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► To cite this version:

Lise M' Barek, Guillaume Mercy, Caroline Gautier, Malika Noquet, Emilie Legros-Lafarge, et al.. The use of the French Dimensional Apathy Scale (f-DAS) to assess apathy in schizophrenia: Properties and profiles. *Journal of Affective Disorders*, 2021, 294, pp.181-188. 10.1016/j.jad.2021.06.081 . hal-03661233

HAL Id: hal-03661233

<https://hal.science/hal-03661233>

Submitted on 2 Aug 2023

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The use of the French Dimensional Apathy Scale (f-DAS) to assess apathy in schizophrenia: Properties and profiles

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1. INTRODUCTION

Apathy can be defined as “the quantitative reduction of self-generated voluntary and purposeful (or goal-directed) behaviour” (Levy and Dubois, 2006; Levy, 2012). This definition focuses on environmental response abilities beyond unwanted automatic actions. It also refers to underlying mechanisms of apathy through attaining goal-directed behaviours (Brown and Pluck, 2000).

There is an increasing recognition of multidimensional components of apathy in transnosographic studies (Marin, 1991; Levy and Dubois, 2006; Levy, 2012; Arnould et al., 2013). In schizophrenia, apathy is part of the negative symptomatology as a sub-syndrome (Foussias and Remington, 2008). Unfortunately, “negative” difficulties are often mentioned through multiple and imprecise terminology. Dimensional approach in schizophrenia could be a mean to enhance our understanding of the nature of apathy and its relationship with cognitive functions or other syndromes such as depression (Bortolon et al., 2018). The triadic Cognitive, Emotional and Auto-activation structure of apathy proposed by Levy and Dubois (Levy and Dubois, 2006; Levy, 2012) is applicable in schizophrenia (Del-Monte et al., 2013).

Data suggest different structures and expressions of apathy across illnesses. In schizophrenia, regarding different tools, nearly half of patients are apathetic (Faerden et al., 2010; Mulin et al., 2011; Yazbek et al., 2014) and Emotional apathy seems to be predominating (Mulin et al., 2011; Yazbek et al., 2014). However, there is inconsistency between methodologies of multidimensional assessment of apathy. As described in table 1, no dimensional tools have been used by referring to a triadic factor structure of apathy regarding to the Levy and Dubois model (Levy and Dubois, 2006; Levy, 2012). The Lille Apathy Rating Scale (LARS; Sockeel et al., 2006), which refers to Stuss and Alexander (2000) conception of apathy and was developed in Parkinson’s disease (Dujardin et al., 2013). Its psychometric properties have been validated in French in schizophrenia (Yazbek et al., 2014). The triadic structure was obtained by the grouping of several cognitive (factor 1 and 4), behavioural (factor 2) and emotional (factor 3) factors. Over nine subscales, seven were revealed by factorial analysis in schizophrenia (Interests, Taking the Initiative, Novelty Seeking, Voluntary Actions, Emotional Responses, Social Life and Self-Awareness).

Table 1. Apathy scales available in schizophrenia.

Scales	References	Validity in schizophrenia	Advantages	Inconveniences (with regard to Levy and Dubois's model (Levy and Dubois, 2006; Levy, 2012)).
Apathy Evaluation Scale (AES)	(Marin et al., 1991)	(Faerden et al., 2008)	Provide a triadic measure of apathy.	Based on the Marin's model (Marin, 1991). Identification in schizophrenia with three subscales: Apathy, Insight, and Social without satisfactory psychometric qualities for the latter two.
Brief Psychiatric Rating Scale (BPRS) Short version (BPRS-E(A))	(Overall and Gorham, 1962) (Mouaffak et al., 2010)	(Overall and Gorham, 1962) (Mouaffak et al., 2010)	Developed especially for psychiatric pathologies.	Despite an abridged version, a satisfactory dimensional measurement of the self-activation and executive aspects isn't accounted for.
Frontal Systems Behavior Scale (FrSBe)	(Grace et al., 1999)	(Velligan et al., 2002)	Multidimensionnal.	Psychometric quality of the subscales is unsatisfactory (Stout et al., 2003). No measurement of the emotional dimension provided.
Lille Apathy Rating Scale (LARS)	(Sockeel et al., 2006)	(Yazbek et al., 2014)	Provides several scoring components.	Four-factor sub-structure but not compliant to Levy and Dubois model (Levy and Dubois, 2006; Levy, 2012)

The self and career Dimensional Apathy Scale (DAS; Radakovic and Abrahams, 2014) provides measurement of three neurobehavioral apathy subtypes: Executive, Emotional and Initiation subscales. The DAS scale has been used in neurodegenerative illnesses and in identifying apathetic profile deficit compared to population of control. Amyotrophic lateral sclerosis is more characterized by initiation apathy independent of physical disability profile (Radakovic et al., 2016; Radakovic et al., 2017). In Parkinson's disease Executive and Initiation apathy are also more often observed (Radakovic et al., 2018). In Alzheimer's disease, profiles show global apathy, with prominent awareness problems in the Initiation and Executive apathy subtypes (Radakovic et al., 2017).

