IMPULSIVE, BUT NOT DISINHIBITED? THE DISSOCIATION BETWEEN IMPULSIVITY AND INHIBITORY CONTROL IN FRONTOTEMPORAL DEMENTIA

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ABSTRACT

Introduction: Behavioral variant frontotemporal dementia (bvFTD) shares clinical, cognitive and behavioral features with Alzheimer's disease (AD), posing a challenge for differential diagnosis. Considering that disinhibition and impulsivity are hallmarks of bvFTD, cognitive and behavioural assessment of such symptoms may be useful for the differential diagnosis between bvFTD and AD. This study aimed to investigate the diagnostic value of neuropsychological tests of inhibitory control and behavioral measures of impulsivity and apathy to distinguish bvFTD from AD.

Methods: Three groups of participants were enrolled: 27 bvFTD patients, 25 AD patients and 24 healthy controls. Groups were matched for gender, education and socioeconomic level. Participants underwent a comprehensive neuropsychological assessment, including tests of inhibitory control (Hayling Test, Stroop, the Five Digit Test [FDT] and the Delay Discounting Task [DDT]). Caregivers completed the Barratt Impulsivity Scale (BIS-11) and the Apathy Scale (AS).

Results: Controls performed better than the clinical groups in most neuropsychological measures. There was no difference between bvFTD and AD for the cognitive measures of inhibitory control, including the DDT. Compared to AD, bvFTD patients were significantly more impulsive (BIS-11: bvFTD 76.1$\pm$9,5, AD 62.9$\pm$13, $p<0.001$) and more apathetic (AS: bvFTD 28.1$\pm$7,8, AD 16.9$\pm$9, $p<0.001$).

Conclusions: **N**europsychological tests of inhibitory control failed to distinguish bvFTD from AD. On the contrary, apathy and impulsivity scales provided good distinction between bvFTD and AD. These results highlight the limits of cognitive measures of inhibitory control for the differential diagnosis between bvFTD and AD, due to the dissociation between cognitive tests and behavioral symptoms.

Keywords: behavioural variant Frontotemporal Dementia; Alzheimer's disease; impulsivity; inhibitory control; delay discounting.

INTRODUCTION

Behavioural variant frontotemporal dementia (bvFTD) shares clinical, cognitive and behavioural features with Alzheimer's disease (AD), posing a challenge for differential diagnosis between these two disorders. In particular, disturbed executive functions that are classically found in bvFTD can also be impaired in AD, such as working memory, mental flexibility, and planning (Perry et al, 2000; Castiglioni, et al., 2006; Hornberger et al., 2010). However, among executive functions, tests of inhibitory control may be useful for the differential diagnosis between bvFTD and AD. Indeed, as disinhibition is a hallmark of bvFTD (Rascovsky et al, 2011), a comprehensive assessment of inhibitory control and impulsivity is potentially more accurate in identifying specific symptoms of bvFTD (O'Callaghan et al., 2013a).

Inhibitory control refers to the ability to selectively supress thoughts or behaviours that are not adaptive or appropriate in the current context (Miyake et al., 2000; Diamond, 2013). Impulsivity is broadly defined as acting prematurely without foresight (Dalley et al., 2011), and a specific sub-type of impulsivity refers to the tendency to prefer an immediate, but smaller, reward, rather than waiting for a larger, although delayed, reward (Rachlin, 2000; Kirby et al., 1991).

The value of tasks of inhibitory control for the clinical diagnosis of bvFTD has been previously investigated. For instance, some authors reported that the Hayling test provides good clinical differentiation between bvFTD and AD (Torralva et al, 2009; Hornberger et al., 2010), although another study did not show a similar result (Flanagan et al, 2016). In contrast, the Stroop test, a classical measure of prepotent response inhibition, has poor diagnostic value in differentiating bvFTD and AD (Collete et al., 2007; Perry et al, 2000).

More recent studies using tasks of delayed discounting tried to overcome the limits of classical inhibitory control tests. The Delay Discounting Task (DDT) requires the participant to make intertemporal choices, deciding between present vs. future reward options. This paradigm may be a reliable model for testing impulsivity (Ainslie, 1975; Odum, 2013). Some reports indicate that DDT can differentiate bvFTD from AD (Lebreton et al., 2013; Bertoux et al., 2015).

