

Non-motor symptoms and activities of daily living in Parkinson's Disease

Sara Becker, M.Sc.

12. October. 2018

Non-motor symptoms (NMS) in Parkinson's Disease (PD)

- ▶ Contribute to reduced quality of life and disability
 - ▶ Often reported as more disabling than motor symptoms
- ▶ Prevalence of at least one NMS:
 - ▶ Barone et al. (2009): 98.6% of 1072 patients
 - ▶ Kim et al. (2013): 100% of 131 patients
 - ▶ Bugalho et al. (2016): 97.7% of 134 patients
 - ▶ Salari et al. (2017): 100% of 81 patients

3 Frequency of occurrence of a range of non-motor symptoms (NMS)*¹⁵

Non-motor symptoms	Mean	Range
Cognitive		
Memory	46%	38–63%
Concentration	39%	30–50%
Depression		
Sadness	43%	23–56%
Anxiety	43%	31–56%
Sleep		
Excessive daytime sleepiness	31%	21–37%
Insomnia	41%	18–53%
REM sleep behaviour disorder	34%	30–39%
Restless legs syndrome	36%	28–41%
Fatigue	42%	31–58%
Pain	31%	18–46%
Gastrointestinal		
Swallowing	25%	16–30%
Constipation	47%	28–72%
Urinary		
Urgency	53%	35–61%
Nocturia	54%	26–67%
NMS Questionnaire (global comparison)		
Parkinson disease patients	8	4–19
Healthy controls	4	2–12

REM = rapid eye movement. * Based on international cohort studies using the Non-motor Symptoms Questionnaire. Data for NMS Questionnaire (global comparison) are number of symptoms. ♦

„DASH“ Score Naismith SL & Lewis SJ. J Clin Neurosci (2011)

53 PD patients without dementia

► Items of the Parkinson's Disease Questionnaire (PDQ-39):

- Depression
- Anxiety
- Sleep disturbances
- Hallucinations

Summed into
one score

- Greater severity of DASH symptoms was strongly associated with poorer working memory and set-shifting (executive functions)

	Coefficient	p
Age, years	0.14	ns
Disease duration	0.31	0.024
Hoehn and Yahr stage	0.30	0.032
PDQ-39 total	0.87	0.000
Beck Depression Inventory-II	0.76	0.000
Mini-Mental State Examination	-0.14	ns
Digit Span forward, total score	-0.35	0.021
Digit Span backward, total score	-0.45	0.001
Logical memory, encoding	-0.21	ns
Logical memory, delayed recall	-0.06	ns
Verbal fluency, animals	-0.01	ns
Trails B-A	0.45	0.001

DASH score = sum of Depression, Anxiety, Sleep and Hallucinations items from the PDQ-39, ns = not significant at $p < 0.05$, PDQ-39 = Parkinson's Disease Quality of Life Questionnaire, Trails B-A, Trailmaking Test Part B – Part A score.

Activities of Daily Living (ADL)

- ▶ Defined as activities necessary for independent living
 - ▶ Loss is a key feature of Parkinson's Disease Dementia (PDD)
- ▶ ADL decline has been linked to dementia in PD
- ▶ **But: Symptoms of PD interfere with virtually all ADL**
 - ▶ Diagnosis of PDD requires ADL deficits be caused by cognitive, not motor, symptoms

