

Longitudinal Course and Predictors of Apathetic Symptoms after Severe Traumatic Brain Injury

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Abstract

Objectives: Apathy is one of the most common behavioral symptoms encountered after traumatic brain injury (TBI). However, very little is known about the longitudinal course and predictors of apathetic manifestations. The aims of the present study were to examine how apathy changes and the predictive value of cognitive factors (memory, attention/executive mechanisms, and multitasking) and personal identity factors (self-esteem and self-efficacy beliefs) for apathy over a period of 10 months.

Method: To this end, 68 participants (32 patients with severe TBI matched with 36 control participants) living in the community were enrolled. At Time 1, participants were given three questionnaires to assess self-esteem, self-efficacy beliefs, anxiety and depression symptoms, and five tasks to assess cognitive processes. Simultaneously, a close relative of each participant completed a questionnaire that assessed lack of initiative/initiative. At Time 2, all questionnaires were re-administered to each patient and their relatives.

Results: Patients displayed a significant lack of initiative/interest at all post-injury assessments. At the individual level, the results revealed that a majority of patients had no change in their apathetic symptoms over the 10-month follow-up, whereas in the others, apathetic symptoms mostly increased. Furthermore, impaired memory was the only mechanism that significantly predicted later apathetic manifestations. Complementary profile analyses indicated that patients with worsening symptoms over the follow-up period showed higher inaccurate memory at Time 1 than patients with stable symptoms.

Conclusions: These results provide valuable insight into the longitudinal evolution and predictors of apathy after TBI, which opens interesting prospects for psychological interventions.

Keywords: Head injury; Traumatic brain injury; Learning and memory; Executive functions; Everyday functions

Introduction

Apathy is one of the most common behavioral symptoms of traumatic brain injury (TBI), with an average estimated prevalence of 45%–50% (Arnould, Rochat, Azouvi, & Van der Linden, 2013). Elevated apathy has been associated with a host of negative consequences, notably on rehabilitation outcomes (Brett, Sykes, & Pires-Yfantouda, 2017), caregiver distress (Bayen et al., 2012) and psychosocial reintegration (Arnould, Rochat, Azouvi, & Van der Linden, 2015). Defined as diminished goal-directed behavior, apathy is commonly divided into three dimensions: lack of initiative, lack of interest, and emotional blunting (Marin, 1991; Levy & Dubois, 2006; Mulin et al., 2011). Lack of initiative corresponds to the incapacity to act or to begin routine and non-routine activities spontaneously (self-initiation) or in response to external stimuli. Lack of interest refers to the incapacity to feel or show an attraction for routine activities or new events, and emotional blunting corresponds to a decrease in positive and negative emotional reactions. Recently, Mulin and colleagues (2011); see also Robert and colleagues (2009),

proposed a set of diagnostic criteria for apathy. According to these criteria, a diagnosis of apathy can be made in the presence of four or more weeks of a loss of or reduction in motivation in at least two of the three proposed apathy dimensions of emotional reactivity, interest and initiative. Despite the clinical significance of apathy, little is known about the longitudinal course and predictors of apathetic manifestations after TBI. However, such findings are much needed to both identify patients who may be at risk of long-term apathetic behaviors and to deploy preventive interventions that are focused on the processes involved in the progression and maintenance of these problematic behaviors.

More specifically, the existing psychological research on apathy in persons with TBI has been exclusively cross-sectional in nature (Starkstein & Tranel, 2012) and mainly focused on the first year after injury (Willemse-van Son, Ribbers, Hop, & Stam, 2009), thus providing little information about how apathy changes over time. As illustrated by a recent literature review (Arnould et al., 2013), approximately 90% of the studies documenting the prevalence of apathy in the TBI population have been performed in the early phase of recovery. Among the reviewed studies, it is noteworthy to mention that the only research conducted after the early phases of injury was the one that reported the highest prevalence rate of apathy (Lane-Brown & Tate, 2009). Indeed, Lane-Brown and Tate (2009) studied 34 individuals on average 6 years after severe TBI and found that 72% were apathetic. Since then, another prevalence study (Monsalve, Guitart, López, Vilasar, & Quemada, 2012) has been performed on a sample of 53 patients with severe TBI, who were assessed between 2 and 4 years ($N = 29$) or 5–8 years ($N = 24$) after their injury. The results showed that almost half of all patients had apathetic manifestations and those between 5 and 8 years after their injury tended to have more frequent and/or severe apathy than the other subgroup. Thus, the few studies that have examined the proportion of apathetic symptoms beyond the early phase of recovery in the TBI population suggest that these symptoms are common, or even more prevalent over time.

More broadly, some longitudinal studies have been performed to assess the progression of functional outcomes in persons with TBI, showing that behavioral disturbances generally tend to persist long after injury (Hammond et al., 2004; Pagulayan, Temkin, Machamer, & Dikmen, 2006; Ponsford et al., 2014; Pretz & Dams-O'Connor, 2013). For instance, Ponsford and colleagues (2014) found that among a cohort of 141 patients with TBI of mixed severity, assessed at 2, 5, and 10 years post-injury using the Structured Outcome Questionnaire (Ponsford, Olver, & Curran, 1995), more than 60% of the sample reported changes in behavioral, emotional, and cognitive domains at all time points. Besides, other studies conducted in stroke patients have identified distinct trajectories of apathetic symptoms over time and found that stable trajectories were the most common (Brodaty, Liu, Withall, & Sachdev, 2013; Mayo, Fellows, Scott, Cameron, & Wood-Dauphinee, 2009; Withall, Brodaty, Altendorf, & Sachdev, 2011). Brodaty and colleagues (2013), which provided the longest follow-up among these studies, interviewed 202 patients during the first 5 years after their stroke and found evidence for three groups of patients showing stable trajectories of apathy over time, at distinct levels (low apathy (48%), minor apathy (29%), and high apathy (12%)), and one group showing a linear increase (11%). Thus, these results revealed that a majority of patients displayed no change in their apathetic symptoms over 5 years, whereas a small proportion of patients showed worsening symptoms. In the same way, it might be expected that the extent of apathetic behaviors remains fairly stable in most patients with TBI, and in some cases, apathy significantly increases with time.