We previously demonstrated that Dimensional Apathy Scale translated into French (f-DAS) was a robust and reliable tool for assessing multidimensional apathy (M'Barek et al., 2018). Since prevalence and profiles of apathy in schizophrenia have never been studied with the f-DAS, we aimed to use this tool to assess apathy in schizophrenia. We also aimed to examine the psychometric properties of the f-DAS, against a standardized measurement of apathy in these patients. Our main objective was to demonstrate the multidimensional characteristic of apathy in schizophrenia and its prominent features. Radakovic and Abrahams (2014) have shown that the DAS allowed a partial overlapping with depression (Radakovic et al., 2016; Radakovic et al., 2018), hence their relationship between f-DAS and depression in schizophrenia was also explored in this study.

2. METHODS

2.1 Procedure and participants

One hundred and twelve subjects participated in the study. A group of 48 patients with schizophrenia was recruited in France from two psychiatric departments providing social rehabilitation ("Réseau Rehab" from Niort's Hospital and "C2RL" Limoges' Hospital). Three patients were excluded due to verbal understanding difficulties during the experiment. Inclusion criteria were: (1) spectrum of schizophrenia according to the DSM-5 criteria (American Psychiatric Association, 2003), (2) absence of psychotic disorder induced by a substance, drug or other medical condition, (3) absence of schizotypal personality disorder in relation to the medical file and confirmed by The Mini-International Neuropsychiatric Interview (MINI; Lecrubier et al., 1998), (4) aged between 18 and 55

years old, (5) stable symptomatology (clinical assessment) during the month prior to inclusion, (6) substantive psychotropic treatment unchanged during the month prior to inclusion (25% change), (7) reading and writing in French acquired. Exclusion criteria were: (1) IQ score < 70 measured by French National Adult Reading (f-NART; Mackinnon and Mulligan, 2005), (2) neurological disorders of vascular, infectious or neurodegenerative origin, (3) dyschromatopsia, (4) taking somatic drugs with a cerebral or mental impact (e.g. corticosteroids), (5) resistance to neuroleptics, (6) addiction to cannabis, alcohol or other substances (> 2 / week) according to DSM-5 criteria, except tobacco, and (7) simultaneous participation in a remediation program targeting neurocognitive deficits. A group of 57 healthy controls was recruited from the general population (flyers distribution, posting information in hospital of Niort and local newspaper reports). They share inclusion and exclusion criteria with patients, although MINI (Lecrubier et al., 1998) was used to exclude control subject with psychiatric disorders. Two subjects were excluded because they showed psychological difficulties. Counselling support was provided for the latter.

2.2 Measures

f-DAS

The French DAS (f-DAS; M'Barek et al., 2018) provides a multidimensional measurement of apathy regarding Levy and Dubois model (Levy and Dubois, 2006; Levy, 2012). It is composed of 24 items assessing Executive, Emotional and Initiation dimensions of apathy. Each item is rated on 4-point Likert scale based on the frequency of occurrence in the last month. The total score is 72. For each subscale, the minimum score is 0 (least apathy) and the maximum 24 (most apathy). The suggested cut-offs is 2 standard deviation above the mean of control group (Radakovic and Abrahams, 2014; Radakovic et al., 2016).

MINI

The Mini-International Neuropsychiatric Interview (MINI; Lecrubier et al., 1998) explores diagnostic (the main Axis I) in psychiatric disorders of the DSM-IV (American Psychiatric Association, 1994) in standardized interview. Based on “yes” and “no” answers, it has been used here, to improve diagnostic

accuracy and avoid associated disorder. Module (B) dysthymia, (D) (hypo) manic and (L) psychotic disorder were used.

f-NART

The French National Adult Reading Test (f-NART; Mackinnon and Mulligan, 2005) is a list of words whose pronunciation cannot be determined from their spelling. It assesses the premorbid intellectual ability in French speakers. It was used to have some knowledge of cognitive performance earlier in life and helps to avoid subjects with intellectual disability.

LARS

Lille Apathy Rating Scale (LARS; Sockeel et al., 2006) is a semi-structured interview of 33 items and gives an overall score divided into nine sub-composite areas. The global score is distributed between -36 and +36. Yazbek et al. (2014) examined the psychometric proprieties of this scale in a sample of schizophrenia patients. They identified a LARS cut-off value of -18. This classification was obtained with the use of control group: [-36; -24] for non-apathetic subjects, [-23; -19] for slightly apathetic subjects, [-18; -13] and for moderately apathetic subjects [-12, +36].

BDI II

The Beck Depression Inventory II (BDI-II; Beck et al. 1996) is used to assess symptoms and characteristic attitude of depression above 13 years of age. It is a self-questionnaire composed of 21 items. The scores range from less than 14 (non-depressed), 14–19 (mild), 20–28 (moderate) and 29–63 (severe symptoms of depression).