One of the limits of neuropsychological tests used to investigate inhibitory functions is that they usually lack ecological validity and do not recapitulate real life situations. In the other hand, behavioural scales that tap into impulsivity are usually made of questions that investigate everyday situations. Therefore, it is possible that these behavioural scales might capture with better accuracy the disinhibition-related disorders associated to bvFTD.

Taken together, there is some evidence that cognitive and behavioural assessment of impulsivity may facilitate the diagnosis of bvFTD. However, it is not clear whether cognitive tasks such DDT and Hayling are superior to behavioural scales in distinguishing bvFTD from AD. Indeed, previous studies (Lebreton et al, 2013; Bertoux et al, 2015) did not include behavioural scales to assess disinhibition. This is a critical point, as some reports showed that the measurement of impulsive behaviour can effectively differentiate bvFTD from AD (Paholpak et al., 2016; Grochmal-Bach et al., 2009), while cognitive tests may fail to do so (Flanagan et al, 2016; Hornberger et al., 2010; Collete et al., 2007; Perry et al, 2000).

The present study aims to assess inhibitory control and impulsivity using neuropsychological and behavioural instruments, in order to determine the accuracy of these tools in the differential diagnosis between bvFTD and AD. As far as we know, this is the first time that the accuracy of the DDT and of other cognitive tests of

inhibitory control are simultaneously compared with a behavioural measure of impulsivity (Barratt Impulsivity Scale; Barratt et al., 1975; Malloy-Diniz, 2010). We further contrasted these tools with a measure of apathy (Apathy Scale; Starkstein, 2001; Guimarães et al. 2009), as quantitatively and qualitatively measures of apathy can also help in the distinction between AD and bvFTD (Fernandez-Matarrubia et al., 2017). Indeed, apathy and disinhibition may co-occur in bvFTD (Le Ber et al, 2006); both constitute the most prevalent neuropsychiatric disorders of bvFTD (Rascovski et al., 2011). Then, carefully characterizing these two behavioural disorders could provide a diagnostic yield for bvFTD.

METHODS

Fifty- two patients were recruited in two Brazilian centres of Cognitive and Behavioural Neurology, located at Belo Horizonte (University Hospital from Universidade Federal de Minas Gerais) and São Paulo (University Hospital from Universidade de São Paulo). All of them fulfilled consensus diagnostic criteria for probable bvFTD (Rascovsky et al., 2011) or AD (McKhann et al., 2011). The AD group included patients at early and moderate stages of the disease. All bvFTD and AD patients underwent structural brain MRI. We did not include patients with neuroimaging disclosing focal lesions or severe vascular lesions.

To improve diagnostic accuracy, patients were clinically followed for at least 18 months after the diagnostic definition and all of them showed clinical progression consistent with the diagnosis.

A subset of patients (eight AD and eight bvFTD) underwent lumbar puncture for cerebrospinal fluid (CSF) biomarkers ($Aß_{42}$, Tau and P-Tau) analyses. For this

subgroup, all AD patients had an "AD CSF biomarker profile", defined by Tau/Aß$_{42}$ > 0.52 (Magalhães et al, 2015). None of the bvFTD patients had this biomarker profile. This procedure was adopted to increase the specificity of the clinical diagnosis. One bvFTD patient had a known genetic mutation (*TARDBP*).

Community-dwelling elderly, with no history of neurologic or psychiatric disorders and intact cognitive assessment constituted the control group.

Groups were matched for education level and socioeconomic status (Table 1). Socioeconomic level was controlled by the Brazilian standard classification (ABEP, 2015).

The local ethics committees approved the study (Project CAAE-17850513.2.0000.5149) and all participants gave written informed consent to participate.

