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The "Interest Game": A Ludic Application to Improve Apathy Assessment in Patients with Neurocognitive Disorders

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Abstract.
Background: Apathy, a highly prevalent behavioral disorder in Alzheimer's disease and other related disorders, is currently assessed using clinical scales as it is for all neuropsychiatric disorders.
Objective: The aim of this study is to propose a new type of assessment using new technologies designed to assess loss of interest by a more implicit and indirect method.
Methods: The Interest Game is a form of interactive self-report, where categories of interests are presented in order to quantify them and identify the activities that constitute them. Two indices can be extracted, the number of categories and the number of activities selected. We compared the scores between three groups: Apathetic (A) and Non-Apathetic (NA) subjects (according to the Apathy Diagnostic Criteria) and controls with no objective cognitive impairment.
Results: 95 subjects were included. Results showed that subjects from the A group had significantly less interests (both categories and images selected) than the NA group. As expected, the control group selected a higher number of categories than the other groups. The diagnosis (minor or major neurocognitive disorder) and level of education had also a significant effect on the number of categories selected. Furthermore, subjects with major neurocognitive disorder (NCD) had significantly less interests than minor NCD group. The number of categories measure was more sensitive than the number of images selected.
Conclusion: The Interest Game is a promising tool to quantify and identify subject interests and differentiate between apathetic and non-apathetic subjects. Future studies should focus on including more apathetic subjects in the minor NCD group and validating this tool with the general population.

Keywords: Apathy, interest, leisure activities, neurocognitive disorders, serious games

INTRODUCTION

Apathy is prevalent across many neurodegenerative, neurological, and psychiatric disorders. It represents the most frequent behavioral and psychological symptom in people with Alzheimer's disease (AD) and related disorders but also in major depression and schizophrenia [1]. A recent review confirmed an increased risk of developing AD in patients with mild neurocognitive disorders (NCD) with apathy [2]. It has been suggested that rather than being a causal risk factor, apathy may be predominantly prodromal to dementia [3, 4].

The diagnostic criteria revised in 2018 [5] defined apathy as a reduction of goal directed activities in three dimensions (behavior/cognition, emotions,

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social interaction) which is not caused by a motor impairment or diminished level of consciousness. Using these criteria, it has been found that apathy is prevalent up to 77% in major NCD [6], and prevalent at 25% in mild NCD.

The cognitive/behavioral dimension is the most frequently observed across different neuropsychiatric pathologies [6, 7]. Subjects with impairment in this dimension are less likely to initiate common activities related to their personal interests. In fact, loss of interest is one of the clinical signs of the cognitive and behavioral component of apathy [8] and a strong predictor for conversion to AD [9]. In parallel, engaging in leisure activities in line with personal interests may reduce the risk of developing cognitive impairment or dementia in elderly subjects [10, 11].

In clinical settings, apathy is essentially assessed during an interview face to face with the patient and/or caregiver using classical evaluation scales (Lille Apathy Rating Scale [12]; Neuropsychiatric Inventory [13]; the Diagnostic Criteria for Apathy [5]) and/or using self-report scales (Dimensional Apathy Scale [14]; Apathy Motivation Index [15]). This type of method may not be very objective in comparison, for instance, to cognitive assessment performed using validated cognitive tests. There is a risk that patients, caregivers, or even clinicians may be influenced by the clinical context, or state of mind during the clinical interview. This could suffer from important variability due to the lack of awareness in patients and thus, a subjective evaluation of apathy presence.

There is emerging evidence that new information and communication technologies (ICT) approaches could provide clinicians with valuable additional information in terms of assessment, and therefore more accurate diagnosis of apathy [16]. ICT instruments that could be employed to assess different aspects and dimensions of apathy include motor, audio, and video sensors but also serious games, which are video games with a 'serious' purpose, such as assessment and/or training [17, 18]. ICT instruments can provide indirect data that can be related to the patient's behavioral characteristics' such as response time that could give information on speed processing and motivation for instance, speech variations and emotions using speech analysis [19] or facial analysis [20] or engagement levels using eye tracking [21].

