RESEARCH ARTICLE

The Source of the Memory Impairment in Parkinson's Disease: Acquisition Versus Retrieval

Nancy D. Chiaravalloti, PhD,[1,2] Naroa Ibarretxe-Bilbao, PhD,[3]* John DeLuca, PhD,[1,2,4] Olga Rusu, MSc,[3] Javier Pena, PhD,[3] Inés García-Gorostiaga, MD,[5] and Natalia Ojeda, PhD[3]

[1]*Kessler Foundation, West Orange, New Jersey, USA*
[2]*Department of Physical Medicine and Rehabilitation, Rutgers New Jersey Medical School, Newark, New Jersey, USA*
[3]*Neuropsychology of Psychiatric and Neurological Disorders Research Team, Department of Methods and Experimental Psychology, Faculty of Psychology and Education, University of Deusto, Bilbao, Spain*
[4]*Department of Neurology and Neurosciences, Rutgers New Jersey Medical School, Newark, New Jersey, USA*
[5]*Department of Neurology, Galdakao Hospital, Galdakao, Spain*

ABSTRACT: Memory deficits are common in persons with Parkinson's disease (PD) even without the presence of a frank dementia. These memory deficits have traditionally been attributed to inability of patients to retrieve information from long-term memory, referred to as the "retrieval failure hypothesis." However, some studies additionally document problems in recognition memory, noted to be inconsistent with the retrieval failure hypothesis. Given the neuroanatomical abnormalities observed in the hippocampus of PD patients and the role of the hippocampus in learning new information, the current study was designed to specifically examine learning abilities in a nondemented PD sample through the application of a learning paradigm, the Open Trial Selective Reminding Test. We examined 27 patients with PD without dementia and 27 age-, gender-, and education-matched healthy controls (HCs) with a neuropsychological test battery designed to assess new learning and memory. Results indicated a significant difference between the groups in terms of their ability to learn a list of 10 semantically related words. However, once the groups were equated on learning abilities, no significant difference was noted between the PD and HC participants in recall or recognition of the newly learned material. The memory deficit observed in nondemented PD patients is thus largely the result of a deficit in learning new information. This finding should be used to guide treatment for memory deficits in persons with PD, and future research should seek to identify novel means of improving new learning in this population.

Key Words: learning; memory; Parkinson's disease; cognition; Open Trial Selective Reminding Test

Cognitive dysfunction is common in Parkinson's disease (PD),[1] often progressing to dementia.[2] Deficits in executive control, visuospatial functioning, and memory have been reported.[1,3-5] Whereas executive dysfunction has been thought of as the hallmark cognitive deficit in PD,[6] deficits in verbal memory are common.[7] Memory deficits are commonly observed on free recall, whereas deficits in recognition and cued recall are thought to be relatively nonexistent or appear later in the disease course.[8,9] This pattern has been interpreted to suggest that material was successfully encoded into memory and that the memory dysfunction in PD is secondary to retrieval deficits,[9,10] referred to as the "retrieval deficit hypothesis." This pattern of memory performance reflects frontal-striatal dysfunction[11] and is consistent with a subcortical dementia syndrome.[12]

The accuracy of the retrieval deficit hypothesis has been questioned,[13] with it being suggested that deficits

*Correspondence to: Dra. Naroa Ibarretxe-Bilbao, Faculty of Psychology and Education, University of Deusto, Universidades, 24, E-48007 Bilbao, Spain; naroa.ibarretxe@deusto.es

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in recognition memory have been overlooked.[14-17] In their meta-analysis, Whittington et al. concluded that a recognition memory deficit does occur in PD and is not limited to PD patients with dementia.[8] Beatty et al.[15] showed that recall and recognition performance was below average in both nondemented PD patients and PD patients with dementia, with neither group performing better on recognition than recall. Higginson et al. similarly demonstrated that nondemented PD patients exhibited deficits on cued recall and delayed recognition commensurate with their deficits in free recall, inconsistent with the retrieval deficit hypothesis.

