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Validity of Spiral Analysis in Early Parkinson's Disease

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Abstract: Spiral analysis is an objective, easy to administer noninvasive test that has been proposed to measure motor dysfunction in Parkinson disease (PD). We compared overall Unified Parkinson Disease Rating Scale Part III scores to selected indices derived from spiral analysis in seventy-four patients with early PD (mean duration of disease 2.4 ± 1.7 years, mean age 61.5 ± 9.7 years). Of the spiral indices, degree of severity, first order zero crossing, second order smoothness, and mean speed were best correlated with total motor Unified Parkinson's Disease Rating Scale (UPDRS) score (all $P < 0.01$), and these indices showed a gradient across worsening tertiles of UPDRS ($P < 0.05$). Spiral indices also correlated with UPDRS ratings for the worst side and worst arm scores as well. The domains of bradykinesia, rigidity, and action tremor were correlated with first order crossing, second order smoothness, and mean speed, where as rest tremor was most highly correlated with degree of severity. This suggests that the spiral analysis may supplement motor assessment in PD, although further analysis of spiral metrics, a larger sample and longitudinal data should be evaluated. © 2007 Movement Disorder Society

Key words: Parkinson disease; kinematics; upper limb; motor control; spiral analysis.

Parkinson's disease (PD) is characterized by the clinical hallmarks of bradykinesia, resting tremor, rigidity and loss of postural reflexes.[1] The Unified Parkinson's Disease Rating Scale (UPDRS) captures these features,[2] and when performed by a trained movement disorder specialist, is a reliable measure of disease severity.[3-6] The UPDRS also correlates with loss of fluorodopa uptake in studies of functional neuroimaging.[7,8] However, the UPDRS is highly examiner-dependent, and less reliable with nonmovement trained neurologists.[9]

Objective, easy to administer, noninvasive quantitative measures which assess motor function might improve the detection of early PD as well as the measurement of disease severity and progression both in clinical trials and clinical practice. A validated kinematic test which quantifies motor function might provide objective, reproducible metrics amenable to statistical analysis in research. Further, few such methods exist to evaluate motor function in PD patients in the clinical setting.

Spiral analysis is a noninvasive system of quantifying motor function based on kinematic and physiologic features derived from handwritten spirals. Spiral analysis provides computer-generated measures of force, speed, time, tightness and uniformity of the spiral to record position, force, and time measurements. The test is based on "unraveling" the two-dimensional drawn spiral picture into a data series that captures its original kinematic information and allows for further computational manipulations and clinical correlations. Spiral data are collected in the x, y, and pressure axes providing virtual "tri-axial" recordings.[10-12]

Spiral analysis thus may be used an objective method of evaluating PD severity, extracting detailed motor features from the standard clinical spiral drawing task. An

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objective measure of motor performance in PD should correlate with disease severity as measured by the UPDRS, though modest correlations are to be expected given the differences between clinical rating scales and computer generated motor measurements. Correlations may be attenuated if spiral analysis captures and quantifies clinically relevant aspects of motor function not measured on the UPDRS. The purpose of this article is to assess the validity of spiral analysis in measuring PD severity in the early stages of disease, by evaluating its cross-sectional association with overall motor UPDRS, as well as subscores for bradykinesia, rigidity, and tremor.

PATIENTS AND METHODS

Seventy-four patients met criteria for the diagnosis of probable PD,[13] and were enrolled in a longitudinal observational study of early PD, defined as disease duration of 7 years or less. Subjects were rated using the UPDRS version 3.0, Part III[2] by neurologists trained in movement disorders, and blinded to spiral performance. The clinician also rated the worse affected side using best clinical judgment. For those subjects on levodopa, spirals were performed in the "on" stage. Spiral data were collected by two research coordinators who were blinded to UPDRS scores. The study was conducted in accordance with the Beth Israel Institutional Review Board and all participants gave informed written consent.

