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Megan Risi graduated in May 2013 from Bridgewater State University with a Bachelor of Science in Psychology. This research was funded by Adrian Tinsley Program (ATP) semester grants, and the 2012 grants including the 2012 ATP (ATP) semester grants, and the 2012, Summer Research Grant. Under the direction of Dr. Sandra Neargarder, (Psychology), Megan completed this research as part of her Honors Thesis in Psychology. This research was presented at various conferences including the 2012 Cognitive Aging Conference in Atlanta, GA and the 2013 National Conference on Undergraduate Research in La Crosse, WI. Megan is currently working as a Research Assistant and plans to continue her education with graduate work in the coming years.

Parkinson's Disease

Parkinson's disease (PD) is a pervasive neurodegenerative disorder with a prevalence rate of approximately 150 out of 100,000 individuals in the United States and Western Europe (Checkoway & Nelson, 1999). The most widely recognized motor symptoms associated with PD include a resting tremor, rigidity, slowness of movement (i.e., bradykinesia), freezing, and gait abnormalities. Non-motor symptoms typically consist of depression, hallucinations, sleep disturbances, fatigue, autonomic nervous system impairment, and cognitive deficits (see e.g., Stacy, 2011). The frequency and severity of these non-motor impairments typically increase with disease duration, and they are not exclusively linked to the motor symptoms (see e.g., Yu et al., 2012).

Cognitive impairment is an understudied aspect of PD, which is often present in the early stages of the disease. It has been estimated that approximately 30-90% of patients who suffer from cognitive impairment will eventually develop a form of dementia that is specifically associated with PD, known as Parkinson's Disease Dementia or PD-D (Williams-Gray, Foltynie, Brayne, Robbins, & Baker, 2007). The wide variation in incidence is primarily due to the lack of criteria in diagnosing dementia in PD and the heterogeneity of the neuropsychological measures used by researchers. While age and disease duration are strong predictive markers of PD-D, cognitive impairment in posterior domains is also considered to be a major risk factor (Dalrymple-Alford et al., 2011; Williams-Gray et al., 2009).

It is believed that changes in cognition occur between the development of PD and the progression to PD-D. Termed mild cognitive impairment (MCI), these changes can be measured through neuropsychological tests that focus on anterior (frontal lobes; executive function) and posterior (temporal and parietal lobes; language, memory, and visuospatial abilities) regions of the brain, which can provide great insight into the progression of PD to PD-D (Miller, Neargarder, Risi, & Cronin-Golomb, 2013).

Research suggests that the presence of MCI within the first few years of PD diagnosis can aid in predicting cognitive outcome in patients. In longitudinal studies by Williams-Gray, et al. (2007, 2009) non-demented PD participants completed a battery of neuropsychological tests that included the National Adult Reading Test to estimate premorbid intelligence, anterior-based tests

(Tower of London, FAS, Switching), posterior-based tests (Pentagon Copy, semantic fluency, pattern recognition memory, spatial recognition memory), the Beck depression index and the Mini Mental State Exam (MMSE) to measure the presence of dementia. The results showed that anterior deficits of executive function, shown on performance on the Tower of London test and the FAS task, were the most common types of cognitive impairment in non-demented PD. In the 2.5 year and 5 year follow up, deficits in performance on semantic fluency and Pentagon Copy, both tests of posterior regions of the brain, were the most significant neuropsychological test predictors of dementia within the cohort, whereas the more common anterior deficits were not. Dementia was defined as performing one standard deviation (SD) below published normative data. Based on the results of this longitudinal research, the authors concluded that posterior cognitive impairment was a significant risk factor in the development of PD-D.

Although previous research clearly demonstrates that MCI in PD patients does in fact exist (Williams-Gray et al, 2007, 2009), it remains unclear how best to characterize it. Specifically, should MCI be defined based on performance that falls 1 SD below the normative mean, 1.5 SDs, or 2 SDs? Should data be compared to published normative data or to an age- and education matched control group wherein assessments are administered in the same environment by the same researcher? If anterior- and posterior-based tests are good predictors of MCI, does an individual have to perform poorly on all tests given within a specific domain (e.g., four out of four anterior tests), or should some other type of criterion be established?