2.3 Statistical analysis

Results were analysed using Python. Statistics analysis were performed using “pandas”, “numpy”, “scipy”, “statsmodels” and “scikit-learn” libraries and data visualisation was obtained using “seaborn” and “matplotlib” libraries. Cronbach’s standardised alpha coefficients were used to assess internal consistency reliability between items of f-DAS scale. Prior to further analysis, validity of the

data was assessed to determine its normality and homogeneity. The Shapiro-Wilk W test was used to evaluate each variable for normality and Levene test and Fisher-Snedecor test to check the homogeneity (see supplementary materials, table S2 and S3, and figure S1). One-way ANOVA were performed to compare mean scores of f-DAS subscales (Executive, Emotional and Initiation) between patients with schizophrenia and controls (patient vs controls). The effect size was estimated with Cohen's term d and classified as small ($d=0.2$), medium ($d=0.5$), or large ($d \geq 0.8$) (Carson, 2012). Concurrent validity was assessed by comparing f-DAS and LARS. Clustering of the patients was performed using agglomerative clustering function from "scikit-learn" library. Prior clustering, the number of five clusters was determined using dendrogram and elbow curve methods (see supplementary materials, figures S3 and S4). Then, for each cluster, z-core were calculated for the three subscales of the f-DAS. To investigate the relationship between the type of apathy and depression level, BDI-II score was used to separate patients with schizophrenia into four groups according to their depression levels (minimal, mild, moderate or severe). The relationship between the type of apathy and depression was then investigated using Pearson correlation. Finally, ANOVAs and post hoc tests were performed to compare the mean of f-DAS subscale scores (Executive, Emotional or Initiation) between each groups of depression level.

3. RESULTS

3.1 Demographic and normative data

The demographic data of patient group and control group are reported in table 2. Healthy controls were matched with controls by age, sex and education level. The premorbid intelligence estimated by the f-NART was between 82.9 and 122.9 for the patient group and between 98.3 and 119.8 for the control group. For the f-DAS scale and subscale, the cut-offs based on ≥ 2 above the mean (Radakovic and Abrahams, 2014; Radakovic et al., 2016) was use to provide normative data (table 3).

Table 2. Demographic characteristics of the sample.

		Patients (N = 45)		controls (N = 55)	
		Measure	Range	Measure	Range
Age (years)	[mean, std]	32.0 (8.2)	19 - 50	35.2 (11.6)	18 - 55
Education (years)	[mean, std]	11.7 (2.0)	9 - 17	13.9 (2.2)	9 - 20
Female gender	[N, %]	16 (35.6%)	-	33 (60.0%)	-
Medications families					
<i>Antidepressants</i>	[N, %]	15 (33.3%)	-	-	-
<i>Anxiolytics</i>	[N, %]	15 (33.3%)	-	-	-
<i>Hypnotics</i>	[N, %]	3 (6.7%)	-	-	-
<i>Neuroleptics</i>	[N, %]	19 (42.2%)	-	-	-
<i>Atypical neuroleptics</i>	[N, %]	36 (80.0%)	-	-	-
<i>Mood stabilizing</i>	[N, %]	4 (8.9%)	-	-	-
Intellectual efficiency (f-NART)	[mean, std]	106.7 (7.8)	82.86 - 122.9	110.0 (6.1)	98.26 - 119.82
Depression level (BDI-II)					
<i>Minimal</i>	[N, %]	21 (46.7%)	-	51 (92.7%)	-
<i>Mild</i>	[N, %]	9 (20.0%)	-	3 (5.5%)	-
<i>Moderate</i>	[N, %]	8 (17.8%)	-	1 (1.8%)	-
<i>Severe</i>	[N, %]	7 (15.6%)	-	-	-
f-DAS	[mean, std]	34.1 (8.9)	21 - 59	20.4 (7.0)	6 - 39
f-DAS [Executive]	[mean, std]	11.4 (4.7)	2 - 22	5.0 (3.0)	0 - 14
f-DAS [Initiation]	[mean, std]	12.5 (4.2)	4 - 21	8.0 (3.2)	0 - 15
f-DAS [Emotion]	[mean, std]	10.1 (3.9)	2 - 18	7.3 (3.4)	1 - 16
LARS	[median, std]	-14.0 (7.4)	-25 - 5	-29.0 (5.7)	-36 - -11

Note: f-DAS: French Dimensional Apathy Scale; LARS:Lille Apathy Rating Scale; f-Nart: French National Reading Test; BDI

II:Beck Depression Inventory II.

Table 3. Normative data on f-DAS (N = 55 controls)

Scale	Mean (SD)	Range	Abnormality cut-off
f-DAS	20.4 (7.0)	6-39	34.4
f-DAS Executive	5.0 (3.0)	0-14	11.0
f-DAS Emotion	7.3 (3.4)	1-16	14.1
f-DAS Initiative	8.0 (3.2)	0-15	14.4

3.2 Psychometrics

Consistency

The overall f-DAS Cronbach's standardized α was 0.87 and can be interpreted as good internal consistency. Overall f-DAS values were acceptable both in the control group (0.79) and in the patient group (0.77). In all groups, the internal consistencies were higher for both Executive (all=0.87) and Initiation subscale (all=0.76) and lower for Emotional (all=0.71).

Validity

There is a statistically significant difference between the means of patient and control groups as determined by one-way ANOVA for f-DAS total score ($F(1, 98) = 72.715, p < 0.001$) and also in Executive ($F(1, 98) = 67.711, p < 0.001$), Emotional ($F(1, 98) = 15.279, p < 0.001$) and initiative ($F(1, 98) = 36.623, p < 0.001$) subscales. (see supplementary materials, table S5). Compared to controls, in schizophrenia, patients are more apathetic, and the difference is large in total of f-DAS score (patient mean score= 34.1; Cohen's $d = 1.7$), in Executive (patient mean score= 11.4; Cohen's $d = 1.6$), in Initiative (patient mean score= 12.5; Cohen's $d = 1.2$) and in Emotional subscales (patient mean score= 10.1; Cohen's $d = 0.8$) (figure 1). The analyses showed that performances on each subscale depend which group they belong to.