UPDRS Subscores

Total motor UPDRS included the total sum of scores for the UPDRS Part III (Items 28–31).[2] A global score for rest tremor was derived by summing the following five items: tremor at rest of all four limbs and face (20). Action tremor score was derived from summation of action or postural tremor (21) of both arms. A global rigidity score was determined from the sum of the rigidity scores (22) for the neck and all four limbs. A global measure of bradykinesia was computed as the sum of the following items: finger taps (23), hand movements (24), and rapid alternating movements (25) for both hands; leg agility (26) for each leg; and body bradykinesia and hypokinesia (31). A total arm bradykinesia measure was also calculated (23, 24, 25). Worse side scores included only those scores that reflected laterality (e.g., not overall bradykinesia for worse side bradykinesia), and the worse arm score included only those scores which pertained to arm function (20–25).

Spiral Collection

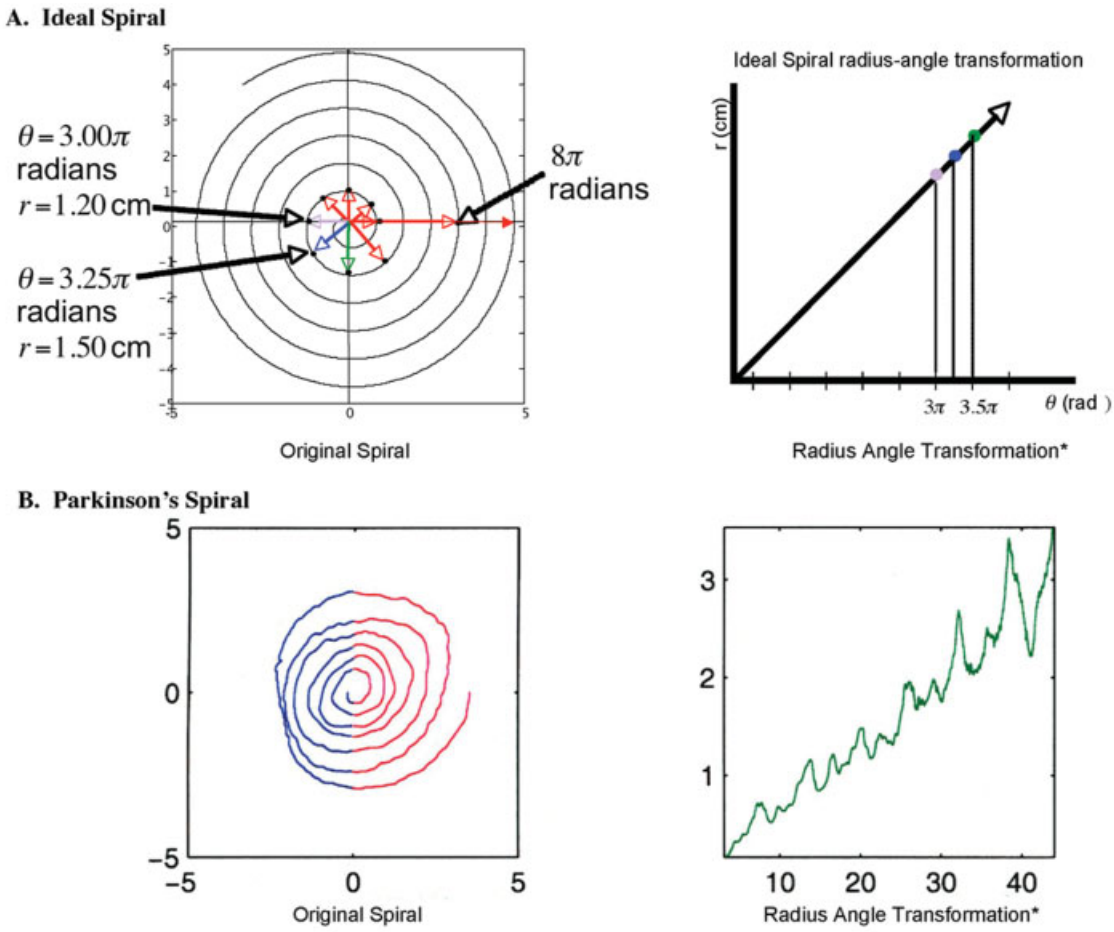
Handwritten spirals were acquired using a digitizing tablet (Intuos 2, Wacom Technology, Vancouver, WA) connected to a microcomputer using proprietary software written in C++.[10] Data were collected in the x-y plane, and in the pressure axis, providing virtual "tri-axial" acquisition. Subjects were seated comfortably and instructed to start in the center of a 10×10 cm box on an 8.5×11 inch white paper and freely draw a spiral of any size within the box. An inked writing pen (not a non-marking computer mouse equivalent) was held in a normal fashion without constraints to allow for full visual feedback. Ten spirals were collected from each hand, and all tracings were monitored on-line for error control. Acquired spiral data were used to calculate the mean degree of severity scores and indices, without outliers removed, for each subject.

