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Cognitive Challenges and What to Do About Them

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Disclosures

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Cognitive Challenges

Subtle Cognitive Changes Can Be Present at Disease Onset

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ARTICLES

Cognitive impairment in incident, untreated Parkinson disease

The Norwegian ParkWest Study

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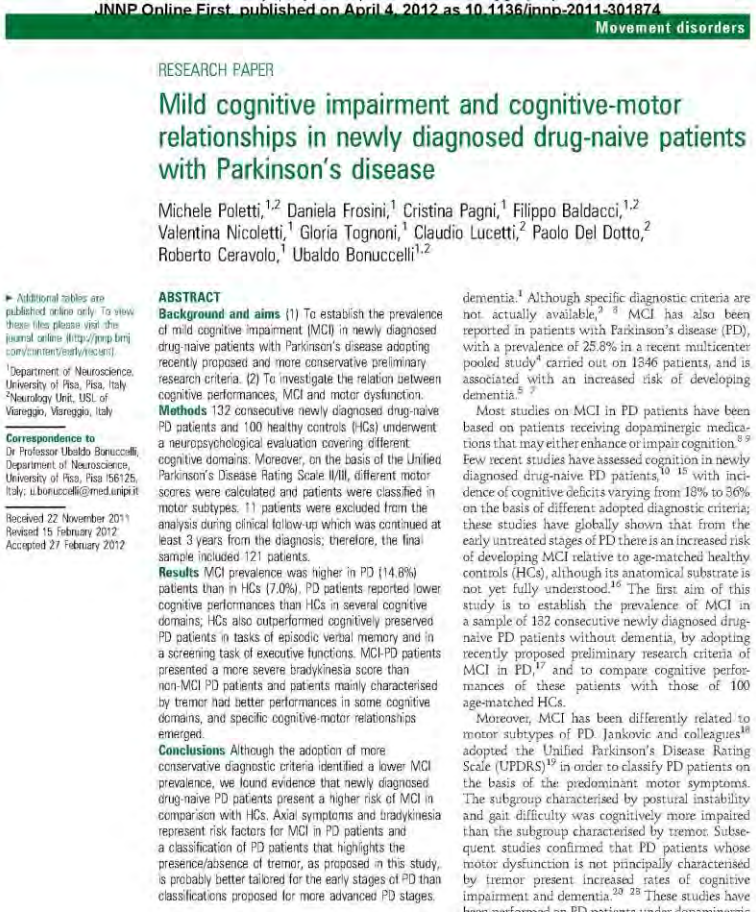
ABSTRACT

Background: Little is known regarding the cognitive impairment in subjects with early, drug-naive Parkinson disease (PD). The aim of this study was to explore the proportion with mild cognitive impairment (MCI) and subtypes in an incidence cohort of untreated PD in Southern and Western Norway.

Methods: A total of 196 non-demented, drug-naive patients who were recruited after an extensive search of all new cases of PD in the area and 201 healthy control subjects completed a battery of neuropsychological tests of verbal memory, visuospatial, and attentional-executive functioning. Subjects were classified as MCI if the age- and education-corrected z-score was falling 1.5 standard deviations below the mean for at least one of the cognitive domains.

Results: The PD group was more impaired on all neuropsychological tests than controls, but the effect sizes were small. The largest effect size was found for verbal memory. A total of 18.9% of the patients with PD were classified as MCI, with a relative risk of 2.1 (1.2-3.6) in PD compared to the control group. Patients with PD with and without MCI did not differ significantly regarding demographic and motor features. Among PD-MCI patients, nearly two-thirds had a non-amnestic MCI subtype, and one third had an amnestic MCI subtype.

Conclusions: The findings demonstrate a twofold increase in the proportion with cognitive impairment in subjects with early, untreated Parkinson disease (PD) compared to controls. This has implications for diagnosis and management of PD. **Neurology® 2009;72:1121-1126**



JNNP Online First, published on April 4, 2012 as 10.1136/jnnp-2011-301874

Movement disorders

RESEARCH PAPER

Mild cognitive impairment and cognitive-motor relationships in newly diagnosed drug-naive patients with Parkinson's disease

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► Additional tables are published online only. To view these files please visit the journal online (http://jnnp.bmj.com/content/early/recent).

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ABSTRACT

Background and aims (1) To establish the prevalence of mild cognitive impairment (MCI) in newly diagnosed drug-naive patients with Parkinson's disease adopting recently proposed and more conservative preliminary research criteria. (2) To investigate the relation between cognitive performances, MCI and motor dysfunction.

Methods 132 consecutive newly diagnosed drug-naive PD patients and 100 healthy controls (HCs) underwent a neuropsychological evaluation covering different cognitive domains. Moreover, on the basis of the Unified Parkinson's Disease Rating Scale II/III, different motor scores were calculated and patients were classified in motor subtypes. 11 patients were excluded from the analysis during clinical follow-up which was continued at least 3 years from the diagnosis; therefore, the final sample included 121 patients.

Results MCI prevalence was higher in PD (14.8%) patients than in HCs (7.0%). PD patients reported lower cognitive performances than HCs in several cognitive domains; HCs also outperformed cognitively preserved PD patients in tasks of episodic verbal memory and in a screening task of executive functions. MCI-PD patients presented a more severe bradykinesia score than non-MCI PD patients and patients mainly characterised by tremor had better performances in some cognitive domains, and specific cognitive-motor relationships emerged.

Conclusions Although the adoption of more conservative diagnostic criteria identified a lower MCI prevalence, we found evidence that newly diagnosed drug-naive PD patients present a higher risk of MCI in comparison with HCs. Axial symptoms and bradykinesia represent risk factors for MCI in PD patients and a classification of PD patients that highlights the presence/absence of tremor, as proposed in this study, is probably better tailored for the early stages of PD than classifications proposed for more advanced PD stages.

