



Behavioral and Psychiatric Symptoms in Dementia (BPSD) Working Group

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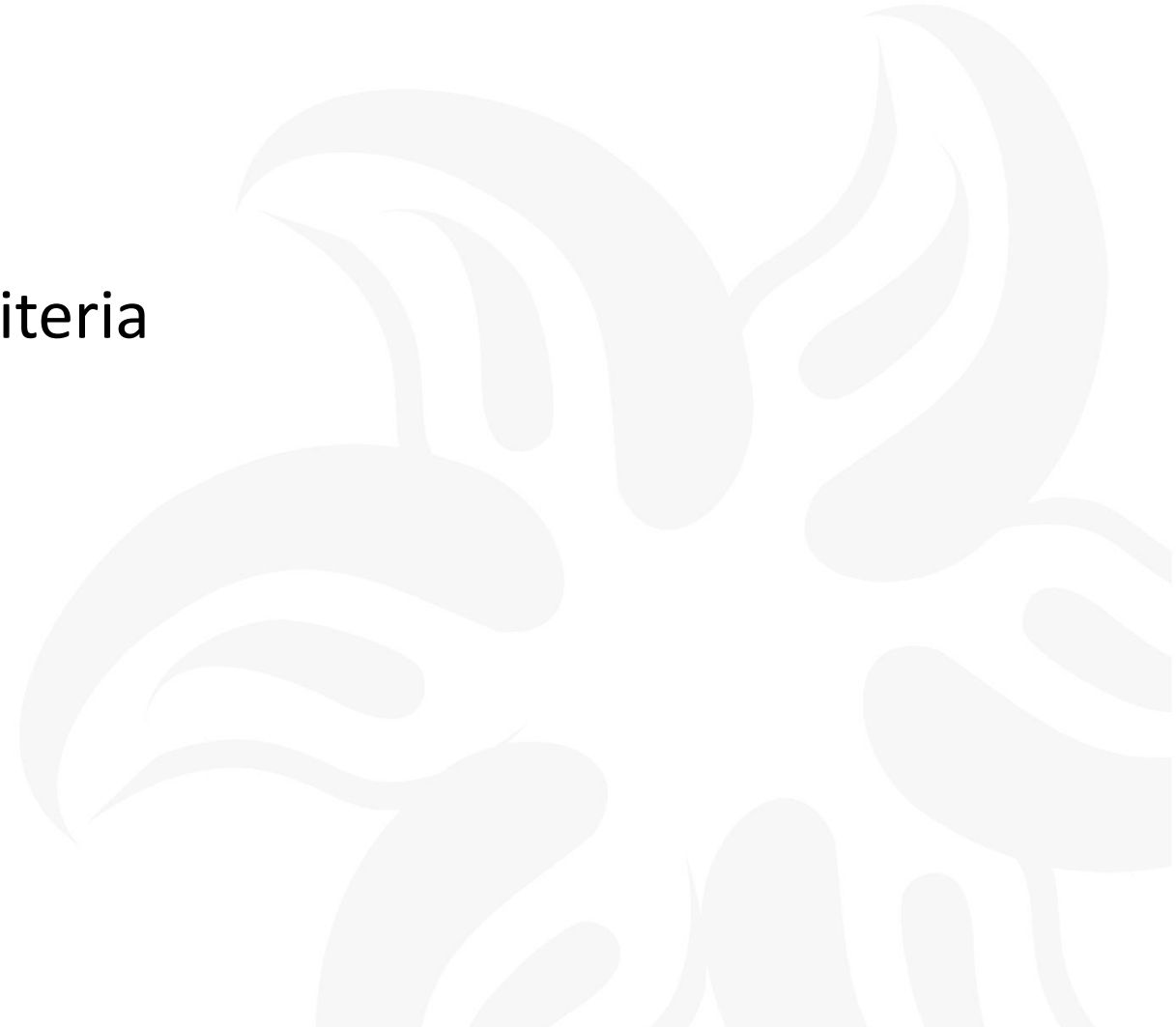
Apathy Workgroup

Chairs: Dr. Krista Lanctôt, Dr. David Miller



Agenda

1. Vision Statement
2. Diagnostic Criteria update
3. Operationalization of diagnostic criteria
4. Issues in Apathy review



Vision Statement

Apathy as a behavioural and psychological symptom in dementia (BPSD) has increasingly been a focus of research over the last 10 years.

This interest has led to the publication of provisional diagnostic criteria and stimulated interest in this syndrome as a treatment target for both Alzheimer's disease and related dementias.

Apathy can both precede and emerge concurrently with cognitive impairment and other BPSD.

The Apathy Working Group brings together industry, academic and drug regulatory experts.

This expertise will be used to define the relevance of apathy and to better understand, recognize and manage apathy within BPSD and provide a basis for further research.

Diagnostic Criteria Update

- Completed consensus process to revise diagnostic criteria
- Submitted diagnostic criteria paper to Alzheimer's & Dementia
 - Submitted manuscript revisions

Operationalization

- Develop companion paper for operationalization of revised diagnostic criteria for apathy in neurocognitive disorders
 - Release it to the public and have clinicians tell us where the difficulties/confusions are once they have had some experience with it
 - Should include primary care and clinical groups, e.g. IPA?
- Who wants to be involved?
- Monthly meetings?

