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► To cite this version:

Delphine Tanguy, Armelle Rametti-Lacroux, Arabella Bouzigues, Dario Saracino, Isabelle Le Ber, et al.. Behavioural disinhibition in frontotemporal dementia investigated within an ecological framework. *Cortex*, 2023, 160, pp.152-166. 10.1016/j.cortex.2022.11.013 . hal-03970275

HAL Id: hal-03970275

<https://hal.science/hal-03970275>

Submitted on 2 Jun 2023

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Behavioural Neurology

Behavioural disinhibition in frontotemporal dementia investigated within an ecological framework



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ARTICLE INFO

Article history:

Received 2 February 2022

Reviewed 23 March 2022

Revised 29 September 2022

Accepted 9 November 2022

Action editor Brad Dickerson

Published online 28 December 2022

Keywords:

Behaviour

Compulsivity

Ecological setting

Impulsivity

Non-pharmacological management

Social disinhibition

ABSTRACT

Disinhibition is a core symptom in behavioural variant frontotemporal dementia (bvFTD) particularly affecting the daily lives of both patients and caregivers. Yet, characterisation of inhibition disorders is still unclear and management options of these disorders are limited. Questionnaires currently used to investigate behavioural disinhibition do not differentiate between several subtypes of disinhibition, encompass observation biases and lack of ecological validity.

In the present work, we explored disinhibition in an original semi-ecological situation, by distinguishing three categories of disinhibition: compulsivity, impulsivity and social disinhibition. First, we measured prevalence and frequency of these disorders in 23 bvFTD patients and 24 healthy controls (HC) in order to identify the phenotypical heterogeneity of disinhibition. Then, we examined the relationships between these metrics, the neuropsychological scores and the behavioural states to propose a more comprehensive view of these neuropsychiatric manifestations. Finally, we studied the context of occurrence of these disorders by investigating environmental factors potentially promoting or reducing them.

As expected, we found that patients were more compulsive, impulsive and socially disinhibited than HC. We found that 48% of patients presented compulsivity (e.g., repetitive actions), 48% impulsivity (e.g., oral production) and 100% of the patients group showed

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<https://doi.org/10.1016/j.cortex.2022.11.013>

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social disinhibition (e.g., disregards for rules or investigator). Compulsivity was negatively related with emotions recognition. BvFTD patients were less active if not encouraged in an activity, and their social disinhibition decreased as activity increased. Finally, impulsivity and social disinhibition decreased when patients were asked to focus on a task.

Summarising, this study underlines the importance to differentiate subtypes of disinhibition as well as the setting in which they are exhibited, and points to stimulating area for non-pharmacological management.

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1. Introduction

Behavioural variant frontotemporal dementia (bvFTD) is one of the most frequent adult-onset neurodegenerative syndromes characterised by progressive deterioration of personality, social conduct and cognition (Rascovsky et al., 2011). Particularly, behavioural disinhibition is very frequent and affect daily lives of both patients and caregivers. Indeed, on average, the disease occurs at the age of 58 (Miller & Llibre Guerra, 2019), when patients are still very active (professionally and personally) and behavioural disturbances extensively interfere with these occupations (Kortte & Rogalski, 2013).

Despite its impact, assessment and characterisation of behavioural disinhibition are still poorly detailed, leading to limited management of these disorders. In a recent review, Magrath Guimet et al. (2021) have reviewed the “existing barriers to diagnosing and interpreting the phenomena associated with what we understand as behavioural disinhibition” and one of the first limitations they highlighted is that many of the instruments used to objectively evaluate behavioural disinhibition are imprecise. Thus, “scales that assess disinhibition globally, such as the NPI (neuropsychiatric inventory), do not capture the spectrum of manifestations associated with behavioural disinhibition, or provide information on the key neural contributors to the observed behaviour”. Moreover, caregivers' questionnaires used to investigate and measure behavioural disinhibition in dementia (Bang et al., 2015; Desmarais et al., 2018; Seeley, 2019) have other methodological limitations, such as observation biases and lack of ecological validity. These tools are often incomplete, not specific enough to identify the subtype of disinhibition and, most of all, provide a subjective measure of behaviour (Migliaccio et al., 2020). Finally, to our knowledge, the issue of when and how disinhibition occurs has not been studied yet. For these reasons, there is a growing need to investigate behavioural disinhibition within an ecological framework, to clarify the description and characterisation of these disorders and to identify environmental factors which may particularly influence (positively or negatively) their manifestation. Within this framework, Magrath Guimet et al. (2021) suggest that ideally a scale for behavioural disinhibition should be able to capture subtypes of this deficit in patients, by distinguishing for example a lack of understanding of social norms from a loss of impulse control.

In bvFTD, compulsivity, impulsivity and social disinhibition are referenced among the diagnostic criteria of the

disease (Rascovsky et al., 2011), reflecting the multifaceted nature of inhibition deficits. As previous work has demonstrated, the stratification of patients based on the presence and severity of aforementioned behavioural disinhibition subtypes suggests different profiles of bvFTD patients (Godefroy et al., 2021). The classification of bvFTD relying on the subtype of inhibition deficits could improve the characterisation of the disease and, most of all, lead to a more appropriate clinical management of behavioural disorders, in turn improving patients' care.

The aims of this study are to provide a better description of behavioural inhibition disorders in bvFTD through an ecological approach. We had three main hypotheses: 1/ the three subtypes of disinhibition (compulsivity, impulsivity and social disinhibition) would present in isolation or in combination with each other; 2/ the three subtypes of disinhibition would relate to distinct neuropsychological profiles and behavioural states; and 3/ guiding individuals' behaviour (i.e., externally-guided behaviour) would limit behavioural disinhibition.

2. Materials and methods

2.1. Cohorts and ethics statement

This study is part of the clinical observational studies C16-87 (ECOCAPTURE pilot) and C15-14 (ECOCAPTURE) promoted by INSERM, the French national institute for biomedical research. It was granted approval by the local Ethics Committee, or “Comité de Protection des Personnes,” on July 7, 2015, and May 17, 2017 respectively, and registered in a public clinical trial registry (<https://clinicaltrials.gov/ct2/show/NCT02496312>; <https://clinicaltrials.gov/ct2/show/NCT03272230>). There were no deviations from the preregistered protocol.

All study participants gave their written informed consent to participate, in line with French ethical guidelines. These studies were performed in accordance with the Declaration of Helsinki. Anonymity was preserved for all participants.

2.2. Participants

A total of twenty-three bvFTD patients were recruited at the Pitié-Salpêtrière Hospital, in Paris. Diagnosis of bvFTD was established according to the International Consensus Diagnostic Criteria (Rascovsky et al., 2011). All patients met the criteria for bvFTD diagnosis. Further inclusion criteria included a Mini Mental State Examination (MMSE; Folstein et al.,

1975) score between 20–30 and being aged below 85. Twenty-four healthy controls (HC) were recruited by public announcement (via a dedicated platform for participant recruitment) and they all had a MMSE score above 27. HC subjects were matched to patients for age, gender, and education level. Exclusion criteria for all participants included current or prior history of neurological disease other than bvFTD, psychiatric disease, and drug abuse. The participants underwent the ECOCAPTURE study including an ecological behavioural protocol and an extensive neuropsychological assessment. The demographic characteristics and neuropsychological scores of the bvFTD patients and HC are detailed in Table 1.

