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# The Apathy Inventory: assessment of apathy and awareness in Alzheimer's disease, Parkinson's disease and mild cognitive impairment

P. H. Robert[1]*, S. Clairet[1], M. Benoit[1], J. Koutaich[1], C. Bertogliati[1], O. Tible[1], H. Caci[2], M. Borg[4], P. Brocker[1,3] and P. Bedoucha[1,4]

[1]*Centre Mémoire, Unité d'Evaluation des Cognitions, Centre Hospitalier Universitaire de Nice, France*
[2]*Service de Pédiatrie Centre Hospitalier Universitaire de Nice, France*
[3]*Service de Gériatrie Centre Hospitalier Universitaire de Nice, France*
[4]*Service de Neurologie Centre Hospitalier Universitaire de Nice, France*

## SUMMARY

**Objective** This study was designed to establish the validity and reliability of the apathy inventory (IA), a rating scale for global assessment of apathy and separate assessment of emotional blunting, lack of initiative, and lack of interest.
**Method** Information for the IA can be obtained from the patient or from a caregiver. We evaluated 115 subjects using the IA, consisting of 19 healthy elderly subjects, 24 patients with Mild Cognitive Impairment (MCI), 12 subjects with Parkinson's disease (PD) and 60 subjects with Alzheimer's disease (AD).
**Results** Internal consistency, item reliability, and between–rater reliability were high. A test–retest reliability study demonstrated that caregiver responses to IA questions were stable over short intervals. A concurrent validity study showed that the IA assesses apathy as effectively as the Neuro Psychiatric Inventory apathy domain. In the caregiver-based evaluation, AD subjects had significantly higher scores than controls, both for global apathy score and for the lack of interest dimension. When the AD patients were subdivided according to diagnostic criteria for apathy, apathetic patients had significantly higher scores than non apathetic patients. With the patient-based evaluations, no differences were found among the AD, MCI and control groups. The scores in the patient-based evaluations were only higher for the PD group versus the control subjects. The results also indicated that AD patients had poor awareness of their emotional blunting and lack of initiative.
**Conclusions** The IA is a reliable method for assessing in demented and non-demented elderly subjects several dimensions of the apathetic syndrome, and also the subject's awareness of these symptoms. Copyright © 2002 John Wiley & Sons, Ltd.

KEY WORDS — dementia; behavior; apathy; motivation; awareness; assessment; Alzheimer's disease; Parkinson's disease; mild cognitive impairment

## INTRODUCTION

Apathy is commonly defined as a lack of interest, emotion and motivation. Apathy is reported to be frequent in patients with stroke, Parkinson's disease (PD), traumatic brain injury, Alzheimer's disease (AD) and depression (Andreasen, 1989; Starkstein *et al.*, 1993; Benoit *et al.*, 1999). However, the clinical definition of apathy is variable, and several authors have attempted to clarify the subject. Berrios and Gili (1995) underlined the 'absence of will', and Marin *et al.* (1991) the 'diminished motivation' of apathetic subjects. More recently, Marin (1996) defined apathy as amotivation in affect, behavior and cognition. In order to study the syndromic validity of apathy, Starkstein *et al.* (2001) operationalized Marin's criteria as follows: (1) lack of motivation relative to the patient's previous level of functioning or the

* Correspondence to: Professor P. H. Robert, Centre Mémoire, Pavillon J, Hôpital Pasteur, 30 avenue de la Voie Romaine, 06002 NICE Cedex 1, France. Tel: (33) 492 03 80 02. Fax: (33) 492 03 83 26. E-mail: Philippe.robert15@wanadoo.fr

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standards of his/her age and culture; (2) presence of at least one symptom belonging to each of the following three domains: (i) diminished goal-directed behavior (lack of effort, dependency on others to structure activity); (ii) diminished goal-directed cognition (lack of interest, lack of concern about one's personal problems); and (iii) diminished concomitants of goal-directed behavior (unchanging affect, lack of emotional responsiveness); (3) the symptoms cause clinically significant distress or impairment in social and occupational functioning; and (4) the symptoms are not due to a diminished level of consciousness or to the direct physiological effects of substances such as narcotics or medications. One of the most interesting aspects of this definition is that the first two criteria underline that a lack of motivation is the cardinal feature of apathy and that such a disturbance could have a separate impact on behavioral, cognitive and affective domains.