Furthermore, technology could also be useful for the direct collection of apathy dimension. This is the case for the assessment of subject's loss of interests. In the classical setup, clinicians ask patients to report their interests using open questions (e.g., "What are your main interests?", "What do you like to do?", "Do you have fewer interests than before?"). Due to the presence of cognitive impairment (memory loss, attentional deficits, linguistic deficits), for elderly patients it is sometimes difficult to respond without being prompted with examples. At present, there is no standardized procedure to collect systematically personal interests. The objective of the present study was to evaluate whether the use of an application called "Interest Game" can be useful to assess the presence of apathy in patients with neurocognitive disorders [10, 11].

METHODS

Population and study procedure

This study was performed as part of the Digital Medicine–Brain, Cognition, Behavior (MNC3) of the University Côte d'Azur. The study was performed in accordance with the Declaration of Helsinki. The protocol was approved by the Ethics Committee (Comité de Protection de Personnes – CPP Est III) (France). MoTap: RCB ID No. 2017-A01366-4). Informed written consent was obtained from all participants before the study. Participants were not included in the study if they had non-corrected visual or auditory impairments.

102 subjects were recruited (35 M; 67 F; mean age: 75.6 years; SD: 7.8 years) at the Research Memory Centre in Nice, France. Subjects were divided into three groups. 48 subjects with mild NCD, 33 subjects with major NCD according to the DSM 5 (American Psychiatric Association, 2013), and 21 healthy control subjects. All subjects underwent a standard assessment including the Mini-Mental State Examination (MMSE) [22] as well as the diagnostic criteria for apathy [5] with a neuropsychologist and a psychiatrist. The Interest Game was then performed in a quiet experimental room with the supervision of a psychologist.

Interest game design and application

Starting from a survey aiming to define the most common interests in elderly people [23], we created 17 categories of interest: "Eating well", "Singing", "Dancing", "Self-care", "Playing", "Family", "The sea", "The mountain", "Nature", "New technologies", "Social interactions", "Sports", "Reading",

"Love", "Museums and arts", "Relaxation and meditation", "TV and cinema". For each category, 6 images were selected representing different activities included in the same category (see Fig. 1).

For example, the sport category includes images of activities such as riding a bike, playing ball games, or sailing. For the "playing" category, different types of game are displayed as cards, video games, or bowling, etc. (see link for more information: http://www.innovation-alzheimer.fr/motivation-application-2/). The images or photographs were either made directly for the purpose of the game or browsed over the Internet (Google Images browser - images without copyright). Among 30 available images per category, 3 clinicians selected together what they considered the six most representative.

The Interest Game is an application designed for a tablet. The final application was developed with Unity (https://unity.com/) and is available on IOS and Android (http://www.innovation-alzheimer.fr/motivation-application-2/).

Procedure

The game was carried out as follows:

1. A category is presented in the form of a question: *Are you interested in* "*category*". (example "sports")
2. The subject answered "Yes" or "No".
3. If the answer was "No", subjects were presented with the next category of interest. If the answer was "Yes", subjects were asked to select among 6 images those they are interested in. They could choose 0 to 6 images. The subject could select and unselect

Three scores were collected: 1) The total *number of categories* chosen by the subject (number of categories answered "yes"). The maximum score was 17. 2) The total number of *images selected* for all the categories answered "yes". The maximum score was 102. 3) The total *duration* of the task.

Statistical analysis

Descriptive statistics were used to present demographic and clinical characteristics. Qualitative variables were presented using frequency and percentage, and quantitative variables were presented using mean and standard deviation (SD). Two types of analyses were conducted. The first one was based on the presence of apathy [healthy controls, apathetic subjects (A), and non-apathetic subjects (NA)] and the second one was based on the diagnostic category (healthy controls, mild NCD, major NCD). Quantitative variables were compared using ANOVA and qualitative variables were compared using the χ^2 test.