Roadmap for apathy research

- Create roadmap for drug development
 - Issues in apathy review – “10 things we still need to know about apathy for drug development”
 - Must haves vs. nice-to-haves
- Outcome measures
- Design considerations
- Biomarkers

Cummings et al., 2015

- All participants should have a reliable caregiver who is willing and able to participate fully in the trial
- Inpatients and outpatients should be evaluated separately
- Patients with AD or PD included in trials should have no history of a clinical stroke

Addressed by upcoming NPS-PIA paper (Mortby et al.)

- Neuroimaging
- Blood-based
- Longitudinal vs. cross-sectional

Discussion



Agitation Workgroup

Chairs: Dr. Cedric O’Gorman, Dr. Paul Rosenberg



Agenda

1. Mission Statement
2. Update on the publication of the Framework publication
3. Review of recent activity in area of AD agitation
 - Publications
 - Oral and Poster Presentations
4. Discussion regarding future projects for the Working Group
5. Any other business

Mission Statement

To address the need for safe and effective medications to treat agitation associated with dementia and to gain consensus amongst experts on a roadmap for optimal clinical trial methodology which may garner regulatory approval.

The Journal of Prevention of Alzheimer's Disease - JPAD
Volume 7, Number 4, 2020

A Framework for Developing Pharmacotherapy for Agitation in Alzheimer's Disease: Recommendations of the ISCTM* Working Group

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J Prev Alz Dis 2020;4(7):274-282

Published online June 26, 2020, <http://dx.doi.org/10.14283/jpad.2020.37>

Publications:

1. Simonetti et al. Neuropsychiatric Symptoms in Elderly With Dementia During COVID-19 Pandemic: Definition, Treatment, and Future Directions. *Front Psychiatry*. 2020 Sep 29; 11: 579842.
2. Cagnin A et al. Behavioral and Psychological Effects of Coronavirus Disease-19 Quarantine in Patients With Dementia. *Front Psychiatry*. 2020 Sep 9;11:578015.
3. Cummings J. Drug Development for Psychotropic, Cognitive-Enhancing, and Disease-Modifying Treatments for Alzheimer's Disease. *J Neuropsychiatry Clin Neurosci*. 2020 Oct 28.
4. Aigbogun MS et al. Real-World Treatment Patterns and Characteristics Among Patients with Agitation and Dementia in the United States: Findings from a Large, Observational, Retrospective Chart Review. *J Alzheimers Dis*. 2020;77(3):1181-1194.
5. Bateman DR et al. Agitation and impulsivity in mid and late life as possible risk markers for incident dementia. *Alzheimers Dement (N Y)*. 2020 Sep 6;6(1):e12016.

Presentations:

1. Circadian rhythm disturbance in agitation of Alzheimer's disease. Paul B. Rosenberg, MD
2. Characterisation of Alzheimer's disease patients with agitation and their Antipsychotic use: a study using the UK Clinical Practice Research Datalink. Ross A. Baker, PhD
3. Efficacy and Safety of AXS-05, a Novel, Oral, NMDA Receptor Antagonist with Multimodal Activity, in Agitation Associated with Alzheimer's Disease: Results from ADVANCE-1, a Phase 2/3, Double-Blind, Active and Placebo-Controlled Trial. Cedric O'Gorman, MD
4. Actigraphy as a proxy biomarker for motoric agitation in Alzheimer disease. Amer M. Burhan, MBChB
5. Poster Biomarkers of agitation in moderate-to-severe Alzheimer's disease patients enrolled in an RCT with nabilone. Myuri Ruthirakuhan, PhD
6. Defining agitation, apathy and other psychiatric symptoms in cognitive impairment and dementia: Why we need to intervene. Mary Sano, PhD
7. Investigating the feasibility of using wearable technologies and machine learning techniques to recognise distress and agitation in people living with dementia. Zeke Steer, MEng

Presentations:

1. EFFICACY AND SAFETY OF AXS-05, A NOVEL ORAL NMDA RECEPTOR ANTAGONIST WITH MULTIMODAL ACTIVITY, IN THE TREATMENT OF ALZHEIMER'S DISEASE AGITATION: RESULTS OF THE ADVANCE-1 TRIAL. C. O Gorman
2. CONSTRUCTING A MORE SENSITIVE CLINICAL TRIAL OUTCOME MEASURE FOR AGITATION IN ALZHEIMER'S DISEASE: INCORPORATING IPA AGITATION CRITERIA. A. De Mauleon
3. BIOMARKERS OF RESPONSE TO NABILONE IN AGITATED PATIENTS WITH MODERATE-TO-SEVERE ALZHEIMER'S DISEASE PATIENTS. M. Ruthirakuhan
4. CAREGIVER PERSPECTIVES ON THE BURDEN AND IMPACT OF AGITATION IN CARING FOR LOVED ONES WITH DEMENTIA/ALZHEIMER'S DISEASE. M. Sanon Aigbogun; R. Baker.

Thought Starters:

- 1. How to successfully implement remote assessments in AD trials to ensure patient safety***
- 2. Use of Biomarkers in Clinical Trials of AD agitation***
- 3. Deep Dive into Clinical Scales for AD agitation – Recommendations to improve clinical relevance and reduce patient and caregiver burden***
- 4. Examination of clinical datasets to evaluate clinical meaningfulness of scales in AD agitation***
- 5. Projects to explore the humanistic and economic impact of AD agitation***
- 6. Other ideas...***