FIGURE 1

Concurrent validity

Considering the scores of patient and control groups, we observed a high correlation between the overall scores obtained for f-DAS and LARS ($r = 0.82, p < 0.001$). A high correlation was also observed in patient group ($r = 0.78, p < 0.001$). Using the recommended cut-offs (2 standard deviations above the mean for the self-version for f-DAS and a score below -18 for LARS), (Yazbek et al., 2014; Radakovic and Abrahams, 2014; Radakovic et al., 2016), 48,9% of the patients were diagnosed as apathetic on total f-DAS scale and 57.8% of the patients on total LARS scale (table 4). Both scales come to the same conclusion for 35 patients (19 apathetic and 16 non apathetic) (Figure2). However, the diagnostics were different for 10 patients. More precisely, 3 patients were classified as apathetic with the f-DAS, but not with the LARS; 7 were classified as apathetic with the LARS, but not with the f-DAS. From a dimensional point of view, 68.9% of the patients are diagnosed as apathetic for at least one dimension (executive, emotional or initiative) of the f-DAS (table 4).

Even though subscales of the f-DAS and the subscales of the LARS are different, we investigated potential correlation between them. Few moderate correlations were observed between f-

DAS subscales and 4 subscales of LARS: The Executive subscale of f-DAS with “Taking the Initiative” and “Voluntary Actions” subscales of LARS ($r=0.62$, $p \leq 0.001$ and $r=0.70$, $p \leq 0.001$, respectively); Emotional subscale of f-DAS with “Emotional Responses” subscales of LARS ($r=0.67$, $p \leq 0.001$); Initiative subscale of f-DAS with “Taking the Initiative”, “Voluntary Actions” and “Social Life” subscales of LARS ($r=0.58$, $p \leq 0.001$, $r=0.58$, $p \leq 0.001$ and $r=0.52$, $p \leq 0.001$ respectively).

FIGURE 2

Table 4. Repartition of apathetic patients on f-DAS and LARS

	Patients (N = 45)		Controls (N = 55)	
	Number of apathetic	Percentage	Number of apathetic	Percentage
No subscale / non-apatetic	14	31.1 %	51	92.7 %
1 subscale	20	44.4 %	3	5.5 %
1 subscale or +	31	68.9 %	4	7.3 %
2 subscales	7	15.6 %	1	1.8 %
2 subscales or +	11	24.4 %	1	1.8 %
3 subscales	4	8.9 %	0	0.0 %
f-DAS Executive	23	51.1 %	2	3.6 %
f-DAS Emotion	9	20.0 %	2	3.6 %
f-DAS Initiative	14	31.1%	1	1.8 %
f-DAS Total	22	48.9 %	2	3.6 %
LARS	26	57.8 %	3	5.5 %

3.3 Specific feature of apathy in schizophrenia

The repartition of patients diagnosed as apathetic, by subscale, was higher in Executive subscale (51.1%) than Initiative (31.1%) and Emotional (20.0%) subscales. Patient group was more impaired in Executive ($z=2.1$) and Initiative subscales ($z=1.4$) than Emotional subscale ($z=0.82$).

Using clustering algorithm over the three dimensions of the f-DAS (executive, emotional and initiative), we identified five clusters within our patients' group. To determine if those clusters correspond to different forms of apathy in schizophrenia, we analysed the scores that the patients obtained in the three dimensions of the f-DAS. To do so, we looked at the 3D projections of the patients' scores. Then, we calculated the z-score of those clusters for the three f-DAS dimensions (figure 3). The cluster 1, shows patients with f-DAS scores close to the cut-offs in the three

dimensions. The cluster 2, shows patients with f-DAS scores higher than the cut-offs in the three dimensions (Executive mean=15.6, $z=2.8$; Initiative mean=18.8, $z=2.7$, Emotional mean=15.8, $z=2.4$). The cluster 3, shows patients with f-DAS scores similar to the mean scores of control group. The cluster 4, shows patients with mean score above the cut off in Executive subscale, close to the cut off in Initiative subscale and similar to the mean score of the control group in Emotional subscale (Executive mean=18.4, $z=4.5$; Initiative mean=14.7, $z=2.1$, Emotional mean=7.1, $z=0$). The cluster 5, shows patients with mean score close to the cut off in Executive subscale and similar to the mean scores of the control group in Emotional and Initiative subscales (Executive mean=12.0, $z=2.3$; Initiative mean=8.0, $z=0$ Emotional mean=4.6, $z=-0.8$).

FIGURE 3

3.4 Apathy and depression

In the patient group, the correlations of BDI II total score and apathy scales are significant and low with f-DAS total score ($r=0.48$; $p<0.001$) and moderate with LARS total score ($r=0.60$; $p<0.001$). Regarding the dimensions of f-DAS, Executive subscale correlates highly with BDI II ($r=0.73$; $p<0.001$) and moderately with Initiative subscale ($r=0.58$; $p<0.001$). Correlation is not significant with Emotional subscale ($r=-0.19$; $p=0.2033$). Within patients' group, 46.7% have no sign of depression, 20.0% mild depression, 17.8% moderate depression, and 15.6% severe depression. The level of depression correlates more strongly with the Executive and Initiative subscale than with the global f-DAS score.

