Cognitive-Motor Interference in Persons with Parkinson Disease

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Learning Objectives

At the end of this session the participant will be able to:

- Discuss the cognitive and motor deficits seen in Parkinson disease (PD)
- Understand the impact of cognitive and motor deficits in PD on daily activities
- Discuss the basis for cognitive-motor interaction and the possible rationale

Outline

- Parkinson disease: Background
- Changes in Cognition
- Cognitive-Motor Interaction - Theoretical Frameworks
- Evidence of Cognitive-Motor Interference
- Rehabilitation for CMI

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Parkinson disease

- 1 to 1.5 million in U.S.
- 6 to 10 million globally
- 60,000 new cases diagnosed each year in U.S.
- Dopaminergic depletion in basal ganglia, disrupts internal balance in basal ganglia activity (Obeso 2008)
  - Clumps of α-synuclein protein, Lewy bodies
- Affects motor and non-motor systems

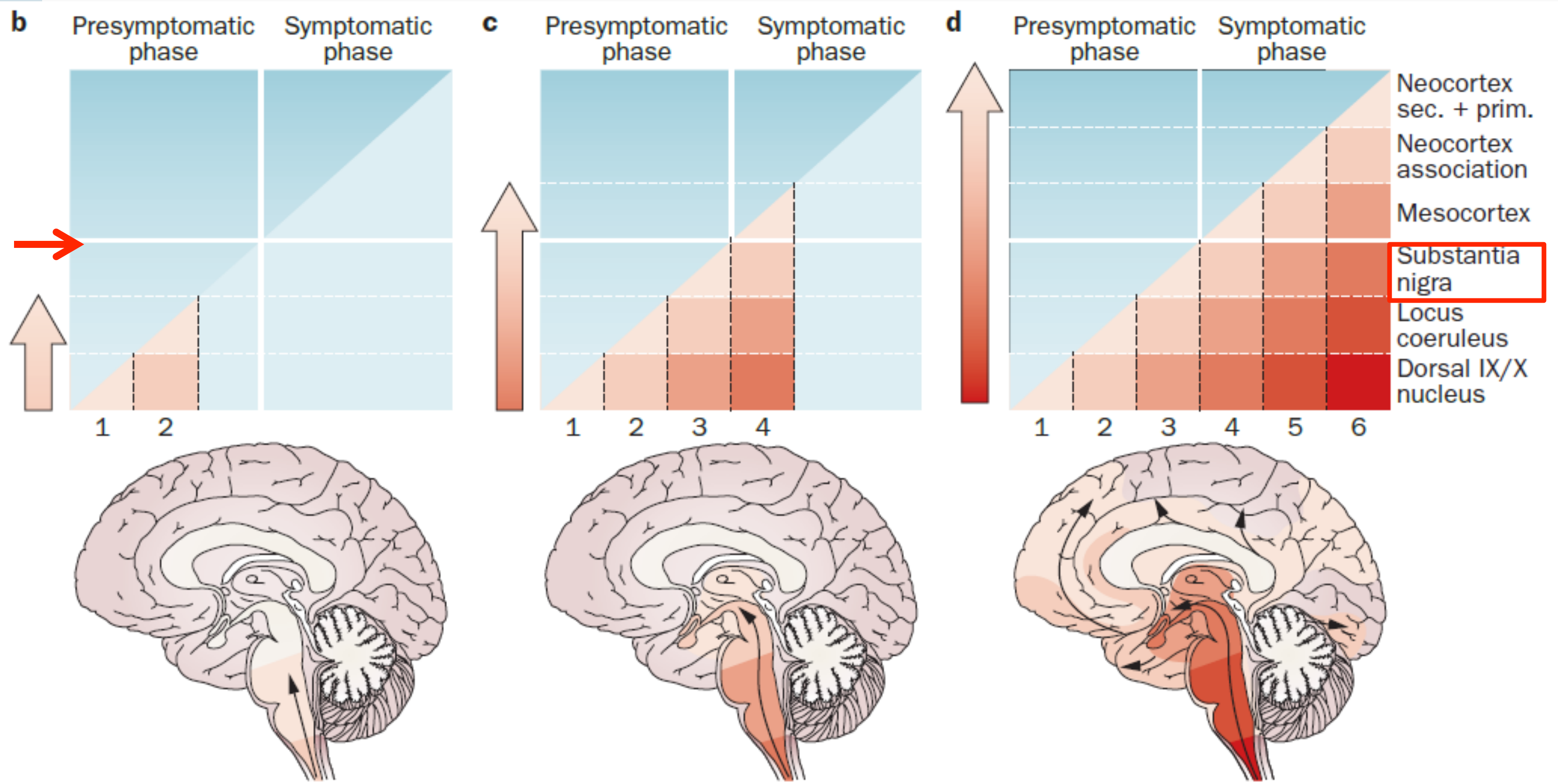
Cardinal motor signs of PD

- **T**remor, rest & postural
  - slow frequency (4-6 Hz), supination/pronation
- **R**igidity
- **A**kinesia (lack of) / Bradykinesia (slowed) / Hypokinesia (small)
- **P**ostural instability
  - retropulsion
  - festination of steps (also speech & thought)
  - freezing of gait (FoG)

Langston 2006, *Annals of Neurology*

Braak's 6 Stages of Pathology in PD

onset up to 10-15 years before symptoms appear



Goedert et al. 2013, *Nature Reviews Neurology*

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Executive Dysfunction in PD

1. Internal control of attention & action is impaired (Brown & Marsden 1988; Jahanshahi 1995)
2. Self-directed formation of strategies is impaired (Taylor 1986)
3. Set shifting is impaired with dysregulation of top-down and bottom-up attention control (Taylor & Saint-Cyr 1995; Cools 2001, 2009)
4. Planning is impaired with decreased activation of PFC and striatum (Lewis 2003)

Dirnberger and Jahanshahi, *J Neuropsychol*, 2013. 7(2):193-224.

Executive Dysfunction in PD

5. Inhibitory control & conflict resolution are impaired, not helped with medication
   – Esp. with more complex tasks, generalized across cog and motor domains (Obeso et al 2011)
6. Dual task performance is impaired in motor and cognitive domains (Benecke 1986; Brown 1991,1993,1998)
   – 12% of variance in CMI on walking speed explained by reduced EF (Brixton test) (Rochester 2008)

Dirnberger and Jahanshahi, *J Neuropsychol,* 2013. 7(2):193-224.

Executive Dysfunction in PD

- 18-36% of newly diagnosed PwPD have cognitive impairment (Aarsland 2009; Foltynie 2004)
- Prevalence of Mild Cognitive Impairment (MCI) in nondemented PD is 27% (Litvan 2011, 2012)
- Majority of these (~60%) progress to PD with dementia (PDD) over 4 years, compared with 20% of PD with normal cognition (Williams-Gray 2007)
- PD-MCI predicts development of dementia, which can occur in up to 80% in PwPD over the long term (Aarsland 1996, 2003)