2.3. Neuropsychological evaluation

All participants carried out extensive cognitive and clinical assessments including a general cognitive assessment with MMSE (Folstein et al., 1975) and the Frontal Assessment Battery (FAB) (Dubois et al., 2000). The Dimensional Apathy Scale-DAS (Radakovic & Abrahams, 2014), used to measure apathy, consisting of three subscales (initiation, cognition and emotional) based on the theoretical model of three forms of apathy (Levy & Dubois, 2006). The DAS has been validated for use in dementia and cut-offs previously published for each subscale are 14 for the presence of executive apathy, 15 for emotional apathy, and 16 for initiation apathy (Radakovic et al., 2016). Depression and anxiety were explored with the Hospital Anxiety and Depression (HAD) Scale (Zigmond & Snaith, 1983). The HAD scale is a screening tool with specific

cut-offs for each subscale. A score of 11 or above is considered a clinically significant disorder, whereas a score between 8 and 10 suggests a mild disorder (Zigmond & Snaith, 1983). Finally, the mini-Social cognition & Emotional Assessment (mini-SEA) orbitofrontal battery was used to assess social cognition including affective and emotional functions (Funkiewiez et al., 2012).

Legal copyright restrictions prevent public archiving of used neuropsychological tests, which can be obtained from the copyright holders in the cited references.

2.4. Behavioural assessment of disinhibition

2.4.1. The ecological protocol

The ECOCAPTURE protocol is an ecological framework with controlled conditions, designed to study behavioural disorders and obtain objective measures of behavioural symptoms, such as apathy or disinhibition (Batrancourt et al., 2019; Godefroy et al., 2021; Tanguy et al., 2022). The protocol mimics a naturalistic situation (i.e., waiting comfortably in a waiting room), and consists of a 45-minute controlled scenario. A general outline of the protocol is schematically presented in Fig. 1B.

Experiments took place within an experimental platform (<https://institutduserveau-icm.org/fr/prisme-human-behavior-exploration-core-facility/>) transformed into a fully furnished waiting room (Fig. 1A). The room is equipped with a six-camera system covering the entire waiting room, which allows the direct observation of the subject and video recording for subsequent analysis.

Table 1 – Demographic, neuropsychological and behavioural characterisation of subjects.

	bvFTD (n = 23)			HC (n = 24)			p-value
	Mean (SD)	Range	>co	NA	Mean (SD)	Range	
Female/Male	8/15			12/12			n.s. ^a
Age (years)	65.7 (8.7)	[45, 80]			63.0 (7.1)	[46, 72]	n.s. ^b
Disease duration (years)	4.1 (2.1)	[1, 10]			n.a		
Education (years)	14.3 (4.8)	[8, 22]			13.8 (2.6)	[8, 18]	n.s. ^c
MMSE (/30)	23.5 (2.7)	[20, 29]			29.5 (.7)	[28, 30]	*** ^d
FAB (/18)	12.6 (3.4)	[5, 18]		1	17.4 (.8)	[15, 18]	*** ^e
HAD (/42)	13.6 (7.0)	[1, 29]			5.9 (3.3)	[0, 16]	*** ^e
Anxiety (/21) (co: 8; 11)	7.6 (4.4)	[1, 17]	7; 5		4.5 (2.3)	[0, 10]	2; 0 *** ^e
Depression (/21) (co: 8; 11)	6.0 (3.3)	[0, 12]	4; 3		1.3 (1.6)	[0, 7]	0 *** ^e
DAS (/72)	30.3 (11.2)	[11, 50]			19.8 (7.7)	[4, 38]	*** ^e
Executive (/24) (co: 14)	10.5 (4.9)	[1, 21]	5		3.9 (3.5)	[0, 15]	1 *** ^c
Emotional (/24) (co: 15)	10.4 (4.0)	[3, 18]	4		9.0 (3.4)	[1, 15]	1 n.s. ^b
Initiation (/24) (co: 16)	9.5 (6.0)	[0, 22]	3		7.0 (3.5)	[1, 14]	0 .d
Mini-SEA (/30)	17.9 (4.4)	[9.2, 24.4]		3	26.5(1.4)	[23.2, 29.6]	*** ^e
Mini-SEA emotion (/15)	8.9 (2.4)	[4.7, 14.1]			13.0 (.9)	[11.1, 14.6]	*** ^e
Mini-SEA faux-pas (/15)	8.6 (3.2)	[2.2, 15]		3	13.6 (1.0)	[11.2, 15]	*** ^e

Data are given as Mean (SD) and Range. If published cut-offs are available, they are notified (co), and the number of participants who fell above the suggested cut-offs are reported. Unavailable data are reported as NA.

ns: non-significant; *p < .1 **p < .05; ***p < .001.

bvFTD: behavioural variant of Frontotemporal Dementia; HC: Healthy Controls; DAS: Dimensional Apathy Scale; FAB: Frontal Assessment Battery; HAD: Hospital Anxiety and Depression scale; Mini-SEA: Mini-Social cognition & Emotional Assessment; MMSE: Mini-Mental State Examination.

^a Chi-square test.

^b Student t-test.

^c Mann–Whitney U test.

^d Poisson generalised linear model.

^e Quasi-Poisson generalised linear model.

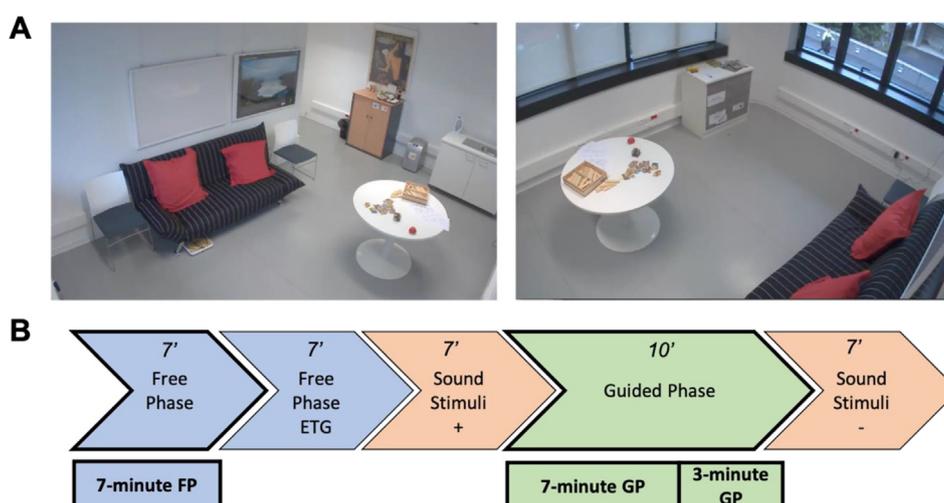


Fig. 1 – Ecological setting. (A) The waiting room; (B) The complete 45-minute ECOCAPTURE protocol: 7-minute free phase; 7-minute free phase with eye-tracking glasses; 7-minute sound stimulus phase (positive stimulus such as favourite music); 10-minute guided phase (devoted to completing the questionnaire) divided in 2 subparts, and 7-minute sound stimulus phase (negative stimulus such as crackling noise). See [Supplementary File 1](#) for details of the additional phases included in the protocol which are not discussed in this paper.