Cognitive Assessment

All participants underwent the same cognitive protocol: Mini-Mental State Exam (MMSE) (Folstein et al., 1975; Brucki, 2003); Frontal Assessment Battery (FAB) (Dubois et al., 2000; Beato et al, 2012), Figure Memory Tests (FMT) (naming, incidental memory, immediate memory, learning, delay recall and recognition) from the Brief Cognitive Battery (Nitrini et al., 2004), verbal fluencies ('FAS' and 'Animals') (Machado et al., 2010), Forwards and Backwards Digit Span (Wechsler, 1997), Stroop-Victoria (Spreen et al., 2006); Hayling (Burgess and Shallice, 1997; Siqueira et al., 2010) and the Five Digits Test (FDT) (Sedó et al., 2015).

Stroop Test is a classical paradigm designed to evaluate the capacity of suppress a prepotent answer in saying colours instead of reading it. Hayling Test evaluates the capacity to inhibit a prepotent verbal answer when completing phrases meaninglessly. FDT evaluates two major executive functions: inhibitory control, in a non-verbal Stroop

like condition, suppressing a prepotent answer in counting numbers rather than saying the stimuli, and cognitive flexibility, alternating two different rules in the same task. FDT was chosen because it is a non-verbal option to Stroop, and it avoids low-formal education effects (de Paula et al., 2011).

Delay Discounting Task (DDT)

The DDT was performed using a computerized version of the original questionnaire (Kirby et al., 1999), created using PowerPoint. Participants were required to choose either an amount of money available today or a larger amount available in the future. The amount of delay (days) and the sum of money varied. A total of 27 forced-choices were presented to participants one at a time, and delayed vs. immediate reward options were randomised to occur on either the left or right side of the screen in equal proportions. Figure 1 illustrates examples of two out the 27 forced-choices. Participants were not awarded any actual monetary payments based on their performance, but they were encouraged to approach the choices as if real money was at stake.

A hyperbolic discount parameter (k) is inferred from subjects' choices on the DDT. Delay discounting is the tendency to discount the present value of a reward as delay to the reward increases, calculated by the equation: $PV = FV/(1 – kt)$, where: PV= Present Value; FV= Future Value; t= time; and, k= slope. A higher k value is consistent with a steeper discounting of future rewards, indicating a higher degree of impulsivity.

The 27 options from DDT were comprised of nine items in three groups: small ($15 - $25), medium ($35 - $55) and large ($75 - $85) values, which refers to the size of the delayed reward. Thus, four parameters are extracted from DDT: a general k for all the 27 items, and separate k values for small, medium and large items. Based on values available in our task, k values could vary from 0.000158 to 0.25.

Behavioural Assessment

Behaviour was assessed by the Apathy Scale (Starkstein et al., 2001; Guimarães et al, 2009) and Barratt Impulsivity Scale 11th version (BIS-11) (Barratt et al., 1975; Malloy-Diniz et al., 2010).

Apathy Scale is formed by 14 items. The Brazilian version is already designed for third-party reporting and presented good correlation with the apathy subscore from the Neuropsychiatric Inventory (Guimarães et al., 2009).

BIS-11 is a self-report scale comprised by 30 items. The participant is required to analyse each item and classify the frequency of that behaviour, using a Likert scale. A higher score means a higher degree of impulsivity. The minimum score is 30 and the maximum is 120. In addition, three partial scores are obtained: motor impulsivity, attentional impulsivity and planning impulsivity (Malloy-Diniz et al., 2010).

Similar to previous studies, the BIS-11 was adapted as a caregiver-report version, in order to avoid a possible anosognosia effect in the patients (O'Callaghan et al., 2013b). Controls completed the BIS-11 original version, but were not evaluated with the Apathy Scale.

Patients were classified as "impaired" or "preserved" regarding their scores on Apathy Scale and BIS-11. For the Apathy Scale, a cut-off of 14 was established to determine impairment, considering that this value exceeds two standard-deviations (SD) from mean value in a healthy-population (Guimarães et al., 2014). For the BIS-11, a cut-off of 82 was established to determine impairment, as this value is 2 SD superior to the mean score from the Brazilian norms (Malloy-Diniz et al., 2015).