As mentioned earlier, another important gap in the literature yet to be addressed concerns the nature of apathetic changes in the TBI population. Indeed, to date, only a few cross-sectional studies have been conducted to investigate the processes related to apathy in persons with TBI. Of these, Andersson and Bergedalen (2002) showed that apathetic manifestations were significantly linked to specific cognitive deficits, namely impaired performance in terms of acquisition and recall memory, executive functions, and psychomotor speed. Recently, Zakzanis and Grimes (2017) found that specific cognitive deficits significantly differentiated patients with real-world disability (i.e., return to work) from those without, but apathy did not. To be more precise, patients who were able to return to work produced significantly higher scores on verbal fluency, memory, and information processing than those who were unable to return to work, whereas both groups did not differ on apathy (elevated apathy scores were observed in the two groups). This suggests that apathetic manifestations are not systematically associated with specific cognitive deficits. Furthermore, several authors have argued that ecological tests are more sensitive to apathy than traditional cognitive measures because such measures do not take into account the demands of the real world that involve multiple processes and self-initiated behaviors (Esposito et al., 2010; Reid-Arndt, Nehl, & Hinkebein, 2007). In line with this, Lengenfelder, Arjunan, Chiaravalloti, Smith, and DeLuca (2015) showed no significant correlations between the apathy subscale of the Frontal Systems Behavior Scale (FrSBe; Grace, Stout, & Malloy, 1999) and various measures of cognitive functioning as assessed by laboratory tasks. In addition, studies have found specific relationships between apathy and multitasking (i.e., the coordination of multiple and simultaneous goal-directed activities) in people with TBI (Burgess, Alderman, Evans, Emslie, & Wilson, 1998; Müller, Czymmek, Thöne-Otto, & Von Cramon, 2006). Besides, some findings in the literature show that apathy can also be underpinned by psychological reactions secondary to brain injury, namely negative self-appraisals. Indeed, TBI studies reported that self-esteem and/or self-efficacy beliefs were significantly associated with lack of initiative and interest (Arnould, Rochat, Azouvi, & Van der Linden, submitted for publication), social participation (Dumont, Gervais,

Fougeyrollas, & Bertrand, 2004) and life goal attainment (Brands, Stapert, Köhler, Wade, & van Heugten, 2014). In line with these results, a recent study conducted in older adults showed that the subjective task demand operated as a mediator between self-efficacy beliefs and lack of initiative/interest (Esposito, Gendolla, & Van der Linden, 2014). In other words, low self-efficacy beliefs lead people to overestimate both task difficulties and effort investment, and such a judgment may play a role in the development of apathy. As suggested by the authors, self-efficacy beliefs could also interact with affective factors such as negative mood, which might contribute to the presence of apathetic manifestations. In this sense, replicated evidence shows that mood has a detrimental effect on motivation and behavior, by increasing the subjective difficulty of the tasks or goals (for reviews, see Gendolla & Brinkmann, 2005). Taken together, the current findings show that cognitive factors (i.e., episodic memory, attention/executive mechanisms, and multitasking) and personal identity factors (i.e., self-esteem and self-efficacy beliefs) contribute to the presence of apathetic manifestations at one point in time. However, nothing is known about the predictive value of these factors for future apathetic manifestations in patients with TBI.

Against this backdrop, the aims of the current investigation were to extend the findings of a previously published study by our research group (Arnould, Rochat, Dromer, Azouvi, & Van der Linden, 2016) in order to examine the longitudinal course of apathy and the predictive value of several factors for apathy over a period of 10 months. To be more precise, we previously conducted a cross-sectional study on a sample of 34 patients with severe TBI, which showed that apathy was negatively related to both episodic memory and multitasking, and that the latter mechanism was the only significant predictor of apathy. In addition, multitasking performance operated as a mediator between episodic memory capacities and apathetic manifestations. Data from this previous study were part of the initial assessment for the present follow-up study. The objectives of the follow-up were threefold. First, we examined the longitudinal course of apathetic symptoms over 10 months in patients with severe TBI, who were discharged home. Second, we sought to determine at the individual level whether distinct trajectories of apathetic behaviors over the follow-up period could be identified among persons with TBI. Third, we aimed to examine the associations between, on the one hand, self-esteem, self-efficacy beliefs and several cognitive processes (i.e., episodic memory, cognitive flexibility, updating working memory, sustained attention, multitasking) and, on the other hand, apathetic manifestations 10 months later. As regards apathetic manifestations, we focused on lack of initiative and lack of interest since emotional blunting has been poorly related to cognitive processes and psychological distress in the literature (Levy & Dubois, 2006). It is of note that studies have shown that lack of initiative and lack of interest are significantly and positively associated with each other (Arnould et al., 2015; Esposito, Rochat, et al., 2014).