Participants were asked to stay in the waiting room before the next tests and received the instructions to make themselves comfortable and enjoy the room. The room contained specific objects that provided opportunities for subjects to interact with their environment and pass the time (games, magazines, food and drink, furniture such as a sofa, chairs, tables, etc.). The protocol was divided in different phases (Fig. 1B), and in particular we explored the 7-minute freely moving phase (7-minute FP) during which the participant was explicitly encouraged to explore the room; the 10-minute externally-guided phase (10-minute GP) involving filling out a questionnaire (this involved questions about items present in/absent from the room, asking the subjects to weigh themselves etc.) and using the necessary resources available in the room (pens of different colours, a weighing scale) to achieve this. The 10-minute GP was divided into two sub-parts: the first one lasting 7 minutes (7-minute GP), dedicated to filling in the questionnaire, and the second one lasting 3 minutes (3-minute GP), during which subjects could eventually return to their previous occupations once the questionnaire has been completed (or abandoned). Between each phase, the investigator entered the room to interact with the participant and provide them with instructions for the next phase (Fig. 1B, see also [Supplementary File 1](#) for the full description of the ECOCAPTURE protocol and of the examiner's interventions in particular). All participants had been told, when included in the study, that the room was equipped with cameras and that they would be filmed. This feature, however, was not emphasised at the start of the experiment so as not to remind participants.

2.4.2. The ethograms and the video-based behavioural metrics

Ethograms are directories or catalogs of behaviours observable under specific conditions, usually grouped into categories according to the kind of behaviour. These behaviours, known

as action patterns, are “discrete, repeatable, identifiable acts that are described in detail” (Lescak, 2018). Moreover, behaviour may be regarded either as instantaneous events or as state events. Instantaneous events are instantaneous, such behaviours can be scored as present, and reported as occurrences. State events have appreciable duration, with a start and stop time, and take a period of time in such a way that allows to calculate behaviour duration (as defined by Lehner: “the behaviour an individual, or group, is engaged in; an ongoing behaviour”) (Lehner, 1996). According to these definitions, certain behaviours were therefore labelled “instantaneous behaviour” and others “state behaviour”, this choice depending on the questions that we are attempting to answer (Altmann, 1974). Moreover, for each specific behaviour from the ethogram, a set of metrics were derived from the collected behavioural data: 1/ the total duration of a behaviour by summing the durations of all occurrences of this behaviour, 2/ the behaviour ratio as the total duration of a behaviour to the total time of the sample session, reported as a percentage, 3/ the time budget as the lists of the percentage of time that an individual spent performing each behaviour, 4/ the number of occurrences of a behaviour during the sample session.

2.4.3. The disinhibition ethogram (instantaneous behaviours)

We selected a list of behaviours of interest related to disinhibition potentially observable in the context of the protocol, according to the definitions of symptoms by Rascovsky et al. (2011), to previous relevant studies in the field (Paholpak et al., 2016; Snowden et al., 2002) and our previous studies (Godefroy et al., 2021; Tanguy et al., 2022). We thus retained 16 behaviours organised into three categories: compulsivity (e.g., repetitive movements or perseveration), impulsivity (e.g., emotional outburst or impulsive motor action) and social disinhibition (e.g., unwarranted or excessive familiar behaviour towards the investigator or lack of manners). The first and co-last authors (DT, BB) supervised the whole process and

edited a handbook with precise guidelines for the coding procedure. All the behaviours were discussed with the other co-authors, and consensus on coding decisions was reached during regular team meetings (with behavioural neurologists present in the team, RM, RL, ILB; and also with AB, VG). In particular, the context of occurrence of a given behaviour was very important to attribute the behaviours to one or another category. For example, if the subject leaves the room, the behaviour is coded as “Disregard for rules or investigator”, reflecting social disinhibition. However, if the subject leaves the room a second time for the same reason, this second exit is coded as “Perseveration”, reflecting compulsivity. The full detailed ethogram called “Disinhibition ethogram” is shown with examples in Table 2. All these selected behaviours were considered as instantaneous behaviours.

Behavioural data was obtained by behavioural coding from 45-minute footage, using a manual video annotation tool (The Observer XT®, Noldus) (DT). Behavioural coding data were collected through the continuous sampling method (all occurrences of behaviours were recorded) and conducted based on the Disinhibition ethogram (Table 2). In our analysis, we were interested in measuring how many times each specific behaviour from the ethogram occurs throughout the 45-minute ECOCAPTURE protocol, in patients versus healthy controls. This analysis yielded a set of 16 metrics (one per behaviour) measuring the number of occurrences of each behaviour, in each participant. These 16 sub-scores were then summed together within each behavioural category (compulsivity, impulsivity, social disinhibition) to obtain three global scores labelled: “compulsivity”, “impulsivity” and “social disinhibition”, in each individual.

Among the 47 subjects, eight videos were coded by two independent coders (DT, VG) to assess the intercoder reliability through the calculation of the intraclass correlation coefficient. The calculated intraclass correlation coefficients were all between .80 and 1, indicating very high reliability. The coders were not blind to the diagnosis nor the hypotheses of this study.

2.4.4. Phase-based metrics

We were interested in the effect of a task guidance on disinhibited behaviours. To do so, we focused on three phases: the 7-minute FP, the 7-minute GP and the 3-minute GP. For each subject, we defined three global scores (for compulsivity, impulsivity and social disinhibition), by generating a set of behavioural disinhibition metrics measuring the total occurrence of disinhibited behaviours per phase. For example, the total occurrence of disinhibited behaviours from the category impulsivity during the 7-minute FP was labelled “FP7_impulsivity”.

2.4.5. Behavioural state ethogram (state behaviours)

Behaviour was measured in an environment (the waiting room) with which patients are encouraged to interact. We wanted to specifically examine factors such as the subjects' activity or posture that may influence behavioural disinhibition.

In order to code individuals' behaviours expressed during the protocol, we relied on a second ethogram: the “Behavioural state ethogram” (Table 3). This ethogram included state

behaviours organised in two discrete behavioural categories: motor pattern and activity scale (see the complete ECOCAPTURE ethograms at Mendeley Data) (Batrancourt et al., 2022). The motor pattern described the posture, as well as the movement and locomotion manifested by the observed individuals (e.g., sitting). The activity scale included four states: 1/ non-activity (the subject showed no apparent activity); 2/ exploration (the subject explored the waiting room and various objects in the room); 3/ activity (the subject was engaged in an activity with a sustained attention); and 4/ transition (the subject moved from one state to another, lasting only a few seconds). For each state within the activity scale, the examiner also selected a modifier to describe the exploration or activity. These modifiers corresponded to items present in the environment with which the subject could interact (e.g., books, magazines, sofa, food and drinks, games). As with the behavioural disinhibition metrics, motor pattern and activity scale were obtained by encoding the video recordings using The Observer XT®. The detailed Behavioural state ethogram is shown in detail in Table 3. As the transition state metric was not further considered, this process generated a set of 18 behavioural state metrics measuring the ratio of time spent in each state behaviour during each phase per subject. The whole set of considered metrics is shown in Table 3.