Stuss *et al.* (2000) suggested that apathy was best described as an absence of responsiveness to stimuli, as demonstrated by a lack of self-initiated action, but they also postulated that different kinds of apathy could be distinguished on the basis of brain region involvement and the underlying neuropsychological mechanisms.

Apathy has been quantified using specific scales such as the Irritability-Apathy scale (Burns *et al.*, 1990), Marin' and colleagues' apathy scale (1991) and Starkstein' and colleagues' 14-item scale (Starkstein *et al.*, 1992). However, in clinical research and in most pharmacological intervention studies, apathy is assessed with the Neuropsychiatric Inventory (NPI) (Cummings *et al.*, 1994), which is the only general behavioral inventory that specifically includes an item on the global evaluation of apathy.

In comparison with the NPI and other existing scales the Apathy Inventory (IA) was designed to provide a separate assessment of the emotional, behavioral and cognitive aspects of apathy mentioned in previously described criteria. The IA is based on the NPI model, and information can be obtained from the spouse or another person intimately familiar with the patient's behavior. Furthermore, the patient him/herself can also be evaluated by direct questioning.

Because apathy is a prominent feature of behavioural changes in AD, we first evaluated the IA in this population. We also tested the IA in Mild Cognitive Impairment (MCI) and PD; indeed, MCI may lead to AD, and apathy is also frequent in PD, a degenerative disease totally different from AD.

In this study we examined the concurrent validity, internal consistency, between–rater reliability and test–retest reliability of the IA, in a population of subjects with MCI, PD or AD, relative to health elderly subjects. Furthermore, IA scores were compared between AD patients with and without a clinical diagnosis of apathy.

## METHODS

### *Apathy Inventory structure and procedure*

The three dimensions assessed in the IA were chosen according to the literature (Landes *et al.*, 2001) and the diagnostic criteria based on the operationalization of the Marin *et al.* scale (1991). Emotional blunting refers to the lack of emotional responses. Lack of initiative refers to diminished goal-directed behavior and lack of interest to diminished goal-directed cognition. The IA consists of two sets of questionnaires, one for caregiver and one for patient-based assessments.

The caregiver version follows the rules and the organization of the NPI. The basic aim of the Apathy Inventory is to obtain information on apathy in patients with brain disorders. It is based on responses gathered from an accompanying person, preferably one intimately familiar with the patient's behavior. The caregiver interview is best conducted in the patient's absence, to facilitate open discussion of behaviors. Questions are asked exactly as written. If the caregiver does not understand, the question can be clarified.

The questions deal with behavioral changes that have occurred since the beginning of the disease. Behavior traits present throughout life and not having changed since onset of the disease are not taken into account, even if they are abnormal. The questionnaire can also be used to measure changes over a specific period of time.

Yes–no questions are posed to determine whether behavior changes are present or absent. If the response is negative, a score of 0 is attributed and the rater proceeds to the next item.

If the response is positive, the frequency and gravity of the item are explored with simple questions ('*How frequently do these problems arise?' and 'How severe are these problems; to what extent do they disturb or handicap the patient?*' For each of the three questions, the maximum score (Frequency 1–4 × Severity 1–3) is 12, giving a maximum total score of 36.

Using the patient-based version, one can evaluate the three dimensions; the score for each dimension is obtained by using a Likert-style scale (1–12): if the symptom is present, the subject is asked to

 

estimate its intensity (from mild at the left-hand end of the scale, to severe at the right-hand end).