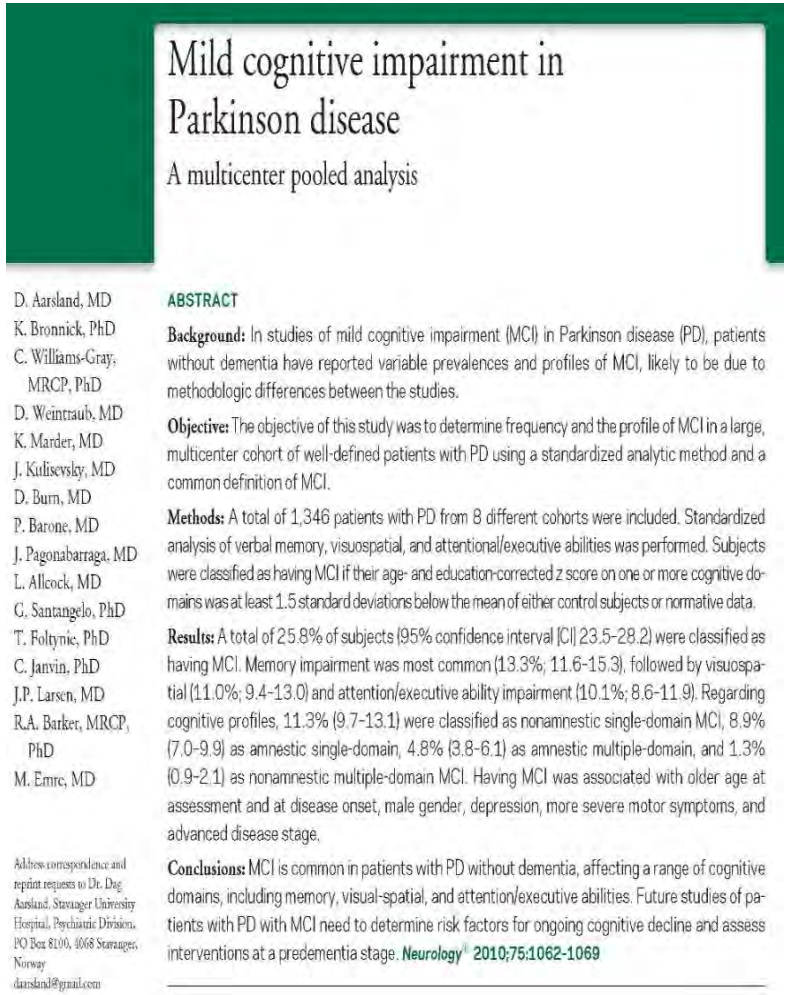
dementia.[1] Although specific diagnostic criteria are not actually available,[2 3] MCI has also been reported in patients with Parkinson's disease (PD), with a prevalence of 25.8% in a recent multicenter pooled study[4] carried out on 1846 patients, and is associated with an increased risk of developing dementia.[5 7]

Most studies on MCI in PD patients have been based on patients receiving dopaminergic medications that may either enhance or impair cognition.[8 9] Few recent studies have assessed cognition in newly diagnosed drug-naive PD patients,[10 15] with incidence of cognitive deficits varying from 18% to 36% on the basis of different adopted diagnostic criteria; these studies have globally shown that from the early untreated stages of PD there is an increased risk of developing MCI relative to age-matched healthy controls (HCs), although its anatomical substrate is not yet fully understood.[16] The first aim of this study is to establish the prevalence of MCI in a sample of 132 consecutive newly diagnosed drug-naive PD patients without dementia, by adopting recently proposed preliminary research criteria of MCI in PD,[17] and to compare cognitive performances of these patients with those of 100 age-matched HCs.

Moreover, MCI has been differently related to motor subtypes of PD. Jankovic and colleagues[18] adopted the Unified Parkinson's Disease Rating Scale (UPDRS)[19] in order to classify PD patients on the basis of the predominant motor symptoms. The subgroup characterised by postural instability and gait difficulty was cognitively more impaired than the subgroup characterised by tremor. Subsequent studies confirmed that PD patients whose motor dysfunction is not principally characterised by tremor present increased rates of cognitive impairment and dementia.[20 25] These studies have

Mild cognitive impairment (MCI) in 10-20% of *de novo* Parkinson's

Variability in Early Changes



Mild cognitive impairment in Parkinson disease

A multicenter pooled analysis

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ABSTRACT

Background: In studies of mild cognitive impairment (MCI) in Parkinson disease (PD), patients without dementia have reported variable prevalences and profiles of MCI, likely to be due to methodologic differences between the studies.

Objective: The objective of this study was to determine frequency and the profile of MCI in a large, multicenter cohort of well-defined patients with PD using a standardized analytic method and a common definition of MCI.

Methods: A total of 1,346 patients with PD from 8 different cohorts were included. Standardized analysis of verbal memory, visuospatial, and attentional/executive abilities was performed. Subjects were classified as having MCI if their age- and education-corrected z score on one or more cognitive domains was at least 1.5 standard deviations below the mean of either control subjects or normative data.

Results: A total of 25.8% of subjects (95% confidence interval [CI] 23.5–28.2) were classified as having MCI. Memory impairment was most common (13.3%; 11.6–15.3), followed by visuospatial (11.0%; 9.4–13.0) and attention/executive ability impairment (10.1%; 8.6–11.9). Regarding cognitive profiles, 11.3% (9.7–13.1) were classified as nonamnestic single-domain MCI, 8.9% (7.0–9.9) as amnestic single-domain, 4.8% (3.8–6.1) as amnestic multiple-domain, and 1.3% (0.9–2.1) as nonamnestic multiple-domain MCI. Having MCI was associated with older age at assessment and at disease onset, male gender, depression, more severe motor symptoms, and advanced disease stage.

Conclusions: MCI is common in patients with PD without dementia, affecting a range of cognitive domains, including memory, visual-spatial, and attention/executive abilities. Future studies of patients with PD with MCI need to determine risk factors for ongoing cognitive decline and assess interventions at a predementia stage. *Neurology*® 2010;75:1062–1069

Parkinson's-MCI is common (25-30%) with inter-individual variability in presentation

- **Executive abilities**
- **Attention**
- **Visuospatial skills**
- **Memory**

It Matters to Patients, Caregivers, and Providers

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Table 3 Final prioritised and ranked uncertainties for the management of Parkinson's disease

	Overarching research aspiration: an effective cure for Parkinson's disease
1	What treatments are helpful for reducing balance problems and falls in people with Parkinson's?
2	What approaches are helpful for reducing stress and anxiety in people with Parkinson's?
3	What treatments are helpful for reducing dyskinesias (involuntary movements, which are a side effect of some medications) in people with Parkinson's?
4	Is it possible to identify different types of Parkinson's, eg, tremor dominant? And can we develop treatments to address these different types?
5	What best treats dementia in people with Parkinson's?
6	What best treats mild cognitive problems such as memory loss, lack of concentration, indecision and slowed thinking in people with Parkinson's?
7	What is the best method of monitoring a person with Parkinson's response to treatments?
8	What is helpful for improving the quality of sleep in people with Parkinson's?
9	What helps improve the dexterity (fine motor skills or coordination of small muscle movements) of people with Parkinson's so they can do up buttons, use computers, phones, remote controls etc?
10	What treatments are helpful in reducing urinary problems (urgency, irritable bladder, incontinence) in people with Parkinson's?