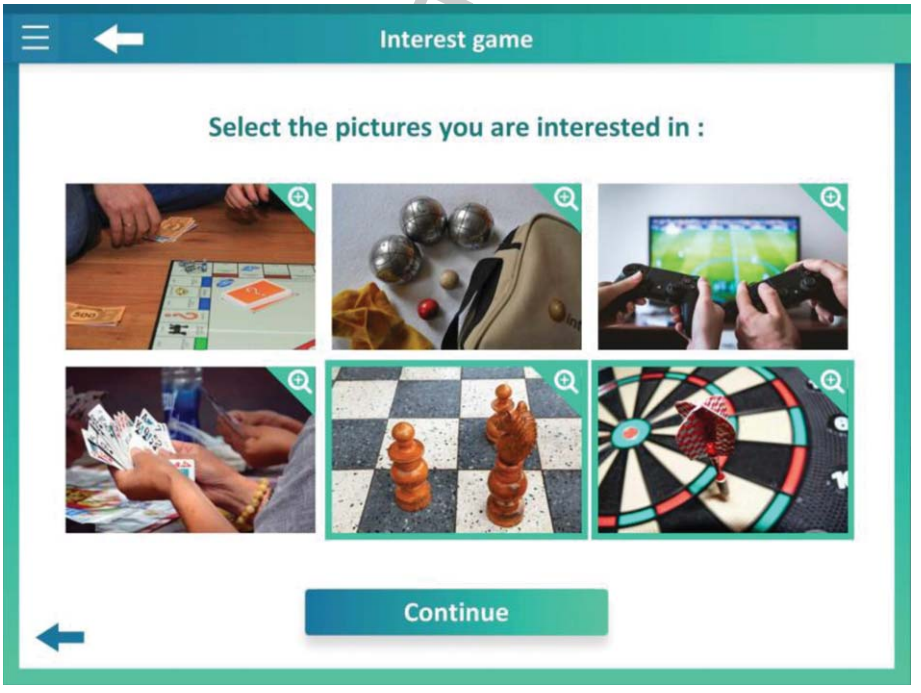

Fig. 1. Screenshot of the Interest Game. When a category is selected, subjects are asked to select among 6 images those they are interested in.

Table 1
Socio-demographic and cognitive variables in control subjects, Non apathetic (NA) and apathetic (A) subjects. One subject education's information is missing

	Control ($n=21$)	NA ($n=45$)	A ($n=36$)	p
Female, n (%)**	17 (81.0%)	32 (71.1%)	18 (50.0%)	**0.035**
Age (y), mean ± SD*	73.3 ± 8.8	75.6 ± 8.0	76.8 ± 7.4	0.278
Level of education, n (%)**				0.200
None/ primary	7 (33.3%)	7 (15.6%)	13 (37.1%)	
Secondary education	7 (33.3%)	22 (48.9%)	14 (40.0%)	
Higher education	7 (33.3%)	16 (35.6%)	8 (22.9%)	
Diagnosis (%)**				–
Mild NCD	– (–%)	35 (77.8%)	13 (36.1%)	
Major NCD	– (–%)	10 (22.2%)	23 (63.9%)	
Control	21 (100.0%)	– (–%)	– (–%)	
MMSE, mean ± SD*	29.5 ± 0.9	23.2 ± 4.3	20.1 ± 5.2	**<0.001**
Categories of interest. mean ± SD*	16.0 ± 0.9	14.0 ± 2.5	11.7 ± 3.1	**<0.001**
Duration, mean ± SD * (s)*	495.5 ± 290.2	574.0 ± 242.1	592.2 ± 248.8	0.111
Images selected, mean ± SD*	57.8 ± 17.5	42.9 ± 19.3	27.9 ± 16.7	**<0.001**

*ANOVA or Kruskal-Wallis; ** χ^2.

When ANOVAs were significant, Tukey *post-hoc* tests were used.

For the following analyses, only apathetic and non-apathetic subjects were included. To evaluate factors associated with the number of categories and the number of images selected, a multiple linear regression analysis was conducted. Variables with a p-value <0.10 in univariate analyses (Pearson's correlation, Student t-test, and ANOVA) were included as factors in the multivariate regression. 95% confidence interval (CI) were reported. A p-value $\leq$0.05 were considered as significant. All statistical analyses were performed using R-3.5.1 free software.