The inability of the retrieval failure hypothesis to fully account for the memory deficits observed in PD has led researchers to hypothesize on a deficit in recognition memory, in addition to the recall deficit. A more parsimonious explanation, however, should be considered: that of insufficient acquisition of information into long-term memory. In fact, such a hypotheses was recently posed by Brønnick et al.,[18] who examined performance on the California Verbal Learning Test-2 (CVLT-2), concluding that memory impairment in early PD was the result of a deficit of learning/encoding and not retention or retrieval. However, the use of standard neuropsychological tests, such as the CVLT, to examine memory deficits is limiting in that they do not provide a complete assessment of learning. Such tests fail to ensure that all participants initially learn the material that is later tested by recall and recognition. In addition, 2-alternative forced choice recognition paradigms, such as that which is used in the CVLT, results in a significantly easier recognition task (i.e., 50% correct by chance), as compared with recall. The examination of the quality by which patients initially learn the stimuli is essential to draw sound conclusions regarding the nature of the memory deficit.

Neuroimaging findings also highlight the possibility of a learning deficit in PD. Reduced dopamine largely affecting frontostriatal circuitry has been associated with cognitive deficits in nondemented patients with PD.[19] Studies have additionally demonstrated the neuroanatomical involvement of the hippocampus in both demented and nondemented patients with PD.[20] Recent work has demonstrated reduced hippocampal volume in nondemented PD patients, compared to controls.[21,22] Another study noted significant age-associated hippocampal atrophy in PD in older (>70) nondemented patients, compared to controls.[23] Other studies have reported on bilateral hippocampal atrophy[24,25] and medial temporal atrophy[26] in nondemented PD patients. Imaging studies have shown reduced hippocampal volumes in nondemented PD patients, which has been related to overall cognitive performance and memory deficits.[20,27] Given the known involvement of the hippocampus in learning, it is likely that learning abilities are affected by PD pathology.

The current study seeks to clarify whether the memory deficit observed in PD is a function of poor initial learning, compromised retrieval, or both. We hypothesized that impairment in initial learning would result in a significant difference between persons with PD and age-, gender-, and education-matched healthy controls (HCs) on the number of trials required to reach a learning criterion[28] on a test that has been used in other clinical populations to test the acquisition versus retrieval hypothesis for impaired verbal memory.[29-31] Another question to be addressed is the potential effect of other cognitive deficits in PD influencing learning and memory, specifically processing speed (PS) and working memory (WM). In our previous work, we have found that WM and, in particular, PS can account, at least in part, for some portion of the variance in learning difficulties.[29] In other pathologies associated with central nervous system dysfunction, our team has demonstrated the relevant role of processing speed slowing on memory abilities and performance in other cognitive domains.[32,33] Because persons with PD often present with PS and WM deficits,[34] this relationship is important to explore in PD.

Methods

Participants

Participants included 27 patients with PD recruited through the Department of Neurology at the Galdakao Hospital (Galdakao, Spain) and the PD Association from Biscay (ASPARBI). Twenty-seven age- and education-matched HCs were also included, recruited from acquaintances of the patients. PD participants were part of a larger study examining cognition in PD.

A neurologist specializing in movement disorders made the diagnosis of PD based on the UK PD Society Brain Bank diagnostic criteria.[35] Other inclusion criteria were (1) age 45 to 75, (2) H & Y disease stages and UPDRS evaluated by the neurologist. Exclusion criteria were as follows: (1) presence of dementia, as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR),[36] and the International Parkinson and Movement Disorder Society clinical criteria for PD dementia (PDD)[37,38]; (2) the presence of other neurological illness or injury (e.g., traumatic brain injury [TBI] or multiple sclerosis [MS]); (3) unstable psychiatric disorders (e.g., schizophrenia); and (4) visual hallucinations, as assessed by the Neuropsychiatric Inventory Questionnaire. The diagnosis of dementia was based on an interview with the patient and the caregiver using the DSM-IV-TR as well as the International Parkinson and Movement Disorder Society's diagnostic criteria for PDD. The algorithm for the diagnosis of dementia in PD (level I) requires (1) a diagnosis of PD, (2) the development of PD preceding