Deane et al. *BMJ Open* 2014;4:e006434.

Patient's Perspective on "Mild" Cognitive Changes

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PERSONAL HISTORY

HAVE YOU LOST YOUR MIND?

More bad news for boomers.

BY MICHAEL KINSLEY

I knew that thinking was involved. I asked my neurologist at the time, and he answered carefully, "Well, after a few years you may lose your edge." Lose my edge? Lose my edge? Oh, shit! I need my edge. My edge is how I make a living. More than that: My edge is my claim on the world. It's why people are my friends, why they invite me over for dinner, perhaps why they marry me. What am I worth to the world if I've lost my edge?

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What to Do About Them

Recent Review Paper

RESEARCH ARTICLE

Modifiable Risk Factors for Cognitive Impairment in Parkinson's Disease: A Systematic Review and Meta-Analysis of Prospective Cohort Studies

Yu Guo, MD,[1] Wei Xu, MD, PhD,[1] Feng-Tao Liu, MD,[2] Jie-Qiong Li, MD, PhD,[1] Xi-Peng Cao, MS,[1] Lan Tan, MD, PhD,[1*] Jian Wang, MD, PhD,[2*] and Jin-Tai Yu, MD, PhD[2*]

[1]*Department of Neurology, Qingdao Municipal Hospital, Qingdao University, Qingdao, China*
[2]*Department of Neurology and Institute of Neurology, Huashan Hospital, Shanghai Medical College, Fudan University, Shanghai, China*

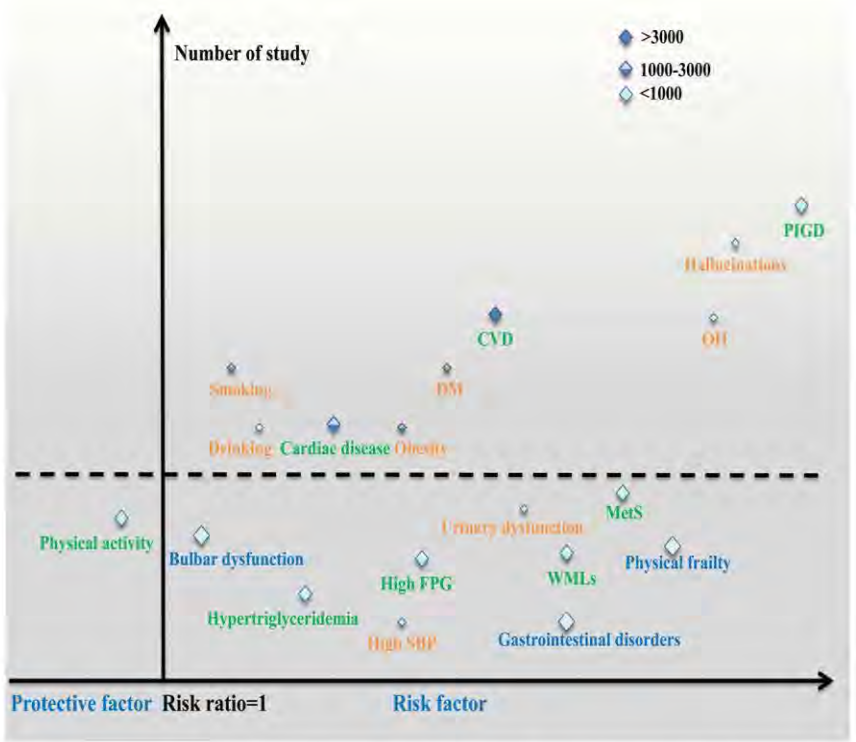

FIG. 4. Factors that show significant association with PD-CI in the systematic review. Sample sizes for factors were classified as <1000, 1000-3000 or >3000; the range of quality score was 6 to 9, the largest size of rhombus represents 6-7 points, the medium size of rhombus represents 7-8 points, and the smallest size of rhombus represents 8-9 points. (CVD, cerebrovascular disease; DM, diabetes mellitus; FPG, fasting plasma glucose; MetS, metabolic syndrome; OH, orthostatic hypotension; PD-CI, Parkinson's disease with cognitive impairment; PIGD, postural-instability-gait disorder; SBP, systolic blood pressure; WMLs, white matter lesions). [Color figure can be viewed at wileyonlinelibrary.com]

Guo et al. *Movement Disorders* 2019;34:876-883.

