. 1 do not reveal noticeable differences, the velocity curves in Fig. 2 reflect important differences between the two participants. The peak velocities for the healthy control participant are nearly doubled from the 2 cm (middle graph) to 4 cm (bottom graph) condition, whereas they remain essentially unchanged for the schizophrenic participants. This inability to scale movement velocity with increasing movement distance was quantified by calculating the slope of the linear regression of the vertical peak velocity versus stroke height. The slope coefficient served as the measure of velocity scaling (VS). In addition, we calculated a measure of movement dysfluency (or lack of smoothness) of the pen movement based on normalized jerk (i.e., the third time derivative of displacement) normalized for stroke size and stroke duration so that the normalized jerk is unitless (Teulings, Contreras-Vidal, Stelmach, & Adler, 1997). Each stroke segment was processed for the dysfluency measure and mean normalized jerk scores across all strokes of the writing pattern were used for statistical analyses.
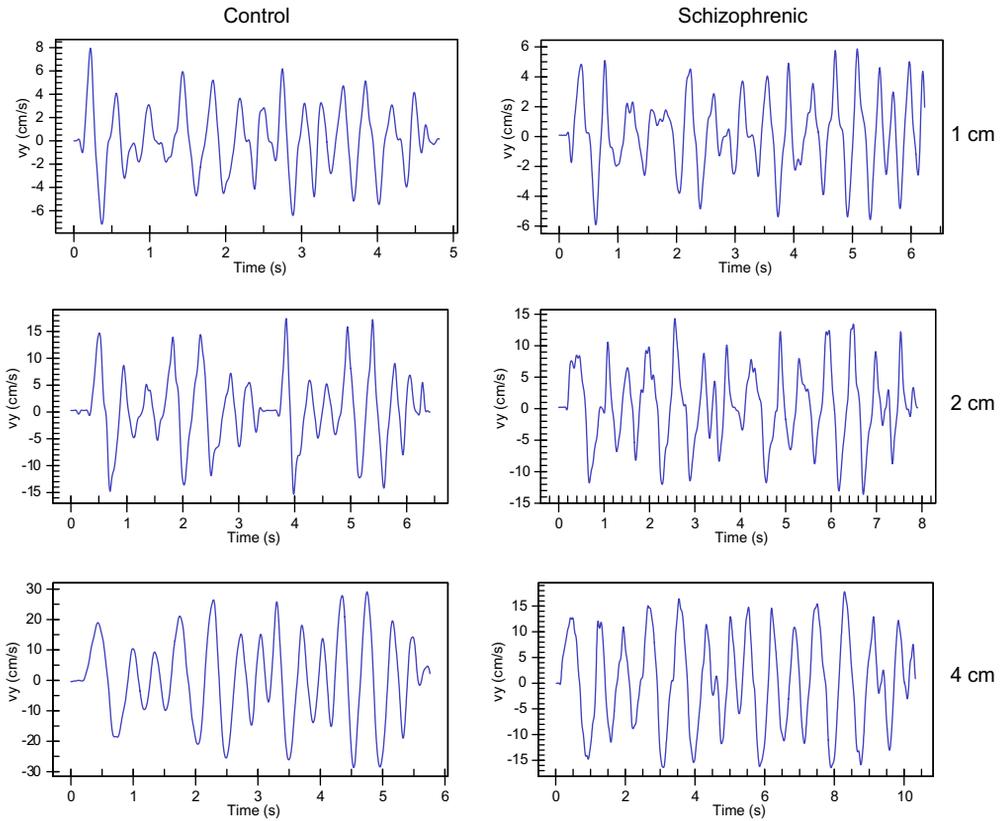
Fig. 2. Vertical stroke velocity waveforms associated with handwriting samples of Fig. 1 from a single healthy control participant (left column) and schizophrenia participant with drug-induced EPS (right column) for the 1 cm (top), 2 cm (middle), and 4 cm (bottom) stroke height conditions.

