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Review Article

Apathy associated with neurocognitive disorders: recent progress and future directions

Krista L. Lanctôt^{a,b,c,*}, Luis Agüera-Ortiz^{d,e}, Henry Brodaty^f, Paul T. Francis^g, Yonas E. Geda^{h,i,j}, Zahinoor Ismail^{k,l}, Gad A. Marshall^m, Moyra E. Mortby^{n,o}, Chiadi U. Onyike^p, Prasad R. Padala^{q,r}, Antonios M. Politis^s, Paul B. Rosenberg^t, Emma Siegel^f, David L. Sultzer^u, Eleanor H. Abraham^a

^aHurvitz Brain Sciences Program, Sunnybrook Research Institute, Toronto, ON, USA

^bDepartment of Psychiatry, University of Toronto, Sunnybrook Research Institute, Toronto, ON, USA

^cDepartment of Pharmacology/Toxicology, University of Toronto, Sunnybrook Research Institute, Toronto, ON, USA

^dCentro de Investigación Biomédica en Red de Salud Mental, CIBERSAM, Madrid, Spain

^eDepartment of Psychiatry & Research Institute Hospital, University Hospital 12 de Octubre, Madrid, Spain

^fCentre for Healthy Brain Ageing and Dementia Collaborative Research Centre, University of New South Wales, Sydney, Australia

^gWolfson Centre for Age Related Diseases, King's College London, London, England

^hDepartment of Psychiatry, Mayo Clinic, Scottsdale, AZ, USA

ⁱDepartment of Neurology, Mayo Clinic, Scottsdale, AZ, USA

^jDepartment of Health Sciences Research, Mayo Clinic, Scottsdale, AZ, USA

^kDepartment of Psychiatry, Mathison Centre for Mental Health Research & Education, Ron and Rene Ward Centre for Healthy Brain Aging Research, Hotchkiss Brain Institute, University of Calgary, Calgary, Canada

^lDepartment of Clinical Neurosciences, Mathison Centre for Mental Health Research & Education, Ron and Rene Ward Centre for Healthy Brain Aging Research, Hotchkiss Brain Institute, University of Calgary, Calgary, Canada

^mCenter for Alzheimer Research and Treatment, Department of Neurology, Brigham and Women's Hospital, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA

ⁿCentre for Research on Ageing, Health and Wellbeing, Research School of Population Health, The Australian National University, Canberra, Australia

^oNHMRC National Institute for Dementia Research, Centre for Research on Ageing, Health and Wellbeing, The Australian National University, Canberra, ACT, Australia

^pDivision of Geriatric Psychiatry and Neuropsychiatry, Johns Hopkins University School of Medicine, The Johns Hopkins School of Medicine, Baltimore, MD, USA

^qGeriatric Research Education and Clinical Center, Central Arkansas Veterans Healthcare System, Little Rock, AR, USA

^rDepartment of Psychiatry, University of Arkansas for Medical Sciences, North Little Rock, AR, USA

^s1st Department of Psychiatry, "Eginition" Hospital, Athens Medical School, National and Kapodistrian University, Athens, Greece

^tDivision of Geriatric Psychiatry and Neuropsychiatry, Johns Hopkins Bayview Medical Center, Johns Hopkins School of Medicine, Baltimore, MD, USA

^uDepartment of Psychiatry and Biobehavioral Sciences, UCLA School of Medicine and VA Greater Los Angeles Healthcare System, Los Angeles, CA, USA

Abstract

Introduction: Apathy is common in neurocognitive disorders (NCDs) such as Alzheimer's disease and mild cognitive impairment. Although the definition of apathy is inconsistent in the literature, apathy is primarily defined as a loss of motivation and decreased interest in daily activities.

Methods: The Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART) Neuropsychiatric Syndromes Professional Interest Area (NPS-PIA) Apathy workgroup reviewed the latest research regarding apathy in NCDs.

Results: Progress has recently been made in three areas relevant to apathy: (1) phenomenology, including the use of diagnostic criteria and novel instruments for measurement, (2) neurobiology, including neuroimaging, neuropathological and biomarker correlates, and (3) interventions, including pharmacologic, nonpharmacologic, and noninvasive neuromodulatory approaches.

*Corresponding author. Tel.: ■■■■; Fax: ■■■■.
E-mail address: krista.lanctot@sunnybrook.ca

Discussion: Recent progress confirms that apathy has a significant impact on those with major NCD and those with mild NCDs. As such, it is an important target for research and intervention.