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Parkinson's Medications

No Differential Long-Term Cognitive Effect for Parkinson's Medications

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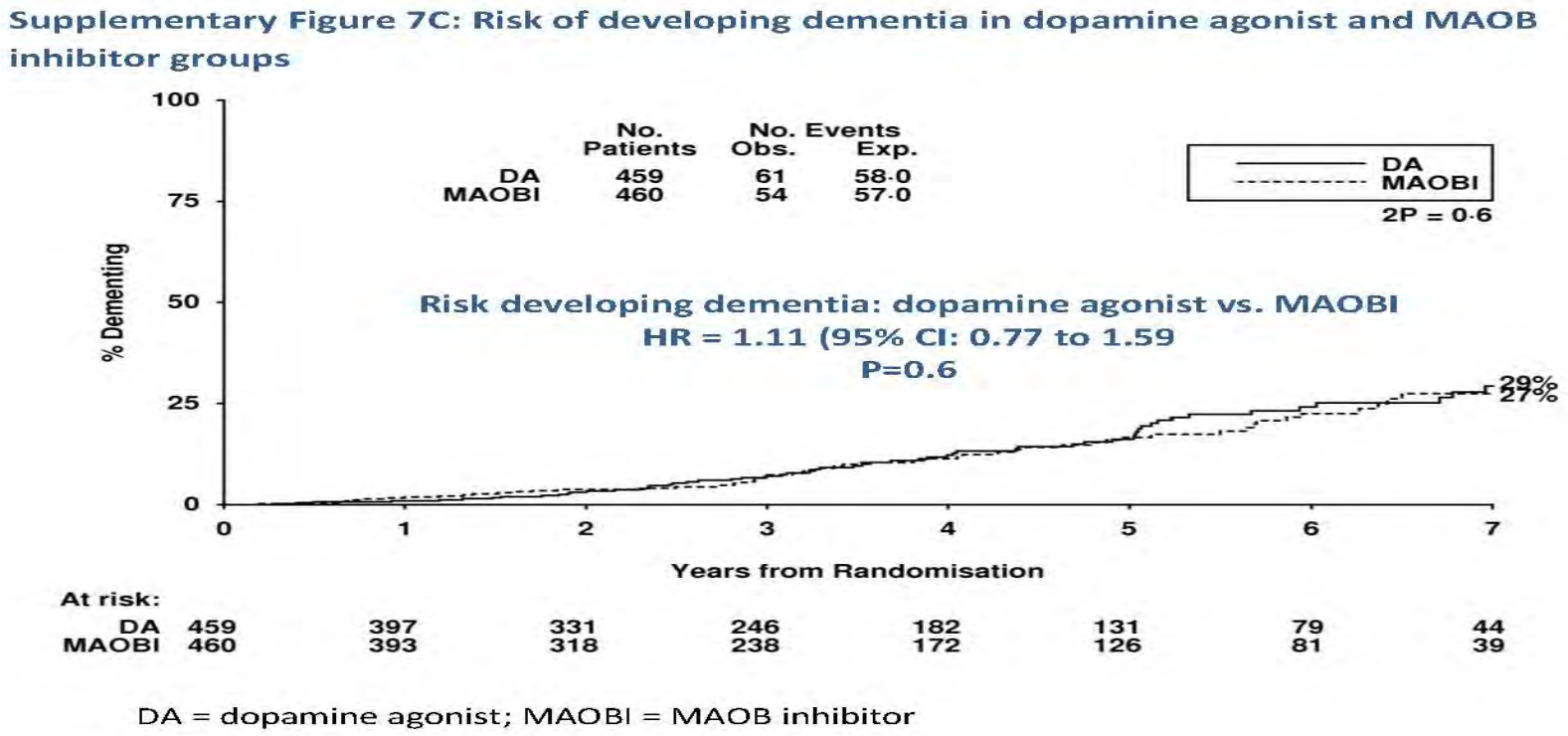

PD MED Collaborative Group. *Lancet* 2014;80:792-799.

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1. Cognitive-Enhancing Medications

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MDS COMMISSIONED REVIEW

Update on Treatments for Nonmotor Symptoms of Parkinson's Disease—An Evidence-Based Medicine Review

Klaus Seppi, MD,[1*] K. Ray Chaudhuri, MD,[2] Miguel Coelho, MD,[3] Susan H. Fox, MRCP (UK), PhD,[4]
Regina Katzenschlager, MD,[5] Santiago Perez Lloret, MD,[6] Daniel Weintraub, MD,[7,8]
Cristina Sampaio, MD, PhD,[9,10]
and the collaborators of the Parkinson's Disease Update on Non-Motor Symptoms Study Group on behalf of the Movement Disorders Society Evidence-Based Medicine Committee

Seppi et al. *Movement Disorders* 2019;34:180-198.

Recent Randomized Controlled Trials (RCTs): Large Unmet Need Still

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TABLE 5. Interventions to treat dementia and nondementia cognitive impairment in PD

Intervention				
Drug class/intervention strategy	Drug/intervention	Efficacy	Safety	Practice implications
Dementia				
Acetylcholinesterase inhibitors	**Donepezil**	Insufficient evidence	Acceptable risk without specialized monitoring[a]	*Possibly useful*[b]
	Rivastigmine	Efficacious	Acceptable risk without specialized monitoring[a]	Clinically useful
	Galantamine	Insufficient evidence	Acceptable risk without specialized monitoring[a]	*Possibly useful*[c]
N-methyl-D-aspartate (NMDA) antagonists	**Memantine**	Insufficient evidence	Acceptable risk without specialized monitoring	Investigational
Nondementia cognitive impairment				
Acetylcholinesterase inhibitors	**Rivastigmine**	*Insufficient evidence*	*Acceptable risk without specialized monitoring*[d]	*Investigational*
Monoamine oxidase B (MAO-B) inhibitors	**Rasagiline**	*Insufficient evidence*	*Acceptable risk without specialized monitoring*	*Investigational*
Nonpharmacological Interventions	**Transcranial direct-current stimulation (T-DCS)**	*Insufficient evidence*	*Insufficient evidence*	*Investigational*
	Cognitive rehabilitation	*Insufficient evidence*	*Insufficient evidence*	*Investigational*

- Only rivastigmine approved in US for Parkinson's cognitive impairment, and study completed 15 years ago now

Recent or Ongoing Trials: Dementia

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- Completed
  - SYNAPSE SYN120 (5-HT_6 antagonist) – negative for cognition (CDR), suggestion for positive effect on neuropsychiatric symptoms and function
  - DBS of nucleus basalis of Meynert (nbM) – negative for cognition (battery), suggestion for positive effect on neuropsychiatric symptoms
- Ongoing
  - LY3154207 (PRESENCE) (D1 agonist) – CDR CoA
  - Ceftriaxone (increases glutamate transporter expression) – ADAS Cog
  - Ambroxol (pharmacological chaperone for GCase) – ADAS Cog
  - Anavex 2-73 (sigma 1 receptor agonist) – CDR CoA
  - Alkahest GRF6021 (proprietary human plasma fractions) – PDD and PD-MCI - safety