### *Population*

115 subjects were included in the study. They comprised 60 consecutively diagnosed patients meeting the ICD-10 criteria for AD, 24 consecutively diagnosed subjects meeting the ICD-10 criteria for MCI, and 12 subjects with PD diagnosed according to conventional clinical criteria. Each PD subject was interviewed to confirm that he or she did not meet the ICD-10 criteria for dementia. Patients were excluded if a new psychotropic treatment had been prescribed less than 15 days before the evaluation. The patients' results were compared with those of a healthy control group composed of 19 individuals with normal neurological and psychiatric evaluations. Controls were selected from among the patients' relatives and among subjects belonging to a senior recreational group.

All the subjects were evaluated at the Nice University Memory Center. The Mini-Mental Score Evaluation (MMSE) and IA were administered to the patients, and NPI and IA were administered to the caregivers. With the exception of the IA, all the evaluations were part of the standard assessment of such patients. All the patients and caregivers gave their informed consent, after the IA procedure had been fully explained to them. Informed consent was also obtained from the caregiver of the most severely impaired subjects.

### *Statistical analysis*

Concurrent validity was determined by comparing the IA individual item and global scores with the NPI apathy frequency × severity scores, using a multiple regression analysis. The NPI and IA evaluations were carried out blind to each other. The same method was used to determine if the IA scores were related to age and the MMSE score. Cronbach's alpha coefficient was calculated to determine internal consistency. Between–rater reliability was determined by having 26 raters score a single caregiver's videotaped responses. Raters participating in this assessment included psychiatrists, psychologists and medical students.

Test–retest reliability was determined by conducting a second interview with the same caregivers. The two interviews were carried out blind to each other. A clinician not involved in the first interview conducted the second interview. Kappa statistic measures were used for between–rater and test–retest reliability. The two interviews were done on the same day by two examiners. One limitation of this procedure is that the caregiver may remember during the second assessment the answers that were provided during the first assessment.

Concurrent validity, internal consistency, and the relation with age and MMSE were calculated both for the overall population and for the AD subgroup. Fourteen IA assessments of AD patients were used for the test–retest study.

The AD group was then subdivided on the basis of diagnostic criteria for apathy (Starkstein *et al.*, 2001); on this basis 14 patients were apathetic (AD/A), and 36 were not apathetic (AD/NA).

Emotional blunting, lack of initiative, lack of interest and the global scores were analysed for the caregiver-based and the patient-based evaluation. Finally, the ratio caregiver/patient-based evaluation was calculated for each of these dimensions. Statistical analysis was based on means and standard deviations, one-way analysis of variance (ANOVA) and the Bonferroni significant difference *post hoc* tests.

## RESULTS

The age, sex, MMSE, NPI apathy, and NPI dysphoria scores for the four groups are presented in Table 1.

Table 1. Demographic and clinical characteristics of the control, MCI, PD and AD subjects

| | AD $n=60$ | PD $n=12$ | MCI $n=24$ | Control $n=19$ |
|---|---|---|---|---|
| Age | 74.90 (7.11) | 64.1 (11.9) | 71.67 (5.92) | 70.68 (8.21) |
| Sex (M/F) | 27/33 | 7/5 | 7/17 | 8/11 |
| MMSE | 22.55 (3.98) | 27.2 (3.5) | 28.21 (1.06) | 29 |
| NPI apathy | 3.36 (4.32) | 2 (3) | 1.50 (3.53) | 0.44 (1.5) |
| NPI dysphoria | 1.93 (2.92) | 3.3 (3.4) | 0.59 (1.37) | 0.19 (0.4) |

Significant differences (one-way ANOVA) for: age: ($F_{3,111}=7.18$; $p<0.001$); MMSE ($F_{3,111}=31.7$; $p<0.0001$); NPI apathy score ($F_{3,111}=3.2$; $p<0.01$); NPI dysphoria score ($F_{3,111}=5.08$; $p<0.01$).