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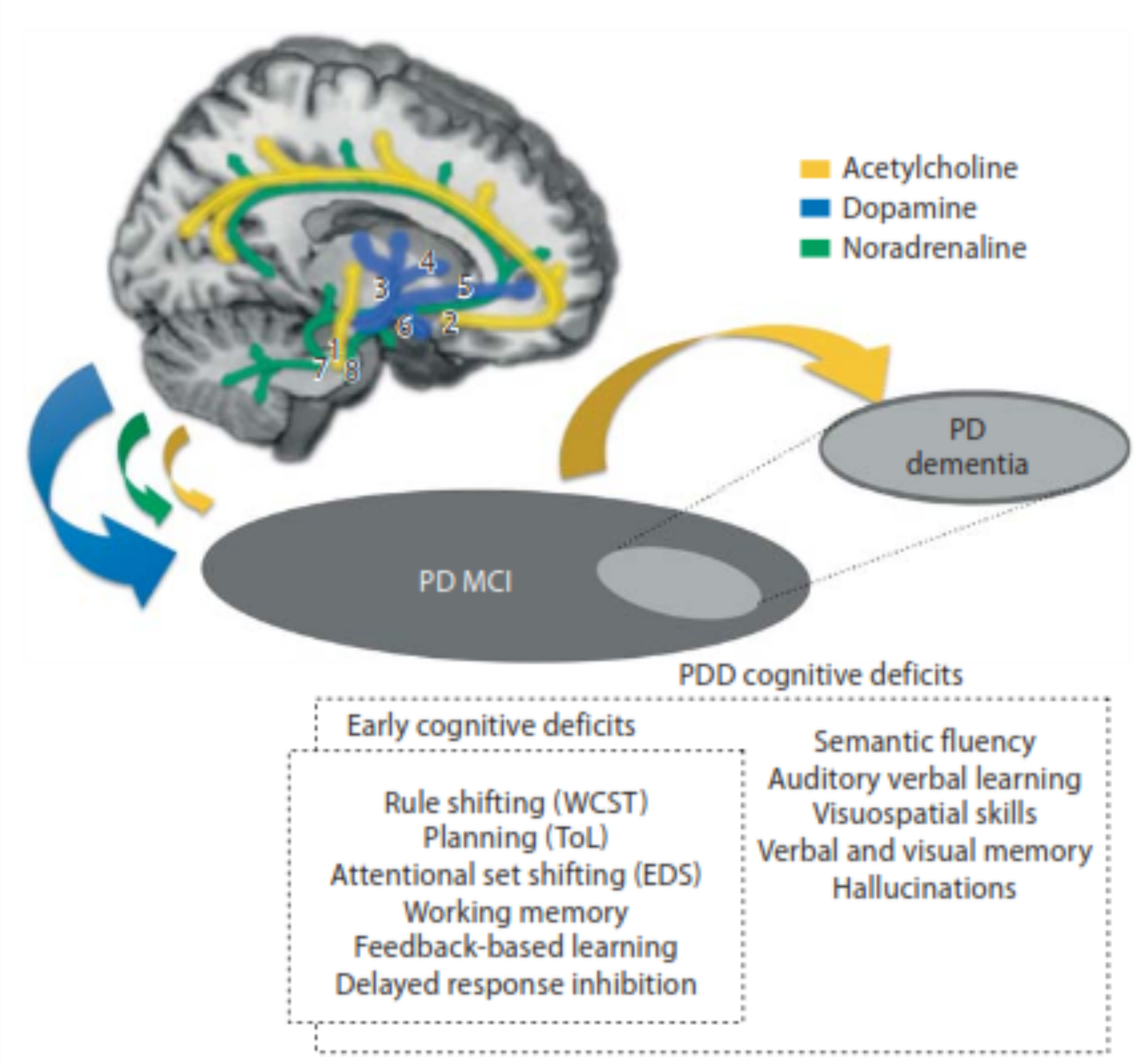
Dual Syndrome Hypothesis



Kehagia et al. *Neurodegener Dis,* 2013. 11(2):79-92.

Hypothesis differentiates between 2 Broad Syndromes

1. PD-MCI
   - Tremor-dominant phenotype
   - Fronto-striatal dysfunction
     - Impaired tests of planning, working memory and executive function
     - Respond to dopaminergic dosing but also overdosing effects
2. PD-D
   - Postural Instability/Gait Difficulty (PIGD) phenotype
   - Posterior cortical and temporal lobe dysfunction
     - Early deficits in visuospatial and semantic fluency
     - Rapid cognitive decline to dementia
     - Cholinergic treatment may help

Kehagia et al. *Neurodegener Dis,* 2013. 11(2):79-92.

Cognitive Flexibility represented differently in the 2 aspects of EF

1. **Attentional control** (Stroop, TMT, Tower of London, Verbal Fluency, Design Fluency)
2. **Abstract reasoning** (Sorting, 20 Questions, Word Context, Proverbs)

- 45% of PwPD had impaired performance on ≥ 1 test
- Impaired group performed significantly worse on attentional control than on abstract reasoning tasks

N = 34 PwPD frontal-type deficits on FAB; 59% H&Y stage 1

Kudlicka et al., *Dement Geriatr Cogn Disord,* 2013. 36(1-2):50-66.

Models of Executive Function and Attention Control

1. Supervisory Attentional System (SAS) (Norman and Shallice 1986)

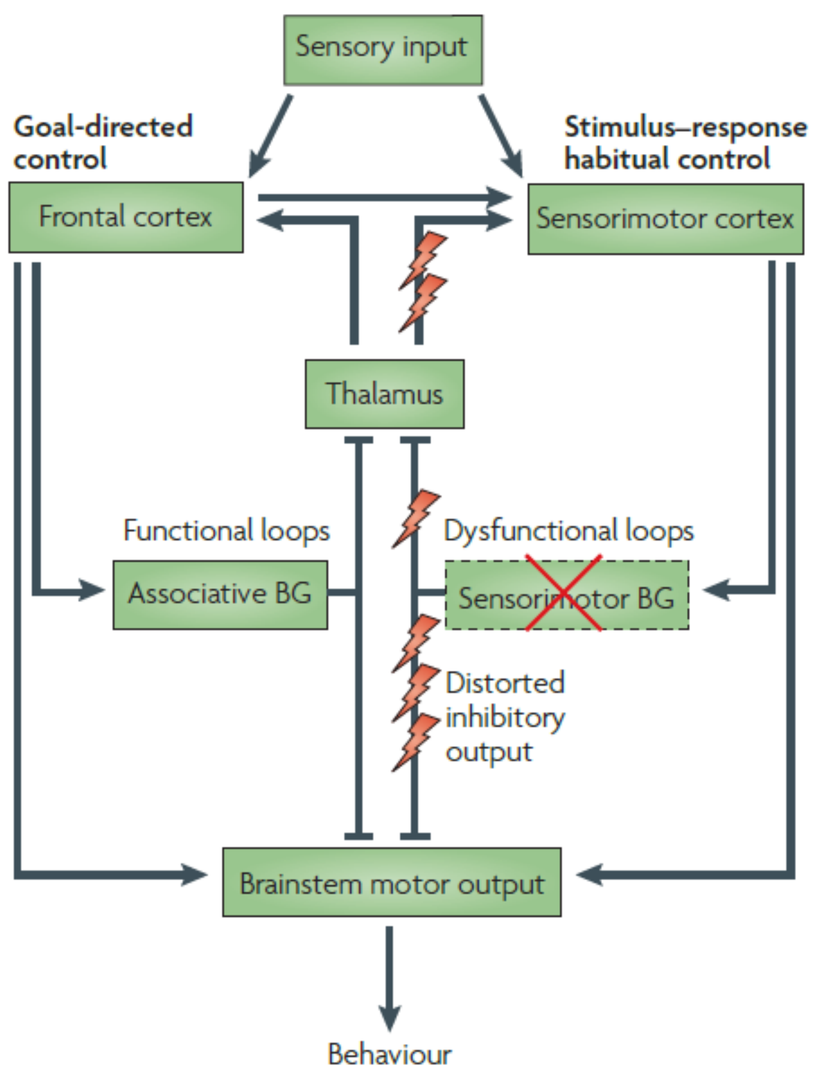
2. Multicomponent Model of Working Memory (Baddeley and Hitch 1974)

– Automatic and Controlled processing in both models

- Controlled - Prefrontal cortex (PFC) analogous to 'central executive' or SAS – allocating attention
- Automatic - Basal ganglia analogous to 'contention schedulers' (Miller and Cohen 2001; Norman and Shallice 1986)

Dirnberger and Jahanshahi, *J Neuropsychol*, 2013. 7(2):193-224.