Recent or Ongoing Trials: MCI

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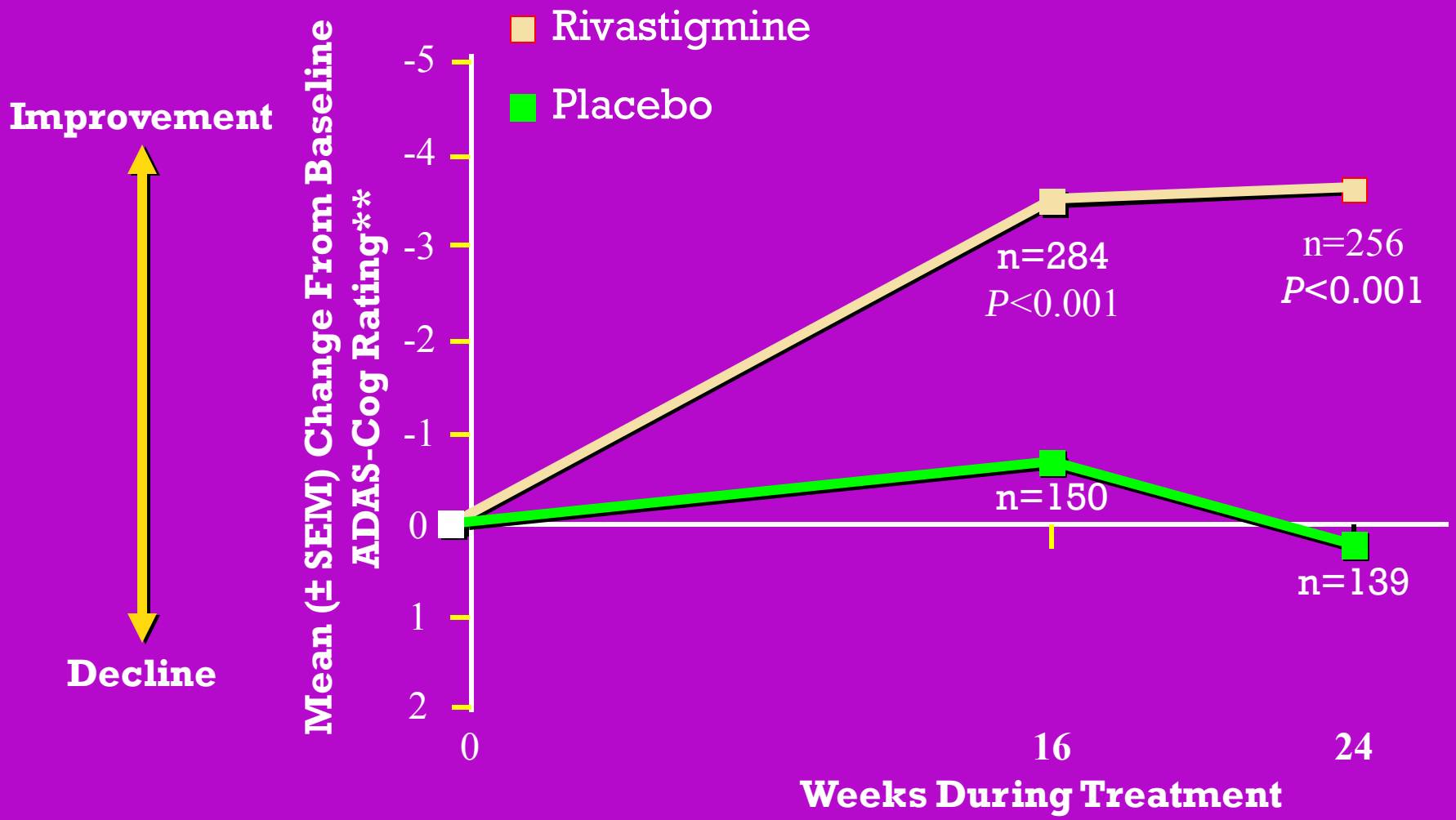
- Completed
  - Atomoxetine (selective NRI) – negative for cognition (composite cognitive outcome), improvement on subjective attention and impulsivity
- Ongoing or Planned
  - Selective α7 nicotinic receptor agonist - AZD0328 - "PD-MIND"
  - tDCS – atDCS to LDLPFC at 2 milliamps (mA) for 20 minutes daily for 5 days
  - rTMS – Each rTMS session consist of 40 trains of 5sec each at 110% of resting motor threshold and 15Hz will be provided at the left DLPFC TMS, NCT03243214
  - DBS of nbM – Activation GPi and nbM for amnestic PD-MCI
  - Exercise – skill-based exercise vs aerobic exercise vs control – for executive dysfunction PD-MCI
  - Cognitive training – Prospective implementation intentions strategies (PRIIS) + existing web-based executive function (EF) computerized cognitive training (CCT) vs. CCT alone vs. control group

Rivastigmine (Acetylcholine) for Parkinson's Dementia



Emre et al. NEJM 2004;351:2509-2518.

Possible Effect for Memantine (Glutamate)

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RESEARCH ARTICLE

International Journal of Geriatric Psychiatry

Memantine improves attention and episodic memory in Parkinson's disease dementia and dementia with Lewy bodies

Keith A. Wesnes[1,2,3], Dag Aarsland[4], Clive Ballard[5] and Elisabet Londos[6]

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Objective: In both dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD), attentional dysfunction is a core clinical feature together with disrupted episodic memory. This study evaluated the cognitive effects of memantine in DLB and PDD using automated tests of attention and episodic memory.

Methods: A randomised double-blind, placebo-controlled, 24-week three centre trial of memantine (20 mg/day) was conducted in which tests of attention (simple and choice reaction time) and word recognition (immediate and delayed) from the CDR System were administered prior to dosing and again at 12 and 24 weeks. Although other results from this study have been published, the data from the CDR System tests were not included and are presented here for the first time.

Results: Data were available for 51 patients (21 DLB and 30 PDD). In both populations, memantine produced statistically significant medium to large effect sized improvements to choice reaction time, immediate and delayed word recognition.

Conclusions: These are the first substantial improvements on cognitive tests of attention and episodic recognition memory identified with memantine in either DLB or PDD.

