APATHY DIAGNOSTIC CRITERIA 2018

ENGLISH VERSION

VERSION FRANÇAISE

APPENDIX

CRITERION A	Yes	No
A quantitative reduction of goal-directed activity either in behavioral, cognitive, emotional or social dimensions in comparison to the patient's previous level of functioning in these areas. These changes may be reported by the patient himself/ herself or by observation of others.		

CRITERION B

B1. BEHAVIOUR & COGNITION Loss of, or diminished, goal-directed behaviour or cognitive activity as evidenced by at least one of the following:	Yes	No
General level of activity: the patient has a reduced level of activity either at home or work, makes less effort to initiate or accomplish tasks spontaneously, or needs to be prompted to perform them.		
Persistence of activity: He/she is less persistent in maintaining an activity or conversation, finding solutions to problems or thinking of alternative ways to accomplish them if they become difficult.		
Making choices: He/she has less interest or takes longer to make choices when different alternatives exist (e.g. selecting TV programs, preparing meals, choosing from a menu)		
Interest in external issue: He/she has less interest in or reacts less to news, either good or bad, or has less interest in doing new things		
Personal wellbeing: He/she is less interested in his/her own health and wellbeing or personal image (general appearance, grooming, clothes, etc.)		

B2. EMOTION Loss of, or diminished emotion as evidenced by at least one of the following:	Yes	No
Spontaneous emotions: the patient shows less spontaneous (self-generated) emotions regarding their own affairs, or appears less interested in events that should matter to him/her or to people that he/she knows well.		
Emotional reactions to environment: He/she expresses less emotional reaction in response to positive or negative events in his/her environment that affect him/her or people he/she knows well (e.g., when things go well or bad, responding to jokes, or events on a TV program or a movie, or when disturbed or prompted to do things he/ she would prefer not to do).		
Impact on others: He/she is less concerned about the impact of his/her actions or feelings on the people around him/her.		
Empathy: He/she shows less empathy to the emotions or feelings of others (e.g., becoming happy or sad when someone is happy or sad, or being moved when others need help).		
Verbal or physical expressions: He/she shows less verbal or physical reactions that reveal his/her emotional states.		

B3. SOCIAL INTERACTION Loss of or diminished, engagement in social interaction as evidenced by at least one of the following:	Yes	No
Spontaneous social initiative: the patient takes less initiative in spontaneously proposing social or leisure activities to family or others.		
Environmentally stimulated social interaction: He/she participates less, or is less comfortable or more indifferent to social or leisure activities suggested by people around him/her.		
Relationship with family members: He/she shows less interest in family members (e.g., to know what is happening to them, to meet them or make arrangements to contact them).		
Verbal interaction: He/she is less likely to initiate a conversation, or he/she withdraws soon from it.		
Homebound: He / She prefer to stays at home more frequently or longer than usual and shows less interest in getting out to meet people		

CRITERION B	Yes	No
The presence of at least 2 of the 3 dimensions (B1, B2, B3) for a period of at least four weeks and present most of the time		

CRITERION C	Yes	No
These symptoms (A - B) cause clinically significant impairment in personal, social, occupational, or other important areas of functioning.		

CRITERION D	Yes	No
The symptoms (A - B) are not exclusively explained or due to physical disabilities (e.g. blindness and loss of hearing), to motor disabilities, to a diminished level of consciousness, to the direct physiological effects of a substance (e.g. drug of abuse, medication), or to major changes in the patient's environment.		

APATHY DIAGNOSIS	Yes	No
Positive if criteria A, B, C and D are present.		

CRITÈRE A	Oui	Non
Il existe une réduction quantifiable de l'activité dirigée vers un but par rapport à l'état précédent de fonctionnement du patient dans les domaines soit des comportements / cognition, des émotions ou des interactions sociales. Ces changements peuvent être rapportés par le patient lui-même ou l'observation extérieure.		