Controlled versus Automatic Processing in PD



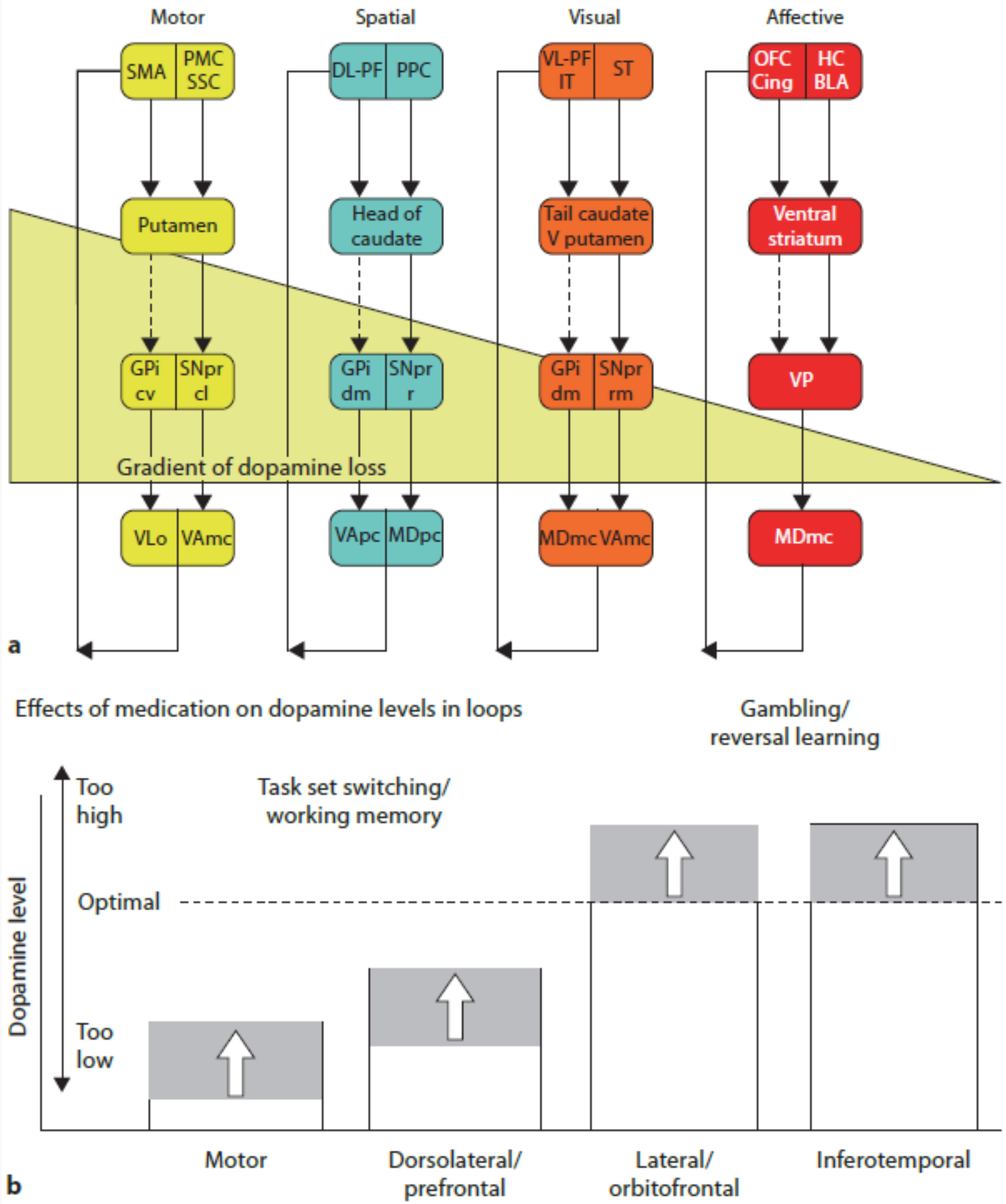
Redgrave et al. *Nat Rev Neurosci,* 2010. 11(11):760-772*.*

Gradient of dopamine depletion in PD: Fronto-striatal loops

Dorsal circuits: planning & WM

Ventral circuits: reward processing and learning

Behavior after withdrawl of DA in PD



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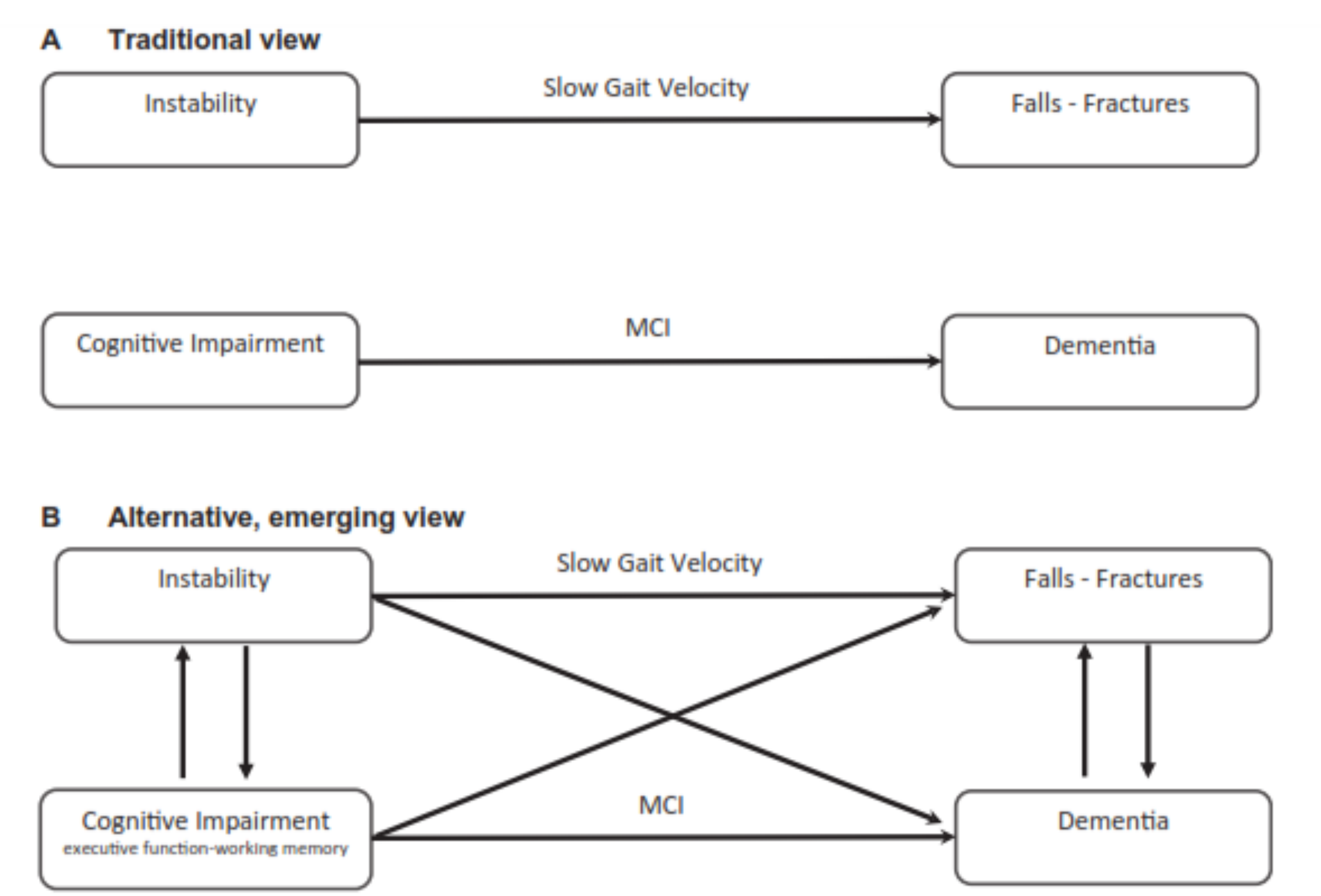
Emerging evidence that:
1) cognition predicts mobility declines & falls and
2) mobility decline & slow gait predict cognitive decline



Montero-Odasso, M., J. Verghese, et al. (2012). *J Am Geriatr Soc* 60(11): 2127-2136.