TABLE 1. Clinical and demographic characteristics of the sample

Characteristics	PD n = 27 Mean (SD)	HC n = 27 Mean (SD)	Test Statistic
Age	68.33 (5.12)	67.00 (5.07)	t = 0.96
Education	11.78 (4.08)	11.56 (4.96)	t = 0.18
Gender	Males = 14 Females = 13	Males = 14 Females = 13	Chi-square = 0.000
Handedness	Right = 27 Left = 0	Right =24 Left = 1 Ambidextrous = 2	Chi-square = 0.204
Estimated premorbid IQ (NART) (raw scores)	23.44 (6.09)	25.59 (3.39)	t = 0.12
Geriatric Depression Scale	2.04 (1.93)	1.37 (1.31)	t = 0.14
Equivalent doses of L-dopa	713.56 (488.44)	n/a	n/a
H & Y stage	Stage 1 = 3 Stage 1.5 = 3 Stage 2 = 20 Stage 3 = 1	n/a	n/a
UPDRS	35.67 (15.87)	n/a	n/a

*All comparisons nonsignificant.
n/a, not applicable.

the onset of dementia, (3) Mini–Mental State Examination below 26, (4) presence of cognitive deficits severe enough to affect daily living, and (5) impairment in more than one cognitive domain, including attention, executive function, visuoconstructive ability, or memory. All patients were symptomatically stable, taking medication, and tested while on their medication. The average levodopa equivalent daily dose was 713.56 (standard deviation [SD]: 488.44).

There were no significant differences between the groups in age, education, gender, handedness, or estimated premorbid full-scale IQ (Table 1). There was also no significant difference between groups in depression. The motor deficit in the PD group was largely mild (H & Y staging: stage 1: 3 patients; stage 1.5: 3 patients; stage 2: 20 patients; stage 3: 1 patient).

Matching of Controls and Patients

Age, education, and gender affect verbal learning and memory.[39] To avoid the challenges associated with using these variables as covariates, we individually matched each PD patient with a control based on age, education, and gender. The following algorithm was applied, based on the methodology of Brønnick et al.[18]: (1) We selected the first unmatched PD patient; (2) we searched for a control that matched the patient exactly on age, sex, and education; (3) if no exact match was found, we accepted a deviance of 1 year on age and education; (4) we increased tolerance limits on age and education to 2 years when necessary; (5) and, finally, increased tolerance limits to 3 years if necessary; (6) if no match was found, the patient was excluded.

Procedure

The study protocol was approved by the ethics committee at the Health Department of the Basque Mental Health System in Spain. All subjects provided written informed consent before participation.

Verbal learning and memory was assessed by the Open-Trial Selective Reminding Test (OT-SRT), which was developed by DeLuca et al.[28-30] based on the traditional SRT,[40] and is designed to assess one's ability to learn new information. The examinee is presented with 10 words over a maximum of 15 trials. Participants continue the list learning until a criterion of complete recall (10 words) on two consecutive trials is achieved. Trial 1 involves a presentation of the list of 10 words. On trials 2 through 15, the participant is reminded only of words that were missed on the preceding trial, but again recalls all the words on the list during the next trial. Training to criterion, instead of administering a fixed number of trials, provides a better quantitative assessment of learning than the traditional fixed trial list-learning paradigm.[28] Thirty minutes after reaching criterion, subjects were once again asked to recall the word list (retrieval from long-term storage). Recognition memory was assessed by asking subjects to identify the original 10 items from among a list of 20 words presented aurally. The dependent variable for both recall and recognition was the number of correct items.

The standard SRT, on which the OT-SRT is derived, has shown good test-retest reliability (internal consistency reliability range: 0.41-0.62; test-retest reliability range: 0.66-0.73).[10] The SRT also correlates highly with other measures of verbal memory, indicating good construct validity,[41] and has been shown to be sensitive in various neurological conditions.[10,29,30]

WM was assessed via the Wechsler Adult Intelligence Scale (WAIS)-III Digit Span,[42] forward and backward, scored as per the standard scoring instructions.[42] PS ability was assessed using the Salthouse Letter Comparison Test, three- and six-letter versions.[43] This measure

TABLE 2. Performance on 30-minute delayed recall and recognition testing by group[a]

Number of Items Correctly Identified	Recall Test		Recognition Test	
	PD	HC	PD	HC
7	1	0	0	0
8	3	3	1	0
9	8	10	2	2
10	15	14	24	25

[a]PD = 27; HC, n = 27; not significant.

of perceptual speed requires the examinee to determine whether two strings of letters are identical or different. In the three-letter version, letter strings that are three characters in length are presented in a printed format. Examinees are instructed to respond "same" or "different" orally, working quickly and accurately. In the six-letter version, the letter strings are six characters in length. The dependent variables were the number of items correct. Letter Comparison has been shown to be sensitive to PS deficits in aging[44] and MS.[45] The Accentuation Reading Test (Test de Acentuación de Palabras; TAP[46]), which is the Spanish version of the National Adult Reading Test (NART), was administered to estimate premorbid intelligence. The Geriatric Depression Scale[47] was also administered to assess depression.