2.5. Statistical analysis

All statistical analyses on demographics, neuropsychological and behavioural data were performed using RStudio 1.2.5033, p -values under .05 being considered as statistically significant. For demographics data, Chi-squared tests were used for gender comparisons, Shapiro–Wilk tests were used to test data normality and Fisher's test for variances equality. For normally distributed data with equal variances, Student t -tests were used. For not normally distributed data, Mann–Whitney U tests were used. For the comparisons of neurocognitive and behavioural data between the two groups, Generalised Linear Models (GLM) were computed using the Poisson family or the quasi-Poisson families when data were overdispersed. Assumptions of the models were verified using the packages RVAideMemoire (Hervé, 2020) and AER (Kleiber & Zeileis, 2008). Correlations were performed for the bvFTD patients' population. We used the Spearman coefficient (r) to build the correlation matrix and to investigate the possible relationships. The Holm–Bonferroni method was used to adjust the p -value for multiple comparisons. In order not to delete either individuals or variables from the analysis because of a few missing data, we estimated the missing values as the median of each of the variables (“imputation by the median”).

2.5.1. Generalised linear mixed models

To evaluate the effects of task guidance on the occurrence of behavioural disinhibition, we performed generalised linear mixed models (GLMM). To compare the occurrence of disinhibited behaviours in the phases of interest which did not have the same duration, we transformed the occurrences data into a ratio (number of behaviours occurred per minute). We built the models using the ratio as dependant variable, the group (bvFTD or HC), the phase (7-minute FP, 7-minute GP, 3-minute GP) and the interaction between them as fixed factors,

Table 2 – The Disinhibition ethogram listing the 16 behaviours of interest related to disinhibition and their definition.

Behaviour label	Definition	Example
Compulsivity		
Utilisation behaviour (Snowden et al., 2002)	Grasping and touching objects of the environment without any contextual reason	Opening and closing the window without any real purpose
Perseveration (Snowden et al., 2002)	Difficulty in shifting mental set and behavioural perseveration	Keep trying to open the tap unsuccessfully (no running water in the room)
Repetitive movements (Rascovsky et al., 2011)	Repeating stereotyped, compulsive/ritualistic behaviours	Rubbing hands
Compulsive eating (Rascovsky et al., 2011)	Eating excessive amounts of food in the absence of real hunger and/or inappropriate foods in the specific context	Eating canned sardines just after breakfast
Impulsivity		
Emotional outburst (Paholpak et al., 2016)	Persistent laughing, crying or swearing alone in the room	Laughing at the sight of the locked box
Inappropriate action (Paholpak et al., 2016)	Doing something very unconventional and thoughtless with an object of the room	Discarding the content of a beverage in the sink
Singing (Paholpak et al., 2016)	Singing alone in the room	Singing “O Christmas Tree” without any reason
Dancing (Paholpak et al., 2016)	Dancing alone in the room	Doing a few dance steps
Self-talking (Paholpak et al., 2016)	Speaking aloud when alone in the room (in the apparent absence of any hallucination)	Commenting on the environment when entering the room
Social disinhibition		
Aggressive behaviour towards investigator (Rascovsky et al., 2011)	Showing hostility, verbal or physical aggressiveness towards the investigator	Angrily yelling “Come in” when the investigator knocks repeatedly at the door
Familiar behaviour towards investigator (Rascovsky et al., 2011)	Showing inappropriate familiarity towards the investigator	Speaking in inappropriately colloquial language
Nudity (Rascovsky et al., 2011)	Exposing inappropriate parts of one's body	Removing one's pants
Harsh handling of objects (Rascovsky et al., 2011)	Handling an object of the room in a way which may cause potential damage, thus showing lack of respect for the investigator's material	Trying to break a locker box instead of searching for the key
Inappropriate gesture or posture (Rascovsky et al., 2011)	Impolite, inappropriate physical behaviour in a social context	Picking one's nose/teeth
Lack of decorum (Rascovsky et al., 2011)	Failing to respect cultural norms of politeness	Yawning, sneezing or coughing without putting hand on the mouth
Disregards for rules or investigator (Rascovsky et al., 2011)	Lack of response to social cues, ignoring instructions given by the investigator	Not answering investigator's questions

and the subjects as random factor. A log-link tweedie distribution was used to analyse the dependent variables as the ratios were continuous, positive and zero-inflated data (Parveen et al., 2016). Models were built using the package *glmmTMB* (Brooks et al., 2017) and assumptions of the models (zero-inflation, under/overdispersion and autocorrelation in residuals) were tested in the *DHARMA* package (Hartig, 2021). Post hoc analyses were performed using the *emmeans* package (Lenth, 2021) and pairwise *t* tests with the Bonferroni correction.

2.5.2. Correlations between disinhibition and activity scale

To explore the relation between variations in disinhibition across phases and variations in activity scale, we built additional variables Δ . For the variable x , Δ_x^1 corresponds to the difference between the scores in the 7-minute GP and the 7-minute FP, while Δ_x^2 corresponds to the difference between the scores in the 7-minute GP and the 3-minute GP. For example, $\Delta_{\text{compulsivity}}^1 = \text{GP7_compulsivity} - \text{FP7_compulsivity}$, $\Delta_{\text{ACT}}^1 = \text{GP7_ACT} - \text{FP7_ACT}$, $\Delta_{\text{ACT}}^2 = \text{GP7_ACT} - \text{GP3_ACT}$. We used Spearman's correlation to investigate the possible relationships between $\Delta_{\text{activity scale}}$ and $\Delta_{\text{disinhibition}}$, in order to determine whether changes in disinhibition scores could be attributed to changes in the subjects' activity, and thus attributable to the task of completing a questionnaire.

2.6. Data availability statement

The pre-processed data that support the findings of this study are available. Anonymized data are available here <http://doi.org/10.17632/6n7p3y3j58.2> (Mendeley repository). ECO-CAPTURE ethograms are available at <https://data.mendeley.com/datasets/mv8hndcd95/2>. However, the conditions of our ethics approval do not permit sharing of the raw video data generated in this study with any individual outside the author team under any circumstances.

The study procedure was pre-registered in Clinical trials registry. We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion criteria were established prior to data analysis, all manipulations, and all measures in the study.

3. Results

3.1. Demographics and neuropsychological characteristics

Demographics and neuropsychological characteristics of all participants are shown in Table 1. BvFTD patients did not differ in terms of age, gender, and education in comparison to HC. The neuropsychological performances, severity of behavioural changes and emotional disorders of bvFTD patients and HCs are presented in Table 1. The bvFTD patients presented a significant decrease in global cognitive efficiency, as revealed by the MMSE ($p < .001$), and a frontal syndrome, as revealed by the FAB ($p < .001$). A significant difference was observed for the DAS (global score as well as the executive dimension) between the two groups ($p < .001$), showing that bvFTD patients were more apathetic than HCs. The results of

the DAS emotional and initiation subscales revealed that the scores were not different between patients and controls, however, the number of individuals who fell above the cut-off was higher in the patient group. The patients were also characterised by significant severity of depressive symptoms and anxiety as measured by the HAD.Depression ($p < .001$) and the HAD.Anxiety ($p < .01$). Regarding the HAD.Depression subscale, among the twenty-three bvFTD patients, four were greater than or equal to eight, including three patients greater than 10, while no HC fell above the cut-off. Regarding the HAD.Anxiety subscale, 11 patients were greater than or equal to eight, including five patients greater than 10, while only two HC was greater than eight.

3.2. Behavioural disinhibition in bvFTD patients and HC

We first investigated the total occurrence of disinhibited behaviours expressed throughout the 45-minute protocol, per category. With regard to behavioural disinhibition, bvFTD patients expressed more compulsivity [$F(1,45) = 21.82, p < .001$], impulsivity [$F(1,45) = 4.27, p = .045$] and social disinhibition [$F(1,45) = 14.25, p < .001$] than HC (Table 4 and Supplementary Fig. 1).