3. Results

Table 1 shows the means (SD) for three dependent variables: vertical pen movement velocity for each size condition, velocity scaling (VS), and normalized jerk for the three participant groups. Low velocities and VS scores, or high normalized jerk scores signify impaired pen movements. Results indicated that both PD and SZ groups are slower

Table 1
Means (SD) of vertical peak velocity, velocity scaling (VS), and normalized jerk per patient group

Movement score	Size (cm)	NC	PD	SZ
Peak velocity (cm/s)	1	9.2 (1.6)	7.1 (3.8)	6.2 (2.4)
	2	14.9 (3.7)	11.5 (4.7)	8.3 (4.0)
	4	28.4 (7.3)	18.6 (6.6)	12.8 (5.4)
VS (cm/s/cm)	1–4	6.2 (2.0)	3.8 (1.6)	1.9 (1.8)
Normalized jerk	1–4	18 (8)	51 (83)	175 (256)

See text for statistical results.

relative to the NC group, particularly for the larger 4-cm movements. Both PD and SZ participants exhibited reduced velocity scaling consistent with parkinsonism, but only the SZ participants were impaired on the measure of smoothness.

Analyses of variance (ANOVA) revealed significant group effects for peak movement velocity for the 1 cm ($F(2, 32) = 3.46$, $p < .05$), the 2 cm ($F(2, 32) = 6.38$, $p < .01$), and the 4 cm ($F(2, 32) = 11.83$, $p < .001$) conditions and for velocity scaling ($F(2, 32) = 12.11$, $p < .001$). Post-hoc Scheffé tests indicated that for the 1 cm and 2 cm height conditions, SZ participants had significantly lower peak velocities than NC participants; whereas there was no difference in peak velocity between the PD and NC participants. For velocities associated with the 4 cm height condition and the velocity scaling score, both the PD and SZ participants had significantly lower values than the NC participants. There was a significant group effect for normalized jerk ($F(2, 32) = 3.49$, $p < .05$), which was mainly caused
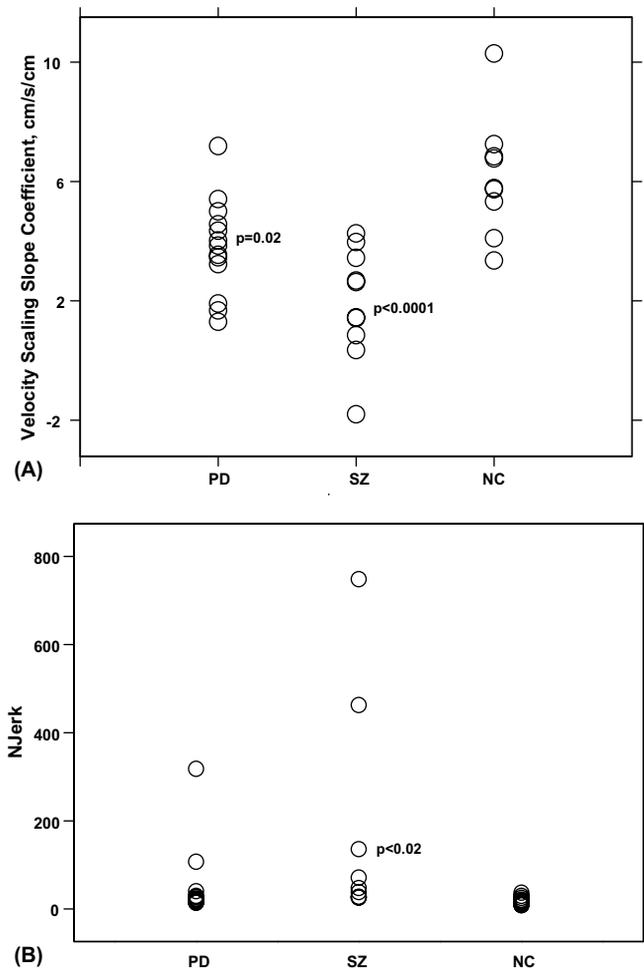

Fig. 3. Scatterplot showing velocity scaling slope coefficients (A) and normalized jerk scores (B) for individual Parkinson's disease (PD), schizophrenic (SZ) and normal control (NC) participants. *p*-values reflect level of significance of the difference with NC.

by the 2 cm stroke height trials ($F(2, 32) = 3.84$, $p < .05$). Post-hoc analyses indicated that the SZ participants had significantly higher normalized jerk scores than the NC participants.

Pen movement velocities were significantly correlated with letter size for the NC ($r = .87$, $p < .001$), SZ ($r = .58$; $p = .001$) and PD ($r = .69$, $p < .001$) groups. Further analyses revealed significant differences in the correlation coefficients between the groups. Specifically, the coefficient for the NC group was significantly higher than the coefficient for the PD ($p = .025$, one-tailed) and SZ ($p = .007$, one-tailed) groups; however the difference between SZ and PD participants was not statistically significant.