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Keywords: Apathy; Alzheimer's disease (AD); Mild behavioral impairment (MBI); neuropsychiatric symptoms (NPS); Neurocognitive disorders (NCD)

1. Introduction

Apathy, defined [1] primarily by a marked loss of motivation [2,3], is seen throughout the spectrum of neurocognitive disorders (NCDs) [4] from mild (e.g., mild cognitive impairment, MCI) to major NCDs (e.g., severe Alzheimer's disease [AD]). Apathy has been considered as both a symptom, with a high prevalence in NCDs, and a syndrome (reviewed by Ishii et al. [5]). Apathy as a syndrome was first described by Marin et al. [3] and International Apathy Workgroup Consensus Diagnostic Criteria have been published describing three separate dimensions consisting of cognitive, affective, and behavioral symptoms [6]. However, much of the research in this field has used the apathy item of the Neuropsychiatric Inventory (NPI) scale to define apathy as a neuropsychiatric symptom (NPS). This article will summarize research on apathy, as defined using any standardized assessment method, noting how it was defined.

The increasing interest in investigating apathy coincides with its recognition as a potential treatment target. Progress has been made in three major areas of research relevant to apathy treatment: phenomenology, neurobiology, and intervention trials. Members of the Alzheimer's Association International Society to Advance Alzheimer's Research and Treatment (ISTAART) Neuropsychiatric Syndromes Professional Interest Area (NPS-PIA) Apathy Workgroup, which is comprised of specialists and investigators from the fields of geriatric medicine, neuropsychiatry, geriatric psychiatry, behavioral neurology, and neuropsychology, describe current research in these areas. Finally, recommendations for future research are made.

2. Phenomenology

2.1. Prevalence of apathy in neurocognitive disorders

The epidemiology of apathy in the setting of NCDs includes estimates of both its incidence and prevalence in normal aging, MCI, and dementia of AD type. Incidence studies, particularly in a population-based setting, are highly informative. In this approach, the incidence of apathy is determined by assembling a cohort of cognitively normal persons free of apathy at baseline and then following them forward in time until the emergence of apathy. Although expensive and complicated, these data are crucial in addressing a knowledge gap. Most epidemiologic studies of apathy in the setting of AD refer to prevalence studies or changes in apathy symptoms over time [7].

The high prevalence of apathy has been well documented in both clinical and community samples, and throughout the spectrum of severity of neurodegenerative conditions, as well as in normal cognitive aging. The frequency of apathy is generally higher in tertiary care settings than in population-based samples due to referral bias [8,9]. In AD, a 1 month prevalence of 72% among 50 outpatients with mild to severe AD has been reported based on the apathy subscale of the NPI, completed by someone who knows the patient well; there was also increased prevalence of apathy as dementia severity worsened [10]. The same group reported the prevalence of apathy to be 51% in mild AD (n = 124), 39% in MCI (n = 28), and 2% in cognitively normal persons (n = 50) [11]. Similarly, Copeland et al. [12] observed a 41% prevalence of "passivity" in a clinic sample of elders suffering a mild cognitive disorder. By contrast, the Cardiovascular Health Study found a 15% prevalence of NPI-defined apathy among MCI subjects and a prevalence of 35.8% in subjects with dementia [13]. The Mayo Clinic Study of Aging [14] measured apathy using the NPI brief questionnaire form (NPI-Q) in a countywide probability sample and reported prevalence rates of 18.5% in MCI and 4.8% among cognitively normal persons. The population-based Kungsholmen project and others have also reported that apathy is common in AD and may be a predictor of disease progression [15]. Despite a variety of apathy scales being used in these studies, data consistently demonstrate that apathy has a high prevalence in both MCI and NCD due to AD.

2.2. Prevalence in preclinical states

Although apathy is common in pre-dementia states such as MCI and its prevalence increases with disease progression [16], it has also been observed in older adults with normal cognitive function [11,14,17,18]. In studies investigating apathy in cognitively normal older adults, prevalence rates have ranged from 2% to 4.8% [11,14,17,18], when it is assessed using the NPI. For example, Lyketsos et al. assessed a sample of 1002 participants from the Cache County Study using the NPI and reported an apathy prevalence of 3.2% in cognitively normal persons [18]. A later study by Onyike et al. assessed apathy in 1033 participants from the same Cache County Study data set and found that 1.4% of cognitively normal older adults (≥ 65 years) had clinically significant levels of apathy (NPI apathy score ≥ 4) [17]. However, when assessed using the Apathy Evaluation

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