Statistics

Descriptive and comparative analyses were performed. Normality was checked with Shapiro-Wilk test. Non-parametrical tests were chosen considering the majority of non-normal distribution found in the different measures, except for behavioural scales, whose distributions were normal. For categorical variables chi-square was used. Kruskal-Wallis and Mann-Whitney pairwise post-hoc comparison were applied for continuous variables, except for behaviour, for which ANOVA with Bonferroni post-hoc tests was applied. In the DDT, within group analyses were performed by the Wilcoxon method in order to evaluate magnitude effects. Receiver Operator Characteristics (ROC) curve analyses were carried out to test diagnostic accuracy. Analyses were performed with Statistical Package for the Social Sciences (SPSS) 22.0 and MedCalc 17.1 softwares.

RESULTS

The final groups consisted of 27 bvFTD patients, 25 AD patients and 24 healthy controls. Table 1 describes sociodemographic data. bvFTD patients were significantly younger than AD; however, age did not differ between clinical groups and controls. Other sociodemographic variables (schooling and socioeconomic level) were similar across groups. AD and bvFTD patients had similar symptom duration.

Considering neuropsychological measures, there were statistically significant differences between clinical groups and healthy controls, with bvFTD and AD scoring worse than controls on most measures (Table 1). There were no significant differences between bvFTD and AD for all measures of executive functions, apart from the "Flexibility" domain from the FDT, in which AD performed significantly worse than

bvFTD. AD patients also performed worse than bvFTD in the delayed recall from the Figure Memory Test.

Regarding the DDT, there were no differences among groups for all parameters. The within group analyses, however, showed that the control group present k values for small rewards statistically higher than their k values for both the large and medium rewards. In contrast, for the bvFTD and AD groups, their k values for the small rewards were only significantly higher than their k values for the larges reward size.

Both apathy and impulsivity measures revealed significant differences between the groups. bvFTD patients were more impulsive than both AD and controls, and were more apathetic than AD patients. Controls and AD did not differ in the impulsivity scale. Considering Brazilian norms for the BIS-11 (Malloy-Diniz et al., 2015), controls' mean score was at the 45^{th} percentile, AD scores were at the 55^{th} percentile and bvFTD mean score were within the 90^{th} – 95^{th} percentile.

The FDT Flexibility score, Apathy score and BIS-11 Total score were analysed in a ROC curve procedure to establish diagnostic accuracy of bvFTD versus AD (Table 3, Figure 2). For the Apathy scale, the cut-off of 19 provided 69.2% sensitivity and 92.6% specificity. The BIS-11 cut-off of 68 achieved 68.2% sensitivity and 80% specificity. FDT Flexibility achieved 86.4% sensitivity and 76.5% specificity with a cut-off of 54 seconds. The composition of a unique score with all three or even two instruments did not improve the diagnostic accuracy significantly.

Patients were classified as "impaired" or "preserved" according to their scores on the Apathy Scale and BIS-11 (Table 2). Only 2.4% of bvFTD patients had alteration neither on apathy nor on impulsivity, while 19.5% of AD patients had similar profile (with significant difference of frequencies between groups, $p < 0.05$). In the other hand,

19.5% of bvFTD patients had impairments on both apathy and impulsivity, while only 4.5% of AD had similar pattern ($p < 0.05$). The two groups exhibited the same percentage of patients having apathy without impulsivity (no statistical difference).

DISCUSSION

This study investigated cognitive and behavioural markers of impulsivity for the differential diagnosis between bvFTD and AD. Behavioural scales (BIS-11 and Apathy Scale) provided better diagnostic accuracy than cognitive measures of inhibitory control, including the DDT, Stroop, and Hayling.

Only one executive parameter ("flexibility" from FDT) was statistically different between bvFTD and AD. Neuropsychological tests of inhibitory control and impulsivity failed to distinguish between bvFTD and AD. Even though impulsivity is a clinical feature of bvFTD, previous studies assessing inhibitory control in bvFTD showed variable results. For instance, there are data showing either difference (Torralva et al, 2009; Hornberger et al., 2010) or absence of difference between bvFTD and AD in the Hayling test of inhibition (Flanagan, 2016). In the present study, bvFTD and AD also did not differ in their performance on the Hayling test. Similarly, there was no difference in Stroop between patient groups, which is in agreement with previous observations showing that this test has poor association with behavioural and anatomical markers of inhibition (Heflin et al., 2011).