Method

Participants and Procedure

The initial study group (Time 1) consisted of 34 non-consecutive adults with severe TBI (28 men, six women) and 36 matched control participants (29 men, seven women). The demographic and injury-related characteristics of these participants were presented in a previous paper (Arnould et al., 2016). Patients were all discharged from the inpatient neurorehabilitation unit at Time 1. The 10-month follow-up (Time 2) took place between 8 and 12 months ($M = 9.77$, $SD = 1.19$) after the initial screening. Two patients from the first study group did not participate at the 10-month follow-up (5.9%) because they were unreachable by phone, despite multiple attempts. The final study group consisted of 32 patients (27 men, five women) aged between 18 and 65 years old ($M = 34.78$, $SD = 13.47$). Their educational level ranged from 7 to 21 years of education ($M = 13.78$, $SD = 3.16$). The time after onset of TBI at the initial assessment ranged from 4 to 277 months ($M = 54.84$, $SD = 60.25$). It should be remembered that participants were included in the study only if there was documented evidence of a severe TBI [Glasgow Coma Scale (GCS) ≤ 8 or post-traumatic amnesia (PTA) > 7 days]. Of the 32 patients assessed at Time 2, the GCS rating was available for 29 (22 had a score of 3–8, five had a score of 9–12 and two had a score of 13–15) and the PTA duration was available for 26 (17 had a PTA > 28 days, seven had a PTA between 8 and 28 days and two had a PTA between 1–7 days). Patients had an initial mean Glasgow Coma Scale score of 7.1 (range: 3–14) and a mean post-traumatic amnesia duration of 59.8 days (range: 5–420). Fifteen patients had sustained their injuries after a motor vehicle accident, nine after a fall, three after a bicycle accident, three after a pedestrian accident, one after a work-related incident and the remaining one had been assaulted. Among the relatives, 43.8% were parents, 37.5% were spouses, 15.6% were friends, and the remaining 3.1% were siblings. As regards post-injury treatment, 20 patients were receiving neuropsychological rehabilitation in an outpatient setting at Time 1, and 16 patients at Time 2. The average number of neuropsychological rehabilitation sessions received per month was 6 ($SD = 7.31$, range 0–24) at Time 1, and 2.7 ($SD = 3.63$, range = 0–12) at Time 2. Each session lasted about 1 hr.

All participants were tested by the same psychologist. No compensation was given for participation. The study was approved by the local ethics committee (CPP Ile de France VIII), and each participant completed an informed consent form

after receiving a complete description of the study. The assessment at Time 1 included three self-administered questionnaires to assess self-esteem, general self-efficacy beliefs, anxiety and depression symptoms, four tasks to assess specific cognitive processes, and one task to assess real-life multitasking. A detailed description of each cognitive measure was presented in a previous paper (Arnould et al., 2016). Since patients may have reduced awareness of their own behavioral disturbances (e.g., Hart, Sherer, Whyte, Polansky, & Novack, 2004), we used an apathy questionnaire completed by the caregivers only. Thus, participants' relatives completed a questionnaire designed to assess apathetic manifestations. All questionnaires were re-administered at Time 2.

Questionnaires

Initiative-Interest Scale. Apathy was assessed with the Initiative-Interest Scale (IIS) (Esposito, Rochat, et al., 2014), which is specifically designed to assess lack of initiative and lack of interest. The scale is composed of 10 items rated on a 4-point Likert scale (*yes, rather yes, rather not, no*), including six items that measure lack of initiative (e.g., “*He is an active person who takes initiative*”) and four items that measure lack of interest (e.g., “*He is interested in many different things*”). The questions were answered by a close relative of the participant, which assessed the apathetic behaviors both at the pre-injury level (retrospectively) and at the current level. The total score ranges from 10 to 40, with higher scores reflecting greater apathetic manifestations. Good psychometric properties have been previously demonstrated in patients with TBI and in elderly people (Cronbach's alpha ranged from .76 to .91), and the exploratory factor analyses revealed that lack of initiative and lack of interest constitute a single dimension (Arnould et al., 2016; Esposito, Gendolla, et al., 2014; Esposito, Rochat, et al., 2014).

Rosenberg Self-Esteem Scale. The Rosenberg Self-Esteem Scale (RSE) (Rosenberg, 1965; French version, Vallière & Vallerand, 1990) is a one-dimensional measure of global self-esteem. This self-report measure consists of 10 statements related to feelings of self-worth and self-acceptance. Five items are phrased in a negative way (e.g., “*I certainly feel useless at times*”), and five items are positively framed (e.g., “*I feel that I have a number of good qualities*”). Each item is answered on a 4-point Likert scale from 1 (*strongly disagree*) to 4 (*strongly agree*). Items with negative statements are reverse scored and the total score ranges from 10 to 40, with a higher score indicating a greater self-esteem. The RSE has been widely used in many studies and has been found to have good validity and reliability within brain injury populations (Carroll & Coetzer, 2011).

General Self-Efficacy Scale. The General Self-Efficacy Scale (GSE) (Schwarzer & Jerusalem, 1995; French validation, M. Dumont, Leclerc, & Deslandes, 2003) is a self-rating scale designed to assess optimistic self-beliefs related to coping with challenges and demands in life. It consists of 10 items scored on a 4-point scale from 1 (*not at all true*) to 4 (*exactly true*). The total score ranges from 10 to 40, with a higher score indicating a greater positive perception of self-efficacy. Studies have shown that the GSE has high reliability, stability, and construct validity (Schwarzer, Mueller, & Greenglass, 1999). Cronbach's alpha ranges from .76 to .90 across a number of different language versions (Luszczynska, Scholz, & Schwarzer, 2005). As there may be an overlap of content between Item 9 of the IIS (“*If something is difficult for me, I try to find other solutions*”) and Item 8 of the GSE (“*When I am confronted with a problem, I can usually find several solutions*”), the latter item was deleted from the measure.