Spiral Analysis

Critical features of spiral execution were expressed as mathematical indices developed using Matlab (The Math Works, Natick, MA), as previously described.[10] Briefly, quantification of the spirals was based on the radius-angle transformations of the two-dimensional spiral pictures that captured the original clinical information (shape, kinematics, dynamics) and allowed for further computations of motor control (see Fig. 1). A matrix of ~50 indices relating to spiral execution including shape, loop tightness, tremors, speed, and writing dynamics were calculated from the transformations.

For this study, we investigated the degree of severity and a subset of indices found to be abnormal in PD.[11,14,15] These included four measures of spatial irregularity (first and second order smoothness, first and second order zero crossing, and tightness), spiral hemipressure, tightness, and drawing speed. Degree of severity provided an overall score of a spiral execution, and was intended as the computerized equivalent to the standard 5-point 0 to 4 clinical rating of a two dimensional Archimedes spiral. It was derived using neural network methods and regression analyses comparing computer indices against ratings by blinded movement disorder neurologists assessing spirals on a 0 to 4 scale from normal control and patient spirals.[10] First order smoothness characterized imperfections in spiral drawing by assessing overall deviation from the ideal spiral shape. Second order smoothness, the first derivative of this value, reflected the rate at which the irregularity changes. Second order zero crossing measured the frequency with which the unraveled spiral transform crossed its own mean, and was another indicator of spiral irregularity.[10]

Tremor was assessed quantifying the number of spiral trials with tremor in the x, y, or pressure axes, averaging tremor frequencies, amplitudes, and axes in the x-y



*Radius-angle transformations were the mathematical equivalents of "unraveling" the spirals; the original two-dimensional (x, y) coordinates expressed in terms of (r,) coordinates.

FIG. 1. Schematic and Parkinson's spiral. (**A**) Ideal Spiral. (**B**). Parkinson's Spiral. *Radius-angle transformations were the mathematical equivalents of "unraveling" the spirals; the original two-dimensional (x, y) coordinates expressed in terms of (r,θ) coordinates.

plane. Mean spiral drawing speed was the determined by averaging the speeds of all adjacent pairs of x, y points over the entire spiral. The speed at each spiral point was calculated as the square root of the sum of the squares of consecutive x, y coordinates over the time difference between points. Tremors had little or no effect on mean spiral speeds because oscillations orthogonal to the spiral line averaged out to the spiral mean. Tightness was calculated as the width between consecutive loops of the spiral, standardized against a reference of five loops per 10 cm based on control data. Hemipressure was calculated as the ratio of the mean value of all pressure data points from the right half compared to the left half of each spiral.

Statistical Methods

To characterize the study population, means and frequencies of demographic variables, UPDRS, and spiral indices were examined. To evaluate the association of spiral analysis with motor scores, correlations of spiral indices with the UPDRS and its subscales were assessed using the Spearman rank correlation coefficient. Because a number of correlations were examined, these were evaluated at the $P < 0.01$ level. Spiral indices with correlation coefficients >0.3, and which were independent or had inherent biological meaning (e.g., speed), were selected to test in the overall models. These indices included speed, second order smoothness, and first order crossing. Degree of severity was also included as this has previously been demonstrated to be associated with PD severity.[16]

The *k*-sample Kruskal-Wallis test was used to determine whether spiral indices varied across tertiles of the total UPDRS motor score. To determine whether the