The PD patients were younger than the AD and MCI patients. The AD patients had significantly lower MMSE scores than both the MCI and the control group ($p < 0.0001$). The AD patients had significantly higher NPI apathy and dysphoria scores than the control subjects. The PD subjects had significantly higher NPI dysphoria scores than the control subjects ($p < 0.001$) and the MCI group ($p < 0.05$). In the overall population, the NPI dysphoria score correlated with the IA caregiver scores for the following items: lack of initiative ($r = 0.32$; $p < 0.05$), lack of interest ($r = 0.4$; $p < 0.001$), global score ($r = 0.37$; $p < 0.01$); in the patient-based evaluation, the NPI dysphoria score correlated with lack of initiative ($r = 0.37$; $p < 0.01$), lack of interest ($r = 0.31$; $p < 0.05$), and the global score ($r = 0.42$; $p < 0.001$). No significant relation was found between the NPI dysphoria scores and the IA caregiver/patient-based evaluation ratio in either the overall population or any of the four diagnostic subgroups.

### *IA validity and reliability*

Concurrent validity was determined by comparing the IA individual item and global scores with the NPI apathy score. The correlations for the overall population and the AD group are presented in Table 2. For the caregiver evaluation, the lack of initiative and the lack of interest correlations reached significance ($p < 0.001$), both for the overall population and the AD subgroup. No such correlation was found in the patient-based assessment. IA item scores did not correlate with age and there was only a significant relation between MMSE and IA caregiver global score ($r = 0.37$; $p < 0.05$).

Table 2. Correlation of Apathy Inventory (IA) scores and the NPI apathy score

| | Overall population Coefficient (SE) | AD group Coefficient (SE) |
|---|---|---|
| IA caregiver-based evaluation | | |
| Emotional blunting | 0.01 (0.09) | 0.03 (0.12) |
| Lack of initiative | 0.23 (0.07)** | 0.22 (0.09)* |
| Lack of interest | 0.63 (0.06)*** | 0.66 (0.08)*** |
| IA patient based evaluation | | |
| Emotional blunting | 0.04 (0.18) | 0.05 (0.36) |
| Lack of initiative | 0.01 (0.16) | −0.23 (0.27) |
| Lack of interest | 0.26 (0.14) | 0.33 (0.24) |

Multiple regression analysis *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$.

As regards internal consistency, the Cronbach alpha coefficient for overall reliability was 0.84 for the caregiver version. Between–rater agreement was very high for all the item scores and the global score (Kappa coefficient 0.99). Regarding test–retest reliability, all the scores correlated: emotional blunting (Kappa = 0.99) lack of initiative (Kappa = 0.97), lack of interest (Kappa = 0.99), and the global score (Kappa = 0.96).

### *Between–group comparisons* (Table 3)

For the caregiver version, *post hoc* analysis indicated that the AD patients had significantly higher scores than the control subjects for 'lack of initiative' and for the global score. For the patient-based assessment, *post hoc* analysis indicated that only the PD group had higher global scores than the other subgroups. The differences were significant relative to the MCI, control ($p < 0.01$) and AD group ($p < 0.05$) for

Table 3. IA scores (mean and SD) in the control, MCI, PD and AD groups

| | AD $n = 60$ | PD $n = 12$ | MCI $n = 24$ | Control $n = 19$ |
|---|---|---|---|---|
| IA-caregiver | | | | |
| Emotional blunting* | 1.73 (3.4) | 1.83 (2.8) | 0.38 (1.3) | 0 |
| Lack of initiative* | 4.05 (4.4) | 3.58 (2.8) | 2 (4.1) | 0.37 (0.8) |
| Lack of interest | 3.42 (4.6) | 2.58 (2.6) | 1.83 (3.9) | 0.68 (2) |
| Global score* | 9.2 (10.4) | 8 (6) | 4.21 (8.6) | 1.05 (2) |
| IA-patient | | | | |
| Emotional blunting† | 0.66 (1.8) | 2.7 (3.5) | 0.39 (1.3) | 0.56 (2.2) |
| Lack of initiative† | 1.52 (2.6) | 2.75 (3.9) | 1.07 (2.3) | 0.05 (0.2) |
| Lack of interest† | 1.56 (2.7) | 3.58 (3.9) | 1 (2.4) | 0.89 (2.2) |
| Global score† | 3.74 (5.9) | 9.1 (8.3) | 2.47 (3.8) | 1.51 (2.9) |

*Significant differences (one-way ANOVA) in the caregiver scores for: emotional blunting ($F_{3,111} = 3.06$; $p < 0.05$); lack of initiative ($F_{3,111} = 5$; $p < 0.01$); total score ($F_{3,111} = 4.94$; $p < 0.001$); no significant difference in the lack of interest dimension ($F_{3,111} = 2.62$; $p < 0.053$).