Hospital Anxiety and Depression Scale. Insofar as apathy and depression frequently coexist in patients with TBI (Andersson, Krogstad, & Finset, 1999), an assessment of anxiety and depression symptoms was included in the study as a control variable. The Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) is a 14-item rating scale that assesses the severity of anxiety symptoms (i.e., generalized anxiety) and depression symptoms (i.e., anhedonia, negative mood and psychomotor retardation) in the previous week. Items are rated on a 4-point scale from 0 (no symptoms) to 3 (severe symptoms). Sum scores are computed for both subscales, ranging from 0 to 21. This scale has been shown to be a reliable, valid measure in individuals with TBI (Schonberger & Ponsford, 2010).

Cognitive Measures

Meeting Preparation Task. The Meeting Preparation Task (MPT) (Levaux, Larøi, et al., 2012; Levaux, Van der Linden, Larøi, & Danion, 2012) is a real-life activity task designed to take into account the multitasking nature of unfamiliar everyday life activities. Participants were required to prepare a room for a meeting that nine people will attend. Participants had to arrange the places, beverages, and materials, while respecting the beverage list and a set of six rules. In addition to involving planning capacities, this task engaged prospective memory (i.e., get coffee from the kitchen 10 min after the beginning of the task) and

updating in pursuit of a goal (i.e., remove the materials of a guest who withdrew from the meeting). Participants' performance was recorded on video and a twofold evaluation was done by independent examiners. The dependent variable retained was the number of inefficiencies (i.e., number of goals/rules that were unachieved/violated). The MPT has been shown to have good convergent validity with the Six Elements Task, a laboratory task designed to assess multitasking (Shallice & Burgess, 1991; French adaptation, Garnier et al., 1998), and to be sensitive to apathy in patients with TBI (Arnould et al., 2016).

Trail Making Test. Cognitive flexibility was evaluated using the Trail Making Test (TMT) (Reitan & Wolfson, 1985). The dependent variable was the completion time for part B minus the time for part A, which further isolates executive functioning from attention (Arbuthnott & Frank, 2000). A higher score reflects poorer cognitive flexibility. The TMT has been shown to be sensitive to the presence of frontal lobe injury (Chan, 2000). In addition, this task has been related to apathetic manifestations in patients with brain injury (Andersson & Bergedalen, 2002).

2-Back "working memory" task. Updating in working memory was assessed by the 2-back subtest of the computerized Test for Attentional Performance (TAP; Zimmermann & Fimm, 2009). The measure retained was the number of omissions. Several studies have demonstrated that the n-back paradigm provides a valid measure of working memory updating (Jaeggi, Buschkuhl, Perrig, & Meier, 2010) and is sensitive to deficits after TBI (Perlstein et al., 2004). In addition, several studies have shown that working memory is involved in apathy (e.g. Esposito, Rochat, Juillerat Van der Linden, & Van der Linden, 2012).

California Verbal Learning Test. Verbal episodic memory was evaluated using the California Verbal Learning Test (CVLT) (Delis, Kramer, Kaplan, & Ober, 1987, 2000). The selected outcome measures were the four factors identified by DeJong and Donders (2009), who examined the latent structure of the CVLT in a clinical sample of 223 persons with TBI. The factors and their related variables are as follows: Attention Span (List A, Trial 1; List B), Learning Efficiency (List A, Trial 5; semantic clustering, recall consistency), Delayed Memory (short-delay free recall, short-delay cued recall, long-delay free recall, long-delay cued recall, recognition hits), and Inaccurate Memory (total intrusions, recognition false positives). Studies have shown significant relationships between this episodic memory task and apathetic manifestations (e.g. Andersson & Bergedalen, 2002).

Simple Reaction Time Task. The Simple Reaction Time Task (SRT) (Volle, Gonen-Yaacovi, Costello Ade, Gilbert, & Burgess, 2011) was designed to assess sensorimotor reaction times (RTs). The variable retained was the intraindividual coefficient of variation (see Stuss, Murphy, Binns, & Alexander, 2003) of RTs, computed by dividing the standard deviation by the mean RT, as a measure of sustained attention. Sustained attention difficulties have recently been associated with a central aspect of diminished goal-directed behavior, namely lack of perseverance (Rochat et al., 2013).

Statistical Analyses

Data were analyzed in SPSS version 23. First, exploratory analyses of each variable were conducted to explore the distribution of the data. Internal reliabilities (Cronbach's alpha) were computed for each of the four questionnaires. Second, a one-way repeated measures ANOVA was used to examine whether patients had experienced significant changes on apathy between pre-injury (retrospectively assessed), Time 1 and Time 2. A series of *t*-tests for independent samples were then performed to compare the performance of patients with TBI and control participants on the neuropsychological tests and questionnaires. Third, we screened for patients presenting a deviant trajectory of apathy over 10 months in comparison with the data obtained from the whole TBI group. To this end, a change score was calculated by subtracting each participant's Time 2 score from his Time 1 score (higher score represent greater increase). Cases with a change score of more than 1.5 SD of the mean of the patient group were considered as showing significant deviance in the direction of either better (negative change score) or poorer (positive change score) evolution of apathy. Mann-Whitney *U* tests were then employed to compare the extreme and non-extreme groups on the various psychological measures. Fourth, a principal component analysis (PCA) was performed to investigate whether the cognitive data could be reduced, and then, Pearson's correlations were used to examine the relationships between cognitive measures, self-related measures, anxiety and depression symptoms, and apathy (at both Time 1 and Time 2). Finally, multiple regression analyses were performed to study the effects of psychological measures on the level of apathy 10 months later. All analyses were two-tailed, with an alpha level set at .05.