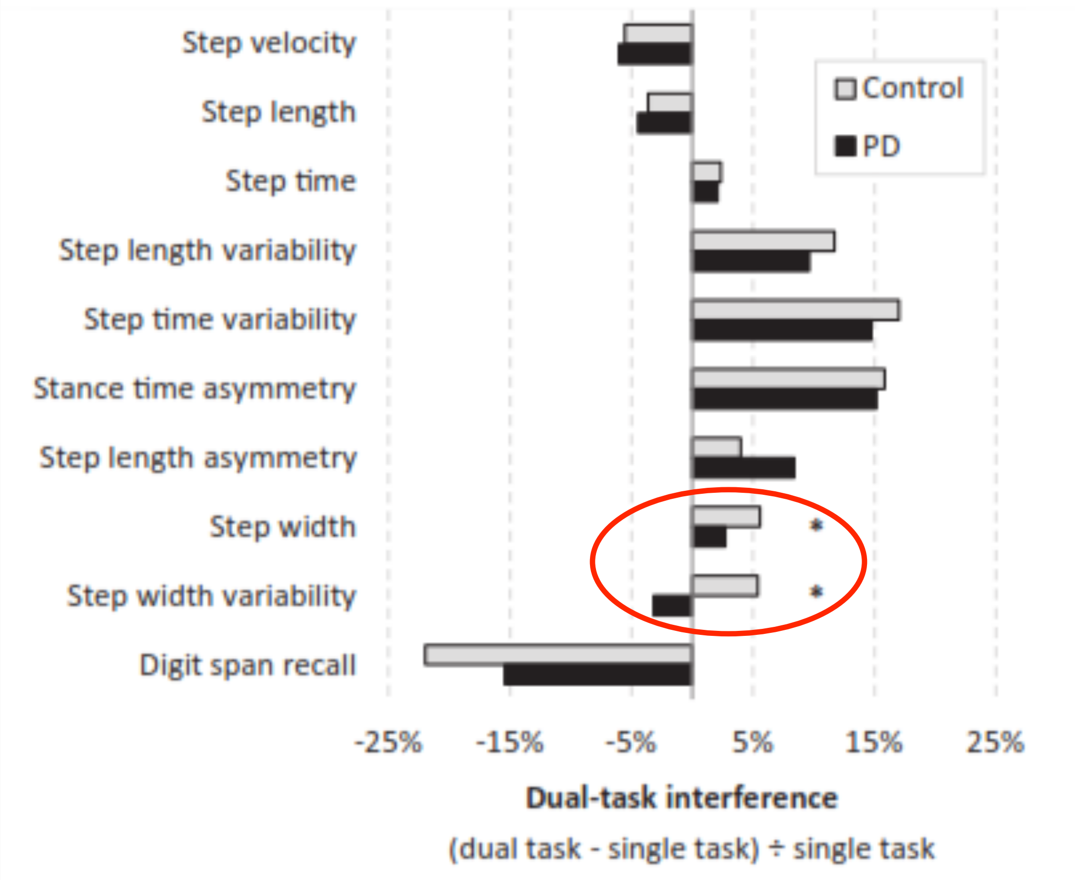
Fear of Falling is Largest Predictor of Walking Speed – single and dual task

TABLE 3. *Regression coefficients of the variables entered into final model for walking speed for each gait outcome*

Outcome	Predictor	β	*P* value	Part correlation	R^2 part correlation
Walking speed (single)	Age	−0.198	0.011*	−0.189	0.04
	Sex	0.219	0.004*	0.214	0.05
	UPDRS-III	−0.180	0.027*	−0.165	0.03
	Freezing	−0.071	0.346	−0.069	0.004
	FES	0.390	<0.001*	0.316	0.10
	Brixton	−0.113	0.143	−0.108	0.01
	HADS-D	0.199	0.022*	0.170	0.03
		R^2 = 0.37; Sig. *F* Change < 0.001			
Walking speed (dual)	Age	−0.149	0.052	−0.144	0.02
	UPDRS-III	−0.312	0.000*	−0.284	0.08
	Freezing	−0.106	0.168	−0.102	0.01
	FES	0.383	<0.001*	0.308	0.10
	HADS-D	0.216	0.012*	0.187	0.04
	Dopamine	0.212	0.007*	0.202	0.04
		R^2 = 0.34; Sig. *F* Change < 0.001			
Interference	UPDRS-III	−0.275	0.002*	−0.275	0.08
	Brixton	0.211	0.015*	0.211	0.05
		R^2 = 0.12; Sig. *F* Change < 0.001			

Rochester et al. (2008). *Movement Disorders* 23(16): 2312-2318.

Dual Task Cost to Postural Control of Gait is greater for PwPD



Control n=184; PD n=121

Rochester, L., B. Galna, et al. (2014). *Neuroscience* 265(0): 83-94.

Dual task interference on gait and cognitive task of digit span recall

Table 3. Results of the ANCOVA to test for dual-task main effects and dual × task interactions for the whole cohort and the subgroup who performed the dual-task + 1 condition, adjusting for age, sex and order of dual-task presentation. *F* (*p*)

Variable	Dual-task main effect		Group × Dual-task interactions	
	Single versus dual-task	Single versus dual-task + 1	Control versus PD (single and dual-task)	Control versus PD (single and dual-task + 1)
Step velocity (m s^{-1})	***26.4 (<0.001)***	***40.3 (<0.001)***	0.094 (0.759)	0.746 (0.390)
Step length (m)	***58.8 (<0.001)***	***52.8 (<0.001)***	1.25 (0.264)	1.04 (0.312)
Step time (ms)	***14.1 (<0.001)***	***18.1 (<0.001)***	0.087 (0.769)	0.005 (0.942)
Step length variability (m)	2.60 (0.108)	***17.0 (<0.001)***	0.433 (0.511)	0.425 (0.516)
Step time variability (ms)	2.76 (0.098)	***17.8 (<0.001)***	0.021 (0.886)	0.017 (0.896)
Stance time asymmetry (ms)	1.22 (0.271)	1.16 (0.284)	0.747 (0.388)	0.427 (0.515)
Step length asymmetry (m)	***6.15 (0.014)***	***5.15 (0.025)***	0.003 (0.957)	0.001 (0.983)
Step width (m)	2.43 (0.120)	***6.67 (0.011)***	***7.61 (0.006)***	***7.55 (0.007)***
Step width variability (m)	2.34 (0.127)	1.07 (0.304)	***9.91 (0.002)***	1.59 (0.210)
Error rate on digit span (% incorrect)	0.731 (0.393)	***15.5 (<0.001)***	0.348 (0.556)	2.12 (0.149)

Values in bold and italics font indicate statistically significant findings ($p < 0.05$).

Rochester, L., B. Galna, et al. (2014). *Neuroscience* 265(0): 83-94.