†Significant differences (one-way ANOVA) in the subjects' scores for: emotional blunting ($F_{3,111} = 4.18$; $p < 0.01$); lack of initiative ($F_{3,111} = 3.04$; $p < 0.05$); lack of interest ($F_{3,111} = 2.88$; $p < 0.05$); total score ($F_{3,111} = 5.36$; $p < 0.001$).

 

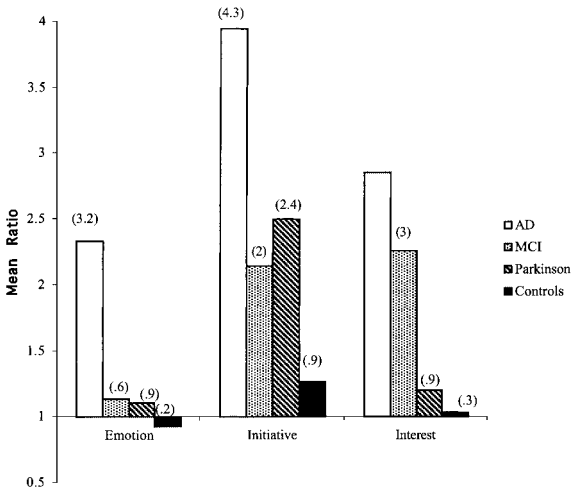


Figure 1. Awareness of apathy in the different subgroups, based on the caregiver/patient-based ratio evaluation. Mean ratio and SD

emotional blunting and the global score, and relative to the control group ($p < 0.05$) for lack of initiative. The caregiver–subject ratio for the three IA items are presented in Figure 1. One-way ANOVA showed no significant difference among the groups as regards the lack of interest ratio ($F_{3,111} = 2.08$), and significant differences for emotional blunting ($F_{3,111} = 2.69$; $p < 0.05$) and lack of initiative ($F_{3,111} = 3.46$; $p < 0.05$). *Post hoc* analysis indicated that the AD patients had significantly higher scores ($p < 0.05$) than the control subjects for these two items.

There were no significant differences in age, MMSE or gender between the apathetic (AD/A) and non apathetic (AD/NA) AD subgroups. One-way ANOVA showed a significant difference among the groups for emotional blunting ($F_{1,58} = 14.95$; $p < 0.001$), lack of initiative ($F_{1,58} = 29.33$; $p < 0.001$), lack of interest ($F_{1,58} = 99.17$; $p < 0.001$) and the global score ($F_{1,58} = 70.83$; $p < 0.001$). There were no significant between–group differences in the IA patient-based evaluation scores.

All the caregiver/subject ratios were significantly higher in the AD apathy group.

## DISCUSSION

This study establishes the reliability and validity of the IA, a new instrument for the assessment of apathy in elderly subjects with and without dementia. The NPI modalities served as a model for analysing the caregiver information in the IA. We found high internal consistency, item reliability, and between–rater reliability. The test–retest reliability study also demonstrated that caregiver responses to IA questions were stable over short intervals. The concurrent validity study showed that the IA assessed apathy as effectively as the NPI apathy domain. The IA has not been compared to the Apathy Scale designed by Starkstein *et al.* (1992), which is an abridged version of the Marin Apathy scale (1991). However, the three IA items are close to the diagnostic criteria derived directly from the Starkstein scale (2001). Using these diagnostic criteria to differentiate apathetic and non-apathetic AD patients indicated significant differences for all the IA parameters between the two subgroups.