The Functional Activities Questionnaire (FAQ) as an ADL measurement

► Constructed FAQ subscores

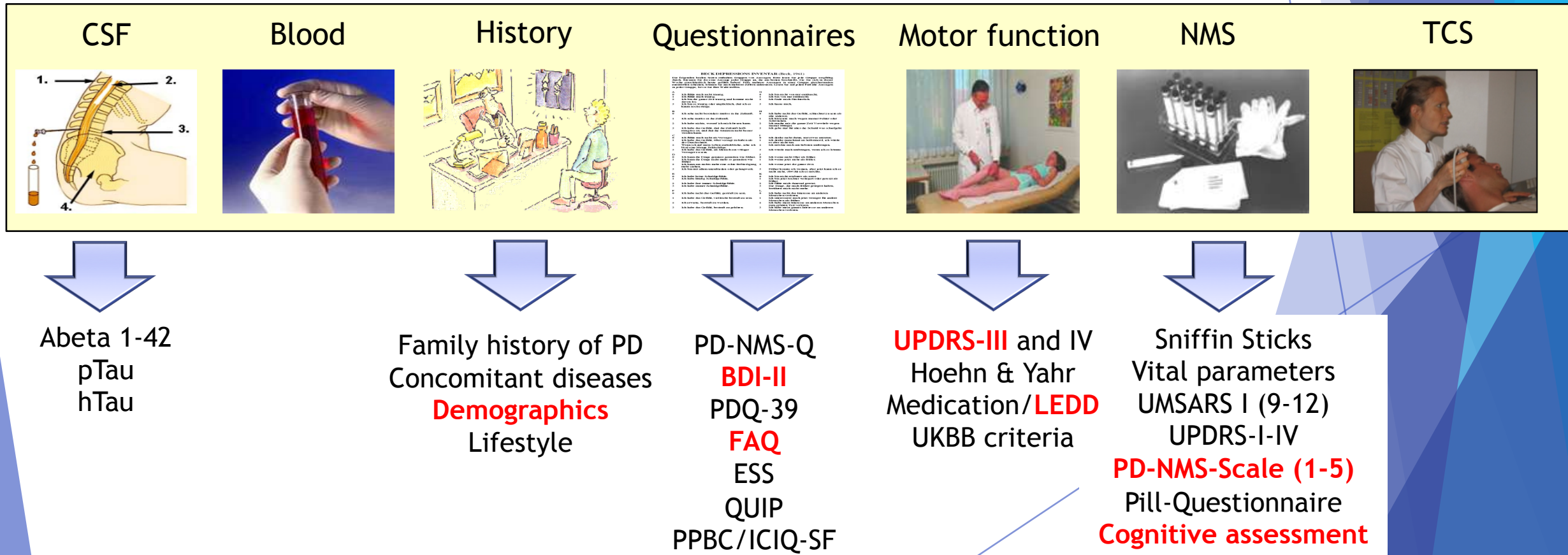
- FAQ_C : Cognitive-driven ADL impairment
- FAQ_M : Motor-driven ADL impairment

Writing checks, paying bills, balancing checkbook	C	
Assembling tax records, business affairs, or papers	C	
Shopping alone for clothes, household necessities, or groceries		M
Playing a game of skill, working on a hobby		M
Heating water, making a cup of coffee, turning off stove after use		M
Preparing a balanced meal		M
Keeping track of current events	C	M
Paying attention to, understanding, discussing TV, book, magazine	C	M
Remembering appointments, family occasions, holidays, medications	C	
Traveling out of neighborhood, driving, arranging to take buses		M
TOTAL SCORE:		

Aims

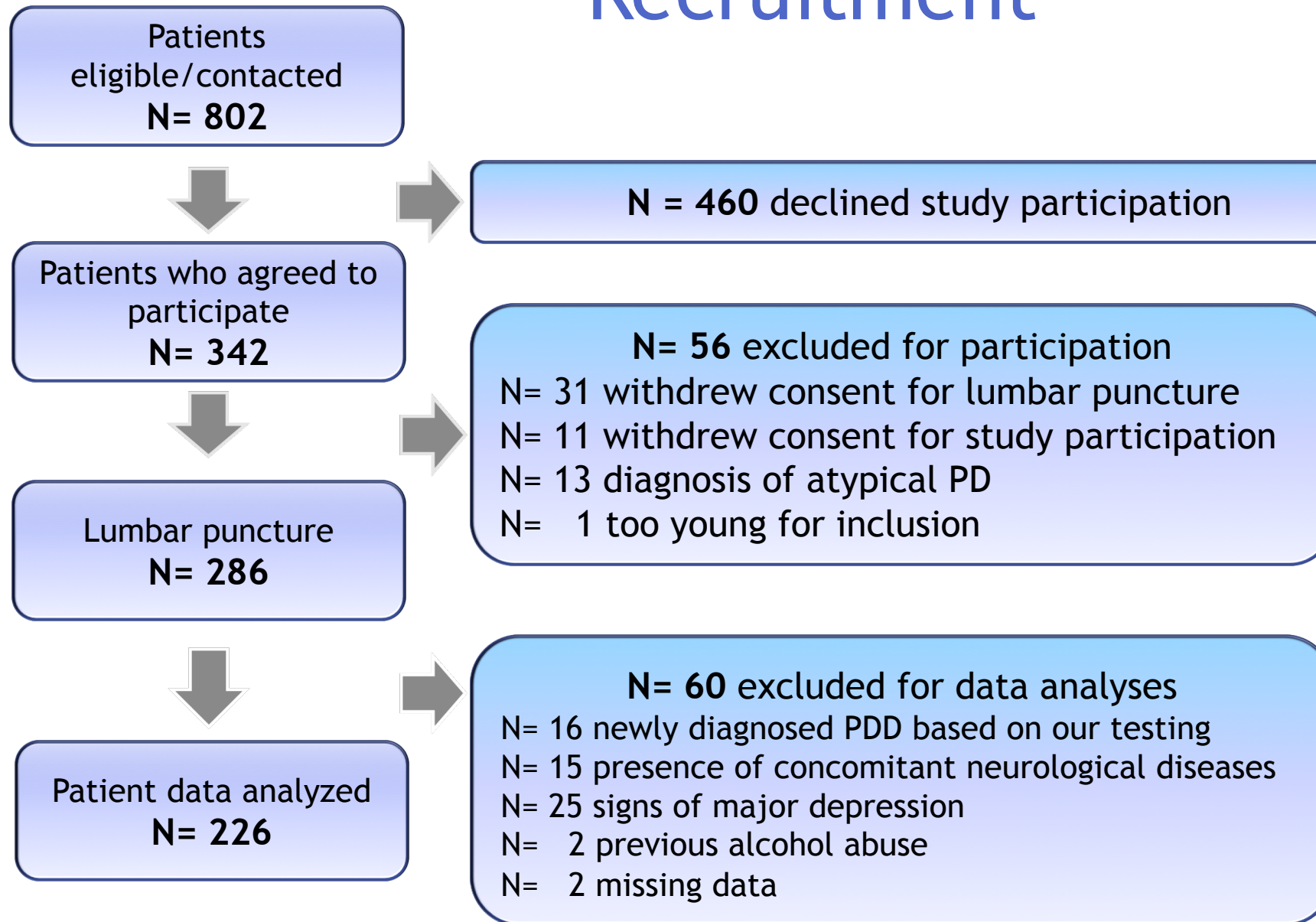
1. Can the DASH score differentiate between PD patients with and without mild cognitive impairment?
2. What is the association of the DASH score to other known risk factors for PDD (age, cognitive decline)?
3. What is the interaction between the DASH and ADL in PD?