TABLE 1. *Clinical features of study participants*

A. *Demographic features of study sample by PD severity*

All subjects (n = 74)		Less severe*	More severe*
Age at testing, mean years (SD)	63.9 (9.64)	63.1 (9.7)	64.7 (9.7)
Age at diagnosis, mean years (SD)	61.5 (9.7)	60.7 (9.8)	62.4 (9.7)
Duration of disease, mean years (SD)	2.4 (1.7)	2.3 (2.0)	2.4 (1.4)
Male, n (%)	38 (51.3)	21 (55.3)	15 (41.7)
Right handed, n (%)	62 (83.8)	30 (78.9)	32 (88.9)
Right side, worst affected, n (%)	40 (54.0)	22 (57.9)	18 (50.0)

B. *Overall UPDRS scores*

	Mean	SD	Range
Total motor UPDRS	10.9	6.3	3–33
Total worst side	5.5	3.0	1.5–16
Total worst arm	4.2	2.3	0.5–12
Total arm Bradykinesia	2.9	2.1	0–10
Total rigidity	2.5	2.1	0–9.5
Total rest tremor	1.3	1.8	0–8.5
Total action tremor	0.91	0.89	0–3.5

*Median total motor score=9.0. For comparison of total motor score groups, all $P > 0.10$. Less severe: motor $\leq$ 9.0, n = 38; more severe: Motor $>$ 9.0, n = 36.

observed associations were independent of age and duration of PD, linear regression models were tested in which UPDRS score was the dependent variable, spiral indices were independent variables, and age was included as a covariate. Analyses were conducted using the Statistical Analysis System SAS version 9.1 (SAS Institute, Cary, NC).

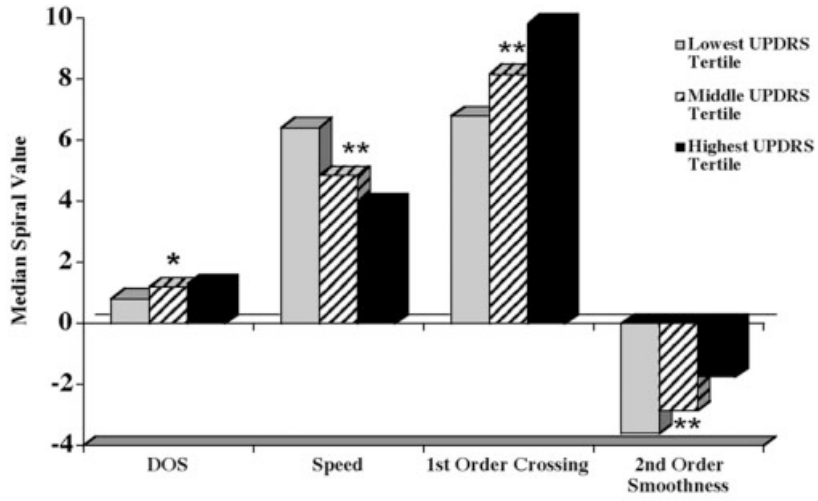
RESULTS

Characteristics of the 74 patients are summarized in Table 1. Of the spiral indices examined, the four with the most prominent correlations with UPDRS were first order crossing, second order smoothness, mean speed, and degree of severity. Each demonstrated statistically significant ($P < 0.01$) correlations of 0.3 or above on at least one portion of the UPDRS.

All four of the spiral indices were independently associated with total motor score on the UPDRS and with total UPDRS for the worst side and for the worst arm, summarized in Table 2. For speed, the associations with UPDRS were inverse. The correlations of spiral indices with UPDRS were similar for the total motor score and

TABLE 2. *Spearman correlation coefficients for spiral variables with UPDRS subscales, r (P-values)*