The present project aims to further examine these questions by administering a series of anterior- and posterior-based tests to a group of non-demented PD patients and their age and education matched controls. Previous research has primarily compared PD and HC participants' performance against published normative data, with no direct comparisons made with an age and education matched control group. It was hypothesized that PD would perform significantly more poorly across all anterior and posterior tests than age and education matched HC participants. A second goal was to examine cognitive performance variation within individuals with PD in an effort to develop subtypes based on patterns of anterior and posterior deficits. Based on previous literature, it was hypothesized that PD participants would fall into one of four cognitive groups (anterior deficit only, posterior deficit only, both deficit, and neither deficit) and that more patients would exhibit anterior-type compared to posterior-type deficits. Further, to determine MCI in PD, various criteria were used such as two deficits in a single domain with cut offs of 1.5 SD, and 2 SD below control participants. Based on previous research (Dalrymple-Alford et al., 2011), it was hypothesized that two deficits of 1.5 SD below the mean in a single domain would provide categorization that is sensitive enough to detect cognitive impairment, yet conservative enough to avoid false positives. The purpose of this research is to further our understanding of the criteria involved in diagnosing MCI in PD.

METHOD

Participants

The study consisted of 61 participants: 34 non-demented PD participants and 27 healthy control (HC) participants who were matched on age [t(60)=.57, p=.96] and education [t(60)=.39, p=.67]. Participants were referred from the Parkinson's Disease Center of Boston University's Medical Center and local support groups, and included individuals who met the clinical criteria for mild to moderate PD as diagnosed by the patients' neurologists. HC participants were recruited from the community.

Measures and Procedures

Participants were given a battery of tests as part of a larger study on PD and cognition. These tests measured anterior- and posterior-type abilities. Anterior tests measured frontal lobe abilities including executive functioning, attention, and decision-making skills. Posterior-type tests measured abilities associated with the parietal and temporal lobes and included visuospatial, visuomotor, visual dependence, spatial reasoning, and memory skills. PD patients were categorized into subgroups based on their performance across the various tests relative to healthy control participants.

Anterior-Type Tests.

The Stroop Color-Word Task. The Stroop Color-Word Task (Stroop, 1935) is a test of executive functioning and measures selective attention, cognitive flexibility, and processing speed. First, participants were presented with a series of "XXXXs" in five columns of 20 words. Each series was presented in one of three colors: green, blue, or red. Participants named the color of each series of "XXXXs" presented as quickly as possible. If the participant was able to complete the list of words, they went back to the beginning to continue reading. The number correct after 45 seconds was recorded. Next, they were presented repeatedly with the words "green," "blue," and "red," that appeared in black (the Stroop word portion). Their task was to read the words as quickly as possible within a 45-second time frame. Finally, they were repeatedly presented with the words "green," "blue," and "red," except now the words were colored such that the color of the word was incongruent with what the word said (e.g., the word blue appeared in red; the Stroop color-word portion). Participants were asked to name the color

in which the words appeared (the response to the above example would be red). Participants were timed and the resulting score was equal to the number correct within a 45-second time frame (dependent variable). Lower scores indicate poorer performance.

The Delis-Kaplan Executive Functioning System (D-KEFS) Verbal Fluency task. The D-KEFS (Delis, Kaplan, & Kramer, 2001) measures verbal fluency. Participants were asked to generate as many words as possible that started with the letter F within a period of one minute. The number of words that were said in each 15-second interval was recorded along with set loss errors and repetitions. This procedure was repeated for the letters A and S. The results from each portion (F, A, and S) were summed to generate a total score (dependent variable). For the category switching portion of the D-KEFS, participants were asked to name as many pieces of fruit and furniture as possible while alternating between categories (e.g., apple, table, banana, chair, etc.) for a period of 60 seconds.

The Trail Making Test. The Trail Making Test (Tombaugh, 2004) measures executive function, specifically attention (Trails A) and set-shifting (Trails B). The Trail Making Test consists of two parts. Trails A has 25 circles with numbers (1-25) in them. Trails B has 25 circles with letters or numbers (A-L, 1-13). The circles are scattered throughout the page in no discernable pattern. Participants were asked to connect the dots in order. For Trails A, the amount of time it took to connect all of the dots was recorded as the dependent variable. For Trails B, each circle had either a number or a letter in it. Participants were asked to connect the dots in order alternating between letters and numbers (1, A, 2, B, etc.). The amount of time it took to connect all the dots was recorded as the dependent variable with lower time indicating better performance.