CRITÈRE B

B1. COMPORTEMENT & COGNTION Perte ou diminution des comportements dirigés vers un but et de l'activité cognitive mis en évidence par la présence d'un des aspects suivants :	Oui	Non
Niveau d'activité général : Le patient présente une réduction du niveau d'activité à la maison soit au domicile ou au travail, fournit moins d'efforts pour initier ou accomplir des tâches de manière spontanée, ou a besoin d'être incité pour les réaliser.		
Persistance des activités : Il/Elle persiste moins dans le maintien d'une activité ou d'une conversation, dans la recherche de solutions à un problèmes ou dans l'élaboration de voies alternatives pour les résoudre lorsqu'elles ils deviennent difficiles.		
Prendre des décisions : Il/Elle a moins d'intérêt et prend plus de temps pour prendre des décisions quand différentes alternatives existent. (par ex pour choisir des programmes tv, préparer des repas, choisir un menu, etc.)		
Intérêt pour des enjeux externes : Il/Elle a moins d'intérêt, réagit moins aux nouvelles quelles soit bonnes ou mauvaises ou à moins d'intérêt pour faire de nouvelles activités		
Bien-être personnel : Il/Elle s'intéresse moins à sa santé et son bien-être ou à son image (apparence générale, toilette, habits, etc.)		

B2. EMOTION Perte ou diminution des émotions mises en évidence par au moins un des aspects suivants :	Oui	Non
Emotions spontanées : Il/Elle montre moins d'émotions spontanées (auto-générée) pour ses propres affaires, ou semble moins intéressé par des évènements qui devraient l'affecter ou affecter ses proches.		
Réactions émotionnelles face à l'environnement : Il/Elle exprime moins de réactions en réponse à des évènements positifs ou négatifs dans son environnement qui le/la touchent directement ou les personnes qu'Il/Elle connait bien (répond à une blague, à des informations à la TV ou aux scènes d'un film, ou quand Il/Elle est perturbé ou incité à effectuer des tâches déplaisantes).		
Impact sur autrui : Il/Elle est moins concerné par l'impact de ses actions ou de ses sentiments ou de ses sentiments envers les personnes qui l'entourent.		
Empathie : Il/Elle a moins d'empathie envers les émotions ou sentiments de l'autre (être heureux ou triste quand l'autre est heureux ou triste ou inversement, triste quand l'autre est triste, ou être touché émotionnellement quand une personne a besoin d'aide)		
Expression verbales ou physiques : Il/Elle montre moins de réactions verbales ou physiques qui indiquent son ressenti émotionnel.		

B3. INTERACTIONS SOCIALES Perte ou diminution de l'engagement dans des interactions sociales mises en évidence par au moins un des aspects suivants :	Oui	Non
Initiatives sociales spontanées : Le patient prend spontanément moins d'initiatives pour proposer des activités sociales ou de loisir à sa famille ou autres.		
Interactions sociales stimulées par l'environnement : Il/Elle participe moins ou est moins à l'aise ou plus ou est indifférent aux activités, sociales ou de loisirs, proposées par son entourage.		
Relations avec les proches : Il/Elle s'intéresse moins aux membre de la famille (par ex savoir ce qu'il leur arrive, les voir ou les contacter)		
Interactions verbales : Il/Elle initie moins ou n'initie plus de conversation, ou l'interrompt précocement.		
Domicile: Il/Elle préfère rester chez lui/elle plus fréquemment ou plus longuement que d'habitude et s'intéresse moins à sortir pour voir ses proches ou ses amis.		

CRITÈRE C	Oui	Non
Les critères A et B causent une altération cliniquement significative des occupations personnelles et sociales, ou d'autres aspects importants du fonctionnement.		

CRITÈRE D	Oui	Non
Les symptômes A et B ne sont pas exclusivement causés par un handicap physique (cécité ou surdité), un handicap moteur, une diminution du niveau de conscience, des effets directs d'une substance (drogues illicites ou traitement), ou de changements majeurs de l'environnement du patient.		

DIAGNSOTIC DE L'APATHIE	Oui	Non
Positif si les critères A, B, C and D sont présent present.		

APPENDIX

Definition:

Goal-directed behaviour/ activity: behaviour aimed toward a goal or toward completion of a task Presumed underlying pathophysiological mechanisms: Apathy is the clinical consequence of various underlying dysfunctions of mental and biological processes required to elaborate, initiate and control intentional/goal-directed behaviour.

How to assess apathy

Interviews for caregiver

AES-I, NPI, IAS, FrSBe, IA, DAIR, KBCI, LARSi, DAS, APADEM-NH

Self report index
AES-S, The Behavioural Assessment of Dysexecutive Syndrome, FrSBe, EDA, NPI-C, DAS, AMI
Clinician's scales
BPRS, PANSS, SANS, AES-C, UPDRS, The Behavioural Assessment of Dysexecutive Syndrome, IAS, FrSBe, IA, DAIR, LARS, sfLARS, NPI-C

Cautions: Due to anosognosia, take with caution patient's report. Select a good caregiver; take into account spouse's biases etc. It is possible in parallel to use other types of scales / assessment tools (eg for depression, anxiety, fatigue..)