Results

Preliminary Analyses

Exploratory analyses of the skewness and kurtosis of each variable revealed that all data were normally distributed, considering that absolute values for skewness and kurtosis greater than 3 and 20, respectively, are judged to be extreme (Weston & Gore, 2006). Specifically, the results showed that skewness ranged from -1.69 to 2.31 and kurtosis from -1.27 to 6.84 . Cronbach's alpha ranged from $.65$ to $.93$ (see Table 1) and indicated that all scales have acceptable to very good internal reliability, whether for the clinical group or the control group.

Comparison Analyses

Comparison of apathy scores before and after TBI. A one-way repeated measures ANOVA was performed on apathy, with the condition (pre-injury, Time 1, Time 2) as the within subject factor. Results indicated a significant effect of condition, $F(2,30) = 12.35$, $p < .001$, $\eta^2_{\text{part}} = 0.45$. A series of post-hoc Bonferroni comparison tests indicated that apathy scores at pre-injury ($M = 17.36$, $SD = 5.31$) were significantly lower than those at each post-injury time point, namely at Time 1 ($p < .001$) and Time 2 ($p < .001$). No significant change in apathy score was observed between Time 1 and Time 2 ($p = .99$). Raw scores for Time 1 and Time 2 are presented in Table 1.

Comparison between TBI patients and control participants on questionnaires and neuropsychological tests. *T*-tests for independent groups were conducted comparing TBI participants' performance on each questionnaire and neuropsychological tests (at both Time 1 and Time 2), to control participants. For the questionnaires, the results revealed significant group differences at the two post-injury assessments on all measures, except for self-esteem (see Table 1). More specifically, compared with control participants, patients had significantly (1) higher scores on apathy [$t(64) = 4.94$, $p < .001$ at Time 1; $t(64) = 4.56$, $p < .001$ at Time 2], depression [$t(64) = 3.07$, $p = .003$ at Time 1; $t(65) = 3.63$, $p = .001$ at Time 2] and anxiety [$t(64) = 2.20$, $p = .03$ at Time 1; $t(65) = 3.28$, $p = .002$ at Time 2], and (2) lower scores on self-efficacy beliefs [$t(64) = -2.70$, $p = .01$ at Time 1; $t(65) = -3.04$, $p = .004$ at Time 2].

For the neuropsychological tests (see Table 2), the results indicated that patients (1) scored significantly below the matched controls on the attention span and delayed memory factors of the CVLT, (2) made more omissions on the TAP 2-back, (3) had more variable RTs on the SRT, and (4) made more inefficiencies on the MPT. In addition, there was a trend toward statistical significance concerning the learning efficiency factor of the CVLT; namely, patients were less efficient in verbal learning than did control participants. However, the groups did not significantly differ on the TMT and the inaccurate memory variable of the CVLT. Cohen's effect size values were moderate to large (ranging from $d = 0.44$ to 0.76).

Comparison of self-beliefs, anxiety and depression symptoms at Time 1 and Time 2. Paired-samples *t*-tests highlighted no significant differences in self-esteem [$t(30) = 0.13$, $p = .89$], in self-efficacy beliefs [$t(30) = -0.18$, $p = .86$], or in anxiety [$t(30) = -0.89$, $p = .86$] between the two post-injury assessments. As regards depression, there was a trend toward statistical significance; namely, patients had more depressive symptoms at Time 2 than at Time 1 [$t(30) = -1.73$, $p = .09$].

Table 1. Means (*SDs*), internal consistency (Cronbach's α) and results of group comparisons on apathy, self-esteem, self-efficacy beliefs, anxiety and depression symptoms for control participants and patients with TBI at Time 1 and Time 2

Measures	Controls		Patients			
	<i>M</i> (<i>SD</i>)	α	Time 1		Time 2	
			<i>M</i> (<i>SD</i>)	α	<i>M</i> (<i>SD</i>)	α
IIS informant	14.60 (3.52)	.77	23.13 (6.33)***	.87	23.13 (7.03)***	.93
RSE	32.30 (4.78)	.86	30.34 (6.59)	.91	30.16 (6.92)	.93
GSE	29.43 (3.57)	.81	26.03 (6.14)*	.92	26.23 (5.4)**	.91
HADS anxiety	5.74 (2.79)	.73	7.94 (4.89)*	.79	8.65 (4.52)**	.78
HADS depression	3.46 (2.56)	.65	6.07 (4.23)**	.75	7.03 (5.14)**	.85

Note: IIS = Initiative-Interest Scale; RSE = Rosenberg Self-Esteem Scale; GSE = General Self-efficacy Scale; HADS = Hospital Anxiety and Depression Scale.

* $p < .05$; ** $p < .01$; *** $p < .001$.

Table 2. Means (*SDs*) and results of group comparisons on demographic and cognitive measures for patients and control participants (*t* tests for independent sample) at Time 1

	TBI patients <i>M (SD)</i>	Control participants <i>M (SD)</i>	<i>t</i>	<i>p</i> -Value	<i>d</i>
Age	34.78 (13.47)	34.33 (12.17)	0.14	.89	0.04
Education	13.78 (3.16)	13.69 (2.38)	−0.13	.80	0.03
SRT ICV	0.26 (0.1)	0.22 (0.08)	1.98	.049*	0.44
TMT (time B minus A)	51.28 (30.89)	40.11 (32.63)	1.45	.15	0.35
TAP 2-back (omissions)	2.66 (2.55)	1.28 (1.91)	2.50	.02*	0.61
MPT inefficiency	1.28 (1.4)	0.63 (0.65)	2.42	.02*	0.60
CVLT attention span	6.19 (2.02)	7.54 (1.75)	−2.97	.004**	0.71
Learning efficiency	32.87 (4.01)	34.49 (3.62)	−1.75	.09	0.42
Delayed memory	11.29 (3.43)	13.43 (2.03)	−3.07	.003**	0.76
Inaccurate memory	3.48 (4.08)	2.32 (3.10)	1.33	.19	0.32

Note: SRT = Simple Reaction Time; ICV = intraindividual coefficient of variation; TMT = Trail Making Test; TAP = Test for Attentional Performance; MPT = Meeting Preparation Task; CVLT = California Verbal Learning Test.