Posterior-type tests.

The Cube and Pentagon Copying tests from the modified Mini Mental State Exam (mMMSE). The Cube and Pentagon Copying tests (Stern, Sano, Paulson, & Mayeux, 1987) measure motor abilities related to vision (visuomotor) and abilities related to the perception of spatial relations involving vision (visuospatial). For these tests, participants copied a 3-D cube and two overlapping pentagons without a time limit. The accuracy of the drawings was the dependent variable with higher scores indicating better performance.

The D-KEFS Verbal Fluency task. The D-KEFS (Delis et al., 2001) measures semantic fluency. Participants named as many animals as possible in one minute. The number of words stated in 15-second intervals was recorded as well as set loss errors and repetitions. Individual words that met the criteria (dependent variable) were counted resulting in a total score with lower scores indicating poorer performance.

The Landmark Line Bisection task. The Line Bisection task (Davidsdottir, Wagenaar, Young, & Cronin-Golomb, 2008; Lee, Harris, Atkinson, & Fowler, 2001) measures spatial perception without motor demands. On a computer screen, participants viewed a horizontal line crossed by a vertical mark that began on either the left or right side of the horizontal line. As the experimenter moved the vertical mark toward the opposite side of the line, participants indicated when the mark reached the perceived center of the line. Each trial started at different sides of center and at different distances resulting in five trials that started to the right of center and five trials that started to the left of center. The distance between the perceived center and the actual center was the dependent variable. The average absolute value of distance from the actual center was taken for the 10 trials with lower numbers indicating less variation and better performance.

The Visual Dependence task. In the Visual Dependence task (Azulay, Mesure, Amblard, & Pouget, 2002; Danta & Hilton, 1975; Davidsdottir et al., 2008), participants viewed a computerized rotating white rod on a black screen presented at an angle (five tilted upward to the right and five tilted upward to the left). The researcher manually rotated the rod from a separate station. The participant was asked to indicate when the rod reached a horizontal position. Scoring was based on how close to horizontal each trial was (dependent variable). The average of 10 trials was used for analysis with lower numbers indicating better performance.

The Delayed condition for the Rey Auditory Verbal Learning Test (RAVLT). The RAVLT-delay (Rey, 1964) measures delayed memory. Participants were given a list of 15 words read in a monotone voice with even spacing. Participants were asked to repeat as many words as they remember from the list in any order. This was repeated 5 times. Then, there was an interference recall wherein the participants were read a new list of words in a monotone voice, then asked to repeat the words in any order. After approximately 20 minutes of neuropsychological testing, the participants were asked to recall the original list (with no additional prompting). The score was the total number of correctly recalled words in the delay portion only with lower scores indicating poorer performance.

RESULTS

Independent groups t-tests with a Bonferroni correction of .008 (.05/6) was used to examine group (i.e. HC and PD) dif-

ferences on the six anterior- and six posterior-type assessments. As illustrated in Table 1, the HC group significantly outperformed the PD group on most tasks including anterior-based tasks of Stroop word and color-word, FAS, switching, Trails A, and Trails B. Similarly, the PD group performed significantly worse on the posterior-based tasks of Line Bisection and RAVLT-delay. See Table 1 for the t-test results, means, and SDs of each group.

Individual PD performance was evaluated to examine within group variability and sensitivity of tests to PD performance. To examine individual performance, means and SDs were calculated for HC participants for each test. PD scores were then converted to z-scores by using the means and SDs of the HC group for each test. For purposes of this project, a deficit was identified as a score that fell at least 1.5 SD below the HC mean for a particular test. The number and percentage of PD participants who exhibited a deficit for the anterior and posterior-type tests according to the 1.5 SD and 2 SD criteria is shown in Table 2. As illustrated, PD participants showed the largest percentage of deficits on Trails A (55.88% and 50% respectively) and the least on semantic fluency (12.50% and 0% respectively). Table 3 shows individual PD performance for each test. Noted deficits and their severity (1.5 SD or 2.0 SD below the HC mean) are provided. Number of deficits on tests ranged from four (switching, cube copy, and semantic fluency) to 19 (Trails A) deficits. Individual performance ranged from zero deficits (five participants) to 10 deficits (one participant).