Key words: memantine; dementia with Lewy bodies; Parkinson's disease dementia; attention; episodic memory; CDR System; automated cognitive tests
History: Received 15 December 2013; Accepted 4 March 2014; Published online in Wiley Online Library (wileyonlinelibrary.com)
DOI: 10.1002/gps.4109

Atomoxetine (Norepinephrine) for Cognition

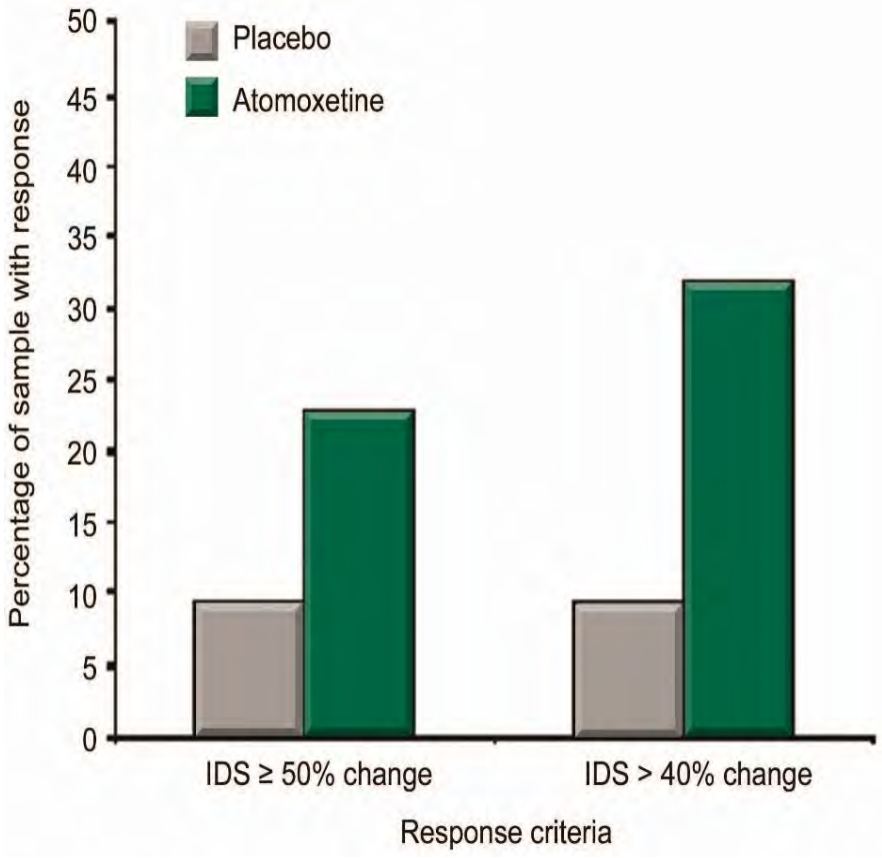

Table 2 Differences in secondary outcome measures by treatment group

	Study visit			
	Baseline	Week 2	Week 4	Week 8
Mini-Mental State Examination[3]				
Atomoxetine	28.12 (0.19)	–	–	28.92 (0.22)
Placebo	28.31 (0.19)	–	–	27.80 (0.22)
Effect (mean group difference in change since baseline, p value)	–	–	–	1.31 (0.41) $p = 0.003$
Epworth Sleepiness Scale[3]				
Atomoxetine	11.69 (0.38)	–	–	9.78 (0.43)
Placebo	11.73 (0.39)	–	–	12.72 (0.45)
Effect (mean group difference in change since baseline, p value)	–	–	–	−2.90 (0.83) $p = 0.001$
State Anxiety[3]				
Atomoxetine	56.08 (1.37)	47.17 (1.44)	47.93 (1.44)	48.00 (1.56)
Placebo	56.23 (1.45)	50.13 (1.48)	52.45 (1.57)	52.84 (1.60)
Effect (mean group difference in change since baseline, p value)	–	−2.81 (2.48) $p = 0.26$	−4.37 (2.54) $p = 0.09$	−4.69 (2.62) $p = 0.08$
Apathy Scale[3]				
Atomoxetine	17.77 (0.56)	–	–	16.86 (0.63)
Placebo	17.42 (0.59)	–	–	17.32 (0.66)
Effect (mean group difference in change since baseline, p value)	–	–	–	−1.80 (1.22) $p = 0.14$
UPDRS part III score[3]				
Atomoxetine	22.16 (0.87)	–	21.09 (0.94)	21.36 (0.98)
Placebo	22.01 (0.90)	–	21.03 (0.98)	20.94 (1.02)
Effect (mean group difference in change since baseline, p value)	–	–	−0.08 (1.65) $p = 0.96$	0.28 (1.70) $p = 0.87$

Weintraub et al. *Neurology* 2010;75:448-455.

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2. Other Cognitive-Enhancing Treatments

Cognitive Training

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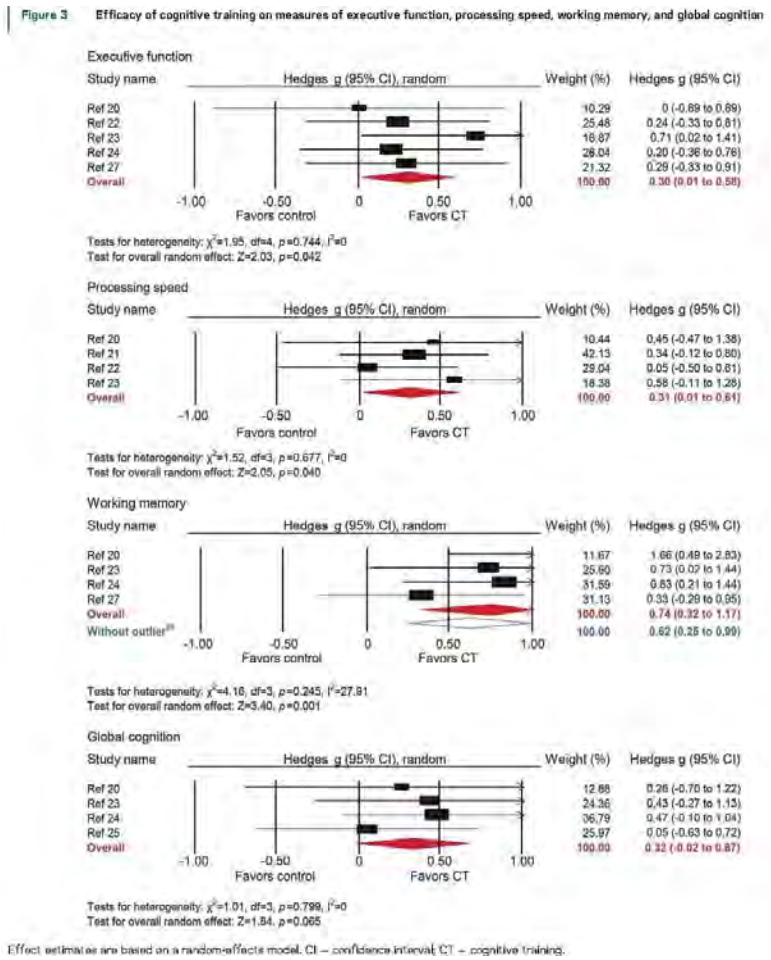

Leung et al. *Neurology* 2015;85:1–9.

