

# **DLB Module**

A Preliminary Discussion

ADC Directors Meeting

Vancouver, BC

April 16, 2016

# Committee Members

- James Galvin, Florida Atlantic University – Chair
- James Leverenz – Cleveland Clinic
- Brad Boeve – Mayo Clinic (Rochester)
- Tanis Ferman – Mayo Clinic (Jacksonville)
- Jennifer Goldman – Rush Medical Center
- Debbie Tsuang – University of Washington
- Carol Lippa – Drexel University
- Daniel Weintraub – University of Pennsylvania
- Douglas Galasko – UC- San Diego
- John Growdon – Harvard University

# Goals

- Develop a companion module to the Uniform Data Set (UDS) to improve characterization of DLB and PDD
- Harmonize efforts with those of the Movement Disorder Society efforts to characterize the non-motor features of Parkinson's disease
- Capitalize on previous efforts to create a FTD module
- Standardize battery of clinical and cognitive tools for DLB and PDD that can be databased at NACC and shared amongst investigators.

# Subcommittees

- Motor and non-motor features of PD (Goldman, Weintraub)
  - Sleep, arousal, attention and fluctuations (Boeve)
  - Behavior and Mood (Tsuang, Lippa)
  - Global clinical tools (Galvin, Leverenz)
  - Neuropsychological tests (Ferman)
  - Biomarkers (Galasko, Growden)
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- Subcommittees could invite *ad-hoc* members to expand expertise

# Action Steps

- Choose instruments and measurements from each workgroup
- Harmonize new data with variables captured as part of UDS 3.0
- Draft sample module
- Instruments or measurements selected should be free of licensing fees or an agreement to make their use free to NIA
- Poll ADCs regarding potential DLB cohorts and any non-UDS measures

# Motor and Non-Motor Features of PD

- Additional consultants: Ray Chaudhuri, David Burn
- Identified deficiencies in quantifying motor symptoms
- Capture age of onset of motor and non-motor symptoms
- Capture evolution of symptoms, particularly prodromal
- Capture common disturbing symptoms such as drooling, dysphagia
- Capture autonomic features
- Harmonize with data collected by UDALL Centers, PPMI, PPPMI, etc.

# Draft DLB Module: Motor and Non-Motor

- MDS-UPDRS
  - Part II: Motor Aspects of Experiences of Daily Living (patient reported)
  - Part III: Motor Examination (clinician reported)
- Estimate age of onset for motor symptoms and prodromal symptoms
  - RBD, olfaction, constipation
- Add sitting and standing BP and Pulse to physical exam
- Autonomic Checklist
  - NMSS
    - Drooling, dysphagia, sexual dysfunction, weight loss, olfaction, vision
  - SCOPA-AUT
    - Bowel, bladder, thermoregulatory

# Sleep, Arousal, Attention, and Fluctuations

- Additional Consultants: Don Bliwise, Ron Postuma
- Capture REM sleep behavior disorder, excessive daytime sleepiness, cognitive fluctuations, and obstructive sleep apnea
- Both patient and informant questions
- UDS 3.0 has several Yes/No questions that may capture the symptoms but no clear determination of how the decision was made that the symptoms were present.



# Draft DLB Module: Sleep and Fluctuations

- Mayo Fluctuations Questionnaire
- Mayo Sleep Questionnaire
- Epworth Sleepiness Scale
- STOP-BANG Questionnaire

# Behavior and Mood

- Additional questions regarding the age of onset for 4 symptoms:
  - Hallucinations
  - Delusions
  - Anxiety
  - Apathy
- Temporal relationship with DOPA-related medications
- Capture presence since disease onset rather than the past 4 weeks

# Draft DLB Module: Behavior and Mood

- Expanded NPI screening questionnaire
  - Delusions
  - Hallucinations/Illusions
  - Anxiety
  - Apathy

# Global Clinical Tools

- Incorporating global functioning in activities of daily living
- Patient-reported (UDS has only caregiver reported)

# Draft DLB Module: Global Clinical Tools

- Focus on Patient-reported activities
- MDS-UPDRS Part II

# Biomarkers

- No additional funding
- No mandate requiring the Centers to prospectively collect any new biomarkers
- Record what biomarkers obtained and whether they are available for sharing – similar to what is done for AD biomarkers

# Draft DLB Module: Biomarkers

- Genetics
- Biofluids
  - DNA
  - Plasma
  - Serum
  - CSF
- Neuroimaging
  - Structural MRI
  - Functional MRI
  - PET
  - DAT scan
  - MIBG