As explained above, we examined PD participants whose z-score fell at least 1.5 SD below the HC group mean as well as a stricter cut-off of at least 2 SD below the HC mean on any given task. For both sets of criteria, participants who had two or more deficits in a single domain (anterior, posterior) were categorized as being deficient in that domain. This subtyping resulted in the establishment of four groups: anterior deficit only, posterior deficit only, anterior and posterior deficit (both), and no deficit in either domain (neither). This categorization for 1.5 SD below showed nine individuals with anterior deficit only, one individual with posterior deficit only, 10 individuals with anterior and posterior deficits (both), and 14 participants with neither deficit. When the cut-off was increased to the stricter 2 SD below the mean, four participants categorized as both moved to the frontal only category, four from the frontal only and one from the both categories moved to neither. This change in categorization maintained the 9 in-

Table 1. Comparison of HC and PD Cognitive Performance. Mean (SD) total score unless indicated otherwise

Test Name	PD (n)	HC (n)	PD Mean (SD)	HC Mean (SD)	95% Confidence Interval	PD-HC significant difference (1-tailed)	Effect Size η2
Anterior-type tests							
Stroop Word score	34	27	32.09 (9.30)	42.11 (8.97)	[12.11, 27.02]	.001*	0.22
Stroop Color-Word score	34	27	85.88 (12.59)	105.44 (16.52)	[5.30, 14.75]	.001*	0.11
D-KEFS FAS	34	27	39.79 (7.55)	54.85 (12.00)	[9.71, 20.40]	.001*	0.20
D-KEFS Switching	17	22	12.94 (3.11)	14.77 (2.83)	[-.10, 3.76]	.03*	0.02
Trails A completion time	34	27	35.11 (10.33)	24.48 (5.17)	[-14.72, -6.56]	.001*	0.23
Trails B completion time	34	27	90.71 (42.98)	54.09 (15.16)	[-52.62, -20.64]	.001*	0.33
Posterior-type tests							
mMMSE Cube Copy	34	27	5.85 (1.40)	6.41 (0.97)	[-.05, 1.16]	0.37	0.05
mMMSE Pentagon Copy	29	25	6.90 (.90)	7.04 (0.68)	[-.30, .58]	0.26	0.12
D-KEFS Semantic Fluency	32	27	22.03 (5.55)	23.85 (5.80)	[-1.14, 4.79]	0.11	0.01
Visual Dependence	34	27	0.51 (0.52)	0.35 (0.26)	[-.37, .04]	0.06	0.001
Line Bisection	34	27	-0.10 (0.77)	0.55 (0.70)	[-.51, .03]	.001*	0.01
RAVLT Delayed recall	17	22	7.24 (3.73)	10.41 (3.53)	[.81, 5.54]	.005*	0.08

* Indicates significant difference at $\alpha = .05$between HC and PD

Table 2. Test Performance Across PD Participants

Test Name	Total PD	Total Deficits -1.5 SD	Percentage	Total Deficits -2 SD	Percentage
Anterior-type tests					
Stroop Word	34	14	41.18	4	11.76
Stroop Color-Word	34	12	35.29	6	17.65
FAS	34	11	32.35	3	8.82
Switching	17	4	23.53	3	17.65
Trails A	34	19	55.88	17	50.00
Trails B	34	16	47.06	14	41.18
Posterior-type tests					
Cube Copy	34	4	11.76	4	11.76
Pentagon Copy	29	9	31.03	2	6.90
Semantic Fluency	32	4	12.05	0	0.00
Visual Dependence	34	7	20.59	7	20.59
Line Bisection	34	10	29.41	8	23.53
RAVLY-delay	17	5	29.41	3	17.65

dividuals with anterior deficit only and one individual with posterior deficit only; however, individuals categorized as being deficient in both fell to five, and neither deficit increased to 19.

Discussion

The first hypothesis stated that PD participants would show more cognitive deficits than HC participants. As predicted, the non-demented PD participants in this study performed significantly worse than the HC participants on several measures of cognition, including all anterior-based tests (Stroop word, Stroop color-word, FAS, switching, Trails A, and Trails B) and two posterior-based tests (Line Bisection and RAVLT delayed recall). These results are in line with previous studies, which have found that anterior deficits as opposed to posterior deficits are more commonly observed in PD (Miller et al., 2013; Williams-Gray et al., 2007, 2009). Contrary to research by Williams-Gray et al. (2009), semantic fluency did not appear to be a strong indicator of posterior cognitive deficits in this PD population, as no significant difference in performance was observed on this measure between PD and HC participants. This may be due to the fact that these PD participants were extremely high functioning whereas Williams-Gray et al. included participants who were more heterogenous in terms of cognitive functioning..