Physical Exercise

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Phase I/II randomized trial of aerobic exercise in Parkinson disease in a community setting

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ABSTRACT

Objectives: To (1) investigate effects of aerobic walking on motor function, cognition, and quality of life in Parkinson disease (PD), and (2) compare safety, tolerability, and fitness benefits of different forms of exercise intervention: continuous/moderate intensity vs interval/alternating between low and vigorous intensity, and individual/neighborhood vs group/facility setting.

Methods: Initial design was a 6-month, 2 × 2 randomized trial of different exercise regimens in independently ambulatory patients with PD. All arms were required to exercise 3 times per week, 45 minutes per session.

Results: Randomization to group/facility setting was not feasible because of logistical factors. Over the first 2 years, we randomized 43 participants to continuous or interval training. Because preliminary analyses suggested higher musculoskeletal adverse events in the interval group and lack of difference between training methods in improving fitness, the next 17 participants were allocated only to continuous training. Eighty-one percent of 60 participants completed the study with a mean attendance of 83.3% (95% confidence interval: 77.5%–89.0%), exercising at 46.8% (44.0%–49.7%) of their heart rate reserve. There were no serious adverse events. Across all completers, we observed improvements in maximum oxygen consumption, gait speed, Unified Parkinson's Disease Rating Scale sections I and III scores (particularly axial functions and rigidity), fatigue, depression, quality of life (e.g., psychological outlook), and flanker task scores ($p < 0.05$ to $p < 0.001$). Increase in maximum oxygen consumption correlated with improvements on the flanker task and quality of life ($p < 0.05$).

Conclusions: Our preliminary study suggests that aerobic walking in a community setting is safe, well tolerated, and improves aerobic fitness, motor function, fatigue, mood, executive control, and quality of life in mild to moderate PD.

Classification of evidence: This study provides Class IV evidence that in patients with PD, an aerobic exercise program improves aerobic fitness, motor function, fatigue, mood, and cognition.

Neurology® 2014;83:413–425

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3. Manage Medical Disorders

Vascular Disorders Contribute to Cognitive Impairment

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- Obesity
- Smoking
- Diabetes
- Hypertension
- Hyperlipidemia

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4. Minimize Harmful Medications

Minimize Anticholinergic Medications

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Use of d
cognitio
Uwe Ehrt,[1] K

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udy
nd[1,6]

eTable 2. Medications Used in Calculating the Total Anticholinergic Burden Score in the Included ADNI and IMAS Samples**

Generic Name	Brand Name	ACB Score
Alprazolam	Xanax	1
Atenolol	Tenormin	1
Atropine	Sal-Tropine	3
Buproprion	Wellbutrin, Zyban	1
Cetirizine	Zyrtec	1
Chlorpheniramine	Chlor-Trimeton, Chlor-Tab, Aller-Chlor	3
Chlorthalidone	Diuril, Hygroton, Thialitone	1
Codeine	Vicodin, Contin, others	1
Cyproheptadine	Periactin, Peritol	2
Darifenacin	Enablex	3
Dexchlorpheniramine	Polaramine	3
Diazepam	Valium	1
Dicyclomine	Bentyl	3
Digoxin	Lanoxin, Digitek	1
Dimenhydrinate	Dramamine, Gravol, others	3
Diphenhydramine	Benadryl, Sominex, Diphenhist, Wal-Dryl, Hydramine, Tylenol PM, Advil PM, Aleve PM, others	3
Doxepin	Silenor, Zonalon, Prudoxin	3
Furosemide	Lasix	1
Hydrocortisone	Cortef, Cortaid	1
Hyoscyamine	Anaspaz, Levsin	3
Isosorbide	Isordil, Ismo	1
Levocetirizine	Xyzal	1
Loperamide	Immodium	1
Meclizine/Buclizine	Antivert, Bonine, Verticalm	3
Methocarbamol	Robaxin	3
Metoprolol	Lopressor, Toprol	1
Nifedipine	Procardia, Adalat	1
Nortriptyline	Pamelor, Aventyl	3
Oxybutynin	Ditropan, Lyrinel, Novitropan	3
Paroxetine	Paxil	3
Prednisone	Deltasone, Sterapred	1
Ranitidine	Zantac, Deprizine	1
Solifenacin	Vesicare	3
Theophylline	Theodur, Uniphyl, Theolair, Slo-bid	1
Timolol maleate	Timoptic, Betimol	1
Tolterodine	Detrol, Detrusitol	3
Trazodone	Desyrel, Oleptro	1
Triamterene	Dyrenium	1
Trospium	Spasmex, Sanctura	3
Venlafaxine	Effexor	1
Warfarin	Coumadin	1

**Medications listed in the anticholinergic burden list (http://www.agingbraincare.org/uploads/products/ACB_scale_-_legal_size.pdf; http://www.bmedreport.com/wp-content/uploads/2011/06/Drugs-on-the-Anticholinergic-Burden-ACB-scale.jpg).

Ehrt et al. *JNNP* 2010;81:160-165.