The DDT also failed to detect differences between bvFTD and AD, in contrast to previous reports (Lebreton et al., 2013; Bertoux et al., 2015). The reasons for the present result remain unclear, but may be due to cultural specificities related to Brazilian background, such as political and economic instability and a history of

hyperinflation, especially in the 1980-1990s. Further studies are required to explore intercultural variability in DDT.

Magnitude effect refers to the finding that discount rates decrease as the amount of reward increases, as subjects are more willing to wait for a larger reward (Green et al., 2004). All groups exhibited magnitude effect on the DDT, showing largest k values for the smallest rewards. Nonetheless, AD and bvFTD patients' differed only between large and small rewards, while controls had different scores between small rewards and both large and medium ones. This suggests that controls discounted small rewards more steeply compared to both of the larger rewards. This finding suggests that patients were less sensitive to magnitude effects, compared to controls.

Apathy is the most common behavioural change in AD (Theleritis et al., 2014; Starkstein, 2001), and is also a core feature of bvFTD (Rascovsky et al, 2007). Our data confirms that apathy is frequent in both conditions. However, apathy is more severe in bvFTD than in AD patients, in accordance to previous reports (Lima-Silva et al., 2015; Liu et al, 2004; Chow, et al. 2009).

There were significant differences between AD and bvFTD in the behavioural measure of impulsivity (BIS-11), which also achieved good accuracy for differential diagnosis, as revealed by ROC analysis. The BIS-11 may be a practical resource to distinguish bvFTD from AD (O'Callaghan et al., 2013b). Another point that may be useful for the differential diagnosis is that the association of apathy and impulsivity disorders is more frequent in bvFTD patients than in AD, with almost 20% of bvFTD cases achieving impaired levels on both scales, while only 4.5% of AD had similar profile.

Taken together, our results highlight the limits of using cognitive measures of inhibitory control for the differential diagnosis between bvFTD and AD. Most tests of inhibitory

control were not specifically designed for neurodegenerative disorders. For instance, the DDT was initially developed to study addiction (Kirby et al., 1999), while the Stroop was originally designed for cognitive screening in young adults (Stroop, 1935).

It is also important to consider that inhibitory control is a set of complex cognitive functions (Dalley et al., 2011; Munakata et al., 2011; Hampshire and Sharp, 2015). Indeed, distinct cognitive abilities are required for efficient inhibitory control. For instance, the DDT may engage diverse cognitive operations, such as prospective memory and emotional processing. Therefore, different cognitive deficits may underlie impulsive behaviour. bvFTD and AD patients may fail in tests of inhibitory control due to deficits in different sub-processes, which are not specifically tapped by most standard tests. Hence, the design of new tests of inhibitory control for the diagnosis of bvFTD should consider more specific sub-processes of this ability.

The development of new cognitive tests for the diagnosis of bvFTD should also take into account the clinical variability of the disease (Whitwell et al, 2009; O'Connor et al, 2017), with patients exhibiting either disinhibited, apathetic or mixed profiles (Le Ber et al, 2006; O'Connor et al, 2017). In our sample, 20% of bvFTD patients had mixed profile. The optimal cognitive diagnosis of bvFTD requires a set of tests tapping into the different possible behavioural aspects of the disease.

This study presents some caveats. The diagnosis was established under clinical basis, and pathological confirmation was not available. However, patients were selected according to consensual criteria and all patients had a minimal follow-up of 18 months and had clinical progression consistent with the diagnosis. Apathy scale was not applied to controls, precluding comparative analyses with this group.

In conclusion, this study highlights the dissociation between cognitive tests of prefrontal functions and behavioural disorders related to these same regions, the “frontal paradox” (Mesulam, 1986; Burgess et al, 2009; Gleichgerrcht et al, 2010; Volle et al, 2012). The present study reinforces this observation, as bvFTD patients presented higher scores of impulsive behaviour than AD and controls, while no differences were observed in tasks tapping inhibitory control. There is a need to develop objective cognitive measures of disinhibited behaviour for clinical use. The gap between behaviour and cognition in bvFTD remains a clinical challenge.