Individual participant data of velocity scaling slope coefficients and normalized jerk scores are presented in Fig. 3A and B, respectively. *p*-values in the figure indicate the significance levels for the comparisons against NC participants. The scatter plots show that 12 of the 13 PD participants had velocity scaling coefficient below the 95th percentile of the NC mean and eight of ten SZ participants had coefficients below this value (3.35 cm/s/cm). For the smoothness measure, 6 of the 10 SZ participants had values greater than the 95th percentile of the normal mean (36.9).

Several correlations between the pen movement variables and independent measures of symptom severity were significant for the PD participants. Specifically, lower VS slope coefficients correlated with higher total scores from Part 3 (motor exam) of the UPDRS ($r = -0.65$, $p < .05$). Peak velocity for the 4-cm stroke height condition was correlated with the total score from Part 3 of the UPDRS ($r = -0.70$, $p < .02$). The relationship between total score of the UPDRS Part 3 and VS slope coefficient for the PD participants is shown in Fig. 4. Similar results were obtained for the SZ participants. VS slope coefficients correlated negatively with the SAEPS score ($r = -0.65$, $p < .05$) and especially with its bradykinesia score (i.e., rapidly alternating hand movements, $r = -0.75$, $p \leqslant .02$).

We examined the relationship between age and gender and the dependent motor variables for each of the three participant groups. As expected, there were no effects of gender for any of the dependent variables across the three participant groups. More importantly,
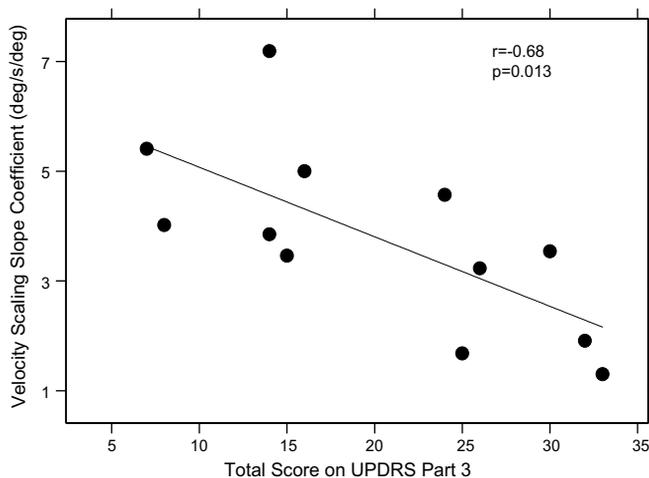

Fig. 4. Scatterplot showing the relationship between velocity scaling and total score of the UPDRS Part 3 in PD participants.

advanced age in the PD participants was significantly related to lower VS slope coefficients ($r = -0.87$, $p < .01$), but not in the SZ or NC participants.

We performed discriminant function analyses to quantify the sensitivity (i.e., the % of SZ or PD participants correctly classified as pathological) and specificity (i.e., the % of NC participants correctly classified as healthy) using the kinematic variables found to be impaired in the PD and SZ groups. Receiver operating characteristic (ROC) analyses revealed 90% sensitivity and 90% specificity for SZ versus NC participants for VS slope coefficient. ROC analyses for PD versus NC participants using the VS slope coefficient revealed 90% sensitivity and 60% specificity.

4. Discussion

We found four important results in this study: first, both schizophrenia (SZ) and parkinsonian (PD) participants exhibited reduced peak velocities in a naturalistic handwriting task compared to normal healthy participants (NC), which shows that medicated SZ patients exhibit bradykinesia characteristic of PD patients. Second, both SZ and PD participants exhibited abnormalities in our velocity scaling (VS) measure when compared with the NC participants. This finding demonstrates that VS is useful as a measure of parkinsonian motor pathology in SZ patients. The findings that VS allows us to distinguish SZ participants with drug-induced parkinsonism from healthy individuals with 90% accuracy and that VS was inversely correlated with observer ratings of bradykinesia in PD and SZ further supports the validity of our measures for quantifying parkinsonism in PD and SZ groups. Third, the SZ participants exhibited abnormalities on a measure of lack of movement smoothness (i.e., normalized jerk); whereas PD participants, with comparable levels of motor pathology exhibited relatively normal smoothness scores on this particular hand writing task. This finding suggests that the motor abnormalities we observed in the SZ participants are likely due to the presence of multiple factors in addition to drug-induced parkinsonism. Fourth, there was a robust relationship between advanced age and impaired velocity scaling in PD. This finding suggests that some aspects of handwriting may be sensitive to the effects of aging on the motor system. The age range was insufficient to detect similar relationships in SZ and NC participants.

