European Psychiatry 54 (2018) 71–76

Contents lists available at ScienceDirect

European Psychiatry

journal homepage: http://www.europsy-journal.com

Original article

Is it time to revise the diagnostic criteria for apathy in brain disorders? The 2018 international consensus group

P. Robert[a,*,1], K.L. Lanctôt[b,1], L. Agüera-Ortiz[c], P. Aalten[d], F. Bremond[a,e], M. Defrancesco[f], C. Hanon[g], R. David[h], B. Dubois[i], K. Dujardin[j], M. Husain[k], A. König[e], R. Levy[l], V. Mantua[m], D. Meulien[n], D. Miller[o], H.J. Moebius[p], J. Rasmussen[q], G. Robert[r], M. Ruthirakuhan[b], F. Stella[s], J. Yesavage[t], R. Zeghari[a], V. Manera[a,e]

[a] CoBTeK IA, Memory Centre, University Cote d'Azur, France
[b] Sunnybrook Research Institute and Departments of Pharmacology/Toxicology and Psychiatry, University of Toronto, Toronto, Canada
[c] Department of Psychiatry, Instituto de Investigacio'n Sanitaria (imas12), Hospital Universitario 12 de Octubre & Centro de Investigacio'n Biome'dica en Red de Salud Mental (CIBERSAM), Madrid, Spain
[d] School for Mental Health and Neuroscience, Alzheimer Center Limburg, Maastricht, Netherlands
[e] STARS team - INRIA Sophia Antipolis, Valbonne 06902, France
[f] Department of Psychiatry and Psychotherapy, Innsbruck Medical University, Austria
[g] Regional Resource Centre of Old Age Psychiatry, Paris Descartes University, Assistance Publique-Hôpitaux de Paris, Corentin-Celton Hospital, Issy-les-Moulineaux, France
[h] Memory Center CMRR, CHU – CoBTeK lab, University Cote d'Azur, France
[i] Centre des Maladies Cognitives et Comportementales (IM2A), Institut du Cerveau et de la Moelle épinière (ICM), UMR-S975, AP-HP, Salpêtrière Hospital, Sorbonne University, Paris, France
[j] Neurology and Movement Disorders, Lille University Medical Center, Inserm U1171, Lille, France
[k] Nuffield Department of Clinical Neurosciences (John Radcliffe Hospital, Oxford OX3 9DU) & Department of Experimental Psychology, University of Oxford, UK
[l] AP-HP, Neurology deparment, Salpetriere hospital Inserm, U 1127, CNRS, UMR 7225, Sorbonne Universités, UPMC Univ Paris 06, UMR S 1127, Institut du Cerveau et de la Moelle épinière, ICM, FRONTlab School of medicine, Sorbonne Universités, Paris, France
[m] Agenzia Italiana del Farmaco, via del Tritone 181, 00187, Rome, Italy
[n] Clinical Research Neurology Lundbeck SAS, Denmark
[o] Bracket, Wayne, PA, USA
[p] moebius-consult GmbH, Baar, ZG, Switzerland
[q] psi-napse, Surrey, UK
[r] EA4712 "Comportement et noyaux gris centraux", Université de Rennes 1, France
[s] Laboratorio de Neurociencias LIM27, Departamento e Instituto de Psiquiatria, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, UNESP - Univ Estadual Paulista, Biosciences Institute, Campus of Rio Claro, SP, Brazil
[t] Department of Psychiatry and Behavioral Sciences, Stanford University, School of Medicine, Stanford University, Stanford, CA, USA

ARTICLE INFO

Article history:
Received 21 April 2018
Received in revised form 19 July 2018
Accepted 24 July 2018
Available online xxx

Keywords:
Apathy
Neuropsychiatry
Brain disorders
Motivation
Behaviour
Emotion
Social interaction
Treatment

ABSTRACT

Background: Apathy is a very common behavioural and psychological symptom across brain disorders. In the last decade, there have been considerable advances in research on apathy and motivation. It is thus important to revise the apathy diagnostic criteria published in 2009. The main objectives were to: a) revise the definition of apathy; b) update the list of apathy dimensions; c) operationalise the diagnostic criteria; and d) suggest appropriate assessment tools including new technologies.
Methods: The expert panel (N = 23) included researchers and health care professionals working on brain disorders and apathy, a representative of a regulatory body, and a representative of the pharmaceutical industry. The revised diagnostic criteria for apathy were developed in a two-step process. First, following the standard Delphi methodology, the experts were asked to answer questions via web-survey in two rounds. Second, all the collected information was discussed on the occasion of the 26th European Congress of Psychiatry held in Nice (France).
Results: Apathy was defined as a quantitative reduction of goal-directed activity in comparison to the patient's previous level of functioning (criterion A). Symptoms must persist for at least four weeks, and affect at least two of the three apathy dimensions (behaviour/cognition; emotion; social interaction;

* Corresponding author at: CMRR Institut Claude Pompidou, 10 rue Molière, 06100 Nice, France.
E-mail address: probert@unice.fr (P. Robert).
[1] Equal contribution.

http://dx.doi.org/10.1016/j.eurpsy.2018.07.008

criterion B). Apathy should cause identifiable functional impairments (criterion C), and should not be fully explained by other factors, such as effects of a substance or major changes in the patient's environment (Criterion D).
Conclusions: The new diagnostic criteria for apathy provide a clinical and scientific framework to increase the validity of apathy as a clinical construct. This should also help to pave the path for apathy in brain disorders to be an interventional target.