ANOVA demonstrated significant differences between apathy total score on f-DAS according to depression level score on BDI II ($F(3,41) = 6.585$; $p<0.001$). Executive subscale ($F(3,41) = 13.067$, $p<0.001$) and Initiative subscale ($F(3,41) = 4.987$, $p<0.01$) scores differ also according to score depression level. There were no significant differences between Emotional subscale regarding depression level ($F(3,41) = 2.018$; $p=0.126$). (see supplementary materials, table S8). In a post hoc analysis, for each subscale, each level of depression mean scores were compared to all others. In Executive subscale, difference in patient group is significant and large between levels minimal-mild ($t(28) = -2.278$, $p<0.05$; Cohen's $d=0.9$), minimal-moderate ($t(27) = -4.942$, $p<0.001$; Cohen's $d=2.0$),

minimal-severe ($t(26) = -5.405, p < 0.001$; Cohen's $d = 2.4$), mild-moderate ($t(15) = -2.169, p < 0.05$; Cohen's $d = 1.0$) and mild-severe ($t(14) = -2.592, p < 0.05$; Cohen's $d = 1.3$). In this dimension no significant difference was observed between levels moderate-severe ($t(13) = -0.194, p = 0.849$). In initiative subscale, there is a significant and large difference between minimal-moderate ($t(27) = -3.630, p < 0.01$; Cohen's $d = 1.5$), minimal-severe ($t(26) = -2.199, p < 0.05$; Cohen's $d = 1.0$) and mild-moderate ($t(15) = -2.671, p < 0.05$; Cohen's $d = 1.3$). The higher the rating is on the BDI II, the greater the degree of severity is on the Executive subscale (figure 4).

FIGURE 4

4. DISCUSSION

During our investigation, we showed that the f-DAS provides a suitable three-dimensional measure of apathy in schizophrenia and that it is a psychometrically robust instrument to distinguish three subtypes of apathy in schizophrenia (Executive, Emotional, and Initiative). We also demonstrated that patients with schizophrenia were significantly more apathetic than the control group in the global score and its three subscales.

In our sample, using the recommended cut-off of the f-DAS (Radakovic and Abrahams, 2014; Radakovic et al., 2016) we identified that 48.9 % of patients were apathetic on f-DAS. For convergent validity, we used the LARS as a gold standard for apathy diagnostic (Sockeel et al., 2006; Yazbek et al., 2014). With this scale, we diagnosed 57.8% of our patients as apathetic. The LARS, correlates highly with f-DAS total score in patients' group ($r = 0.78, p < 0.001$). Our ratio of apathetic patients corresponds to the results obtained in the previous study of the gold standard (47.3% of prevalence in Yazbeck et al., 2014) and other measure of apathy prevalence (51% in Faerden et al., 2010). However, this is a binary classification, and it can be improved using the dimensional characteristic of the f-DAS. Considering the impairment on one subscale, or more a way of classification of our patients (regarding f-DAS subscale cut-off), the prevalence of apathy in schizophrenia increases to 68.9% of our patients. Despite dimensional tools available in schizophrenia, prevalence of apathy in

schizophrenia could be largely underestimated. Correlations are moderate between f-DAS dimensions and 4-subcales of LARS (Taking the Initiative, Voluntary Actions, Emotional Responses and Social Life). In their factorial analysis, Yazbek et al. (2014) didn't identify Concern and Everyday productivity subscales. In our study, these subscales correlations were also low or negligible with any dimension of f-DAS (as also Interest, Novelty seeking and Self Awareness). But the comparison with the LARS, total score and subscale is limited. First, to suggest the LARS cut-off in schizophrenia, in absence of validated measures of apathy in schizophrenia, Yazbek et al. (2014) used a unidimensional measure of negative symptomatology, the Scale for Assessment of Negative Symptoms (SANS; Andreasen, 1982), factor "lack of motivation" as gold standard. Secondly, the LARS was initially a four-factor structure (Sockeel et al., 2006) and was designed to provide a global score of apathy and categorical severity of apathy. This limits the adjustment of f-DAS in each dimension. Further research is needed to compare the f-DAS to other three-dimensional scales when they become available.

Through our profile analysis of patients with schizophrenia, we showed that Executive and Initiative dimensions were the most prevalent in patients' group. We could also identify five clusters within our patients, suggesting that five different profiles of apathy could be described in patient with schizophrenia. Cluster 1 is composed of patients with a mean score of f-DAS close to the value of the cut-off in each dimension. The classification of apathetic by cut-off is a binary system, meaning that all these patients can't be diagnostic as apathetic. Nevertheless, this group can be qualified as "vulnerable group" in the three dimensions of apathy. Three other clusters have noticeable features (cluster 2, 4 and 5). In Cluster 2, most of patients are apathetic in each dimension (above or close to the cut-off in each f-DAS subscales). In Cluster 4, most of patients are impaired in Executive and Initiative dimensions (above the cut-off in Executive subscale and close to the cut-off in Initiative subscale), and in cluster 5 most of patients are apathetic in Executive subscale (close or above the cut-off in Executive subscale). Finally, cluster 3 shows patients with apathetic profile like the control group, except for Emotional dimension which was slightly higher but still lower than the cut-off value. These results differ from other studies in schizophrenia. Mulin and al. (2011), identify emotional aspects of apathy but not auto-activation. Beyond the problematic measure of apathy, it is possible that