The IA caregiver assessment was used to determine the level of apathy and separate evaluation of the emotional, behavioral and cognitive aspects of apathy in four groups of subjects. The AD patients had significantly higher global and lack of initiative scores than the controls. The standard deviations showed large differences in the apathy scores within the AD group. When diagnostic criteria were used to classify apathetic and non-apathetic AD subjects, the IA scores were significantly different between the two subpopulations. This type of subdivision also reveals different brain perfusion patterns, as evaluated by SPECT (Migneco *et al.*, 2001): compared to control subjects, apathy-free AD subjects had significantly lower perfusion of inferior temporal regions (left fusiform gyrus, left parahippocampal area) and occipital regions (left gyrus lingualis). In contrast, apathetic AD subjects had significantly decreased perfusion of the left anterior cingulate, the right inferior and medial gyrus frontalis, the left orbitofrontal gyrus, and the right gyrus lingualis (Benoit *et al.*, 2002).

The MCI patients' scores fell between those of the AD patients and the controls, and the largest difference between the MCI and healthy subjects was observed for the 'lack of initiative' dimension. As in the AD group, the standard deviation showed large IA score differences within the MCI group. However, given the small number of MCI subjects, it was impossible to divide this population into apathy/non apathy subgroups. It would be interesting in future to determine if behavioral symptoms such as lack of initiative are an additional clinical marker of progression from MCI to dementia.

Either the caregiver or the patient can be interviewed for the IA. However, the patient-based scores did not correlate with the NPI apathy score and showed no differences between the AD, MCI and control groups. The scores obtained in the patient-based evaluations were only significantly higher in the PD

group in comparison to the control group for the emotional blunting, lack of initiative and global scores.

This double evaluation takes into account the conventional caregiver/subject ratio technique used to measure awareness. It has already been demonstrated that AD patients are significantly less aware of their deficits than are their caregivers (Auchus *et al.*, 1994; Seltzer *et al.*, 1997; Starkstein *et al.*, 1997; Wagner *et al.*, 1997). Comparing AD and PD patients, Seltzer *et al.* (2001) demonstrated that, in general, both groups rate themselves as being less impaired than do their caregivers. However, the two diagnostic groups differed significantly on awareness discrepancy measures in the cognitive domain. In their ratings of patients' cognitive skills, AD caregivers consider them significantly more impaired than do the patients themselves, whereas PD caregivers and patients do not differ significantly in their assessments. Using the same method, Starkstein *et al.* (2001) showed that apathy in AD was associated with the patients' poor insight into their apathy syndrome. The present study confirms these results and shows that the awareness was most lacking for the emotional blunting and lack of initiative dimensions. Alternatively, however, the low ratings of AD patients could be related to their difficulty in remembering behavioral changes that occurred before disease onset.

The use of this type of technique raises the question of the validity of the ratio technique. One might argue that the ratio technique is too dependent on severity of the disturbances rated by the caregiver. This was not the case in the PD group. Subjects with a neurodegenerative disease other than AD had high IA caregiver and patient evaluation scores, demonstrating that it is possible to be aware of one's own apathetic symptoms. It seem that this result was not totally explained by the presence of depressive symptoms, as there was no correlation between the NPI dysphoria score and the IA ratio. However, as a specific assessment of depression was not done, depressive symptoms remain a possible confounding factor.

In summary, the IA is a rapid and reliable method for assessing several dimensions of the apathetic syndrome, and also the subject's awareness of these symptoms. Future studies should look at potential dissociations between the cognitive, emotional and behavioral dimensions of apathy in other disorders, such as fronto-temporal dementia and major depression, together with the respective influence on daily life activities of the apathetic syndrome itself and the patient's awareness of it.

KEY POINTS

- Apathy is one of the most frequent behavioral symptoms of Alzheimer's disease (AD) and other dementias, and must be carefully evaluated.
- The Apathy Inventory is a reliable tool for assessing the emotional, behavioral and cognitive dimensions of the apathy syndrome, and also the subject's awareness of these symptoms.
- AD patients had poor awareness of their emotional blunting and lack of initiative.

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