The 2018 criteria for Apathy and rationales for update

Philippe Robert

Apathy Diagnostic Criteria meeting
13 July 2019 - Los Angeles

B1. BEHAVIOUR & COGNITION
Loss of, or diminished, goal-directed behaviour or cognitive activity as evidenced by at least one of the following:

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, etc.)

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:

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:

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.

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SURVEY CENTRES

POPULATION CHARACTERISTICS

<table>
<thead>
<tr>
<th>Overall population (N=188)</th>
<th>No Apathy (n=106)</th>
<th>Apathy (n=82)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean [SD]</td>
<td>Mean [SD]</td>
<td>p-value*</td>
</tr>
<tr>
<td></td>
<td>72.58 [8.54]</td>
<td>76.30 [7.82]</td>
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</table>

<table>
<thead>
<tr>
<th>Major Cognitive disorders (N=75)</th>
<th>No Apathy (n=106)</th>
<th>Apathy (n=82)</th>
<th>p-value*</th>
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</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean [SD]</td>
<td>Mean [SD]</td>
<td>p-value*</td>
</tr>
<tr>
<td></td>
<td>73.17 [8.44]</td>
<td>77.27 [9.12]</td>
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<tr>
<td>MMSE</td>
<td>19.45 [2.43]</td>
<td>18.34 [2.63]</td>
<td>&lt;.001</td>
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<table>
<thead>
<tr>
<th>Minor Cognitive disorders (N=77)</th>
<th>No Apathy (n=106)</th>
<th>Apathy (n=82)</th>
<th>p-value*</th>
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<tbody>
<tr>
<td>Age</td>
<td>Mean [SD]</td>
<td>Mean [SD]</td>
<td>p-value*</td>
</tr>
<tr>
<td></td>
<td>73.84 [8.59]</td>
<td>77.48 [7.32]</td>
<td>0.005</td>
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<tr>
<td>MMSE</td>
<td>23.98 [2.33]</td>
<td>23.73 [3.94]</td>
<td>&lt;.001</td>
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</table>

<table>
<thead>
<tr>
<th>Anxiodepression (N=21)</th>
<th>No Apathy (n=106)</th>
<th>Apathy (n=82)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean [SD]</td>
<td>Mean [SD]</td>
<td>p-value*</td>
</tr>
<tr>
<td>68.00 [9.94]</td>
<td>74.50 [8.31]</td>
<td>6.120</td>
<td></td>
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<tr>
<td>MMSE</td>
<td>28.33 [0.56]</td>
<td>23.62 [4.04]</td>
<td>&lt;.001</td>
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</tbody>
</table>

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Frequency of subjects presenting the full Apathy Diagnostic Criteria

WITH APATHY

<table>
<thead>
<tr>
<th>SCD</th>
<th>Mild NCD</th>
<th>Major NCD</th>
<th>AFD</th>
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</thead>
<tbody>
<tr>
<td>10</td>
<td>25.5</td>
<td>60</td>
<td>87.1</td>
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</table>

Criterion B sensitivity & specificity of each dimension
**B1 Behaviour / cognition**

NO

YES

**B2 Emotion**

**B3 Social Interaction**

Repartition of examples presence in dimension B1 for all the population (n = 188)

Examples are empirically divided in Behavior / Cognition / Mixt cognitive & behavior

**B1. BEHAVIOUR & COGNITION**

Loss of, or diminished, goal-directed behaviour or cognitive activity as evidenced by at least one of the following:

**Categories**

Clinicians panel choice

**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, etc.).

**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 her/his own health and wellbeing or personal image (general appearance, grooming, clothes, etc.).

Dimension B1 showed the highest Sensitivity (followed by B3), meaning that its presence was strongly associated to presence of apathy (DCA+).

This suggests that merging behavior and cognition in a single category lead to a strong apathy index, which is easier to use in the clinical practice because deficits in behavior and cognition are hard to distinguish.
Appendix

http://www.innovation-alzheimer.fr/assessment/

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 hypomorphic 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.

http://www.innovation-alzheimer.fr/motivation-application-2/

17 questions for 17 interests

Are you interested in eating well?
Are you interested in playing?
Are you interested in the family?
Are you interested in the Sea?
Are you interested in Love?
Do you like reading?
Is the Sport interesting?
Do relaxation and meditation interest you?
Are you interested in Dance?
Do you like singing, music?
Do you like Mountain?
Are you interested in Nature?
Are you interested in movies / TV?
Are you interested in social relations?
Are you interested in museums / Arts?
Are new technologies of you interest for you?
Is the self-image of interest to you?

Apathy Diagnostic Criteria 2009 vs 2018

<table>
<thead>
<tr>
<th>Apathy Criteria</th>
<th>2009</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>30 (57,7)</td>
<td>2 (3,8)</td>
</tr>
<tr>
<td>Yes</td>
<td>0 (0,0)</td>
<td>20 (38,5)</td>
</tr>
</tbody>
</table>

Kappa coefficient: 0,92
Concordance (%): 96,2

n = 21
n = 41
n = 33

N = 52
Rationales for update & Suggestions

- Disease specificity
- Pharmacological research
- Strategic decision
- To be connected with the 2018 criteria
- Non pharmacological approach
- Concepts and definition of apathy
- Operationalization