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Table 1: Demographical, clinical, neuropsychological and behavioural results

	Controls [n=24]	**bvFTD [n=27]**	**AD [n=25]**	**p-value**
Male:Female	6:18	14:13	13:12	ns[1]
Age (years), mean (SD)	70.8 (8.3)	67.8 (9.8)	74.6 (9.7)*	<0.05b[3]
Education (years), mean (SD)	11.5 (3.8)	11.9 (3.6)	11.6 (5.3)	ns[2]
Disease duration (years), mean (SD)	NA	4.1 (2.2)	2.9 (1.2)	ns[2]
Family income, mean (SD)	39.6 (12.1)	33.0 (10.3)	35.7 (11.8)	ns[2]
MMSE, mean (SD)	28.6 (1.3)	25.2 (3.5)	24.3 (2.8)	<0.001a[3]
PDMT – delayed recall, mean (SD)	NA	4.9 (2.5)	3.9 (2.2)	<0.05b[3]
FAB, mean (SD)	14.7 (2.2)	12.6 (3.2)	12.96 (2.9)	<0.001c[3]
Fluency (FAS), mean (SD)	34.7 (9.5)	23.5 (11.5)	26.5 (12.9)	<0.05a[3]
Fluency (Animals), mean (SD)	17.2 (3.8)	10.5 (3.99)	10.60 (4.6)	<0.05a[3]
Stroop Colour – time (sec.), mean (SD)	15.3 (1.8)	22. 4 (11.2)	25.3 (18.1)	<0.01a[3]
Hayling Test				
- part A–time (sec.), mean (SD)	17.9 (5.4)	36.8 (33.7)	26.1 (8.6)	<0.01a[3]
- part B–score (PQt), mean (SD)	9.7 (4.0)	6.96 (4.7)	5.5 (3.6)	<0.05d[3]
- part B–scaled error (PQl), mean (SD)	10.2 (7.1)	18.2 (13.2)	17.4 (9.6)	<0.05c[3]
Five Digits Test				
- switching – Time (sec.), mean (SD)	**68.5 (15.3)**	**74.4 (23.1)**	**115.7 (50.7)**	**<0.05bd[3]**
- switching – Errors, mean (SD)	1.8 (2.9)	5.9 (6.2)	8.5 (8.7)	ns[2]
- flexibility (sec.), mean (SD)	**43.5 (13.7)**	**43.9 (18.7)**	**84.1 (45.1)**	**<0.001bd[3]**
Delayed Discounting Test				
- general k, mean (SD)	0.0722 (0.8907)	0.0531 (0.0856)	0.0580 (0.0696)	ns[2]
- large k, mean (SD)	0.0619 (0.0914)	0.0563 (0.0917)	0.0546 (0.0730)	ns[2]
- medium k, mean (SD)	0.0774 (0.0891)	0.0626 (0.0961)	0.0673 (0.0905)	ns[2]
- small k, mean (SD)	0.0974 (0.0988)	0.0662 (0.0873)	0.0884 (0.0893)	ns[2]
Apathy score, mean (SD)	*NA*	*28.1 (7.8)*	*16.9 (9)*	*<0.05b*[4]
Barrat Impulsivity Scale – 11th				
- total score, mean (SD)	**59.4 (8.1)**	**76.1 (9.5)**	**62.9 (13.5)**	**<0.05bc[6]**
- motor score, mean (SD)	19.7 (2.96)	22.7 (5.9)	20.1 (4.8)	ns[5]
- attention score, mean (SD)	**15.1 (3.0)**	**18.8 (3.3)**	**14.9 (4.7)**	**<0.05bc[6]**
- planning score, mean (SD)	**24.6 (4.3)**	**34.7 (4.3)**	**27.9 (7.1)**	**<0.05bc[6]**