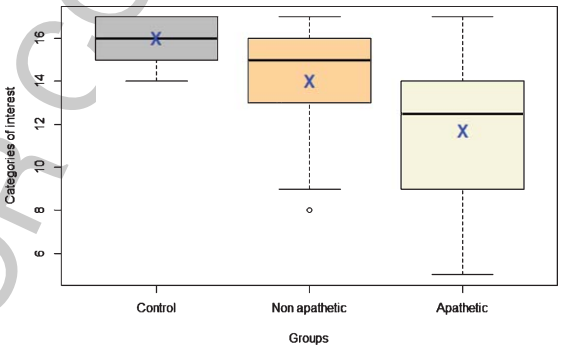

Fig. 2. Number of categories selected according to the diagnostic criteria for apathy (Controls, Non apathetic, Apathetic) with mean and SD.

RESULTS

Group comparison based on the presence of apathy

For the analyses participants were divided into three groups: healthy controls, apathetic subjects (A), and non-apathetic subjects (NA) according to the Apathy diagnostic criteria. Characteristics and clinical information of each group are reported in Table 1. No significant differences in age and education were found across three groups (all ps $\geq$ 0.20). The proportion of male and female differed significantly across three groups ($\chi^2=6.7$, $p=0.033$), with a higher proportion of females in the Control and NA groups compared to the A group. As expected, MMSE score was significantly different across the three groups ($F=33.3$; $p<0.001$). Specifically, *post-hoc* Tukey's HSD tests showed that the control group had significantly higher MMSE scores than the two NCD groups, and that the NA group had significantly higher MMSE score than the A group ($p<0.004$).

Significant differences on the number of selected categories ($F=20.5$; $p<0.001$) and images ($F=18.8$; $p<0.001$) were found, with more categories and images selected by the control group compared to the A and NA group, and more categories and images selected for the NA group compared to the A group (All *post-hoc* Tukey's HSD tests were significant ($p<0.010$) (see Fig. 2). No significant difference was found ($p=0.11$) for the duration.

Group comparison based on the diagnostic category

Clinical and cognitive results for the control, mild NCD, and major NCD groups are reported in Table 2. No significant difference was found among

the three groups for the age, sex, and level of education. As expected, the level of cognitive impairment indexed by the MMSE score, differed significantly between the three groups ($F = 110.2$; $p < 0.001$), with MMSE score being higher for the control group compared to the two NCD groups, and higher for the mild NCD group compared to the major NCD group (all *post-hoc* Tukey's HSD tests were significant, $p < 0.001$). In the mild NCD and major NCD groups, 36 subjects were apathetic according to the diagnostic criteria (44.4%) and 45 non apathetic (55.6%). No subject was apathetic in the control group. The percentage of subjects suffering from apathy in the major NCD group (69.9%) was significantly higher compared to the mild NCD (26.2%) ($\chi^2 = 12.7$, $p < 0.001$).

The ANOVA showed a significant difference for the number of selected categories ($F = 16.0$; $p < 0.001$) and for the number of selected images ($F = 20.5$; $p < 0.001$), with both number of categories and number of images being higher for the control group compared to the two NCD groups, and higher for the mild NCD group compared to the major NCD group (all *post-hoc* Tukey's HSD tests were significant, $p < 0.010$).

Regression analysis

Number of categories

Univariate analyses. The univariate linear regression analysis conducted on the number of categories of interest revealed no significant correlation with age ($r = 0.11$, $p = 0.308$) and MMSE ($r = 0.18$, $p = 0.118$). Independent ANOVAs conducted on the number of categories of interest revealed a significant effect of education level ($F = 4.0$, $p = 0.022$), presence of apathy ($T = 3.7$, $p \leq 0.001$), and diagnosis ($T = 2.8$, $p = 0.007$). No significant effect of gender was found ($T = -0.7$, $p = 0.468$). Thus, education level, presence of apathy and diagnosis were used as regressors in the multivariate analyses.

Multivariate analysis. Multiple linear regression conducted on the number of categories of interest revealed a significant effect of education, with subjects with higher education reporting a higher number of interest categories compared to subjects with low or no education (Adj Coeff = 1.8 95% CI = [0.1; 3.5], $p = 0.042$). A difference in the number of categories was also observed according to the presence of apathy. NA subjects reporting a higher number of categories of interest compared to A subjects (Adj Coeff = 1.6, 95% CI = [0.3; 3.0], $p = 0.020$). No significant effect of diagnosis was found (Adj Coeff = –0.9, 95% CI = [–2.3; 0.5], $p = 0.187$).