3.2.1. Occurrence of behavioural disinhibition in bvFTD patients and HC

In order to better describe the occurrence of behavioural disinhibition and the possible overlap of its various subtypes, we investigated the presence of at least one disinhibited behaviour for each disinhibition subtype in each subject (Table 5). We found that 48% of patients presented compulsivity, 48% impulsivity and 100% of the patients group showed social disinhibition. In comparison, only 4% of HC presented compulsivity, 58% impulsivity and 66% social disinhibition. Among the patients, 26% exhibited both social disinhibition and compulsivity, 26% exhibited both social disinhibition and impulsivity, and 22% showed all three subtypes of disinhibition. Among HC, 17% did not show any disinhibited behaviour.

3.2.2. Disinhibition symptoms intensity

Fig. 2 reports the intensity of the behaviour, i.e., the number of occurrences of each instantaneous behaviour from the disinhibition ethogram (16 behaviours) throughout the 45-minute protocol, in each subject, and the differences between bvFTD patients and HC. Clear differences in intensity can be appreciated. The highest frequencies were reported in compulsivity (up to 51 “repetitive actions” in one of the patients) and impulsivity (up to 41 “talking to oneself” in one of the patients) (see also Supplementary Fig. 2 and Supplementary Fig. 3). The social disinhibition symptom includes three behaviours (“Inappropriate gesture or posture”, “Lack of decorum”, “Disregard for rules or investigator”) often observed among the bvFTD patients, but with a relative lower intensity compared with compulsivity and impulsivity (Fig. 2 and Supplementary Fig. 4).

3.2.3. Relationships between disinhibition, neuropsychological data and state behaviours

We found that compulsivity negatively correlated with the mini-SEA recognition subtest ($r = -.70, p_{\text{adjust}} < .001$), and

Table 3 – The Behavioural state ethogram listing the behaviours included in the motor pattern and activity scale behavioural categories, and their definition. The behavioural state metrics collected during the 7-minute FP, the 7-minute GP and the 3-minute GP sample sessions.

Behaviour label	Definition	Phases		
Motor pattern				
Sitting	Subject sits on the sofa or on a chair. Subject is seated on the sofa or on a chair.	FP7_SIT	GP7_SIT	GP3_SIT
Standing	Subject stands up. Subject is standing.	FP7_STD	GP7_STD	GP3_STD
Walking	Subject walks and moves around the room. Subject moves at least two steps.	FP7_WLK	GP7_WLK	GP3_WLK
Activity scale				
Non-Activity	Subject shows no apparent activity.	FP7_NACT	GP7_NACT	GP3_NACT
Exploration	Subject explores the waiting room and objects in the room.	FP7_EXP	GP7_EXP	GP3_EXP
Activity	Subject is engaged in an activity, with a sustained attention over a period of 10 sec, for the specific reading and playing activities, or regarding the completion of the questionnaire	FP7_ACT	GP7_ACT	GP3_ACT
Transition	A short-term state (a few seconds) from one state to another. Resuming a task quickly following an interruption.			
Abbreviations: FP7 = free phase, GP7 = first 7 minutes of guided phase, GP3 = final 3 minutes of guided phase. SIT = sitting; STD = standing; WLK = walking; NACT = non activity; EXP = exploring; ACT = activity.				

that mini-SEA recognition subtest positively correlated with the FAB ($r = .61$, $p.adjust < .05$). Fig. 3J shows the correlation matrix.

During the 7-minute FP, the bvFTD patients spent more time inactive (22%) than the controls (5%). Both groups spent a large proportion of time on activities (up to 53% in bvFTD and 68% in HC) (Fig. 3A). In the bvFTD patients, the time spent on activities was divided between playing games (41%), reading (26%), and food and drink related activities (33%). The HCs spent a large proportion of their time reading (63%) (Fig. 3B). The comparison of bvFTD with HC on the 7-minute FP metrics showed significant differences for FP7_NACT and FP7_Read ($p < .05$, $p < .01$, respectively), and a trend difference for FP7_ACT ($p < .1$) (Fig. 3C). During the 7-minute GP, the two groups spent more time in activity (up to 80% in bvFTD and 81% in HC) (Fig. 3E). During the 3-minute GP, the bvFTD patients spent less time in activity (54%) than the controls (70%) (Fig. 3F) which showed a trend towards significance ($p < .1$) (Fig. 3H).

Concerning the correlation between the disinhibition and the state behaviours during the 7-minute FP in bvFTD patients, FP7_social_disinhibition negatively correlated with FP7_ACT ($r = -.60$, $p.adjust < .05$). Fig. 3D shows the correlation matrix.

3.3. Context of occurrence of disinhibited behaviours

3.3.1. Factors affecting the production of disinhibited behaviours

We found different effects of group and phase on the occurrence of the three disinhibition subtypes during the protocol. Firstly, we found a significant effect of group on compulsivity (GLMM Tweedie, Type II Wald Chi-square test: $X^2 = 5.037$, $p = .025$) with bvFTD patients being more compulsive than HC. Interestingly, we found no effect of phase on the manifestation of this disinhibition subtype. Secondly, there was no effect of group on the occurrence of impulsivity, but there was a significant effect of phase ($X^2 = 9.297$, $p = .009$) with less

impulsivity in the 7-minute GP than in the 7-minute FP ($p = .047$). Finally, concerning social disinhibition, there was a significant effect of group ($X^2 = 5.685$, $p = .017$), bvFTD patients being more socially disinhibited than HC. There was also an interaction between group and phase ($X^2 = 6.340$, $p = .042$) with a trend for bvFTD patients to be less socially disinhibited in the 7-minute GP than in the 7-minute FP ($p = .092$). When looking at each phase separately, bvFTD patients showed more social disinhibition than HC in the 7-minute FP ($p = .005$) and in the 3-minute GP ($p = .014$), but not during the 7-minute GP ($p = .598$) (Fig. 3G).

3.3.2. Influence of activity on behaviour

We found a negative correlation between $\Delta_{activity}^1$ and $\Delta_{social\ disinhibition}^1$ ($r = -.67$, $p.adjust < .01$), and a positive correlation between $\Delta_{non\ activity}^1$ and $\Delta_{social\ disinhibition}^1$ ($r = .58$, $p.adjust < .05$). Thus, interestingly, in bvFTD patients, the more activity increased (or non-activity decreased) between the 7-minute FP and the 7-minute GP, the more social disinhibition decreased (Fig. 3I). We did not find any correlations between compulsivity, impulsivity with motor pattern and activity scale.

4. Discussion

In the present work, we explored inhibition disorders in an original semi-ecological situation, by distinguishing three categories of disinhibition: compulsivity, impulsivity and social disinhibition, in order to better characterise behavioural disinhibition in bvFTD. We first described the phenotypical heterogeneity of disinhibition in bvFTD patients and HC, emphasising the greater presence of social disinhibition. We then examined the relationships between the observed behaviours and the neuropsychological scores, highlighting the association of compulsivity with emotion recognition. We finally identified aspects of the context that might play a role in the occurrence of social disinhibition, such as being active and engaged in a task.