Statistical Analysis

Shapiro-Wilk's tests were used to assess the distribution of the data. The OT-SRT numbers of trials to reach the learning criterion, recall, and recognition measures were not normally distributed. Therefore, Mann-Whitney's U tests were used to examine differences between PD and HC groups on those variables. For normally distributed variables (scores of the Letter Comparison Task and scores on WAIS-III Digit Span), one-way analysis of variance was conducted. Pearson product moment correlations were utilized to examine the relationship between learning and memory, PS, and WM.

Results

PD participants required significantly more trials to reach the learning criterion (mean rank: 33.26), as compared to the HC group (mean rank: 21.7; $U(1,52) = 209$; $Z = 2.71$; $P = 0.007$), demonstrating a medium effect size (r = 0.37). Results indicated no significant difference between groups in terms of performance on both number of words correctly recalled ($P = 0.939$) and number of words correctly recognized on the OT-SRT ($P = 0.618$; Table 2). The median number of words recalled after a 30-minute delay was 10 for both groups, and the median number of words recognized correctly was 10 for both groups. Results were similar on other measures of performance on recognition testing. Twenty-four of the twenty-seven PD participants and 25 of the 27 HC participants made no false-negative errors on recognition testing. False-positive errors were divided into semantically related and unrelated errors on the to-be-remembered list of words. Twenty-six of the twenty-seven PD participants and 25 of the 27 HCs made no semantically unrelated false-positive errors. Although all participants made more semantically related than nonsemantically related false-positive errors, performance of the two groups did not differ, with 11 of the 27 PD participants making one semantically related false-positive error and 2 of the 27 making three semantically related false-positive errors. Similarly, 10 of the 27 HCs made one semantically related false-positive error. Small effect sizes were noted for both recall (r = 0.01) and recognition (r = 0.06).

There was a significant difference between the groups on PS such that the HC groups performed at higher levels overall than the PD group on the six-letter Letter Comparison Task ($F(1,52) = 7.15$; $P < 0.05$). There was no significant difference between the groups on the three-letter Letter Comparison Task.

Although there was no significant difference between groups in terms of simple WM abilities, as observed on WAIS-III Digit Span forward, a significant difference was observed between groups on complex manipulation in WM, as noted on WAIS-III Digit Span backward ($F(1,52) = 7.76$; $P < 0.01$).

Table 3 presents intercorrelations between memory performance on the OT-SRT, PS ability on the six-letter Letter Comparison task, and Complex WM (WAIS-III Digit Span backward) by group. No significant correlations were noted between learning and memory performance and PS and WM performance in either group.

Discussion

Impaired memory functioning is common in PD, largely attributed to an inability to retrieve information from long-term storage.[8,9] To provide support for

TABLE 3. Intercorrelations between learning and memory performance and PS and WM performance by group

Variables	PD n = 27	HCs n = 27
OT-SRT trials to criterion × six-letter LC	−0.102 ns	0.241 ns
OT-SRT trials to criterion × Digits Backward	−0.123 ns	0.059 ns
OT-SRT 30-minute recall × six-letter LC	0.254 ns	0.320 ns
OT-SRT 30-minute recall × Digits Backward	0.041 ns	0.169 ns
OT-SRT recognition hits × six-letter LC	0.033 ns	−0.109 ns
OT-SRT recognition hits × Digits Backward	−0.089 ns	−0.117 ns
Six-letter LC × Digits Backward	0.600 $P < 0.001$	0.530 $P < 0.01$

LC, Letter Comparison; ns, not significant.

this conclusion, it has frequently been reported that recall performance is impaired, whereas recognition performance is intact.[16,17] However, several studies have noted deficits in recognition memory as well and have hypothesized deficits in both recall and recognition in PD patients. The current study employed a technique to directly test whether impaired verbal memory was the result of deficient learning versus impaired retrieval in PD. Consistent with Brønnick et al.,[18] we noted a clear learning impairment in non-demented patients with PD, when compared to age- and education-matched HCs. The PD group required significantly more trials to initially learn a list of words than did age- and education-matched HCs. However, after controlling for differences in acquisition of information (i.e., training to a learning criterion), performance on recall and recognition between groups did not differ. These results suggest that memory impairment in PD may not be secondary to retrieval failure, but may, in fact, be the result of an impaired ability to learn new information effectively.