Limit Narcotic and Benzodiazepine Medication Use

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- Benzodiazepines can be associated with (1) sedation, (2) gait/balance impairment and (3) cognitive changes
- Opioid epidemic in U.S. currently
  - Also non-narcotics like tramadol
- Also, effects of medical or recreational marijuana on cognition unclear but of some concern

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5. Treat Common Parkinson's Non-Motor Symptoms

Numerous Psychiatric Symptoms

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- Psychosis
  - Lowering Parkinson's medications, use of antipsychotics
- Depression
  - Multiple antidepressants with benefit in Parkinson's
- Anxiety
  - Antidepressant first line, then benzodiazepines
- Apathy
  - Stimulants used clinically, bupropion too

Poor Sleep Is Bad for the Brain

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Actigraphically-defined sleep disturbance in Parkinson's disease is associated with differential aspects of cognitive functioning

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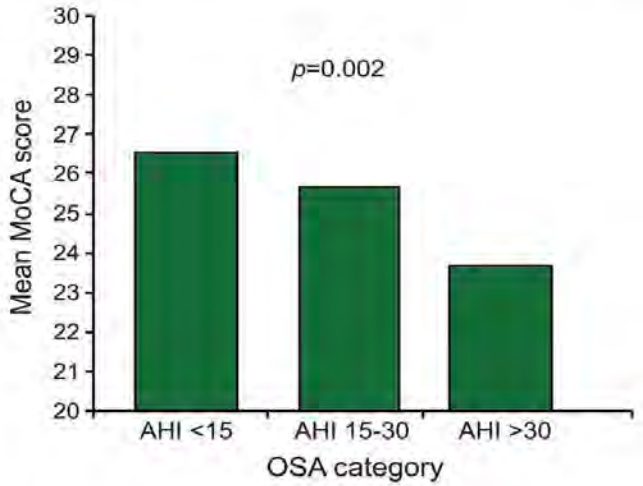
ABSTRACT

The frequency of sleep disturbance and cognitive impairment in Parkinson's disease has led to the suggestion that these processes might share common neural circuitry. This study aimed to identify the relationships between measures of cognitive functioning and an objective measure of sleep disturbance. Ninety-five patients with idiopathic Parkinson's disease and 48 healthy controls underwent neurological and neuropsychological examination. They wore an actigraphy watch for 2 weeks, from which a measure of nocturnal sleep efficiency was calculated. Multiple regression models showed that working memory and verbal memory consolidation were significantly associated with sleep efficiency, as well as education and age. By contrast, verbal fluency and attentional set-shifting were not associated with sleep efficiency, after accounting for age and education. These findings reveal that nocturnal sleep disturbance in Parkinson's disease is associated with specific cognitive difficulties, rather than a global pattern of cognitive dysfunction. This may in part reflect common neural underpinnings.

Figure Mean Montreal Cognitive Assessment (MoCA) score by apnea-hypopnea index (AHI) category



Relationship between MoCA scores and obstructive sleep apnea (OSA) severity. AHI <15: AHI <15 respiratory events per hour of sleep; AHI 15–30: AHI between 15 and 30 respiratory events per hour of sleep; AHI >30: AHI >30 respiratory events per hour of sleep.

Mery et al. *Neurology* 2017;88:1-9.
Gunn et al. *J of Clin Neuroscience* 2014;21:1112-1115.

Orthostatic Hypotension Affects Cognition

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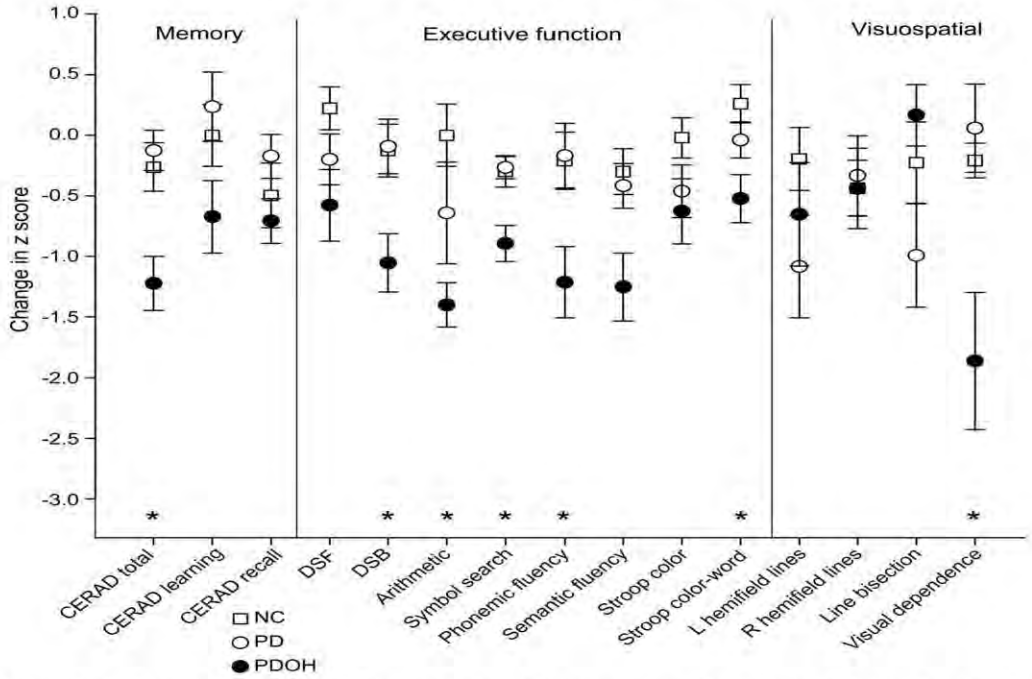
Figure Cognitive performance reflected as group-specific (normal control [NC], Parkinson disease [PD], Parkinson disease with orthostatic hypotension [PDOH]) change from baseline following tilt



Prior to analysis of change, all raw scores on cognitive measures were converted to group-specific *z* scores, where the mean and SD in the supine position of each specific group (NC, PD, PDOH) were used to determine relative within-group performance while under upright tilt. Values reported are for within-group *z* score change for each measure. Error bars represent standard error. *NC vs PDOH, $p < 0.01$.

Centi et al. *Neurology* 2017;88:17-24.

Conclusion: Action Steps

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- Ask to be screened for cognitive abilities routinely
- Use cognitive-enhancing medications when indicated
- Engage in cognitive and physical exercise (as tolerated)
- Treat vascular and other medical risk factors
- Minimize anticholinergic, narcotic and benzodiazepine medication use, and be wary of marijuana use
- Treat psychiatric, sleep and other key non-motor symptoms
- Be involved in clinical research, and partner involvement is key too