It is interesting to note that while SZ and PD participants were slower than NC participants, the effect was particularly apparent for the larger 4 cm movements. As the involvement of the proximal arm joints increases with writing size, greater impairment of larger handwriting movements may imply a deficit involving the proximal rather than the distal arm joint an provide clues about the involvement of different joints in parkinsonism. Wang, Bain, Aziz, and Liu (2005) examined spiral drawing movements in patients with parkinsonian tremor performed under different degrees of arm restraint and found that tremor was driven predominantly by the shoulder, or proximal, joint. While none of our PD or SZ participants exhibited significant tremor, it is possible that bradykinesia affecting arm movements may follow a similar pattern.

Our findings are consistent with previous literature on handwriting and limb movements in PD. Teulings and Stelmach (1991) and Van Gemmert, Teulings, Contreras-Vidal, and Stelmach (1999) showed that while medicated PD participants undershot pen movement distances when instructed to increase the stroke height, their movement times were normal. This implies a failure to increase movement velocity in order to attain the proper

movement amplitude while maintaining normal temporal control. Van Gemmert, Adler, Teulings, and Stelmach (2004) reported that relative to medicated PD patients (and their healthy controls) the unmedicated patients were impaired in their ability to scale peak acceleration with increasing stroke size during drawing of an outward spiral. Similar phenomena have been observed in other movement types. For example, studies of single joint wrist rotation showed that patients with parkinsonian bradykinesia are not properly scaling movement velocity with increasing movement amplitude (Caligiuri et al., 1998; Pfann, Buchman, Comella, & Corcos, 2001; Robichaud, Pfann, Comella, & Corcos, 2002). Patients with more severe motor signs, particularly bradykinesia, exhibited lower velocities and lower velocity scaling (VS) scores. Studies of limb movement have reported both slowed movement and impaired velocity scaling in PD (Pfann et al., 2001; Robichaud et al., 2002).

Our measure of velocity scaling exhibited high levels of sensitivity and specificity. Regarding sensitivity, we were able to correctly identify 90% of the PD and 90% of the SZ participants using only the velocity scaling variable. The velocity scaling measure exhibited better specificity against SZ (90%) than against PD (60%) participants. Thus suggests that some NC participants exhibited VS slope coefficients within the PD range, but well below the range for SZ participants.

Velocity scaling in general expresses the ability to increase velocity almost proportionally with an increase in amplitude so that total movement duration remains virtually constant. Our findings are consistent with previous literature of single joint wrist rotation showing patients with parkinsonian bradykinesia do not properly scale movement velocity with increasing movement amplitude (Caligiuri et al., 1998; Pfann et al., 2001; Robichaud et al., 2002).

Unlike the PD participants, SZ participants exhibited a breakdown in the smoothness of pen movements based on analyses of normalized jerk. Thus, performance on the velocity scaling and normalized jerk measures was dissociated in PD but not SZ. Because both participant groups exhibited clinical evidence of parkinsonism, we hypothesize that the velocity scaling measure may carry information about the extrapyramidal motor system. On the other hand, since only the SZ participants exhibited symptoms of psychosis, we hypothesize that increased normalized jerk levels may carry information about the extent of impairment of motor functions in schizophrenia. This hypothesis is supported by previous studies of motor control in schizophrenia. For example, w found that hand force steadiness error was related to specific aspects of psychopathology in unmedicated schizophrenia patients (Caligiuri & Lohr, 1994; Cortese et al., 2005). Since participants from these two previous studies had never been exposed to antipsychotic medications, we reasoned that the motor impairments were likely an inherent component of the illness. Insofar as normalized jerk measured during dynamic movement in the present study can be considered analogous to force steadiness, measured during static posture, the present findings suggest that the breakdown in smoothness of movement, the breakdown in steadiness during posture, and psychosis may share a common neurobiologic mechanism in schizophrenia.

An interesting finding of the present study was the relationship between older age and impaired velocity scaling in PD. Aging is known to impair motor performance (Potvin, Syndulko, Tourtellote, Lemmon, & Potvin, 1980) largely through loss of dopaminergic neurotransmission (Mahant & Stacy, 2001). Our findings that older PD participants exhibited greater handwriting abnormalities than younger PD participants indicate that age and

disease may act synergistically to amplify the impairment. This is an important issue that awaits further research employing larger samples of participants.