the course of the disease impacts the expression of apathy. Longitudinal effect was already observed in apathy. In schizophrenia, global apathy is found in 50% of patients with a first psychotic episode, then in 40% in the following year. Among patients with apathy from the onset of the disease, 30% of them still had it a year later (Faerden et al., 2010). Emotional dimension could be sensitive to longitudinal effect. Wei et al. (2019) uses the DAS to study apathy across dementia syndromes and disease stage. Emotional apathy was more prominent in early stage in behavioural-variant of front temporal dementia and executive apathy is more severe in late stage Alzheimer Disease. It will be interesting to observe the predominance of the different dimensions of apathy in schizophrenia in a longitudinal study.

Recently, Raffard et al. (2019) proposed a longitudinal study to identify factors that best predict apathy dimensions on the LARS. Anticipatory pleasure and sensibility to punishment were among predictors of cognitive apathy and sensibility to punishment predicted emotional apathy. Schizophrenic patients also tend to overestimate the cost of the effort to perform an action and this leads to a decrease in goal-directed behaviours (Hartmann-Riemer et al., 2015). The limbic pathway and the processes related to the emotional evaluation of environmental signals enabling decision-making to have a key role in the Emotional / Affective dimension of the model of Levy and Dubois (Levy and Dubois, 2006; Levy, 2012). The model of Stuss (2011) allows in the operationalization of so-called "emotional" processes: the regulation of behaviour using decision-making tasks. To improve understanding of emotional mechanism in apathy, Emotional dimension identified with f-DAS scale could be investigated with decision-making tasks in schizophrenia.

The divergent validity of f-DAS is good and shows weak correlation between f-DAS total and BDI II. There were statistically significant differences between group means of f-DAS and BDI II (Executive and BDI II; Initiative and BDI II). We already demonstrated this lack of correlation between Emotional dimension and depression, in our previous study of the translation of DAS (M'Barek et al., 2018) and there is a robust effect across illnesses. Indeed, in Amyotrophic Lateral Sclerosis Disease (Radakovic et al., 2016), Alzheimer Disease (Radakovic et al., 2017) and Parkinson Disease (Radakovic et al., 2018) no correlation between this subtype and depression was found either. These results overcome the opposition of these concepts and show how necessary it is to develop better understanding of their co-dependence in a multidimensional point of view. The f-DAS

combined with a measure of depression could contribute to improving the understanding of the effect of some antidepressants such as selective serotonin reuptake inhibitors (SSRIs) and adverse effects on emotional experience identified in literature (Padala et al., 2020).

Limitations linked to the gold standard or longitudinal effect have already been exposed but other limits can be stated for this study. Firstly, the sample size could be improved to increase generalization or result through predictive modelling. This study stresses on quality of participation for groups (patients and controls) and strict inclusion criteria, such as the use of several pre-tests. Bigger sample size should be accompanied by a longer study to guarantee the quality of sample and because persons with diagnosis of schizophrenia sometimes needed time to build up confidence which impacted the recruitment speed. Secondly, the difference of gender in the sample of this study must be pointed out. For the control group, participation was only on a voluntary basis and was largely female. The recruitment method for control group of this study on a voluntary basis can be improved. However, it should be noted that males were most recruited in the patient group because in schizophrenia the male prevalence is approximately two-fold higher than compared to females (Gourier-Frery et al., 2014). Although this was not the focus of our study, no correlation could be demonstrated between gender and other results (see supplementary materials, figure S5 and table S10).

In summary, we propose to apply to schizophrenia a dimensional scale based on Levy and Dubois triadic model of apathy; (Levy and Dubois, 2006; Levy, 2012) which has never been done. Overall, the f-DAS has good psychometric quality in schizophrenia. However, it must be pointed out that the prevalence of apathy in a dimensional point of view could be underestimated in schizophrenia. Divergent validation underlines the lack of correlation between Emotional subscale of f-DAS and depression which is robust in literature. The f-DAS can be helpful in other studies to understand overlapping between depression and specific dimensions of apathy. The Emotional aspect of apathy needs to be understood deeply.

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The use of the French Dimensional Apathy Scale (f-DAS) to assess apathy in schizophrenia: Properties and profiles