Information and Communication technologies (ICT)

There is evidence that apart from the currently used assessment methods for apathy, new ICT approaches could provide clinicians with valuable additional information for detection and therefore more accurate diagnosis of apathy. Actigraphy and methods used to monitor motor activity and rest-activity rhythms had already demonstrated to be accurate and related to apathy. Other methodologies (voice analysis, video analysis, use of serious games) already are used but only at the moment in research setting.

Caution: Such technologies must be used and interpreted with caution in patients with movement disorders (Parkinson's disease, Huntington's disease, progressive supranuclear palsy,…). These patients often have reduced total activity, in relation with their motor symptoms. In the same way, they speak slowly, with an hypophonic voice, have a low speech rate due to speech and respiratory disorders. They also have an hypomimic face that can give the impression they do not react to emotion while it is not really the case. Hence, the proposed measures need to be used with reservations. What is needed for pharmacological clinical trials - To provide the scientific rational (biological basis) for targeting specific dimensions; - To provide the relation with the product intended for development (mechanism of action); To provide justification for the choice of endpoint.

The criteria are presented in: European Psychiatry 54 (2018) 71–76

The supplements (table 1,2,3) are included below

Supplementary Table 1. Participants in the expert panel

Name	Domain of expertise
P.Robert*[1], K. L. Lanctôt*[2]	Experts in the field of apathy in Europe and North America. Philippe Robert organized the 2008 expert meeting, and Krista Lanctot is expert in pharmacological approaches. She makes the link with other scientific association involved in clinical trials (ISTCM and ISTAART).
L. Agüera-Ortiz[3,] P. Aalten[4,] C.Hanon[7], R.David[8], B.Dubois[9], K. Dujardin[10], M. Husain[11], A. König[5], R. Levy[12] V. Manera [1,5], F.Stella[19], J. Yesavage[20]	Clinicians and researchers experts in apathy and behavioral disturbances.
F. Bremond[1,5]	Engineer in informatics and specialist of the use of ICT for the assessment of behavioral disturbances.
G., M. Ruthirakuhan[2], R. Zeghari[1]	PhD students in Nice and in Toronto working directly for their thesis on apathy.
M. Defrancesco[6], D. Meulien[14], D. Miller[15], H.J. Moebius[16], J. Rasmussen[17]	Experts belonging to the ISTCM and ISTAART groups.
V. Mantua[13]	Expert in an European agency. Please take note that the opinions expressed in this manuscript are the personal views of the Author and may not be understood or quoted as being made on behalf of or reflecting the position of the Italian (AIFA) or European (EMA) Medicines Agency or any of their Committees. The mention of commercial products, their sources, or their use in connection with material reported herein is not to be constructed as either an actual or implied endorsement of such products by any Public Department or Health and/or Payer Services.

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Supplementary Table 2: Delphi round 1 and 2; Questions, and responses obtained from the expert panel and from clinicians belonging to the French Research Memory Centre network

Round 1			
General questions		**Experts Score*** (Mean, SD) / 5	**Clinicians Score**** (Mean, SD) / 5
1. How important is it to have apathy diagnostic criteria for			
	The clinical practice	4.4 (.7)	3.6 (.7)
	Research	4.8 (.4)	4.2 (.8)
2. For clinical purposes, how important are the diagnostic criteria for the following targets?			
	To improve prevention strategies	4.3 (.8)	3.0 (.8)
	To improve diagnostic and assessment strategies	4.7 (.5)	3.8 (.8)
	To help clinicians in the choice of the pharmacologic treatments	4.2 (1.0)	3.5 (.7)
	To help clinicians in the choice of the <u>non</u> pharmacologic treatments	4.2 (.9)	3.8 (.6)
	To help family caregivers to understand the pathology and put in place care strategies	4.0 (1.0)	4.0 (.6)
	To help professional caregivers to understand the pathology and put in place care strategies	4.1 (.8)	3.9 (.7)
3. For research purposes, how important are the diagnostic criteria for the following targets?			
	To improve the understanding of the phenomenology	4.5 (.6)	4.1 (.9)
	To improve the understanding of the neuroanatomical and biological correlates	4.6 (.5)	4.2 (.8)
	To improve the population selection criteria in pharmacological clinical trials	4.7 (.8)	4.4 (.8)
	To improve the population selection criteria in non-pharmacological clinical trials	4.6 (.6)	4.3 (.9)
Criteria specific questions		**% of responses** (17 responses)	**% of responses** (11 responses)
4a. Title: Is it important to modify the title and to replace apathy with another terminology?			
	Yes	65	63
	No	35	27
	Don't know / Prefer not to answer	0	10
4b. If so, what terminology would you suggest employing?			
	Motivation deficits	17.5	0
	Motivation disorders	17.5	67
	N/A, Don't know / Prefer not to answer/Other	65	33
5. Criterion A: do you agree with the current formulation?			
	Yes	70	
	No	30	
	Don't know / Prefer not to answer	0	
6. Criterion B: do you agree to simplify and rephrase the difference between self-initiation and environment stimulated events?			
	Yes	65	
	No	12	
	Consider 2 versions of the criteria (1 for clinical purposes, 1 for research)	18	
	Don't know / Prefer not to answer	5	
7. Criterion B: do you agree to add questions for the criteria operationalization?			
	Yes	76	