# Neuropsychological Tests

- Additional Consultants: David Salmon, Alex Troster, Brenna Cholerton
- Two goals:
  - Not add burden to ADCs
  - Discriminate between DLB and AD
- Domains lacking or under-represented in UDS 3.0:
  - Attention, Executive function, and Visual-Spatial Perceptual tasks
- Add approximately 20 minutes to the UDS 3.0 battery



# Draft DLB Module: Neuropsychology

- Modified Stroop Color-Word-Interference Task
- test of attention, processing speed, and executive function.
- There is evidence that it distinguishes between DLB/PDD and AD

Word Condition	RED	RED
	GREEN	BLACK
	BLACK	GREEN
Color Condition	#####	#####
	#####	#####
	#####	#####
Interference Condition	RED	RED
	GREEN	BLACK
	BLACK	GREEN

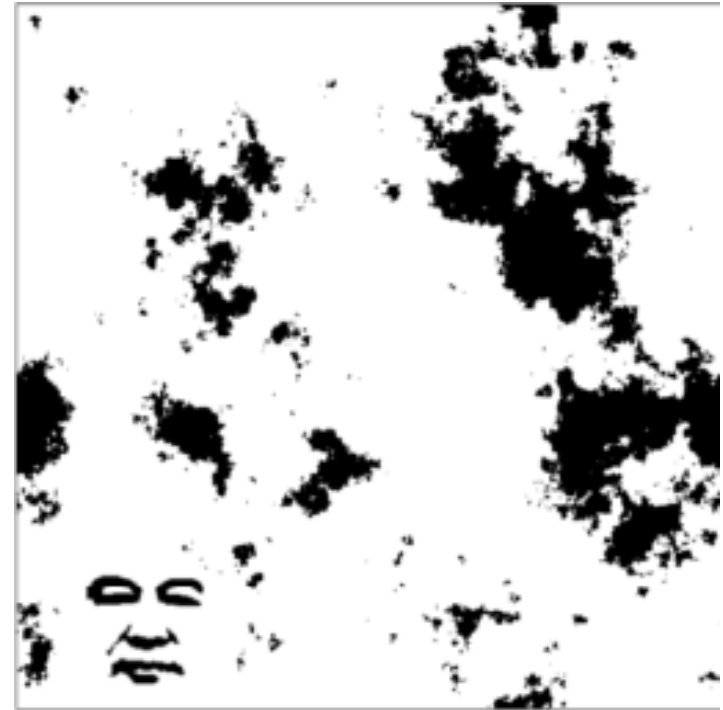
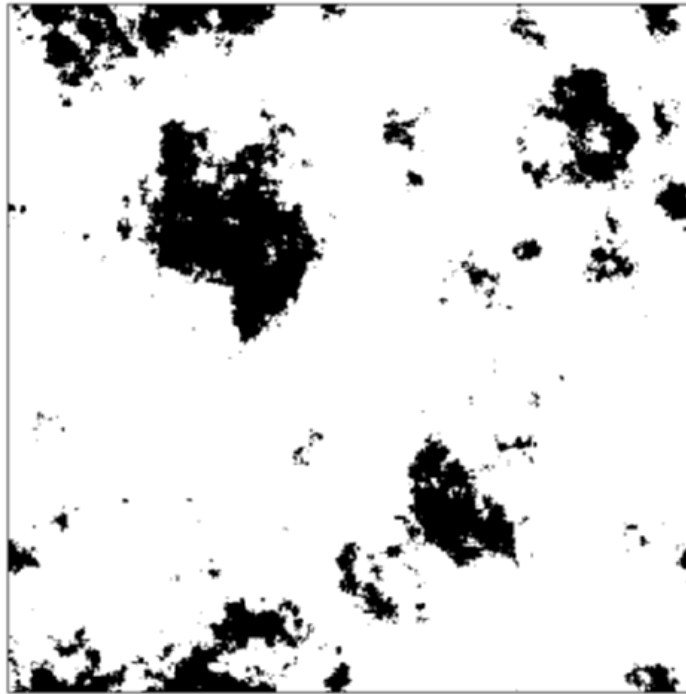
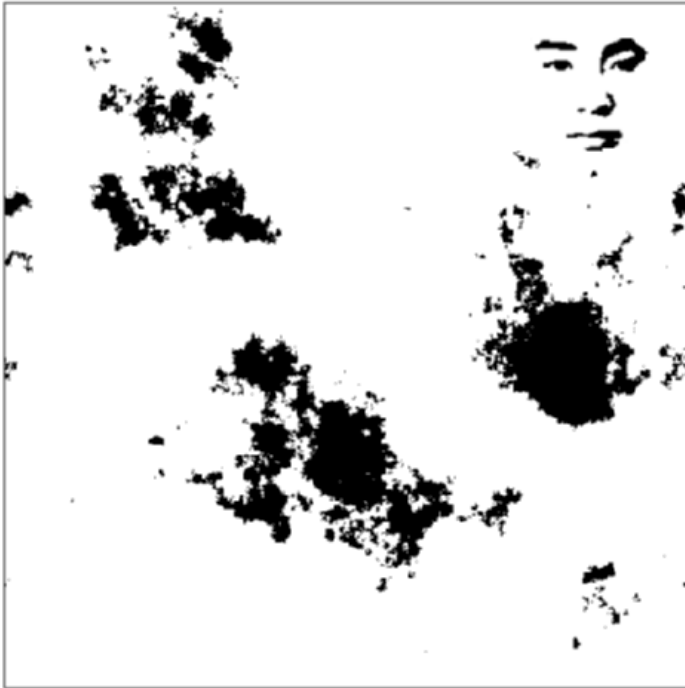
	Raw
Word Score	
Color Score	
Color-Word Score	