Spatiotemporal and Variability Measures of Gait are all Impaired by Dual Tasking

Table 4.
Descriptive Statistics for Gait Spatiotemporal Measures, Gait Variability Measures, and Dual-Task Cost[a]

Variable	Single Task		Dual Task			Dual-Task Cost Log_{10} (Dual/Single)	
	$\bar{X}$ (SD)	Range	$\bar{X}$ (SD)	Range	*P*	$\bar{X}$ (SD)	Range
Stride time (s)	1.1 (0.1)	0.90 to 1.39	1.3 (0.3)	0.92 to 2.44	<.001*	0.06 (0.01)	−0.03 to 0.24
Stride length (m)	1.2 (0.2)	0.52 to 1.46	1.0 (0.2)	0.32 to 1.44	<.001*	−0.04 (0.008)	−0.20 to 0.01
Step width (m)	0.1 (0.03)	0.03 to 0.13	0.08 (0.03)	0.03 to 0.14	.002*	0.03 (0.01)	−0.21 to 0.17
Swing time (%)	38.2 (2.5)	30.48 to 41.91	35.9 (3.1)	25.65 to 40.37	<.001*	−0.03 (0.004)	−0.10 to 0.01
Walking speed (m/s)	1.0 (0.2)	0.46 to 1.38	0.9 (0.2)	0.26 to 1.22	<.001*	−0.09 (0.01)	−0.34 to 0.03
Stride time variability (s)	0.03 (0.02)	0.01 to 0.10	0.08 (0.1)	0.02 to 0.67	.01*	0.32 (0.07)	−0.36 to 1.54
Stride length variability (m)	0.04 (0.02)	0.02 to 0.12	0.05 (0.04)	0.02 to 0.22	.06	0.06 (0.04)	−0.55 to 0.52
Step width variability (m)	0.4 (0.2)	0.09 to 1.16	0.3 (0.1)	0.10 to 0.78	<.001*	−0.10 (0.02)	−0.45 to 0.23
Swing time variability (%)	0.04 (0.02)	0.02 to 0.12	0.06 (0.05)	0.02 to 0.28	.02*	0.14 (0.04)	−0.28 to 0.97

[a] Asterisk denotes significance.

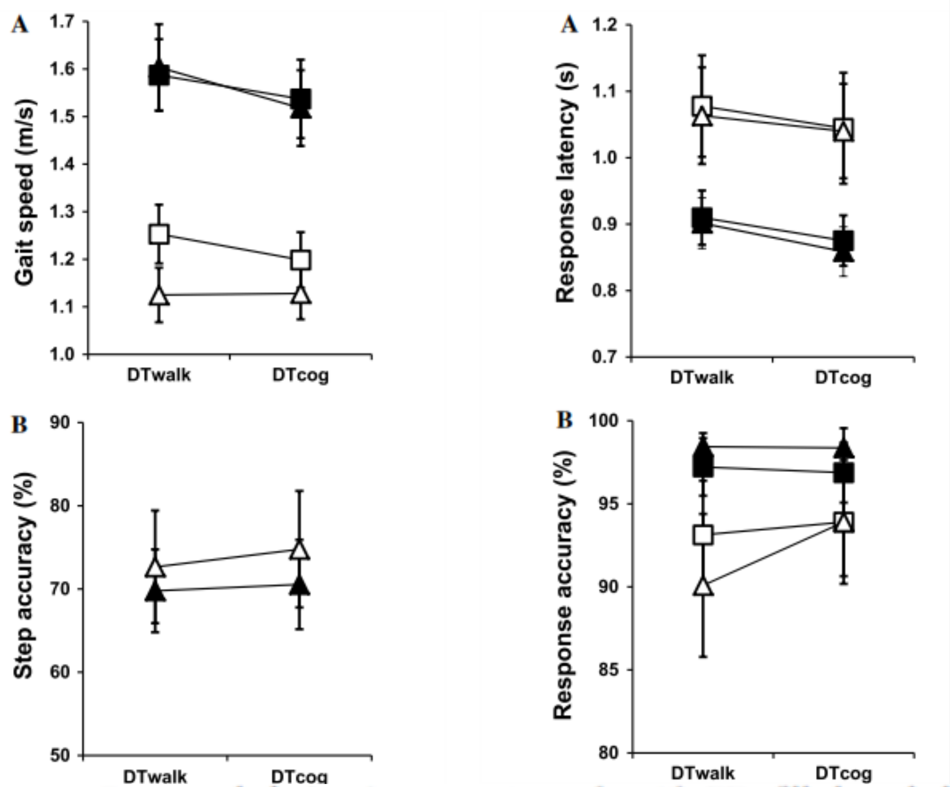
PD n=35

Different control mechanisms for Temporal and Postural aspects of gait

- Stride length and gait speed (temporal aspects) were associated with processing speed measures
- Step width variability (postural aspect) was significantly associated with executive function and attention measures.
- These associations were affected differently by dual-tasking
  - only dual task cost to stride length was associated with processing speed
- Slowed overall processing may indicate shared system underlying gait and cognition

Stegemoller et al. (2014). *Phys Ther* 94(6): 757-766.

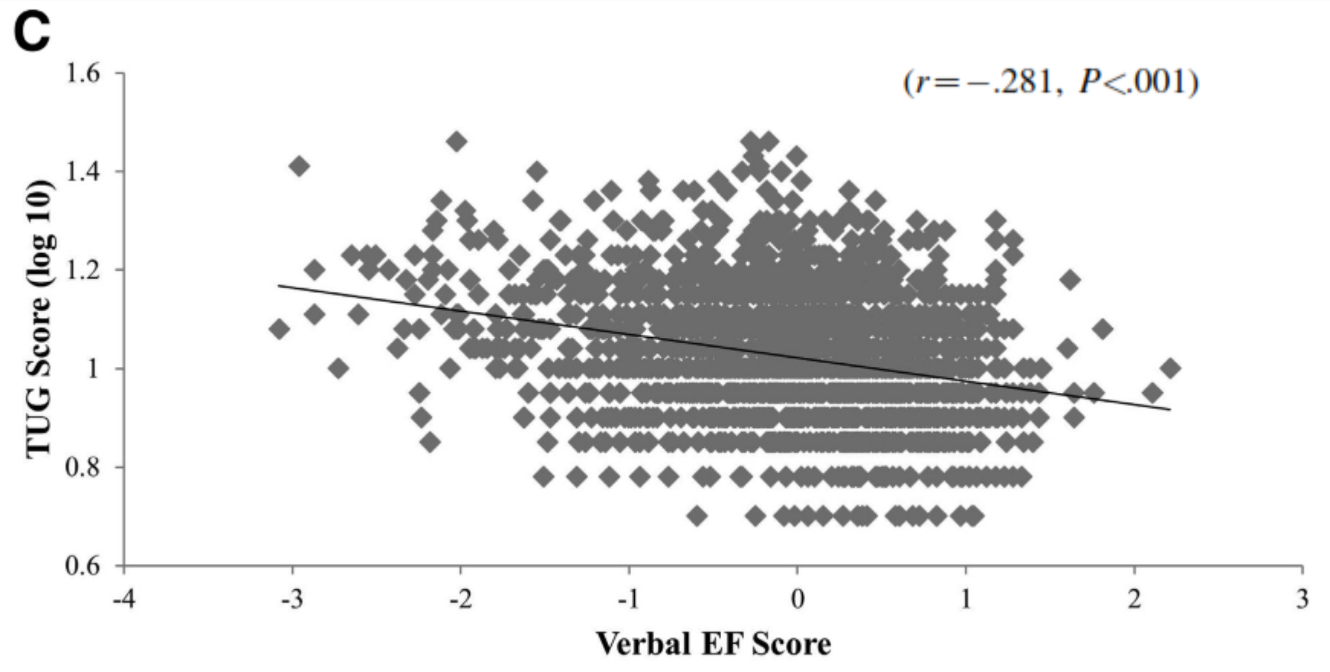
For PwPD the ability to change walking as instructed depends on task complexity



error. *Open symbols* (△,□) represent people with PD; *filled symbols* (▲,■) represent healthy older adults. *Squares* (□,■) represent the UB condition; *triangles* (△,▲) represent the NB condition. DT_{walk} indicates the dual-task condition with instructions to focus on walking; DT_{cog} indicates the dual-task condition with instructions to focus on the cognitive task

Kelly, V. and A. Shumway-Cook (2014). *Exp Brain Res* 232(1): 263-271.