	No	12	
	Don't know / Prefer not to answer	12	
8. Criteria C: This criterion indicates that the criteria are not only related to the dementia field. Is it important to keep this specification?			
	Yes	65	
	No	24	
	Don't know / Prefer not to answer	12	

Round 2		**% of responses** (10 responses)
9. The majority of responses indicated to keep the term apathy in the title. If it is possible to have a subtitle, which one would you suggest?		
	Motivation disorders	20
	Motivation deficits	80
10. Criterion A: The majority of responses indicated to keep the current definition. Some alternatives were also suggested: do you agree with the following?		
	To replace "motivation" with "motivation and drive"	17
	To replace "motivation" with "goal-directed behaviour"	67
	To replace "functioning" with "performance"	17
	To specify the domains included in criterion B	50
11. Do you agree to include in the diagnostic criteria document a brief glossary in order to define: "motivation", "goal-directed behaviour" and other notions of interest?		
	Yes	100
	No	0
12. Criterion B: The majority of responses indicated to simplify and rephrase the difference between self-initiation and environment stimulated events, and to add questions for the criteria operationalization (same number of examples). Furthermore, some important modifications were suggested. Please indicate if you agree with the following proposals:		
	If there is the presence of environment-stimulated deficits (no reaction to environmental stimuli), indicate a higher degree of apathy	62.5
	Modify the 3 present domains (1/Cognition; 2/Behaviour; 3/Emotion) with the following domains: 1/ Behaviour-Cognition; 2/ Emotion; 3/ Social interaction	62.5
13. Criterion C: The majority of responses indicated that is important to keep the indication that the criteria are not only related to dementia. This underlines the dimensional level of the diagnostic criteria. More generally this raises the question of the criteria use for various disorders (eg dementia, non dementia), users (clinician, researchers), practices (daily clinic, research, clinical trials). Do you agree with the following proposals?		
	To have 2 levels of descriptions (1 for the clinical practice, 1 for research)	12.5
	To add in the annex suggestions on how to assess the different apathy domains (including caregiver's scales, ICT, etc.)	87.5
	To add in the annex indications according to the type of disorder	75

Quantitative rating for general questions: 5-point rating scale: 1= Not important at all; 2= Not very important; 3= Important; 4= Very important; 5= Extremely important.
* Expert's scores: scores provided by the participants of the expert meeting (N=17).

** Clinician's scores: scores provided by clinicians belonging to the French Research Memory Centre network (responses obtained by 11 out of the 17 centres).