- Different from the copyrighted version
- Similar to the one normed by the Mayo group
- Developing norms

# Draft DLB Module: Neuropsychology

- Noise-Pareidolia (Yokoi et al, 2014)
- There are two types of images:
  - An array of ink blots with a facial image in one corner
  - An array of ink blots with no facial image
- Responses are recorded
  - Is there a face: Yes or No
  - Point to where the face is
- The scores are based on the number of:
  - Correct answers: “Yes” when there is a face or “No” when there is no face
  - Pareidolia: “Yes” when there is no face or “Yes” when there is a face but points to the wrong place
  - Missed responses: “No” when there is a face
- Yokoi and colleagues tested small sample of 34 DLB, 34 AD and 29 Controls.
  - Mean percentage of illusory responses as 15.4 (SE=3.2) for DLB compared to 1.9 (SE=1.1) for AD, and 1.9 (SE=1.1) for Controls.
  - No differences in the number of misses between AD and DLB, though the Controls had fewer misses.
  - ROC analysis: the illusory responses with a cut-off of 2.5% had a sensitivity of 0.71 and specificity of 0.80.
- 40 items
- Takes anywhere from 5 to 20 minutes

# Draft DLB Module: Neuropsychology



# Harmonization with EU –JPND Effort

	Level 1	Level 2
Cognition		
Staging	<b>CDR</b>	CGI-S, CGI-C
Global	MMSE, <b>MOCA</b>	
Memory	CERAD word list	<b>Benton visual retention test</b>
Visuospatial	Degraded letter test (VSOP)	Benton line orientation
Executive	Similarities (WAIS)	<b>Stroop test</b>
Attention	Adaptive digit ordering	<b>Trail making test</b>
Language	<b>Fluency, animals</b>	<b>Boston Naming, 15-item</b>
Psychiatric Symptoms		
Profile	<b>NPI Questionnaire</b>	<b>NPI</b>
Depression	<b>NPI item 4, GDS-15</b>	Cornell scale
Apathy	<b>NPI item 7</b>	Apathy evaluation scale
Psychosis	<b>NPI items 1+2</b>	CUSPAD misidentification, NEVI

	Level 1	Level 2
Other		
Quality of life	QoL-AD	
Caregiver burden	Zarit burden inventory	
Autonomic	<b>Orthostatics, NMSS</b>	ECG
Sleep	<b>Sleep items, NMSS</b>	<b>Mayo sleep questionnaire</b>
Motor	<b>UPDRS III</b> , timed up-and-go	Finger tapping, <b>H &amp; Y</b>
Fluctuations	<b>Mayo fluctuation scale</b>	Fluctuation assessment scale
Falls	<b>Semi-quantitative question</b>	Tinetti scale
ADLs	<b>FAQ</b>	
Milestones	CDR=3, admission, death	

# Next Steps

- ADCs (11/29 responded)
  - 1 LBD cohort, 1 planned
  - 1 MDS-UPDRS, 2 UPDRS, 2 Mayo Fluctuation Scale
- Draft version submitted NACC
- Distribute draft DLB Module to ADCs for review and comments
- Revisions based on comments