4.1. Behavioural disinhibition in the population

We found that our ecological/ethological approach was able to discriminate bvFTD patients from HC. BvFTD patients were, as expected, more compulsive, impulsive and socially disinhibited than HC. In particular, social disinhibition seems to be more detected by our ecological approach than in previous non-ecological studies relying on questionnaires (65%–98% according to [Bang et al., 2015](#); and [Desmarais et al., 2018](#)). On the other hand, *compulsivity* emerges less in our cohort than what was previously described (71%–80% of patients according to [Miller & Llibre Guerra, 2019](#); [Seeley, 2019](#)). Concerning impulsivity, we identified this pathological behaviour in 48% of our sample and this is the first time that behavioural impulsivity has been reported in bvFTD. It is important to note that differences in assessments could account for variability across studies.

In a more descriptive way, it is interesting to note that each bvFTD patient presented at least one socially disinhibited behaviour, often associated with compulsivity and/or impulsivity. Our behavioural data suggested four groups of bvFTD patients: 1) patients presenting only social disinhibition, 2) patients with social disinhibition and compulsivity, 3) patients with social disinhibition and impulsivity, and 4) patients presenting the three subtypes of disinhibition. The cumulative presence of all the symptoms could be considered as an

index of disinhibition syndrome severity, with four behavioural profiles of graded severity. In the same vein, in a previous study, we found that patients with a broad pattern of atrophy in bilateral frontal and orbitofrontal regions showed, in addition to social disinhibition, a higher frequency of compulsive and impulsive behaviours than the other groups ([Godefroy et al., 2021](#)). Thus, these behaviours could be considered as the clinical manifestations of a more severe disease, possibly associated with more extensive cortical atrophy. Interestingly, previous work suggests such anatomical and behavioural disinhibition subtypes of bvFTD patients ([Ranasinghe et al., 2016](#)). A longitudinal study of these same patients showed that each behavioural and anatomical subtype evolved differently over time ([Ranasinghe et al., 2021](#)). Another study found that, within the three main genetic forms of FTD, an increase in the prevalence of disinhibition over the course of the disease could be noted ([Benussi et al., 2021](#)). Though disinhibition can be more or less present depending of patients' genetic mutation, it is likely that several behavioural profiles exist at the beginning of the disease, and that with the progression of the disease, the evolution of these symptoms leads to a greater risk of developing all forms of behavioural disinhibition.

Among HC, a majority of subjects also exhibited some disinhibited behaviours, mainly impulsivity or social disinhibition. However, while the presence or absence of these two categories of disinhibition in the healthy population is close to what can be observed in patients, there is a significant difference in the frequency of these behaviours, with the HC group showing far fewer. It is this high frequency of such behaviours in bvFTD patients which argues for its pathological nature. However, the presence of disinhibited behaviours with low frequency in HC suggests the existence of a continuum of disinhibition ranging from normal to pathological states.

Table 4 – Behavioural characterisation of subjects.

	bvFTD (n = 23)	HC (n = 24)	p-value
Female/Male	8/15	12/12	n.s. ^a
	Mean (SD)	Mean (SD)	
Compulsivity	11.9 (18.6)	.2 (.8)	*** ^b
Utilisation behaviour	.3 (1.1)	0 (0)	n.s. ^b
Perseveration	.6 (2.3)	0 (0)	. ^b
Repetitive movements	9.9 (16.6)	.2 (.8)	** ^b
Compulsive eating	1 (3.3)	0 (0)	*
Impulsivity	9.9 (18.6)	3.1 (4.8)	* ^b
Emotional outburst	1.5 (3.9)	.5 (.7)	n.s. ^b
Inappropriate action	.8 (2)	.2 (1.2)	. ^b
Singing	.4 (1.9)	0 (0)	n.s. ^b
Dancing	.4 (1.6)	0 (0)	n.s. ^b
Self-talking	6.7 (12.5)	2.3 (3.8)	n.s. ^b
Social disinhibition	9.9 (7.8)	3.1 (4.4)	*** ^b
Aggressive behaviour towards investigator	.2 (.6)	.1 (.6)	n.s. ^b
Familiar behaviour towards investigator	.2 (.6)	.3 (.7)	n.s. ^b
Nudity	0 (0)	.01 (.2)	n.s. ^b
Harsh handling of objects	.3 (.7)	.1 (.4)	n.s. ^b
Inappropriate gesture or posture	4.2 (4.5)	1.6 (3.9)	** ^b
Lack of decorum	1.9 (3)	.9 (1.5)	n.s. ^b
Disregards for rules or investigator	3.1 (4.6)	.1 (.3)	*** ^b

Data are given as Mean (SD).

ns: non-significant; $p < .1$ * $p < .05$; ** $p < .01$; *** $p < .001$.

bvFTD: behavioural variant of Frontotemporal Dementia; HC: Healthy Controls.

^a Chi-square test.

^b Quasi-Poisson generalised linear model.

4.2. Correlation with cognitive, clinical and behavioural data

To provide a complete description of these behavioural disinhibition symptoms, we examined correlations with neuropsychological scores and other behavioural data.

According to [Fig. 3J](#), we found that compulsivity correlated negatively with performance on tests of emotion recognition. These findings concerning the neuropsychological correlates of disinhibition are in line with previous works, compulsive behaviours being commonly correlated with executive dysfunctions in obsessive compulsive disorders (OCD) ([Abramovitch et al., 2011](#); [Cetinay Aydin & Gulec Oyekcin, 2013](#)) and normal development ([Pietrefesa & Evans, 2007](#)).

We also found that the more activity increased (or non-activity decreased) between the phases the more social disinhibition decreased ([Fig. 3I](#)). Therapeutic intervention with meaningful activities such as puzzles, games and reading have already described as effective management to decrease agitation related to boredom and inactivity ([Keszycki et al., 2019](#)). However, benefits can be inconsistent, depending on the subjects' interests, highlighting the importance of tailoring activities to patients ([Kolanowski et al., 2011](#)). Moreover, the ability to maintain attention towards a task, such as reading, which was a common activity in controls in our study,

Table 5 – Percentage of subjects showing at least one disinhibited behaviour in each behavioural category.

	BvFTD (<i>n</i> = 23)			HC (<i>n</i> = 24)		
	Female	Male	Total	Female	Male	Total
Compulsivity	75%	33%	48%	8%	0%	4%
Impulsivity	50%	47%	48%	75%	42%	58%
Social disinhibition	100%	100%	100%	67%	67%	66%
None	0%	0%	0%	8%	25%	17%
Compulsivity only	0%	0%	0%	0%	0%	0%
Impulsivity only	0%	0%	0%	25%	8%	17%
Social disinhibition only	0%	40%	26%	8%	33%	21%
Comp & Social only	50%	13%	26%	8%	0%	4%
Imp & Social only	25%	27%	26%	50%	33%	42%
Comp & Imp & Social	25%	20%	22%	0%	0%	0%

bvFTD = behavioural variant frontotemporal dementia; HC = healthy controls; Comp = Compulsivity; Imp = Impulsivity; Social = Social Disinhibition.