Supplementary Table 3: Apathy Scales and interviews

	Scale for:	*Apathy dimensions** Apathy specific ***	*Original study population*
Brief Psychiatric Rating Scale (BPRS) *[1] Overall and Gorham (1962)*	Clinician	Emotion No	Paranoia Schizophrenia Depression
Positive and Negative Syndrome Scale (PANSS) *[2] Kay et al. (1987)*	Clinician	Emotion, Social Interaction No	Schizophrenia
Scale for the Assessment of Negative Symptoms (SANS) *[3] Andreasen (1989)*	Clinician	Emotion, Social interaction No	Schizophrenia
Apathy Evaluation Scale (AES-S/I/C) *[4] Marin et al. (1991)*	Self-report Caregiver Clinician	Cognition, Behavior, Emotion Yes	AD (Alzheimer's disease), Brain injury, Major depression
Apathy Scale (AS) *[5] Starkstein et al. (1992)*	Clinician	Cognition, Behavior, Emotion Yes	PD (Parkinson's disease)
Neuropsychiatric Inventory (NPI) *[6] Cummings et al. (1994)*	Caregiver	Cognition, Behavior, Emotion No	Dementia
Unified Parkinson's Disease Rating Scale (UPDRS) 1 item *[7] Martinez-Sarriez et al. (1994)*	Clinician	Cognition, Behavior No	PD
The Behavioural Assessment of Dysexecutive Syndrome (DEX) *[8] Wilson et al. (1996)*	Clinician Self-report	Cognition, Behavior, Emotion No	Brain injury
Irritability-Apathy Scale (IAS) *[9] Burns et al. (1997)*	Caregiver Clinician	Cognition, Behavior No	AD HD (Huntington disease)
Frontal Lobe Personality Scale (FLOPS) now known as the Frontal Systems Behavior Scale (FrSBe) *[10] Grace et al. (1999)*	Self-report Caregiver Clinician	Cognition, Behavior No	Brain injury (frontal lobe)
Neuropsychiatric Inventory Questionnaire (NPI-Q) *[11] Kaufer et al. (2000)*	Caregiver	Cognition, Behavior, Emotion No	AD

L'échelle d'appréciation de la démotivation (EDA) *[12]* Chantoin et al. (2001)	Self-report	Cognition, Behavior, Emotion Yes	Dementia (especially memory disorders)
Apathy Inventory (AI) *[13]* Robert et al. (2002)	Caregiver Clinician	Cognition, Behavior, Emotion Yes	Dementia
Dementia Apathy Interview and Rating (DAIR) *[14]* Strauss & Sperry (2002)	Caregiver Clinician	Behavior No	Dementia
Key Behavior Change Inventory (KBCI) *[15]* Belanger et al. (2002)	Caregiver	Cognition, Behavior, Emotion No	Elderly memory disorder
Lille Apathy Rating Scale (LARS) *[16]* Sockeel et al. (2006)	Clinician	Cognition, Behavior, Emotion, Social Interaction Yes	PD
Lille Apathy Rating Scale short form (sfLARS) *[17]* Dujardin et al. (2013)	Clinician	Cognition, Behavior, Emotion, Social Interaction Yes	PD
Informant based Lille apathy rating scale (LARS-i) *[18]* Dujardin et al. (2008)	Caregiver	Cognition, Behavior, Emotion, Social Interaction Yes	PD
Neuropsychiatric Inventory (NPI-C) *[19] de* Medeiros et al (2010)	Clinician	Behavior, Cognition, Emotion No	Dementia
Abbreviated Apathy Evaluation Scale (AES-10) *[20]* Leontjevas et al. (2012)	Caregiver	Cognition, Behavior, Emotion Yes	Dementia
Apathy in institutionalized persons with dementia (APADEM-NH) *[21]* Aguera-Ortiz & al (2015)	Caregiver	Cognition, Behavior, Emotion Yes	Dementia
Dimensional Apathy Scale (DAS) *[22]* Radakovic & Abrahams (2014) *[23]* Radakovic et al. (2016)	Self-report Caregiver	Cognition, Behavior, Emotion, Yes	Neurodegenerative Diseases AD, PD, ASL***
Apathy motivation index (AMI) *[24]* Ang et al. (2017)	Self-report	Cognition, Behavior, Emotion, Social Interaction Yes	Healthy adults

* Based on the following classification coming from the Apathy diagnostic criteria 2018: Behavior & Cognition; Emotion; Social interaction.
** Yes = the scale is apathy specific. No = the scale assesses apathy as a subdomain.
*** ALS (amyotrophic lateral sclerosis). The scale also proposes a Dimensional Apathy Framework. Furthermore, the discrepancy between self-ratings and informant/carer-ratings on the

DAS have been used to define the awareness deficit in dementia, and are described in the following papers:

Radakovic, R., Starr, J. M., & Abrahams, S. (2017). A novel assessment and profiling of multidimensional apathy in Alzheimer's disease. Journal of Alzheimer's Disease, 60(1), 57-67.

Radakovic, R., & Abrahams, S. (2018). Multidimensional apathy: evidence from neurodegenerative disease. Current Opinion in Behavioral Sciences, 22, 42-49.

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