Importantly, deficits in complex WM and PS were noted in the current sample. Such deficits have been shown to negatively affect the learning and memory process in other neurologically impaired populations.[45,48] However, correlational analyses conducted on the current data revealed no significant relationship between learning and memory performance, PS deficits, and complex WM deficits in the current sample. This indicates that the learning deficit observed herein could reflect a hippocampally mediated learning deficit that is potentially amenable to cognitive rehabilitation focused specifically on learning.[49] The likelihood of a hippocampally mediated learning deficit in persons with PD is consistent with the wealth of data highlighting the presence of hippocampal atrophy in persons with PD.[20]

Although the current findings may appear inconsistent with the majority of the PD literature to date, the differences in the conclusions drawn can be explained by a clear understanding of the methodological differences between the current work and the existing literature. When drawing conclusions regarding the integrity of recall and recognition abilities, it is essential that testing methodology ensures that participants effectively learn the to-be-remembered information to an equivalent degree. Without controlling for initial learning, one cannot truly conclude retrieval failure because reduced recall performance may reflect poor initial learning. Such methodology to control for initial learning has not been applied in previous learning and memory research in PD. Previous PD memory research has not controlled for the amount of information acquired during learning. Individuals with PD have been shown to learn less than healthy individuals,[18] but their deficient performance on delayed recall trials could be the result of poor initial learning or poor retrieval of information from long-term storage. In fact, when one applies methodology that controls for initial learning, as done in the current study, recall and recognition performance in individuals with PD is equivalent to that observed in an age- and education-matched healthy sample. This is consistent with work that has been done in other neurological samples, including MS[28-30] and TBI.[31] It is therefore clear that assessments of new learning and memory functioning in neurological samples, including PD, must employ techniques that allow for a complete assessment of new learning abilities. The open-trial SRT is one such measure.

The open-trial SRT allows the clinician to continue presenting learning trials until the patient meets the preestablished learning criterion; he or she can then compare the number of trials needed to reach that learning criterion to normative data.[28] Other existing memory measures do allow an assessment of learning ability. The California Verbal Learning Test,[51,52] The Hopkins Verbal Learning Test,[53] and the Memory Assessment Scales[54] all provide a measure of total learning across five learning trials that provides information as to the pace at which the patient is learning the new information. However, the open-trial SRT goes beyond these more traditional assessment techniques by providing information as to when a learning criterion is actually met (i.e., controlling for initial acquisition), allowing the clinician to determine the extent of the impairment in learning abilities. Furthermore, by providing the opportunity for patients to actually learn the new information through additional learning trials, the evaluation of recall and recognition abilities is more accurate.

It is important to consider the reasons for which the provision of additional trials is effective in enabling the PD group to demonstrate intact recall and recognition abilities. We do not believe that it is the simple addition of more learning trials (e.g., repetition) that improves recall and recognition performance, a finding supported by work in an MS sample.[55] In contrast, we believe that the additional trials provide the opportunity to improve the quality of encoding. Encoding is not defined as simply learning new information. Rather, encoding is defined as "the process of interpreting items and organizing them into memory units" (Begg and Green, 1988[56]; p. 234), implying that a deeper semantic and organizational process is applied, resulting in increased recall and recognition. Learning strategies that promote a deeper semantic encoding of the to-be-learned information promotes increased recall.[57-59] Similarly, Bellazza and Young[60] showed that it is the improved organization of the encoded material resulting that improves future recall, not simply the provision of additional learning opportunities.

The clinical significance of the findings of the current study cannot be overstated. The finding of impaired acquisition and intact retrieval in PD has significant

implications for rehabilitation and treatment of memory deficits in patients with PD. The present data suggest that interventions should focus on improving acquisition of the memory trace, rather than methods to facilitate retrieval (e.g., memory book). The results of the present study show that when information is adequately acquired, retrieval (i.e., recall and recognition) will be within normal limits.