Slower TUG and worse Verbal EF are associated



Verbal Executive Function:

- Verbal fluency - Word generation (animals)
- Verbal Working Memory – immedediate & delayed recall

Timed Up and Go performance and Verbal Executive Function performance predict Quality of Life measures

Table 3 Correlation coefficients and regression model for each PDQ-39 domain

	Correlation Coefficients				Regression Model				
	TUG Score		EF Score			TUG Score		EF Score	
PDQ-39 Domains	*r*	*P*	*r*	*P*	Adjusted R^2	β	*P*	β	*P*
Mobility	.37	<.001	−.22	<.001	.26	.27	<.001	−.06	.004
ADL	.27	<.001	−.19	<.001	.16	.19	<.001	−.07	.001
Emotion	.17	<.001	−.10	<.001	.04	.14	<.001	−.03	.141
Stigma	.04	.074	.01	.631	Not entered	Not entered		Not entered	
Social	.09	<.001	−.07	.003	.05	.05	.044	−.01	.808
Cognition	.24	<.001	−.24	<.001	.11	.16	<.001	−.16	<.001
Communication	.20	<.001	−.18	<.001	.13	.12	<.001	−.08	<.001
Pain	.16	<.001	−.01	.534	.05	.13	<.001	Not entered	

Abbreviation: ADL, activities of daily living.

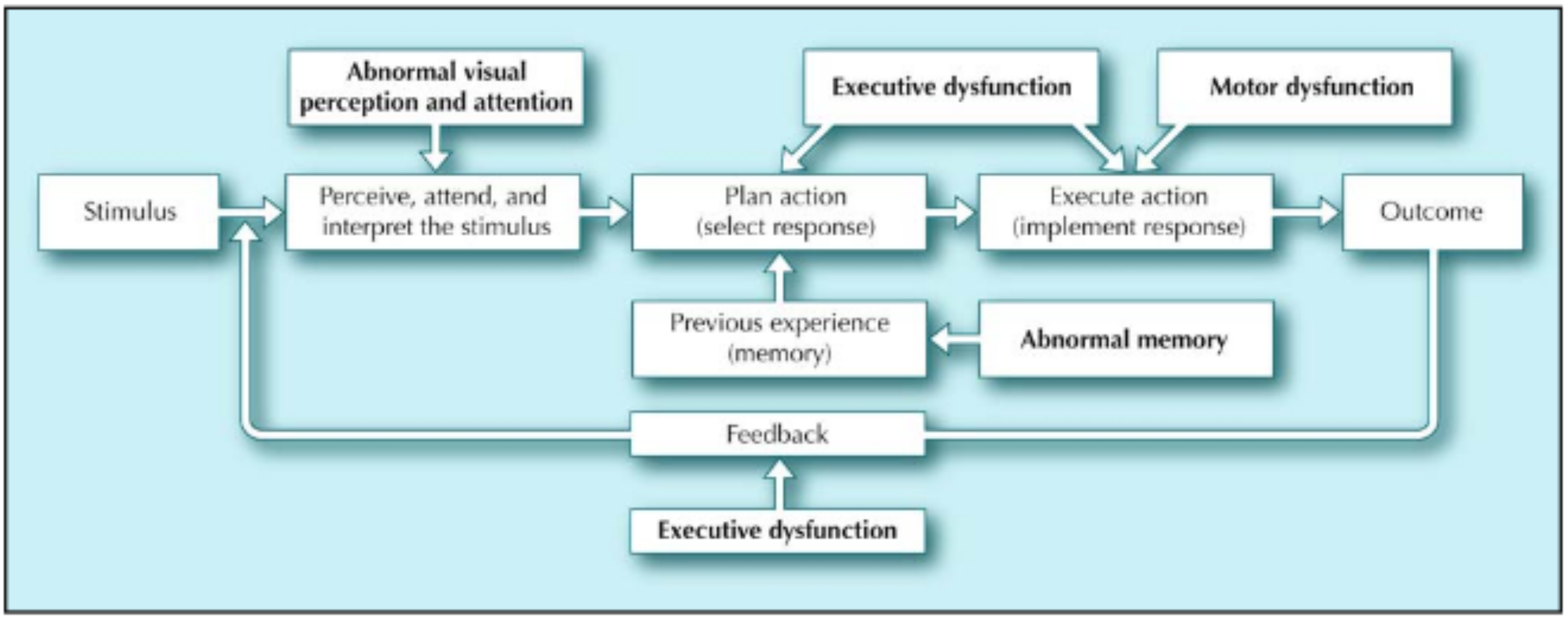
Stegemöller et al. (2014). *Arch Phys Med Rehab* 95(4): 649-655.

Driving and PD

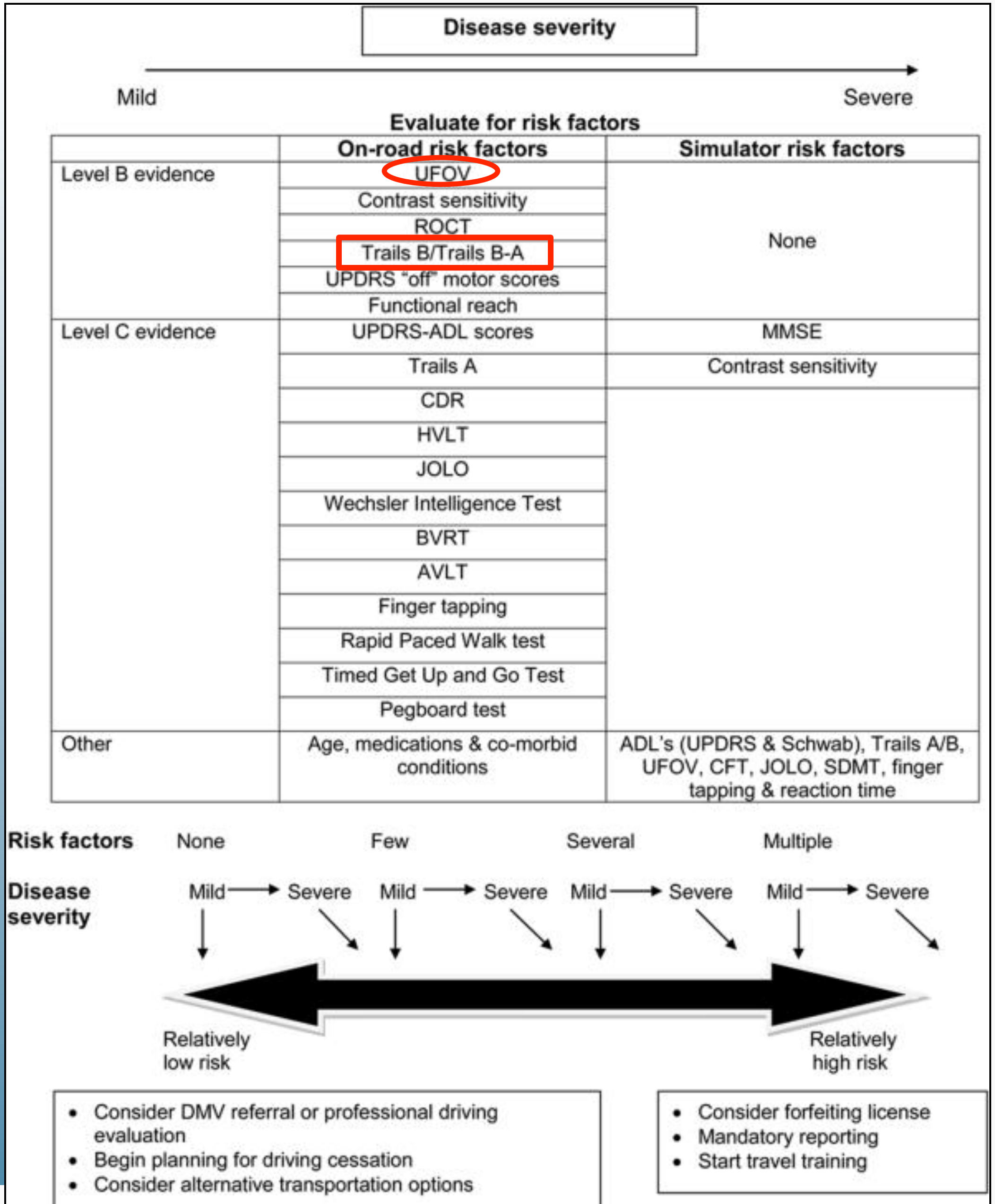
- Car accidents 2 to 5 times higher for PwPD
- Approach traffic signals more slowly, yet decelerate later and fail to stop before entering the intersection
- Impaired in navigating curves, steering accuracy, speed adaptation, maintaining constant lane position and lane changing
- Increased reaction times to brake and steer
- Greater decline in driving skills with a concurrent auditory task