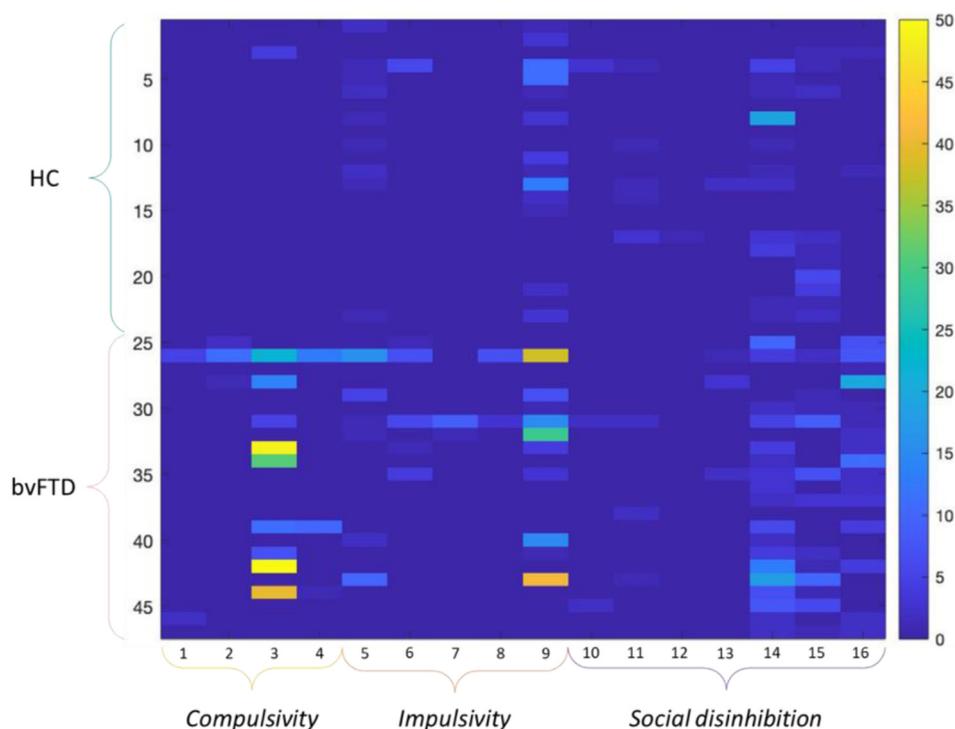


Fig. 2 – Occurrence and intensity of the three subtypes of behavioural disinhibition in behavioural variant frontotemporal dementia patients (*n* = 23) and healthy controls (*n* = 24). Each row represents one subject, each column corresponds to a disinhibition behaviour as defined in the Disinhibition ethogram. Intensity of recorded behaviour frequency is represented by the colorbar on the right. From left to right, the *Compulsivity* columns correspond to: 1. Utilisation behaviour, 2. Perseveration, 3. Repetitive movements, 4. Compulsive eating; the *Impulsivity* columns correspond to: 5. Emotional outburst, 6. Inappropriate action, 7. Singing, 8. Dancing, 9. Self-talking; and the *Social Disinhibition* columns correspond to: 10. Aggressive behaviour towards investigator, 11. Familiar behaviour towards investigator, 12. Nudity, 13. Harsh handling of objects, 14. Inappropriate gesture or posture, 15. Lack of decorum, 16. Disregards for rules or investigator. bvFTD = behavioural variant frontotemporal dementia; HC = healthy controls.

suggests relative cognitive preservation, which could also explain a lower level of social disinhibition in these patients.

4.3. Occurrences of disinhibited behaviours

The guided phase of the protocol resulted in a decrease of impulsivity and also affected the level of social disinhibition:

bvFTD patients presented higher frequency of social disinhibition in the free phase and at the end of the guided phase, but not during the guided phase. The guided phase reduced impulsivity and social disinhibition in bvFTD patients, standardising behaviours in patients and HC. At the end of the guided phase, patients had often completed the questionnaire or abandoned doing so, therefore went back to normal