We believe that improving efficiency during acquisition is likely key to improve subsequent recall and recognition in PD. Whereas providing additional learning trials is one method of improving memory performance in persons with PD, other strategies to improve learning have been identified as effective in other neurological populations. Such techniques include self-generated learning,[57,61] spaced learning,[58,62] and retrieval practice.[59] Future research should focus on using such methods of enhancing learning efficiency to improve memory in patients with PD. Additionally, given the executive impairments that have been documented in PD, future research examining the role of executive functioning in acquisition is clearly warranted. ■

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References

1. Muslimovic D, Post B, Speelman JD, Schmand B. Cognitive profile of patients with newly diagnosed Parkinson disease. Neurology 2005;65:1239-1245.
2. Hely MA, Reid WG, Adena MA, Halliday GM, Morris JG. The Sydney multicenter study of Parkinson's disease: the inevitability of dementia at 20 years. Mov Disord 2008;23:837-844.
3. Foltynie T, Brayne CE, Robbins TW, Barker RA. The cognitive ability of an incident cohort of Parkinson's patients in the UK. The CamPaIGN study. Brain 2004;127:550-560.
4. Aarsland D, Bronnick K, Larsen JP, Tysnes OB, Alves G. Cognitive impairment in incident, untreated Parkinson disease: the Norwegian ParkWest study. Neurology 2009;72:1121-1126.
5. Eigh E, Domellof M, Linder J, et al. Cognitive function in early Parkinson's disease: a population-based study. European Journal of Neurology 2009;16:1278-1284.
6. Owen AM, James M, Leigh PN, et al. Fronto-striatal cognitive deficits at different stages of Parkinson's disease. Brain 1992;115:1727-1751.
7. Dubois B, Pillon B. Cognitive and Behavioral Aspects of Movement Disorders. Jankovic J, Tolosa E, eds. Baltimore, MD: Lippincott, Williams & Wilkins; 1998.
8. Whittington CJ, Podd J, Kan MM. Recognition memory impairment in Parkinson's disease: power and meta-analyses. Neuropsychology 2000;14:233-246.
9. Mahurin RK, Feher EP, Nance ML, Levy JK, Pirozzolo FJ. Cognition in Parkinson's disease and related disorders. In: Parkes RW, Zec RF, Wilson RS, eds. Neuropsychology of Alzheimer's Disease and Related Disorders. New York: Oxford University Press; 1993.
10. Lezak MD, ed. Neuropsychological Assessment. New York: Oxford University Press; 1995.
11. Cooper JA, Sagar HJ, Jordan N, Harvey NS, Sullivan EV. Cognitive impairment in early, untreated Parkinson's disease and its relationship to motor disability. Brain 1991;114:2095-2122.
12. Cummings JL, Benson DF. Subcortical dementia. Review of an emerging concept. Arch Neurol 1984;41:874-879.
13. Tröster AI, Fields JA. Frontal cognitive function and memory in Parkinson's disease: Toward a distinction between prospective and declarative memory impairments? Behavioral Neurology 1995;8:59-74.
14. Higginson CI, Wheelock VL, Carroll KE, Sigvardt KA. Recognition memory in Parkinson's disease with and without dementia: evidence inconsistent with the retrieval deficit hypothesis. J Clin Exp Neuropsychol 2005;27:516-528.
15. Beatty WW, Ryder KA, Gontkovsky ST, et al. Analyzing the subcortical dementia syndrome of Parkinson's disease using the RBANS. Arch Clin Neuropsychol 2003;18:509-520.
16. Flowers KA, Pearce I, Pearce JM. Recognition memory in Parkinson's disease. J Neurol Neurosurg Psychiatry 1984;47:1174-1181.
17. Taylor AE, Saint-Cyr JA, Lang AE. Frontal lobe dysfunction in Parkinson's disease. The cortical focus of neostriatal outflow. Brain 1986;109:845-883.