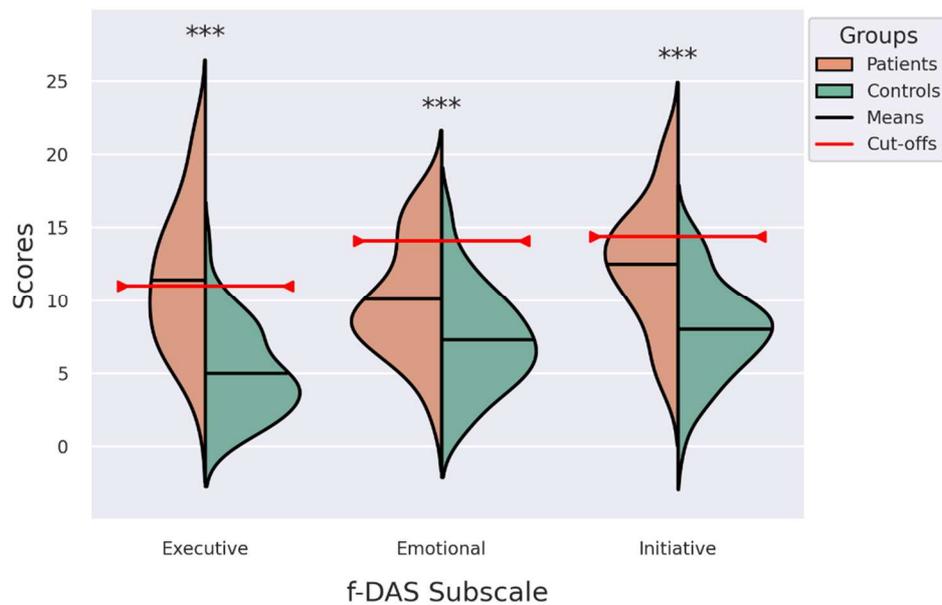


Figure 1, f-DAS, French Dimensional Apathy Scale: Violin plots represent the distribution of the f-DAS subscale scores in patients with schizophrenia (left) and controls (right). For each subscale and each group, the mean score is indicated by the black horizontal line (f-DAS Executive: meanpatient = 11.4, meancontrol = 5.0, f-DAS Emotional: meanpatient = 10.1, meancontrol = 7.3, f-DAS Initiative: meanpatient = 12.5, meancontrol = 8.0). For each subscale, cut-off is indicated by the horizontal red line. Statistical significance of means difference between patient and control is indicated by stars (* for a p-values ≤ 0.05 , ** for a p-value ≤ 0.01 and *** for a p-value ≤ 0.001).