	Spiral variable			
UPDRS scale	1st order crossing	2nd order smoothness	mean speed	DOS
Total motor	0.42 (0.0002)	0.41 (0.0003)	0.41 (0.0002)	0.29 (0.01)
Total worst side	0.39 (0.0006)	0.42 (0.0002)	0.38 (0.0007)	0.37 (0.001)
Total Worst arm	0.39 (0.0006)	0.44 (<0.0001)	0.39 (0.0006	0.42 (0.0002)
Bradykinesia				
Total arm	0.27 (0.02)	0.30 (0.01)	028 (0.02)	0.21 (0.07)
Total worst arm	0.23 (0.05)	0.28 (0.02)	0.34 (0.003)	0.21 (0.08)
Total worst side	0.23 (0.04)	0.32 (0.006)	0.29 (0.01)	0.22 (0.06)
Rigidity				
Total	0.04 (0.70)	0.22 (0.06)	0.25 (0.03)	0.15 (0.20)
Worst side	0.01 (0.90)	0.23 (0.05)	0.29 (0.01)	0.12 (0.30)
Worst arm	0.05 (0.70)	0.30 (0.01)	0.31 (0.008)	0.15 (0.20)
Rest tremor				
Total	0.10 (0.40)	0.15 (0.19)	0.09 (0.42)	0.27 (0.09)
Worst side	0.12 (0.32)	0.18 (0.13)	0.13 (0.26)	0.31 (0.007)
Worst hand	0.16 (0.16)	0.23 (0.05)	0.16 (.16)	0.38 (0.0008)
Action tremor				
Total	0.40 (0.0004)	0.33 (0.004)	0.24 (0.04)	0.27 (90.02)
Worst hand	0.30 (0.008)	0.36 (0.002)	0.18 (0.11)	0.30 (0.009)



*=P<0.05, **=P<0.01 using Kruskal-Wallis test; Lowest UPDRS tertile corresponds to the mildest disease and highest to worst disease in early PD group.

FIG. 2. Spiral analysis indices by tertiles of UPDRS. $*P < 0.05$, $**P < 0.01$ using Kruskal-Wallis test; Lowest UPDRS tertile corresponds to the mildest disease and highest to worst disease in early PD group.

for the UPDRS subscale specific to the worse affected side and for the worse arm. First order crossing and second order smoothness were each significantly correlated with UPDRS subscales pertaining to bradykinesia, while mean speed was inversely associated. Degree of severity was not correlated significantly with bradykinesia subscales. Second order smoothness was positively and mean speed was negatively correlated with indices of rigidity, while degree of severity and first order crossing did not show significant correlations. The correlations of spiral indices with UPDRS subscales for rest tremor did not show a consistent pattern. The only significant correlations were for rest tremor in the worse hand with degree of severity and second order smoothness. In contrast, each of the spiral indices showed significant associations with UPDRS subscales for action tremor.

Figure 2 shows the median values for spiral indices by tertile of UPDRS total motor score. For each index, there is a graded association across tertiles of this summary motor score (Kruskal-Wallis $P \leq 0.01$ for first order crossing, second order smoothness, and mean speed, $P \leq 0.05$ for degree of severity). Linear regression models adjusting for age and duration of PD at the time of spiral indicated that correlations of spiral indices with UPDRS scores were independent of these covariates. Neither age nor duration of disease was a significant predictor, and neither covariate substantially affected the relation between UPDRS and spiral index (data not shown).

DISCUSSION

Spiral drawing is a standard neurologic test that is commonly performed but rarely quantified. Spiral analysis is a computerized method of analyzing kinematic behavior of the upper limb based on spiral drawing on a digitizing tablet that provides objective and reliable indices of motor function in a short and easy to administer test.[10] In this study, we demonstrate that certain spiral indices correlate with the motor UPDRS scores, and suggest that spiral analysis may serve as a supplement to the UPDRS.

Handwritten spirals have been used clinically to evaluate movement disorders and specifically have been applied to study writing speed and tremor subjectively[17-19] and objectively.[20] Other handwriting studies using a digitizing tablet have demonstrated an association between severity of Parkinsonism, letter size and time to perform the task, but did not specifically demonstrate a relationship between the letter parameter and UPDRS score.[21] Spiral analysis using a digitizing tablet has been used to correlate with dyskinesia in advanced patients with severe UPDRS scores.[22] To our knowledge, this is the first study utilizing spiral analysis in a cohort of early treated PD patients and directly demonstrating an association with the UPDRS rating scale in this group.

Several spiral analysis indices, particularly second order smoothness, degree of severity, and mean speed correlate with all subscales in the domain. There is a greater correlation, in order of magnitude, with the arm

then the side then the whole body. This would be expected as the spiral is drawn with the hand. The significant association with total motor UPDRS scores in patients with early PD suggests that spiral analysis may provide valid measures not only of the upper arm motor but overall motor function in early PD. As the spiral is a psychometric task, it may indeed be measuring subcortical or cortical circuits which express as parkinsonian features in parts of the body other than the arm. However, this may be due, in part, to arm scores generally driving the total UPDRS, strengthening the correlations between spiral drawing and total UPDRS.