18. Brønnick K, Alves G, Aarsland D, Tysnes OB, Larsen JP. Verbal memory in drug-naive, newly diagnosed Parkinson's disease. The retrieval deficit hypothesis revisited. Neuropsychology 2011;25:114-124.
19. Owen AM. Cognitive dysfunction in Parkinson's disease: the role of frontostriatal circuitry. Neuroscientist 2004;10:525-537.
20. Ibarretxe-Bilbao N, Tolosa E, Junque C, Marti MJ. MRI and cognitive impairment in Parkinson's disease. Mov Disord 2009;24(Suppl 2):S748-S753.
21. Camicioli R, Moore MM, Kinney A, et al. Parkinson's disease is associated with hippocampal atrophy. Mov Disord 2003;18:784-790.
22. Junque C, Ramirez-Ruiz B, Tolosa E, et al. Amygdalar and hippocampal MRI volumetric reductions in Parkinson's disease with dementia. Mov Disord 2005;20:540-544.
23. Bouchard TP, Malykhin N, Martin WR, et al. Age and dementia-associated atrophy predominates in the hippocampal head and amygdala in Parkinson's disease. Neurobiol Aging 2008;29:1027-1039.
24. Bruck A, Kurki T, Kaasinen V, Vahlberg T, Rinne JO. Hippocampal and prefrontal atrophy in patients with early non-demented Parkinson's disease is related to cognitive impairment. J Neurol Neurosurg Psychiatry 2004;75:1467-1469.
25. Jokinen P, Bruck A, Aalto S, et al. Impaired cognitive performance in Parkinson's disease is related to caudate dopaminergic hypofunction and hippocampal atrophy. Parkinsonism Relat Disord 2009;15:88-93.
26. Tam CW, Burton EJ, McKeith IG, Burn DJ, O'Brien JT. Temporal lobe atrophy on MRI in Parkinson disease with dementia: a comparison with Alzheimer disease and dementia with Lewy bodies. Neurology 2005;64:861-865.
27. Ibarretxe-Bilbao N, Junque C, Marti MJ, Tolosa E. Brain structural MRI correlates of cognitive dysfunctions in Parkinson's disease. J Neurol Sci 2011;310:70-74.
28. Chiaravalloti ND, Balzano J, Moore NB, DeLuca J. The Open-Trial Selective Reminding Test (OT-SRT) as a tool for the assessment of learning and memory. Clin Neuropsychol 2009;23:231-254.
29. DeLuca J, Barbieri-Berger S, Johnson SK. The nature of memory impairments in multiple sclerosis: acquisition versus retrieval. J Clin Exp Neuropsychol 1994;16:183-189.
30. DeLuca J, Gaudino EA, Diamond BJ, Christodoulou C, Engel RA. Acquisition and storage deficits in multiple sclerosis. J Clin Exp Neuropsychol 1998;20:376-390.
31. DeLuca J, Schultheis MT, Madigan NK, Christodoulou C, Averill A. Acquisition versus retrieval deficits in traumatic brain injury: implications for memory rehabilitation. Arch Phys Med Rehabil 2000;81:1327-1333.
32. Genova HM, Deluca J, Chiaravalloti N, Wylie G. The relationship between executive functioning, processing speed, and white matter integrity in multiple sclerosis. J Clin Exp Neuropsychol 2013;35:631-641.
33. Ojeda N, Pena J, Schretlen DJ, et al. Hierarchical structure of the cognitive processes in schizophrenia: the fundamental role of processing speed. Schizophr Res 2012;135:72-78.
34. Liozidou A, Potagas C, Papageorgiou SG, Zalonis I. The role of working memory and information processing speed on Wisconsin Card Sorting Test performance in Parkinson disease without dementia. J Geriatr Psychiatry Neurol 2012;25:215-221.

35. Daniel SE, Lees AJ. Parkinson's Disease Society Brain Bank, London: overview and research. J Neural Transm Suppl 1993;39: 165-172.

36. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Washington, DC: American Psychiatric Association; 2000.

37. Emre M, Aarsland D, Brown R, et al. Clinical diagnostic criteria for dementia associated with Parkinson's disease. Mov Disord 2007;22:1689-1707; quiz, 1837.

38. Dubois B, Burn D, Goetz C, et al. Diagnostic procedures for Parkinson's disease dementia: recommendations from the movement disorder society task force. Mov Disord 2007;22:2314-2324.