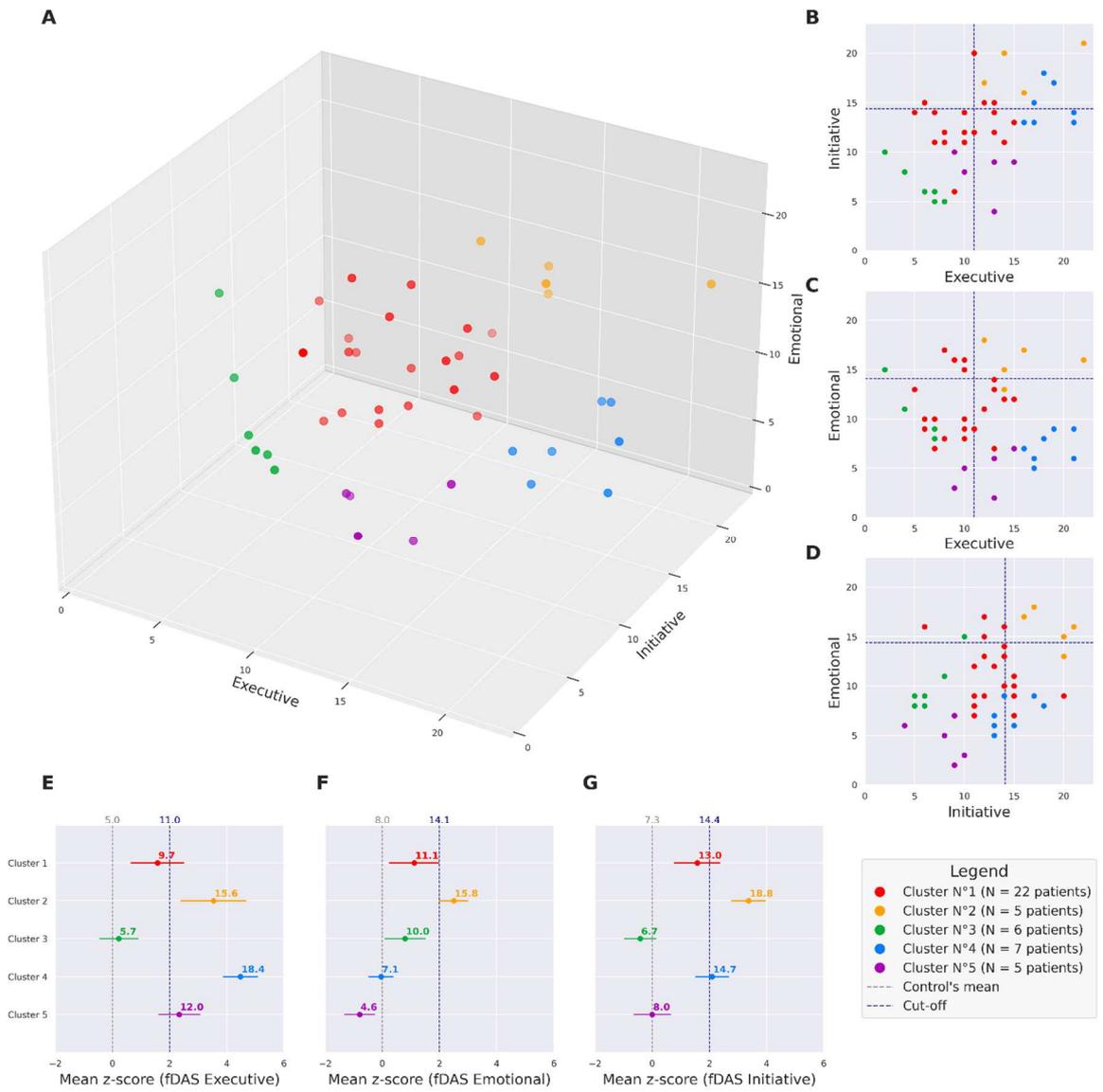


Figure 3. Profiling of apathy in patients with schizophrenia. (A) 3D projection of the patients scores for f-DAS Executive, f-DAS Emotional and f-DAS Initiative subscales. Each dot represents one patient and is coloured depending on the cluster it belongs too. (B, C and D) 2D projections of the patients' scores, respectively: f-DAS executive in function of f-DAS initiative, f-DAS executive in function of f-DAS emotional and f-DAS initiative in function of f-DAS emotional. The dash lines indicate the cut-off in the corresponding subscale. (E, F and G) Plot of the mean z-score of the different clusters in the three subscales of the f-DAS (executive, emotional and initiative respectively). Horizontal lines indicate the standard deviation of the corresponding z-score. Scores indicated on the graphs correspond to the mean of the subscale score for each cluster. The middle dash lines indicate the cut-off in the corresponding subscale and the dash lines on the left indicate the mean score of the control group in the corresponding subscale.

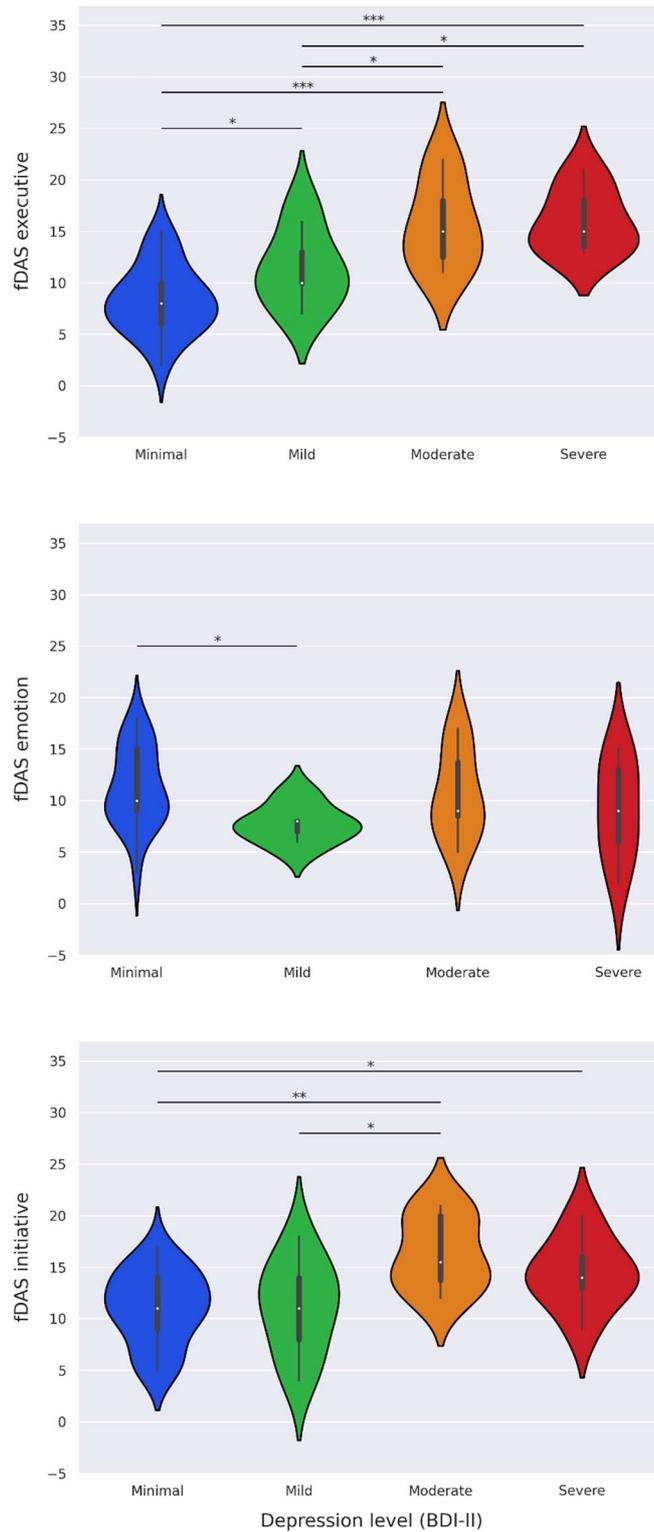


Figure 4. Distribution of patients' score in f-DAS subscales in function of their depression level. Violin plot illustrate the distribution of the f-DAS subscales (Executive, Emotional or Initiation) scores for patients with schizophrenia according to their level of depression (from left to right: minimal, mild, moderate and severe). For each subscale, statistical significance of means difference between two groups is indicated by stars (* for a p-values ≤ 0.05 , ** for a p-value ≤ 0.01 and *** for a p-value ≤ 0.001).