The current project directly compared PD performance to that obtained by age and education matched control participants from the greater Boston area. The majority of researchers who study PD-MCI, however, compared their obtained PD group data to published normative data. This remains the case even when a control group was included as a part of the research study (Williams-Gray et al., 2007, 2009). The control group comparison method was chosen over the use of published norms in order to minimize demographic differences that might skew the data. Published normative data are often inconsistent when accounting for demographic variables such as education. Our PD sample was highly educated, ranging from 13 years (one participant) to 21 years (two participants) of education with a mean of 17.09 years. Our matched controls had a range of 14 years (two participants) to 21 years (two participants) of education with a mean of 17.30 years. Less well-matched normative data may have indicated less cognitive impairment in our PD group thereby masking changes in cognition.

The second hypothesis stated that PD participants would fall into one of four cognitive groups: anterior deficit only, posterior deficit only, both deficit, and neither deficit. As demonstrated by the data, the numbers of PD participants that were categorized in the groups changed as a function of the criteria adopted for inclusion. As predicted, PD participants exhibited more cognitive deficits on anterior-based tasks when compared to posterior-based tasks. These results were consistent with the literature on cognitive performance in PD participants (see e.g., Williams-Gray et al. 2009).

There are no set diagnostic criteria for MCI in PD. The Movement Disorder Society recently assembled a task force to clarify MCI in PD, but used various ways to establish a diagnosis. These guidelines suggested that multiple domains be assessed with many neuropsychological measures, but did not come to a consensus as to which measures to use and urged additional research to determine these measures. To diagnose MCI, they suggested that a deficit should be found on at least two tests within a single domain. Determining a cognitive deficit on a test had various options. A deficit could be determined if the patient scored between 1 and 2 SD below matched normative data. If available, a significant decline on serial cognitive testing or estimated premorbid abilities could be considered a cognitive deficit in the corresponding domain (e.g. executive function, visuospatial abilities). Finally, if a patient had undergone neuropsychological testing previously, reported a change in cognition, and fell at least 1 SD below previously tested abilities, a score of less than 1 SD below published norms was sufficient to determine a deficit on that task (Litvan et al., 2012).

Determining a deficit within a domain varies among researchers. Some studies have emphasized the need to show a deficit on two tests within a single domain (see e.g., Williams-Gray at al., 2007, 2009). Dalrymple-Alford et al. (2011) proposed that one deficit across two domains (e.g. one anterior test and one posterior test) was sufficient for the categorization of MCI in PD. Researchers in Taiwan (Yu et al., 2012) considered a domain impaired if the participant scored 1.5 SD below normative data on a minimum of one test within that domain. With so many variations, it is clear that more research is needed to establish reliable and valid guidelines.

MCI was evaluated using cut-off values of 1.5 SD below the HC participants' mean and 2 SD below the HC participants' mean with two deficits in a single domain (anterior or posterior) constituting a deficit in that domain. When 1.5 SD below the HC participants' mean was used, nine PD participants were categorized as having anterior deficits, one PD participant was categorized as having posterior deficits, 10 PD participants were categorized as having both deficits, and 14 PD participants were categorized as having neither deficit. When the more strict cut-off of 2 SDs was used, anterior and posterior grouping remained the same (nine and one respectively), but the PD participants classified as both deficits was decreased to five and neither deficit increased to 19.

The type and number of neuropsychological tests used to determine this subtyping is needed in future research. Many of the investigations into PD-MCI have used various neuropsychological tests. Other research into PD-MCI has used unbalanced numbers of tests between domains. For example, Dalrymple-Alford et al. (2011) used 12 anterior-based cognitive tests and eight posterior-based tasks. The more tests you have for a single domain, the more opportunity there is to find deficits within that domain. When the number of tests is unbalanced, the testing can appeared skewed to uncovering deficits within the domain with more tasks.