Furthermore, individual spiral indices correlate with domain subscores suggesting that spiral analysis may be useful even if single domains are tested. It is of interest that different spiral indices correlate better with some domains than others. Second order smoothness, which measures deviation from the ideal spiral shape, correlates with bradykinesia, rigidity, and action tremor but not rest tremor. Mean speed is associated with rigidity, bradykinesia, and action tremor, but not rest tremor. First order crossing correlates with bradykinesia and action tremor but not rigidity or rest tremor. It is of interest that rest tremor was not highly correlated with most of the spiral indices except for degree of severity, a measure that indirectly incorporated tremor when it was developed with computer-derived scales based on expert physician assessments.

Despite that the UPDRS shows excellent reliability among trained movement disorder experts, physicians in training and general neurologists do not perform the UPDRS as reliably.[9] Furthermore, some spiral indices relate to complex issues in motor control or to clinical measures such as rigidity, which cannot be rated from a videotape. Therefore, objective measures are valuable both to assist nonmovement disorder neurologists and provide accurate, measures of difficult to quantify clinical dysfunction such as rigidity. Computerized spiral analysis results cannot replace clinical measures such as rigidity, but they correlate well with UPDRS counterparts to provide objective measures to supplement the clinical exam.

The UPDRS was selected as the external referent because it is a widely used, well validated measure of motor function in PD, making it an excellent proxy for severity of PD.[23] Though it is the best available external referent, like all clinical rating scales it is not a perfect measure. Because the UPDRS is based on a 5-point (0–4) ordinal scale changes of less than a full point between adjacent scores are difficult to measure. Further, like other clinical rating scales, the UPDRS is an ordinal and not a ratio scale; thus a 1-point difference from 0 to 1 and from 2 to 3 may not reflect changes of equivalent magnitude within a domain or across the domains combined to generate summary scores. Finally, the excellent test retest reliability in untreated early and more advanced treated disease,[3,6,24] has not been evaluated in early treated disease.

Spiral indices were significantly correlated with total motor UPDRS scores and domain scores indicating that these measures capture important aspects of motor function in early PD. The magnitude of the association may appear modest, with Spearman correlation coefficients ranging from 0.29 to 0.44. Given that we are examining the relationship between a clinical rating scale and quantitative analysis of motor function, two very different kinds of measurement, these apparently modest correlations are very good. Several factors are likely to contribute to these modest correlations. First, measurement error or unreliability in either the UPDRS or the spiral analysis or both will attenuate the measured association between them. Second, the UPDRS may measure important aspects of PD (true score variance) not captured by spiral analysis. Finally, the spiral analysis may capture important aspects of motor function in PD not captured by the UPDRS. To identify true score variance captured by one measure or another each of them must be assessed against an external referent such as neuroimaging, measures of clinical course, treatment effect, or functional status. This has been evaluated for the UPDRS,[23,25-27] but not for spiral analysis.

Spiral analysis is a continuous, linear measure that may supplement the UPDRS by providing data on small changes, which would be particularly useful in early PD when the overall UPDRS scores may be small. It is important to assess objective metrics that perform similarly to the motor portion of the UPDRS and also have the potential to quantify mild disability and intermediate points in disease progression. It is therefore possible that some of the uncorrelated variance with spirals represents true score variance of severity of PD that is captured by the spiral but not by the UPDRS.

Our study demonstrates that spiral analysis is a noninvasive neurophysiologic test that correlates with the UPDRS, and may be useful in the assessment of severity of parkinsonian signs. We found that spiral analysis may provide objective measures of otherwise potentially difficult to assess clinical scales such as of rigidity.[28,29] Additional research, including clinimetric studies of the reliability of spiral analysis in PD patients and of the indices themselves, as well as study with larger sample followed longitudinally, are necessary to confirm the progressive worsening in spiral performance within individuals, and to further assess the utility of this measure.

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