* $p < .05$; ** $p < .01$.

Individual Profile Analyses

Further analyses were performed to screen for patients presenting a deviant trajectory of apathy over the 10-month follow-up in comparison with the data obtained from the whole TBI group. The mean-level change in apathetic manifestations was .01 ($SD = 4.5$), with a minimum of -12 (greater decrease) and a maximum of $+10$ (greater increase). Four patients were detected with a change score more than $+1.5 SD$ from the mean of all patients and one patient was detected with a change score less than $-1.5 SD$. Thus, results revealed that 27 patients (84.4%) displayed no change in their apathetic symptoms over the 10-month follow-up, four patients (12.5%) showed worsening of apathetic symptoms, and one patient (3.1%) showed improving of apathetic symptoms.

Mann–Whitney U tests were then conducted to compare on the various measures patients with stable symptoms versus patients with worsening symptoms. The results revealed that (1) the level of apathetic symptoms at the baseline assessment did not differ between the two subgroups ($M = 23.44$, $SD = 6.84$ vs. $M = 21.25$, $SD = 1.89$, $U = 37$, $p = .35$), and (2) patients with worsening symptoms exhibited a higher level of inaccurate memory on the CVLT ($M = 9.01$, $SD = 3.52$) than did patients with stable symptoms ($M = 2.78$, $SD = 3.52$, $U = 96.5$, $p = .008$). In addition, contrary to patients who displayed no change in their apathetic symptoms, those with high apathy increase scored significantly above the controls on the inaccurate memory factor of the CVLT ($U = 116.5$, $p = .004$). Finally, the two subgroups did not significantly differ on demographic and injury-related characteristics (age, educational level, time since injury, severity of trauma, and number of neuropsychological rehabilitation sessions). It is of note that the time since onset of injury was highly variable from one patient with worsening symptoms to another (two patients were assessed at 17 months, one patient was assessed at 141 months, and the remaining one at 277 months after injury). The only patient who displayed a significant improvement of its apathetic manifestations over the follow-up period was assessed at 8 months after injury.

Factor Analysis of the Various Cognitive Measures

A PCA (with varimax rotation) was performed on the set of specific cognitive measures in order to extract processing components, and the relationships between these processing components and the 10-month follow-up apathy scores were examined. Specifically, the variables included in the analysis were the intraindividual coefficient of variation derived from the SRT, the TMT part B minus part A time scores, the number of omissions on the TAP 2-back, and the four factors of the CVLT. The results of the PCA revealed the presence of two components with eigenvalues exceeding 1, which explained 34.1% and 22.5% of the variance. The first factor consisted of five variables representing memory capacities (i.e., variables related to the CVLT and TAP 2-back) and the second factor was composed of the other two variables, which are more representative of executive and attentional capacities (i.e., variables related to TMT and SRT). Component loadings for the memory factor and the executive/attentional factor are presented in Table 3. The Kaiser–Meyer–Olkin measure was .58, Bartlett's test of sphericity reached statistical significance ($p < .001$), and the correlation between the two components was not significant ($r = .01$, $p = .99$).

Correlation Analyses

Pearson correlations were computed in the TBI group between the demographic and injury-related characteristics, cognitive measures, self-related measures, anxiety and depression symptoms, and apathy (at both Time 1 and Time 2). The results revealed that apathy scores at Time 2 were positively related to apathy scores at Time 1 ($r = .78, p < .001$) and the number of inefficiencies on the MPT ($r = .43, p = .01$). In addition, apathy scores at Time 2 were significantly associated with the memory factor ($r = -.54, p = .001$), indicating that the better the memory performance at Time 1, the lower the apathy score at Time 2. For the injury-related characteristics, a negative correlation was observed between GCS rating and apathy at Time 2. Finally, as regards the relationships between the clinical data at Time 2, the results revealed that apathy was negatively associated with self-esteem ($r = -.39, p = .03$) and self-efficacy beliefs ($r = -.48, p = .005$). No other correlations reached statistical significance.

Regression Analysis

A regression analysis was performed to determine the specific contribution of each component at Time 1 in lack of initiative and interest at Time 2. More specifically, we included as predictors the apathy score at Time 1, the memory factor, the number of inefficiencies in the MPT, and GCS score as a control variable (see Table 4). There was no multicollinearity and residuals were normally distributed. The results revealed that the apathy score at Time 1 and memory factor were the best predictors of apathy at Time 2, although GCS score was also a significant predictor of apathy at Time 2 [adjusted $R^2 = .71, F(4, 24) = 18.07, p < .001$].