Stolwyk et al. (2006). *Movement Disorders* 21(12): 2096-2100; Klimkeit et al. (2009). *Neurosci Biobehav Rev* 33(3): 223-231.

Cognitive - Motor Dysfunction Impacts Information Processing for Driving



Uc and Rizzo (2008). *Curr Neurol Neurosci* 8(5): 377-383.



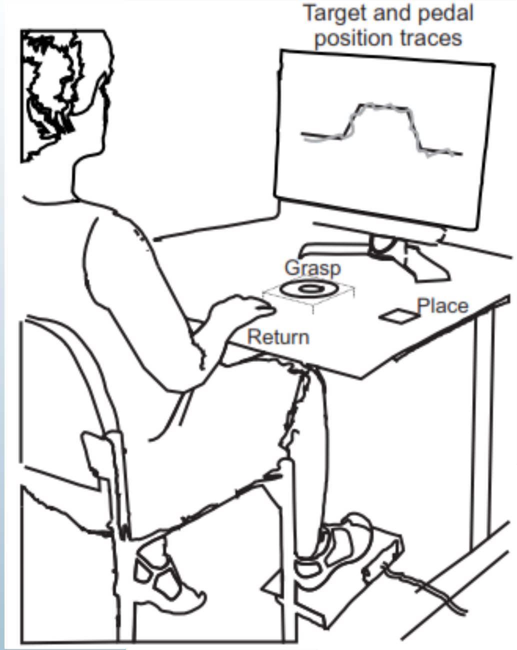
Hierarchy of Risk Factors for driving in PD

N = 55; H&Y stage 2&3.
Rapid Pace Walk

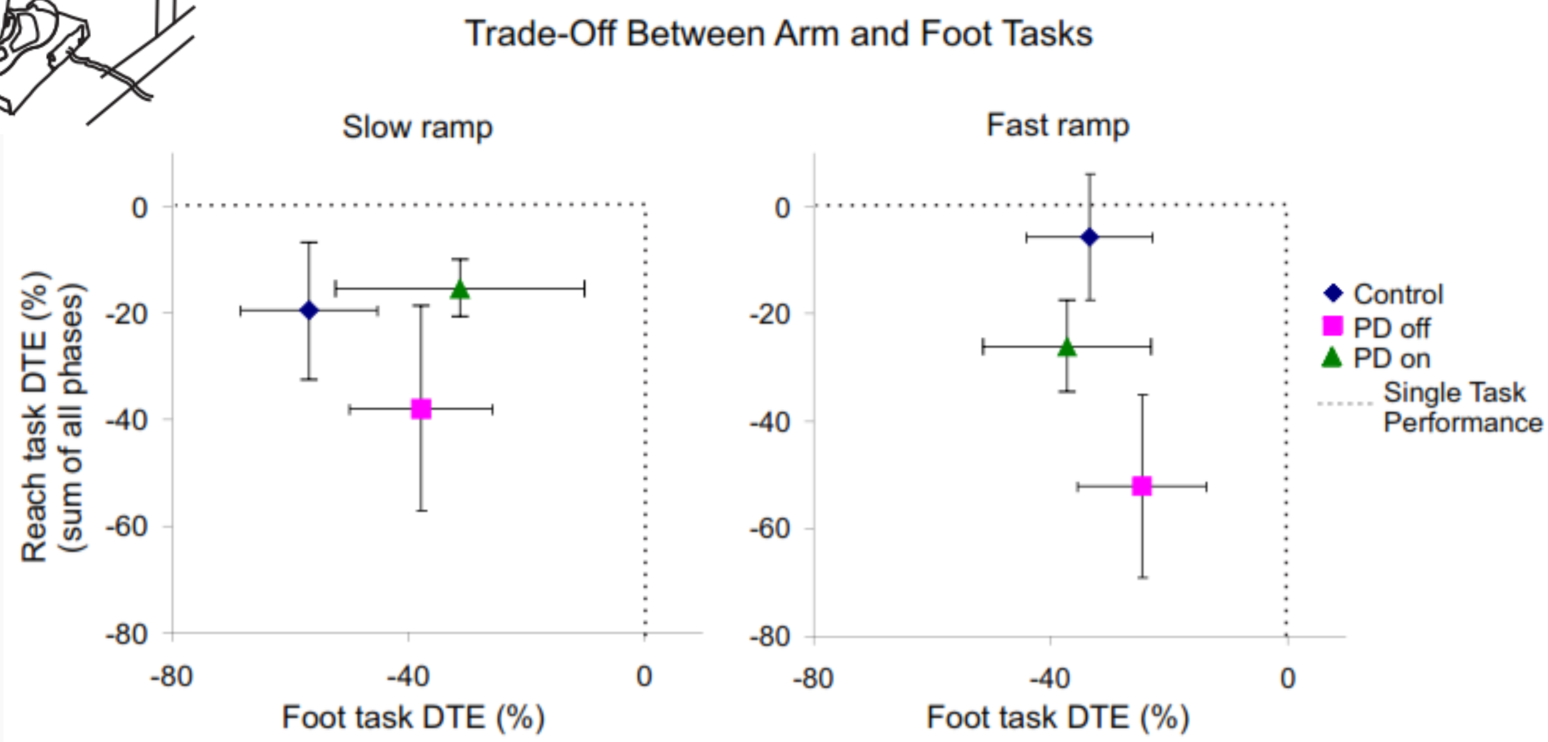
- Cutoff ≥6 s
- Sensitivity 71%
- Specificity 78%

ADL = activities of daily living;
AVLT = Auditory Verbal Learning Test;
BVRT = Benton Visual Retention Task;
CDR = Clinical Dementia Rating Scale;
DMV = Department of Motor Vehicles;
MMSE = Mini-Mental State Examination;
ROCT = Rey-Osterrieth Complex Figure Test;
HVLT = Hopkins Verbal Learning Test;
JOLO = Judgment of Line Orientation;
SDMT = Symbol Digit Modalities Test;
UFOV = Useful Field of View.