ABC-PD Study: Amyloid-beta in CSF as a risk factor for cognitive dysfunction in Parkinson's Disease



Recruitment

ABC PD



Neuropsychological Assessment

► Cognitive classification using Level II criteria

- PD-CN, cognitively normal
- PD-MCI, mild cognitive impairment in PD

Domain	Test	Subtest
Global Cognitive Screening	Mini-Mental State Examination	
	Montreal Cognitive Assessment	
Attention & Working Memory	Wechsler Adult Intelligence Scale (WIE)	Digit-Symbol Test
		Letter-Number-Sequencing
Memory	Consortium to Establish a Registry For Alzheimer's Disease (CERAD-PLUS)	Word List Recall of Word List Recall of Constructional Praxis
Executive Functions	CERAD-PLUS	Semantic Fluency Phonemic Fluency Trail Making Test Part B
Language	CERAD-PLUS	Boston Naming Test
	WIE	Similarities
Visuospatial Abilities	CERAD-PLUS	Constructional Praxis
	Leistungsprüfsystem 50+ (LPS 50+)	Fragmented Words

DASH Score Construction

	DASH PDQ-39 (Naismith) Symptoms based on scale from 0 (never) to 4 (always)	DASH NMS-Scale Symptoms assessed over last month, scored with respect to severity (0 none - 3 severe) and frequency (1 rarely - 4 very frequently)
	Due to having Parkinson/s Disease, how often during the last month have you...	
Depression	17. ...felt depressed?	3.10. Does the patient seem sad or depressed or has he/she reported such feelings?
Anxiety	21. ...felt anxious?	3.9. Does the patient feel nervous, worried or frightened for no apparent reason?
Sleep Disturbances	30. ...unexpectedly fallen asleep during the day?	2.3. Does the patient doze off or fall asleep unintentionally during daytime activities? (For example, during conversations, during mealtimes, or while watching television or reading)
Hallucinations	33. ...had distressing dreams or hallucinations?	4.13. Does the patient indicate that he/she sees things that are not there?
Maximum Points	16	48