Overall, research into PD-D is highly varied and subject to limitations such as a participant's inability to continue with research for reasons of motor impairment, dementia resulting in the inability to complete a neuropsychological battery, and high morbidity and mortality rates, making longitudinal research difficult. Because of these factors, a large pool of participants is needed. It is important to test newly diagnosed PD participants to obtain a baseline score on neuropsychological tests to better understand the course of the disease. Finally, by continuing the research for 10 or more years, the progression to dementia in PDs may be better understood, resulting in more precise risk factors being identified. Through continued research, better understanding of PD and its progression to dementia will aid in the care of the patients

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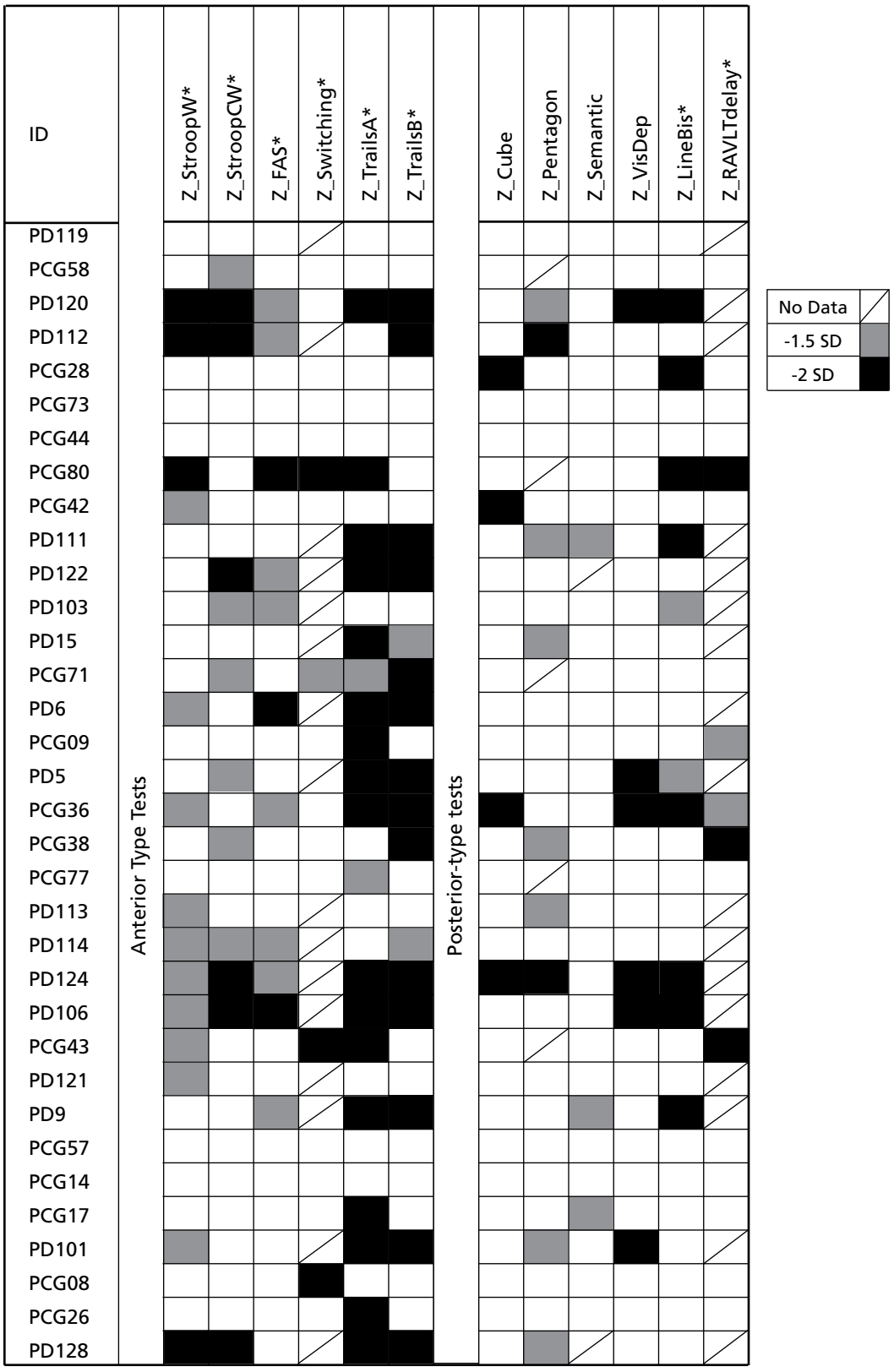
Table 3. Individual PD Performance



* Test showed significant difference between PD and HC