Crizzle et al. (2012). *Neurology* 79(20):2067-2074.



Dual Task Costs to Arm task and Foot task differ between PwPD and Controls



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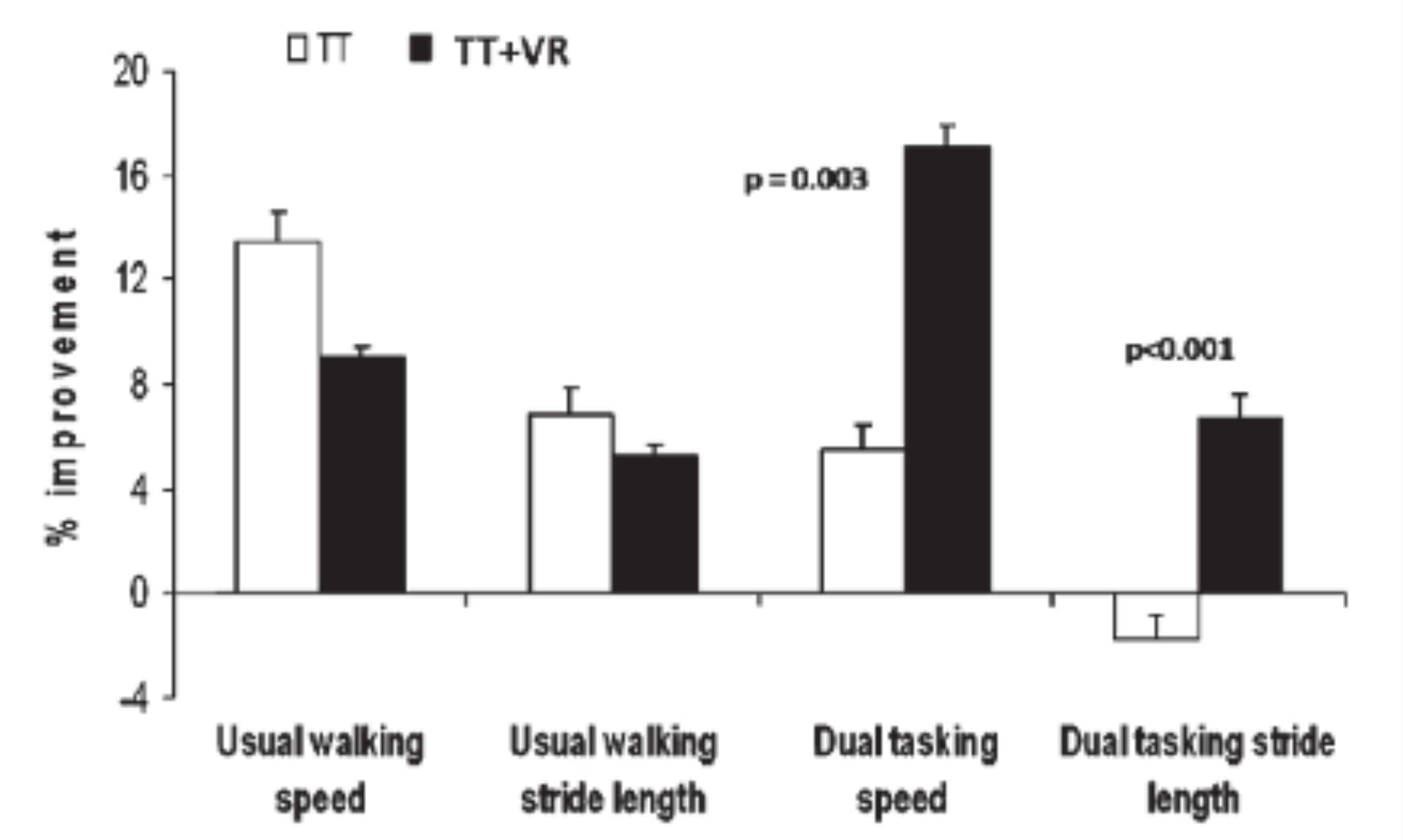
Dual task performance improvement greater after Virtual Reality training on Treadmill then TT alone (3x/wk x 6 weeks)



Mirelman et al. (2011). *J Gerontol A Biol Sci Med Sci* 66A(2):234–240.

Training improved all aspects of gait, most retained after 1 month

Table 2. Training Effects on Gait Measures

Test Condition	Pretraining	Posttraining	Follow-Up (1 month)	p Value
Usual gait				
Speed (m/s)	1.16 ± 0.18	1.26 ± 0.20*	1.28 ± 0.19†	.006
Stride time (s)	1.08 ± 0.07	1.04 ± 0.05*	1.04 ± 0.09	.021
Stride length (cm)	123.08 ± 17.22	129.78 ± 18.20*	133.18 ± 15.65†	.043
Dual-task gait				
Speed (m/s)	1.01 ± 0.23	1.17 ± 0.15*	1.13 ± 0.17	.032
Stride time (s)	1.15 ± 0.11	1.10 ± 0.07*	1.08 ± 0.09†	.016
Stride length (cm)	113.07± 23.70	121.31 ± 24.21	126.32 ± 15.88†	.046
Gait during endurance testing				
Speed (m/s)	1.01 ± 0.18	1.16 ± 0.18*	1.13 ± 0.16†	.004
Stride time (s)	1.13 ± 0.24	1.04 ± 0.07*	1.06 ± 0.13	.246
Obstacle negotiation				
Speed (m/s)	0.96 ± 0.19	1.17 ± 0.22*	1.17 ± 0.20†	.001
Stride time (s)	1.10 ± 0.09	1.05 ± 0.07*	1.06 ± 0.10	.232
Stride length (cm)	147.97 ± 16.97	160.66 ± 17.79*	161.46 ± 17.47†	.019

Notes: *p* Values in the right column are for the overall repeated measures analysis of variance models.
* Significant immediate effects at posttraining.
† Significant retention effects as compared with baseline evaluation analyzed in post hoc analysis.

Mirelman et al. (2011). *J Gerontol A Biol Sci Med Sci* 66A(2):234–240.

Training improved cognitive tasks and reduced dual task cost by 56% - Clinical improvements retained

Table 3. Training Effects on Cognitive and Clinical Measures

1 month

	Pretraining	Posttraining	Follow-Up	*p* Value
Cognitive				
Number of errors made during serial subtraction	1.5 ± 1.8	1.0 ± 1.2	0.8 ± 1.2	.16
Dual-task cost	13.9 ± 14.8	6.9 ± 8.4*	12.8 ± 7.6	.05
Trail Making Test A (s)	69.0 ± 15.9	57.2 ± 11.9*	—	.003
Trail Making Test B (s)	141.4 ± 34.9	120.4 ± 18.2*	—	.05
Clinical				
UPDRS motor —part III	26.5 ± 7.6	23.5 ± 6.6*	24.7 ± 7.1†	.02
Four Square Step Test (s)	13.3 ± 2.5	11.6 ± 1.6*	11.9 ± 1.6†	.009
Quality of life (PDQ-39)	27.4 ± 15.9	19.4 ± 13.6*	23.6 ± 14.5	.04

Notes: *p* Values in the right column are for the overall repeated measures analysis of variance models. PDQ = Parkinson's disease quality of life questionnaire; UPDRS = Unified Parkinson's Disease Rating Scale.

* Significant immediate effects at posttraining.

† Significant retention effects as compared with baseline evaluation as analyzed in post hoc analysis.

Mirelman et al. (2011). *J Gerontol A Biol Sci Med Sci* 66A(2):234–240.

Thank you