Number of images

Univariate analyses. The univariate linear regression analysis conducted on the number of selected images revealed no significant correlation with age ($r = -0.04$, $p = 0.754$), but a significant positive correlation with the MMSE score ($r = 0.38$, $p \leq 0.001$). Independent ANOVAs conducted on the number of images revealed a significant effect of education level ($F = 4.1$, $p = 0.021$), presence of apathy ($T = 3.7$, $p \leq 0.001$), and diagnosis ($T = 4.1$, $p < 0.001$). No significant effect of gender was found ($T = -0.2$, $p = 0.805$). Thus, education level, presence of apathy and diagnosis were used as regressors in the multivariate analyses.

Multivariate analysis. Multiple linear regression conducted on the number of selected images revealed a significant effect of education, with subjects with higher education reporting a higher number of image compared to subjects with low or no education

Table 2
Socio-demographic and cognitive variables in control subjects, mild NCD and major NCD subjects. One subject education's information is missing

	Total ($N = 102$)	Mild NCD ($n = 48$)	Major NCD ($n = 33$)	Control ($n = 21$)	p
Female, *n* (%)**	67 (65.7%)	30 (71.4%)	20 (60.6%)	17 (81.0%)	0.131
Age (y), mean ± SD *	75.5 ± 8.0	75.6 ± 7.8	76.8 ± 7.6	73.3 ± 8.8	0.280
Level of education, n (%) **					0.689
None/ primary	27 (26.7%)	10 (20.8%)	10 (31.3%)	7 (33.3%)	
Secondary education	43 (42.6%)	22 (45.8%)	14 (43.8%)	7 (33.3%)	
Higher education	31 (30.7%)	16 (33.3%)	8 (25.0%)	7 (33.3%)	
Presence of ADC, n (%) **					**<0.001**[a]
Control	21 (20.6%)	– (–%)	– (–%)	21 (100.0%)	
No	45 (44.1%)	31 (73.8%)	10 (30.3%)	– (–%)	
Yes	36 (35.3%)	11 (26.2%)	23 (69.7%)	– (–%)	
MMSE, mean ± SD *	23.4 ± 5.4	24.8 ± 3.0	17.5 ± 3.9	29.5 ± 0.9	**<0.001**

*ANOVA or Kruskal-Wallis; ** χ^2; [a]Comparison between major and mild NCD groups.

(Adj Coeff = 11.2 95% CI = [0.6; 21.9], $p = 0.039$). A difference in the number of image was also observed according to the diagnosis, with mild NCD subjects reporting a higher number of images compared to major NCD subjects (Adj Coeff = 12.0 95% CI = [3.5;20.6], $p = 0.007$). NA subjects reported almost significantly more images compared to A subjects (Adj Coeff = 8.6, 95% CI = [–0.1;17.3], $p = 0.052$).

DISCUSSION

In the present study we investigated the interest of employing an application, the "Interest Game" developed in the context of the "MoTap" project, to help clinicians in apathy assessment through a playful game-like interface. The results collected on a sample of people with mild and major neurocognitive disorder (NCD) showed that the application could differentiate apathetic (A) from non-apathetic (NA) individuals.

The application allows to collect two types of indexes. The first one is the number of categories of interests, potentially indicating levels of motivation represented by the number of categories that the participants reported to be interested in, after being prompted by a single purpose question ("Are you interested in . . . .?"). The second index is the number of images selected for the categories of interests, collected using a forced-choice format ("Which of these images are you interested in?"). Interestingly, the multivariate analysis showed that the number of categories of interest significantly differentiated apathetic versus non apathetic subjects, whereas the number of selected images significantly differentiated patients according to their diagnosis (minor versus major NCD). One hypothesis concerning this difference is that the ability to report the number of images requires more cognitive resources, and this task may be less adapted to patients with severe cognitive impairment [24]. However, it is important to underline that the level of education played an important role on the results. We found significant differences according to the level of education regarding the number of selected categories and images. Therefore, participants with higher level of education chose a larger number of categories and images of interest.