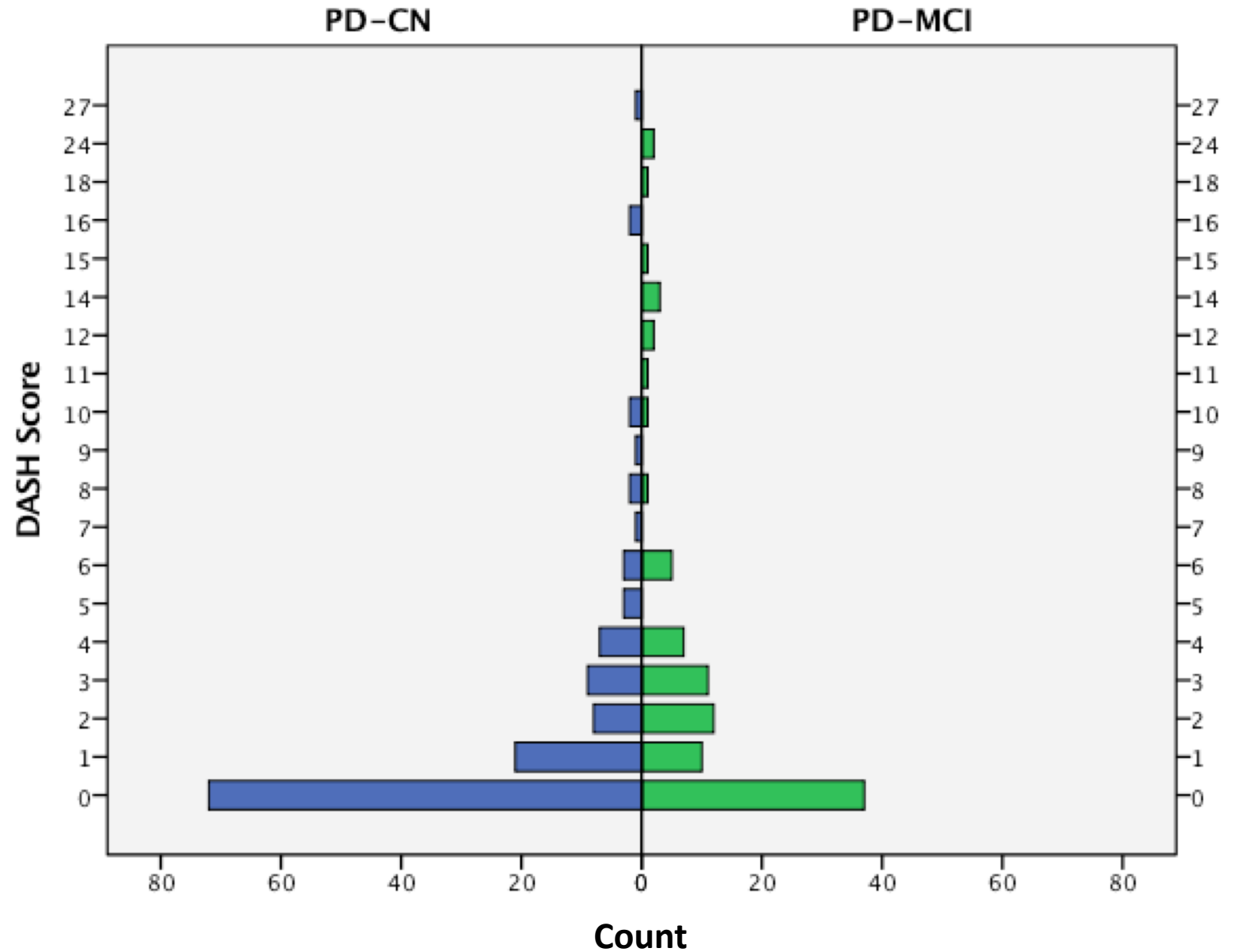
Demographics

	Total sample N=226	PD-CN n=132	PD-MCI n=94	p-value PD-CN vs. PD-MCI
Male Gender: n (%)	145 (64.2)	85 (64.4)	60 (63.8)	1.00
Age (years)	66.19 (48.07-83.67)	65.52 (48.07-79.93)	67.78 (50.01-83.67)	0.04
Education Years	13 (8-21)	13 (8-21)	12 (8-21)	0.08
Age at Onset (years)	60.58 (36.43-79.49)	60.03 (36.43-77.63)	61.29 (41.02-79.49)	0.21
Disease Duration Years	3.88 (0-18.40)	3.64 (0.11-18.40)	4.87 (0-15.37)	0.08
LEDD	487.13 (0-1574)	422.50 (0-1574)	542.50 (0-1380)	0.005
UPDRS-III (0-108)	25 (1-56)	22 (1-56)	28.50 (3-52)	<0.001
Hoehn & Yahr: n (%)				0.002
1	30 (13.3)	22 (16.7)	8 (8.5)	
2	129 (57.1)	83 (62.9)	46 (48.9)	
3	65 (28.8)	26 (19.7)	39 (41.5)	
4	2 (0.9)	1 (0.8)	1 (1.1)	
BDI-II Score (0-20)	6 (0-19)	6 (0-19)	7 (0-19)	0.09
MoCA (0-30)	26 (16-30)	27 (18-30)	25 (16-30)	<0.001