39. van Hooren SA, Valentijn AM, Bosma H, et al. Cognitive functioning in healthy older adults aged 64-81: a cohort study into the effects of age, sex, and education. Neuropsychol Dev Cogn B Aging Neuropsychol Cogn 2007;14:40-54.

40. Buschke H. Selective reminding for analysis of memory and learning. J Verb Learn Verb Behav 1973;12:543-550.

41. Larrabee GJ, Levin HS. Memory self-ratings and objective test performance in a normal elderly sample. J Clin Exp Neuropsychol 1986;8:275-284.

42. Wechsler D. Wechsler Memory Scale—third edition. San Antonio, TX: The Psychological Corporation; 1997.

43. Salthouse TA, Babcock RL. Decomposing adult age differences in working memory. Dev Psychol 1991;27:763-776.

44. Salthouse TA. The processing-speed theory of adult age differences in cognition. Psychol Rev 1996;103:403-428.

45. Chiaravalloti ND, Stojanovic-Radic J, DeLuca J. The role of speed versus working memory in predicting learning new information in multiple sclerosis. J Clin Exp Neuropsychol 2013;35:180-191.

46. Gonzalez M. Creación y validación de un test de lectura para el diagnóstico del deterioro mental en el anciano. Madrid: Universidad Complutense de Madrid; 1991.

47. Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression rating scale: a preliminary report. J Psych Res 1982-1983;17:37-49.

48. DeLuca J, Chelune GJ, Tulsky DS, Lengenfelder J, Chiaravalloti ND. Is speed of processing or working memory the primary information processing deficit in multiple sclerosis? J Clin Exp Neuropsychol 2004;26:550-562.

49. Chiaravalloti N, Moore NB, Nikelshpur OM, DeLuca D. An RCT to treat learning impairment in MS. Neurology 2013;81:2066-2072.

50. Gaudino EA, Chiaravalloti ND, DeLuca J, Diamond BJ. A comparison of memory performance in relapsing-remitting, primary progressive and secondary progressive, multiple sclerosis. Neuropsychiatry Neuropsychol Behav Neurol 2001;14:32-44.

51. Delis D, Kramer JH, Kaplan E, Ober BA, eds. California Verbal Learning Test: Adult Version. San Antonio, TX: The Psychological Corporation; 1987.

52. Delis DC, Kramer JH, Kaplan E, Ober BA. California Verbal Learning Test—Second Edition. San Antonio, TX: Psychological Corporation; 2000.

53. Brandt J. The Hopkins Verbal Learning Test: development of a new memory test with six equivalent forms. Clin Neuropsychol 1991;5:125 -142.

54. Williams JM. Cognitive Behavior Rating Scale. New York: Psychological Assessment Resources; 1991.

55. Chiaravalloti ND, Demaree H, Gaudino EA, DeLuca J. Can the repetition effect maximize learning in multiple sclerosis? Clin Rehabil 2003;17:58-68.

56. Begg I, Green C. Repetition and trace interaction: superadditivity. Mem Cognit 1988;16:232-242.

57. Chiaravalloti ND, Deluca J. Self-generation as a means of maximizing learning in multiple sclerosis: an application of the generation effect. Arch Phys Med Rehabil 2002;83:1070-1079.

58. Goverover Y, Hillary FG, Chiaravalloti N, Arango-Lasprilla JC, DeLuca J. A functional application of the spacing effect to improve learning and memory in persons with multiple sclerosis. J Clin Exp Neuropsychol 2009;31:513-522.

59. Sumowski JF, Chiaravalloti N, Deluca J. Retrieval practice improves memory in multiple sclerosis: clinical application of the testing effect. Neuropsychology 2010;24:267-272.

60. Bellaza FS, Young DR. Chunking of repeated events in memory. J Exp Psychol Learn Mem Cogn 1989;15:990-997.

61. Lengenfelder J, Chiaravalloti ND, DeLuca J. The efficacy of the generation effect in improving new learning in persons with traumatic brain injury. Rehabil Psychol 2007;52:290-296.

62. Goverover Y, Arango-Lasprilla JC, Hillary FG, Chiaravalloti N, Deluca J. Application of the spacing effect to improve learning and memory for functional tasks in traumatic brain injury: a pilot study. Am J Occup Ther 2009;63:543-548.