1. Introduction

Apathy is a pervasive neuropsychiatric symptom of most neurocognitive, neurodegenerative, and psychiatric disorders. It represents the most common behavioural and psychological symptom in people with Alzheimer's disease [1] and Huntington's disease [2], and is prevalent in other neurodegenerative conditions, such as Parkinson's disease [3] and vascular dementia [4]. It is also found among substantial proportions of individuals following stroke and traumatic brain injury [5], and psychiatric conditions such as major depressive disorder [6] and schizophrenia [7]. The presence of apathy significantly affects the patient's quality of life [8], and in neurodegenerative disorders is associated with a faster cognitive and functional decline [9], representing a risk factor for the conversion from Mild Cognitive Impairment to Alzheimer's disease [10]. For all these reasons, identifying apathy early in disease progression is considered a clinical and research priority.

In major contributions [11–14], apathy was defined as a lack of motivation that persists over time and causes identifiable functional impairment. Three dimensions of apathy were identified, including deficits in goal-directed behaviour, goal-directed cognitive activity, and emotions. In 2008, a task force was set up during the European Psychiatric Association congress to develop diagnostic criteria for apathy [15]. Based on these diagnostic criteria, a patient is classified as apathetic when he/she meets four criteria (A-D). Criterion A specifies the presence of a loss of (or diminished) motivation in comparison to the person's previous level of functioning, which is not consistent with his age or culture. These changes in motivation may be reported by the patient himself or by the observations of others. Criterion B stipulates the presence of symptoms in at least two of three domains (behaviour, cognition, and emotion) for a period of at least four weeks and present most of the time. These symptoms can be detected either in self-initiated or environment-stimulated activities. Criterion C specifies that the symptoms (A - B) must cause clinically significant impairment in personal, social, occupational domains, or other important areas of functioning. Finally, Criterion D specifies that the symptoms (A - B) should not exclusively explained or due to physical or motor disabilities, to diminished level of consciousness or to the direct physiological effects of a substance.

These diagnostic criteria for apathy are now widely used in clinical and research practice for patients with neurodegenerative and neuropsychiatric disorders (e.g., [16]).

In the last decade, there have been considerable advances in the domain of apathy in brain disorders, including the apathy biological and neural based (e.g., [17]). First, the definition of apathy as a disorder of 'motivation' (Criterion A) has been extensively criticized (e.g. [18],), as 'motivation' is a psychological interpretation of behavioural internal states, which may be difficult to measure objectively. At the same time, the construct of *goal directed behaviour/activity* - construed as a set of related processes by which an internal state is translated, through observable action, into the attainment of a goal (e.g., [19]) - is increasingly used in the domain of neuroscience, and it has been proposed to be a useful to operationalize apathy, particularly in clinical contexts. Second, the different apathy domains (criterion B) have been object of discussion, and most particularly: a) the distinction between the 'behaviour' and 'cognition' domains and its relevance in clinical practice [20]; b) the importance of adding the 'social interaction' as a domain of apathy [21]; c) the importance of considering alternative proposals on apathy subtypes based on the underlying disrupted mechanisms (for instance, the 'emotional–affective', 'cognitive' and 'auto-activation' apathy subtypes [18]. Third, finer assessment tools for apathy have been developed, based on classical instruments (e.g., interviews and self-reports; see [17] for a review) but also on new Information and Communication Technologies (ICTs, e.g., [22]). However, no consensus has been reached so far on the role of ICTs in the apathy assessment, and on their relations to classical apathy measures.

Finally, the therapeutic strategy is an important aspect to consider. Despite the lack of an established pharmacological treatment for apathy with a strong evidence base (e.g., [23]), preliminary data on apathy treatment efficacy are emerging [24], with a research focus on drugs [25] and repetitive transcranial magnetic stimulation [26], often accompanied by non-pharmacological approaches [27]. Having diagnostic criteria for apathy based on the last advancements in the clinical research that reach a wide consensus among the scientific, regulatory and medical community is therefore crucial. These would, for example, allow clinical trials to be designed with a well-defined population and more sensitive apathy outcome measures, and thus obtain wider acceptance regarding the effectiveness of prevention and/or treatment strategies.

Given all these advances, a group of experts in the domain of apathy in brain disorders (leaded by PR and KL) decided to revise the diagnostic criteria for apathy proposed in 2008. The main objectives were to: a) revise the definition of apathy (criterion A); b) update the list of apathy dimensions (criterion B); c) operationalize the diagnostic criteria using examples of clinical situations and areas of possible impairment (criterion B); and d) suggest appropriate and updated apathy assessment tools.

2. Methods

2.1. Task force

Participants were selected based on their expertise in the domain of apathy in brain disorders. Some of these experts already participated to the 2008 expert meeting. These included, among others, clinicians and researchers from a) the CoBTeK-IA lab and Memory centre of the University Côte d'Azur, a lab with a focus on how to assess apathy using ICT); b) the French Memory Centre network, which includes 17 research memory centres located in the French university hospitals, c) the ISCTM (International Society for CNS Clinical Trials and Methodology) Apathy Workgroup; d) the ISTAART (International Society to Advance Alzheimer's Research and Treatment) Neuropsychiatric symptoms professional Interest Area.

The final task force included 23 experts (researchers, health care professionals and representatives of one regulatory body and