Analyses: a:Controls≠ others; b:AD ≠ bvFTD; c:Controls ≠ bvFTD; d: Controls ≠ AD
Tests: 1: Chi-square; 2: Kruskal-Wallis; 3: Mann-Whitney; 4:t-test Student; 5: ANOVA; 6: Bonferroni post-hoc test.
In bold, measurements which differed statistically between dementia groups, and between one dementia group (either AD or bvFTD) and controls (Apathy Scale was not applied to controls).
AD: Alzheimer's disease; bvFTD: behavioural variant frontotemporal dementia ; MMSE: Mini-Mental State Examination ; FAB: Frontal Assessment Battery ; FAS: Phonemic fluency test ; PDMT: picture drawings memory test; ns: not significant; NA: not applied

Table 2: Apathy and Impulsivity association

			Group		Total	Chi-square Pearson
			bvFTD	AD		
Apathy & BIS-11	Apathy: - BIS-11: -	% of cases	11.1%	88.9%	100.0%	0.011
		Expected	48.9%	51.1%	100.0%	
		% from total	2.4%	19.5%	21.9%	
	Apathy: + BIS-11: -	% of cases	50.0%	50.0%	100.0%	
		Expected	48.6%	51.4%	100.0%	
		% from total	26.8%	26.8%	53.6%	
	Apathy: + BIS-11: +	% of cases	80.0%	20.0%	100.0%	
		Expected	49.0%	51.0%	100.0%	
		% from total	19.5%	4.9%	24.4%	

Table 1: Results for Receiver Operator Characteristics (ROC) Curve analysis

Instrument	**Area under the curve (AUC)**	**Standard Error**	**Confidence interval (95%)**	**p value**
BIS-11 Total score	0.788	0.0713	0.634 a 0.898	0.001
Apathy Total score	0.828	0.0616	0.695 a 0.920	<0.0001
Flexibility-FDT	0.832	0.0671	0.677 a 0.932	<0.001

BIS-11: Barratt Impulsivity Scale 11th version

FDT: Five Digit Test

Figure 1 - Title: Examples of the Delay-Discounting Task

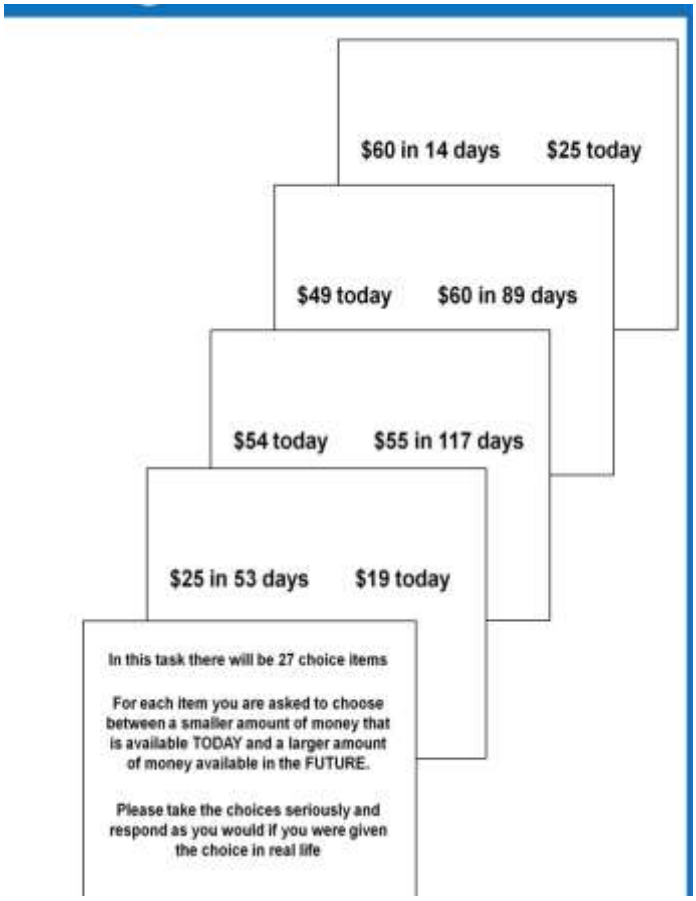

Figure 2 - Title: Receiver Operator Characteristics (ROC) Curve for Apathy, Barratt Impulsivity Scale (BIS-11) and Five Digit Test - Flexibility