One question raised by this study is whether the pen movement smoothness abnormality observed in SZ might be related to psychopathology. Unfortunately, severity ratings of psychosis were not available for all of the study participants and we were unable to control for this factor in the analyses. There is evidence in the literature that approximately 30–40% of unmedicated SZ participants exhibit motor disturbances similar to those reported in this study (Cortese et al., 2005). Thus, it is possible that the excessively high normalized jerk scores we observed for the SZ participants may reflect psychopathology rather than drug-induced parkinsonism.

Research on handwriting in PD has led to the development of technologies for quantifying kinematic and temporal aspects of fine movements and their disorders. Objective handwriting measurements have been shown to be superior to subjective visual examination in distinguishing untreated from treated PD patients (Adler, Teulings, & Stelmach, 1997; Van Gemmert et al., 2004).

Hypokinesia is a clinical hallmark of Parkinson's disease (Berardelli, Rothwell, Thompson, & Hallett, 2001) and often manifests as micrographia. Changes in handwriting can be observed early in the progression of the disease (Becker, Muller, & Braune, 2002) and can be attributed to any of several pathophysiologic mechanisms including insufficient recruitment of muscle force, underscaling of muscle force, or a deficit in the scaling of motor output appropriate for the task (Berardelli et al., 2001). Findings from studies of the physiological and programming bases of handwriting deficits in PD (e.g., Teulings & Stelmach, 1991; Van Gemmert, Adler, & Stelmach, 2003; Van Gemmert et al., 1999; Van Gemmert, Teulings, & Stelmach, 2001) have advanced our understanding of the role of the pathophysiology of parkinsonian movement disorders. Moreover, research on handwriting in PD has led to the development of technologies for quantifying kinematic and temporal aspects of fine movements and their disorders. Objective handwriting measurements have been shown to be superior to subjective visual examination in distinguishing untreated from treated PD patients (Adler et al., 1997; Van Gemmert et al., 2004).

Modern studies of handwriting in PD have approached the problem in terms of a central, motor programming deficit (Margolin & Wing, 1983). Margolin and Wing found that PD patients were able to produce appropriate letters during handwriting, but could not maintain adequate force to produce normal letter size. They drew upon previous work by Hollerbach (1981), who modeled handwriting by two separate oscillators: a vertical oscillator for production of letter height and a horizontal oscillator for production of letter width. According to Margolin and Wing, inadequate force generation would have a greater impact on the vertical than horizontal oscillator during handwriting. These results illustrate the advantage of the kinematic analysis of handwriting movements to quantify central motor programming deficits, such as those found in PD. Contreras-Vidal and Stelmach (1995) modeled dopamine depletion in PD using handwriting movements. The three-vector handwriting simulation (based on the neural network model of Bullock, Grossberg, & Mannes, 1993) showed that the PD simulation had a progressive decrease in letter size and an increase in movement time compared with the normal simulation. They concluded that dopamine depletion reduces the pallidothalamic gating and prevents the rescaling of the motor program governing movement speed.

There were several features of the handwriting signal that were not examined in the present study. For example, we did not analyze the frequency of the continuous movement

signal. Spectral analyses of drawing or writing movements may differentiate voluntary from involuntary handwriting movements, particularly tremor. In a previous study of handwriting movements in PD participants Liu, Carroll, Wang, Zajicek, and Bain (2005) reported that the voluntary component was characterized as movements having spectral peaks less than 1.0 Hz, with involuntary components such as dyskinesia and action tremor having peak frequencies in the 1.0–5.0 Hz and 6.0–10.0 Hz range, respectively. Employment of spectral analyses in the study of handwriting movements in schizophrenia patients treated with neuroleptic medications may be particularly helpful in identifying individuals at risk for developing tardive dyskinesia.

In conclusion, the results of the present study support that the specific analysis of pen movements in terms of velocity scaling and dysfluency of handwriting is useful in detecting subtle changes in motor control related to age, symptom severity, and adverse effects of psychotropic medications. A brief assessment of pen movement during handwriting can serve as a screening tool for medication-induced motor side effects. Early detection and monitoring of these motor side effects could become useful to monitor and adjust medication regimes and reduce non-adherence and possibly relapse in patients with schizophrenia.

Acknowledgments

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