Results are expressed as *Median (Range)*, except where noted

Results

DASH-NMS score was significantly higher in the PD-MCI group compared to the PD-CN group ($p=0.037$)



Correlations with the DASH score

	r_s	p -value
Age	0.10	0.13
LEDD	0.06	0.36
UPDRS-III Total Score	0.11	0.09
MoCA Total Score	-0.23	<0.001
Executive Functions	-0.07	0.26
Attention/Working Memory	-0.18	0.006
Memory	-0.12	0.08
Visuspatial Functions	-0.19	0.005
Language	-0.13	0.05
FAQ _C	0.28	<0.001
FAQ _M	0.21	0.002

Regression Analysis

- ▶ Results of the linear regression showed that the only statistically significant predictor of the DASH score was cognitive-driven ADL impairment ($p=0.009$)

	B-weight	<i>t</i>	<i>p</i> -value	95 % Confidence Interval	
				Lower Bound	Upper Bound
MoCA	-0.06	-0.77	0.44	-0.29	0.13
Attention/ Working Memory	-0.03	-0.39	0.70	-1.07	0.72
Visuospatial Functions	-0.13	-1.77	0.08	-1.33	0.07
Language	0.07	0.89	0.37	-0.47	1.25
FAQ _C	0.26	2.64	0.009	2.65	18.32
FAQ _M	0.07	0.79	0.43	-4.52	10.55

Conclusion

- ▶ DASH Score is related to severity of cognitive impairment
 - ▶ Primarily associated to cognitive-driven ADL impairment
- ▶ Combination of both factors may define a group of patients at risk for conversion to PDD
- ▶ Long-term studies are needed to evaluate the predictive value of the FAQ subscores as well as the DASH score
 - ▶ Currently in progress (4 year follow-up of our cohort)

Thank You to...

PD Dr. Inga Liepelt-Scarfone
Prof. Dr. Daniela Berg
Prof. Dr. Walter Maetzler
AG Neurodegeneration

ABC-PD Team:

Alena Bäumer
Sarah Caliendo
Friederike Klumpp
Katja Michaelis
Susanne Nußbaum
Jessica Pollock
Maren Rüdiger-Albers
Patricia Sulzer
Zuzanna Tkaczynska
Ina Wiedmann



Correlations DASH (expanded)

	DASH	Age	LEDD	UPDRS-III	MoCA	Executive Functions	Attention /Working Memory	Memory	Visuospatial Functions	Language	FAQ _C	FAQ _M	FAQ _Q
DASH		.10	.06	.11	-.23**	-.07	-.18**	-.12	-.19**	-.13*	.28**	.21**	.05
Age	.10		.05	.04	-.41**	-.17**	-.11	-.08	.00	-.02	.14*	.09	.01
LEDD	.06	.05		.30**	-.07	-.09	-.08	-.08	-.16*	-.13*	.12	.18**	-.08
UPDRS-III	.11	.04	.30**		-.19**	-.21**	-.27**	-.11	-.12	-.10	.18**	.38**	-.20**
MoCA	-.23**	-.41**	-.07	-.19**		.44**	.46**	.39**	.37**	.47**	-.27**	-.17*	-.13*
Executive Functions	-.07	-.17**	-.09	-.21**	.44**		.63**	.47**	.42**	.47**	-.23**	-.17*	-.05
Attention/ Working Memory	-.18**	-.11	-.08	-.27**	.46**	.63**		.39**	.40**	.48**	-.36**	-.26**	-.12
Memory	-.12	-.08	-.08	-.11	.39**	.47**	.39**		.37**	.33**	-.20**	-.13*	-.09
Visuospatial Functions	-.19**	.00	-.16*	-.12	.37**	.42**	.40**	.37**		.40**	-.18**	-.18**	-.02
Language	-.13*	-.02	-.13*	-.10	.47**	.47**	.48**	.33**	.40**		-.30**	-.22**	-.14*
FAQ _C	.28**	.14*	.12	.18**	-.27**	-.23**	-.36**	-.20**	-.18**	-.30**		.57**	.43**
FAQ _M	.21**	.09	.18**	.38**	-.17*	-.17*	-.26**	-.13*	-.18**	-.22**	.57**		-.36**
FAQ _Q	.05	.01	-.08	-.20**	-.13*	-.05	-.12	-.09	-.02	-.14*	.43**	-.36**	

*Correlation is significant at the 0.05 level

** Correlation is significant at the 0.01 level

Presence of each DASH Symptom (extra)

Presence of Depression was statistically significant between PD-CN and PD-MCI groups ($p=0.041$)