Discussion

The objectives of the study were to examine the longitudinal course of apathy and the predictive value of cognitive factors (i.e., episodic memory, cognitive flexibility, updating working memory, sustained attention, and multitasking) and personal identity factors (i.e., self-esteem and self-efficacy beliefs) for apathy over a period of 10 months. The main findings can be summarized as follows. Firstly, our results showed that the mean score for lack of initiative/interest did not differ between Time 1 and Time 2, and both scores were significantly higher when compared to either pre-injury condition or control participants. At the individual level, 27 patients (84.4%) displayed no change in their apathetic symptoms over the 10-month follow-up, four patients (12.5%) showed worsening symptoms, and one patient (3.1%) showed improving symptoms. Secondly, with regard to the relations between cognitive factors, personal identity factors and apathy, correlation and regression analyses revealed that (1) memory difficulties and apathy at Time 1 were the best predictors of apathy at Time 2; (2) injury severity as assessed by the GCS was also a significant predictor of apathy at Time 2; (3) multitasking deficits at Time 1 correlated with

Table 3. Component loadings for the mnesic factor and the executive/attentional factor

	Mnesic factor	Executive/attentional factor
TAP 2-back (omissions)	-0.38	-
CVLT attention span	0.53	-
Learning efficiency	0.76	-
Delayed memory	0.87	-
Inaccurate memory	-0.76	-
SRT ICV	-	0.81
TMT (time B minus A)	-	0.73

Note: SRT = Simple Reaction Time; ICV = intraindividual coefficient of variation; TMT = Trail Making Test; TAP = Test for Attentional Performance; CVLT = California Verbal Learning Test.

Table 4. Multiple regressions for lack of initiative and interest

Dependent variable	Predictor variable	<i>B</i>	<i>SE</i>	<i>t</i>	<i>p</i> -Value	β
IIS Time 2	(Intercept)	14.32	3.93	3.65	.001**	-
	IIS Time 1	0.54	0.14	3.96	.001**	.54
	GCS	-0.65	0.24	-2.76	.011*	-.30
	Mnesic factor	-2.24	0.75	-3.00	.006**	-.36
	MPT inefficiency	0.29	0.58	0.51	.615	.06

Note: IIS = Initiative-Interest Scale; GCS = Glasgow Coma Scale; MPT = Meeting Preparation Task.

* $p < .05$; ** $p < .01$.

apathy 10 months later; and (4) patients with worsening symptoms during the follow-up period were found to have a more inaccurate memory at Time 1 than patients with stable symptoms.

To our knowledge, this is the first longitudinal follow-up study to show that apathetic manifestations are common and highly persistent beyond the early stage of recovery in patients with severe TBI. Indeed, the level of lack of initiative/interest was significantly greater at all post-injury assessments compared to pre-injury level and that of control participants. More specifically, the results revealed that a majority of patients displayed no change in their apathetic symptoms over the 10-month follow-up, whereas in the others, apathetic symptoms mostly increased. First, these findings are congruent with recent studies conducted with people living in the community after acquired brain injury, which highlighted that individuals exhibit a profound reduction in activity participation and a decline in achieving life goals (Brands et al., 2014; Goverover, Genova, Smith, Chiaravalloti, & Lengenfelder, 2017). Second, our results point in the same direction as longitudinal studies of post-stroke apathy showing that stability represented the most common trajectory of apathetic manifestations over time. To be more precise, our findings and those obtained by Brodaty and colleagues (2013) and Mayo and colleagues (2009) showed that approximately 85%–90% of patients had apathetic symptoms that remained longitudinally stable. In addition, the small proportion of patients who exhibited a significant change over time mostly experienced a linear increase in apathy. Thus, in accordance with several findings in the literature, the present study showed that apathetic manifestations are unlikely to improve with time in persons with TBI, indicating that the development of targeted and effective rehabilitation for apathy and related dysfunctions is of prime importance (Arnould et al., 2013; Cassar, Applegate, & Bentall, 2013).

Regarding the mechanisms underlying apathy, of the seven measures of cognitive function and personal identity examined, only memory performance was a significant predictor of later apathetic manifestations. More precisely, patients who have deficits in verbal episodic memory and/or updating working memory at one point in time after the early phase of recovery are likely to display lack of initiative/interest 10 months later. These results corroborate and extend previous cross-sectional studies showing that these two components of memory are significantly related to apathetic symptoms (Andersson & Bergedalen, 2002; Esposito et al., 2012; Robert et al., 2006). Moreover, our data are consistent with several studies that have demonstrated the predictive validity of memory performance in relation to later return to productivity in the TBI population (Cifu et al., 1997; Dawson, Levine, Schwartz, & Stuss, 2004; Green et al., 2008). For instance, Green and colleagues (2008) found that memory function at 5 months post-injury was significant in predicting return to productivity (i.e., paid and voluntary employments, school, parenting, home-making and participation in cultural and physical activities) at 1 year in a sample of 63 patients with moderate to severe TBI. Thus, in line with previous studies, our findings showed that memory difficulties constitute a risk factor for long-term apathetic behaviors in patients with TBI. Specifically, episodic memory deficit could lead to apathy because of its significant affect on the ability to remember to do something in the future (Burgess, 2000; Schmitter-Edgecombe & Wright, 2004), namely maintaining the contents of the intended actions (i.e., the objective, constraints, or context). Further, a deficit in updating and monitoring the contents of working memory could affect the achievement of goal-directed behaviors insofar as relevant information would not be updated and thus not taken into account in the action plans.

In addition, we found that patients with worsening apathy over the follow-up period made a significantly greater number of intrusions and/or false positive recognitions during verbal episodic retrieval at Time 1 than patients with stable apathy. It is of note that very few studies have to date considered this qualitative aspect of memory in the investigation of the relationships between apathy and memory. As an exception, Figved and colleagues (2008) showed that, among various cognitive measures, apathetic manifestations were specifically related to the production of intrusions during an episodic recall task in patients with multiple sclerosis. Thus, it appears that the link between memory errors and apathy has a specific character, suggesting that the mechanisms underlying the production of these errors could constitute a key component of diminished goal-directed behaviors. In this regard, memory distortions have often been associated with cognitive control deficits, in particular the inability to inhibit irrelevant or interfering information (Dobbins, Foley, Schacter, & Wagner, 2002; Dockree et al., 2006; Shimamura, 1994). In line with our hypothesis, some studies have shown that difficulties in resisting proactive interference in working memory were significantly associated with lack of perseverance (Gay, Rochat, Billieux, d'Acremont, & Van der Linden, 2008; Gay et al., 2010), which is a key aspect of goal-directed behavior (Esposito, Rochat, et al., 2014). Consequently, memory difficulties related to inhibition impairments could have a significant affect on project completion and goal-directed behavior. Further studies should clarify the links between inaccurate memory and apathy, by exploring the cognitive mechanisms involved in the production of memory errors.