This is in line with studies suggesting a positive correlation between educational attainment and the frequency of leisure activities [25, 26]. Moreover, many studies have demonstrated that education level and participation on leisure activities have an important link to cognitive reserve [11, 27–30]. Therefore, education needs to be considered when determining the optimal score on the Interest Game for each subject.

The presence of apathy significantly affects the patient's quality of life and the caregiver's burden [31, 32]. In NCD, apathy can appear at the early stages of the disease progression [4] even in people with subjective cognitive decline, a condition characterized by cognitive complaints without objective decline in cognitive testing [33]. The presence of apathy is associated with a faster cognitive and functional decline [2, 34] representing a risk factor for the conversion from mild cognitive impairment to AD [35, 36]. Critically, preliminary evidence suggests that interventions targeting apathy in people with mild cognitive impairment (through repetitive transcranial magnetic stimulation) may be effective to improve the global cognitive functioning [37]. Thus, identifying apathy early in the disease progression and putting in place early treatment options could offer new opportunities to prevent dementia or to postpone clinical deterioration. In this context, developing instruments that help clinicians in an early, objective, and ecological apathy assessment is a research priority [16].

Taken together, these results suggest that the Interest Game can represent an additional objective tool next to existing scales and interviews to assess apathy, and in particular its cognitive dimension [5, 38]. This is important because apathy was significantly associated with worse functional abilities, with the strongest effects in mild dementia [39]. Indeed, loss of interest is one the most prevalent dimension of apathy in neurocognitive disorders [6, 7]. The Interest Game allows to specifically assess interests in external issues: "The person has less interest, reacts less to news of any kind, good or bad, or has less interest in doing new activities".

Despite these promising results, the study suffers from several limitations. The first one is the limited number of subjects and the unbalanced number of apathetic subjects per diagnostic group, with 26.2% of apathetic participants in the mild NCD group, and 68.8% of apathetic participants in the major NCD group. This is in line with the prevalence rates observed in the recent survey, which reported that the behavior/cognition domain of apathy was always present for apathetic subjects with mild and major NCD and prevalent at 37% and 60% for non-apathetic

patients with mild and major NCD [6]. However, for research purposes, inclusion of more apathetic subjects with mild NCD could be useful. A second limitation concerns the stage of development of the Interest Game application. The version used for the study did not allow to collect precise information on the types of interests selected by the subjects (e.g., social activities versus individual ones). It is important in the next version to include this feature in order to match the selected categories and images with the apathy domains behavior/cognition, emotion, and social interaction. Finally, it would be important to verify the existence of correlations between Interest Game scores and validated apathy scales, such as the Dimensional Apathy Scale [14] or the Apathy Motivation Index [15], which allow to better quantify apathy severity.

Two aspects in the application need to be implemented. First, it is important to increase the number of interest categories, although the present version of the application can already differentiate between individuals with and without apathy. We hypothesize that these differences would probably be more extensive with a larger number of categories. The current number comes from practical purpose in order to cover the maximum number of options and at the same time provide a brief task. Secondly, level of education needs to be considered. This parameter in a much larger sample could be of great help in determining a cut off score.

In addition, it is noteworthy that the Interest Game was not developed only to provide a quantitative measure of subject's interests. It is meant to be used together with a clinician as an instrument to facilitate interaction and dialogue on the patient's interests. In this way, the Interest Game can provide additional qualitative and valuable information on what is meaningful to a patient, which allows to design more personalized and effective treatment plans. Recent reviews and recommendations showed that the most effective non-pharmacological treatment for apathy were the ones tailored to each subject's interest [40, 41]. This is further underlined in a recent editorial from Starkstein [42] indicating that "*It is likely that a generic approach to activities may fail to produce positive changes in many patients. What is therefore required is a* "*tailor-made*" *approach, designing specific activities depending on individuals*' *interests and capacities*". Since the Interest Game makes it possible to clearly identify patients' interests, it can be a useful tool in a therapeutic context.

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The data that support the findings of this study are available from the corresponding author upon reasonable request.

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