Another aspect of our results merits further discussion. Indeed, contrary to our previous cross-sectional study indicating that multitasking was a predictor of apathy (Arnould et al., 2016), the present findings showed that multitasking at Time 1 did not predict apathy at Time 2. More precisely, we only found a significant correlation between multitasking and later apathetic manifestations. These results are in line with a recent longitudinal study conducted on individuals with schizophrenia (Raffard et al., 2016), in which baseline multitasking performance was found to be a predictor of apathy at baseline—as assessed by the factor including diminished interest measured according to the Lille Apathy Rating Scale (Sockeel et al., 2006; Yazbek et al.,

2014)—but not at 1-year follow-up. Hence, it could be argued that the relationship between multitasking and apathy goes in the opposite direction, namely that lack of initiative/interest may play a role in the presence of later multitasking difficulties. In this sense, several longitudinal studies have shown that apathy is a highly significant predictor of cognitive and functional decline in elderly people with or without dementia (Clarke, Ko, Lyketsos, Rebok, & Eaton, 2010; Starkstein, Jorge, Mizrahi, & Robinson, 2006). For instance, Clarke and colleagues (2010) reported that, in a sample of 1136 community-dwelling older adults, apathetic manifestations at baseline were associated with significant decline in cognitive functioning at 1 year follow-up, even after adjustment for baseline age, level of education and depression at follow-up. Moreover, a study showed that among the three dimensions of apathy, namely emotional blunting, lack of initiative, and lack of interest, only the latter one was predictive of cognitive decline (Robert et al., 2008), which suggests that diminished interest may possibly constitute a key symptom in the progression of cognitive difficulties. Likewise, some authors have stated that interest has a strong motivational and goal-orientated component, particularly for exploration, information seeking, and learning (Sansone & Smith, 2000; Silvia & Kashdan, 2009). Thus, it may be possible that apathetic manifestations, especially lack of interest, could compromise the execution of multitasking in patients with TBI. Nevertheless, this hypothesis should be examined more directly.

Several limitations of the study should be acknowledged. First, our sample of patients was small, and therefore the results can only be generalized with caution. Second, the sample was highly heterogeneous in terms of time since injury, which might be a limitation. Indeed, although time since injury did not significantly correlate with apathetic manifestations in the present study and in various cross-sectional studies (e.g., Andersson & Bergedalen, 2002; Lane-Brown & Tate, 2009), it is possible that recovery stage might influence test results and ratings. Further longitudinal studies are needed to examine the longitudinal course of apathetic manifestations in patients with TBI, by assessing apathetic manifestations at specific post-injury time points (e.g., each year after injury). Third, the evaluation of apathetic symptoms was only based on caregivers' assessments and not on a self-report rating scale. However, the use of a scale that was completed by the caregivers only could lead to a mis-estimate of the behavioral disorder assessment because these problematic behaviors may sometimes happen without the caregivers' knowledge (Rochat, Beni, Billieux, Annoni, & Van der Linden, 2011). In addition, the processes related to the development of apathy could differ between patients and external observers (Arnould et al., submitted for publication). In this sense, numerous studies have shown that behavioral complaints by persons with TBI were much more related to psychological reactions (e.g., emotional distress) than performances on cognitive tests (Chamelian & Feinstein, 2006; French, Lange, & Brickell, 2014). Thus, additional studies are needed to explore the predictive validity of various mechanisms for future self-reported apathetic behaviors. Fourth, embedded measures of performance validity were not employed in the present study, which might be a limitation. Indeed, although malingering has been primarily reported in patients with mild TBI, some studies have been published on patients with moderate or severe TBI who have been found to demonstrate symptom exaggeration and feigning (Bianchini, Greve, & Love, 2003; Boone & Lu, 2003). Finally, other types of variables such as environmental factors could also underlie apathetic manifestations following severe TBI. For instance, a recent longitudinal study showed that litigation procedure was a significant predictor of lower participation, autonomy and psychiatric function in a group of patients with severe TBI (Bayen et al., 2017). Future studies are needed to investigate the influence of environmental factors such as the legal status on the occurrence of apathetic manifestations in the TBI population.

To conclude, the main results of this study showed that, after the early phase of recovery, the majority of patients with severe TBI displayed no change in their apathetic symptoms over the 10-month follow-up, and a small proportion of patients showed worsening symptoms. In addition, impaired memory constitutes a risk factor for long-term apathetic behaviors. Further studies are needed to confirm these results and to explore the role of memory and cognitive control impairments in the occurrence of apathy, as well as the potential predictive value of apathetic manifestations on later cognitive difficulties. More generally, it is essential to adopt a multifactorial and integrative approach to apathy that takes into account the various mechanisms at play in the facets of apathy, as well as the interactions between the mechanisms involved, and the bidirectional relationships between the various mechanisms and apathetic manifestations. Such an approach seems to have the potential to capture the diversity and complexity of the apathetic manifestations occurring after TBI, and thus to enable the development of targeted and effective rehabilitation.

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Conflict of Interest

There are no conflicts of interest to disclose.

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