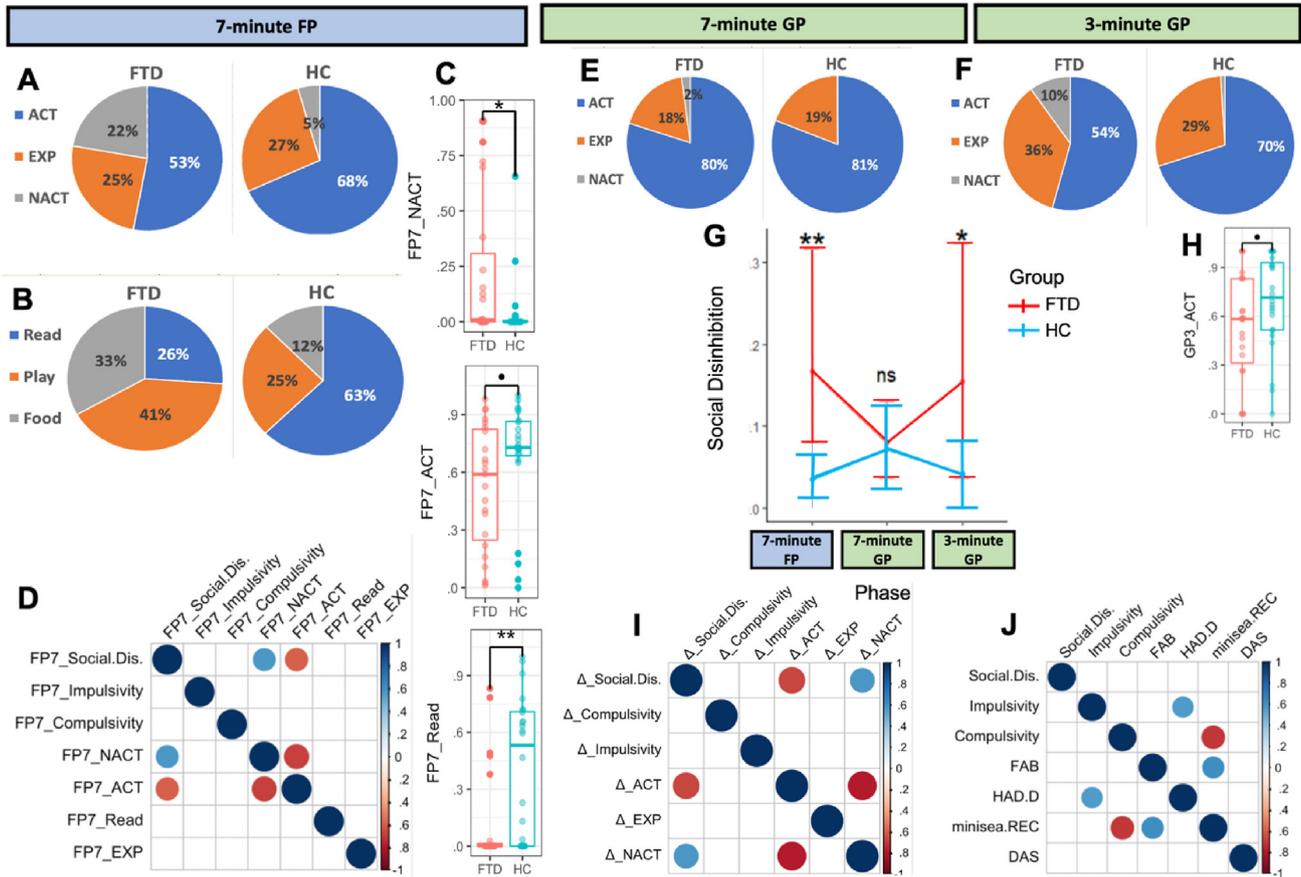


Fig. 3 – Relationships between disinhibition, neuropsychological data and state behaviours. The behaviour of 23 bvFTD patients and 24 HCs was observed, and the behavioural data were collected based on the Disinhibition ethogram and the Behavioural state ethogram, throughout the 45-minute EOCAPTURE protocol, and three sample sessions: 7-minute FP, 7-minute GP, 3-minute GP. (A) Time budget in bvFTD patients and HCs for the 7-minute FP. (B) Time budget regarding specific activities in bvFTD patients and HCs for the 7-minute FP. (C) Distribution of FP7_NACT, FP7_ACT, FP7_Read, in the two groups (bvFTD patients, HCs). (D) Correlation matrix in bvFTD patients between the disinhibition metrics and the behavioural states metrics, for the 7-minute FP. (E) Time budget in bvFTD patients and HCs for the 7-minute GP. (F) Time budget in bvFTD patients and HCs for the 3-minute GP. (G) Scores of social disinhibition across phases in bvFTD patients and HC. (H) Distribution of GP3_ACT in the two groups (bvFTD patients, HCs). (I) Correlation matrix in bvFTD patients between the disinhibition metrics and the behavioural states metrics, for the variation between the 7-minute GP and the 7-minute FP. (J) Correlation matrix in bvFTD patients between the disinhibition metrics (global scores collected throughout the 45-minute EOCAPTURE protocol) and the neuropsychological scores. Abbreviations: FTD = behavioural variant frontotemporal dementia; HC = healthy controls; FP = Free Phase; GP = Guided Phase; FP7 = free phase; GP3 = final 3 minutes of guided phase NACT = the ratio of time spent in non-activity during the sample session; EXP = the ratio of time spent in exploration during the sample session; ACT = the ratio of time spent in activity during the sample session; Read = the ratio of time spent in reading activity during the sample session; Play = the ratio of time spent playing games during the sample session; Food = the ratio of time spent in food and drink related activities during the sample session; DAS = the Dimensional Apathy Scale; FAB = the frontal assessment battery; HAD = the Hospital Anxiety and Depression scale; HAD.D = the Depression subscale of the HAD; Minisea = the mini-Social cognition & Emotional Assessment; Minisea.REC = the facial emotion recognition test of the Minisea. * $p < .05$, ** $p < .01$, *** $p < .001$ for significant differences between the groups; • $p < .1$, for trend differences between the groups. ns = non-significant.

activities and social disinhibition as well as impulsive behaviours increased again. Indeed, once the questionnaire was completed, there was no longer a framework to guide patients' behaviours, and features of disinhibition were expressed again. This pattern has often been observed in proposed therapies (e.g., therapeutic activities, multisensory stimulation or music therapy), where “undesired” behaviours

decrease only during the activity time and do not present evidence for long-lasting benefits (Keszycki et al., 2019).

Concerning compulsivity, performing a task, such as completing a questionnaire, did not affect the occurrence of the behaviour. On the contrary, some patients even showed more repetitive actions at the beginning of the task, most likely because feeling under pressure to complete it correctly.

Thus, our results make it clear that the three subtypes of disinhibition were not modulated in the same way by performing a task and highlight the importance of defining and differentiating these subtypes present in each patient, since their management should be adapted to each profile.

We investigated the relationship between changes in activity scale and behavioural disinhibition during the guided phase. We found that a reduction of social disinhibition was related to an increase of activity. This task was therefore particularly effective in reducing inappropriate behaviour. Unfortunately, no activity scale correlated with measures of impulsivity. One of the possible explanations is that impulsivity was present in fewer patients, and this could explain the lack of significance. The results suggest that the way the environment is set up can influence the type of disinhibited behaviour seen in patients which is in line with previous studies indicating that a stable and structured environment is beneficial for the patient (Shinagawa, 2015). Moreover, a study has shown that abnormal behaviour can be prevented by maintaining a calm and non-irritating environment for patients with frontotemporal dementia (Young et al., 2018), with daily routine and limited new items. Structuring the environment by reducing background noise and or visual distractions can facilitate the focus on a task completion, limiting wandering and agitation (Kortte & Rogalski, 2013). Similarly, Evan et al. recommend to act on the environment to limit impulsive behaviours for example by limiting temptations for Parkinson's disease (Evans et al., 2009). If environmental demands exceed the patient's cognitive abilities, stress may manifest in a variety of abnormal and undesirable behaviours (Barton et al., 2016; Richards & Beck, 2004). Taken together, these findings further underline the importance of differentiating the subtypes of disinhibition present in each patient and adapting non-pharmacological intervention accordingly, since impulsive and compulsive behaviours seem to be relatively opposite in the way they can be managed.

Memory and visuospatial functions are relatively spared in most cases of bvFTD, at least at the beginning of the disease (Rascovsky et al., 2011), thus focusing on these preserved abilities (e.g., during neuropsychological rehabilitation and speech/language therapy) seems to be a relevant approach. Using the patients' preserved procedural memory, by introducing old games and hobbies for example, is successful in reducing compulsive and impulsive behaviours as well as social disinhibition (Ikeda et al., 1995). Setting up activities in line with former hobbies or asking to complete a task with a meaningful purpose (here, completing a questionnaire for the medical team's needs) may motivate the patient to focus on an occupation and reduce disinhibition behaviours. In this way, helping with domestic tasks (such as cooking, cleaning, gardening, etc., in a safe way) would be beneficial for patients but also for caregivers by lightening their workload.

Pilot studies in FTD patients have already described tailored activities as appropriate interventions to address behavioural disturbances (O'Connor et al., 2019) and there is evidence for the potential benefit of Positive Behaviour Support in reducing disinhibited behaviours (O'Connor et al., 2020). Thus, developing and implementing tailored support seems promising in managing disinhibition. Many non-pharmacological interventions are proving effective in

managing behavioural inhibition disorders in other diseases, such as dementia (Cohen-Mansfield, 2001), attention-deficit/hyperactivity disorder (Richardson et al., 2015) and autism (Zarafshan et al., 2017). Non-pharmacological interventions have also been explored in other neuropsychiatric symptoms such as apathy, with promising management strategies using tailored activities based on the patient's cognitive and physical profile (Manera et al., 2020). However, the literature examining treatments for disinhibition in the case of non-pharmacological intervention remains scarce in the context of dementia (Keszycski et al., 2019), and this area should be further investigated in the future.

4.4. Limitations

The present study has some limitations. Firstly, we acknowledge the small sample size of bvFTD patients, the difficulty of recruitment being partly explained by our "heavy" study's protocol (two days of experimental protocol). In addition, we applied highly selective inclusion criteria (e.g., MMSE score >20) due to the need to include patients at a very early stage, which reduced the number of patients available for the study. At the same time, this allowed us to explore in detail patients in the early stages of the disease while avoiding the confounding effect of advanced neurodegeneration on behaviour. Finally, as self-report questionnaires may be biased due to possible anosognosia in patients, it would be interesting in future studies to also use a caregiver-rated scale for a more objective reporting of these disorders.

This study is the first to investigate disinhibition in an ecological setting and the potential for its reduction using tailored activities. Such symptoms are described as one of the major causes of stress for caregivers (Cheng, 2017; Davis & Tremont, 2007) and therefore present an important target for management strategies. These results should be further studied by investigating several groups of patients with a larger sample. This would improve our understanding of the progression of the disease and highlight behavioural disinhibition heterogeneities among bvFTD patients, leading to personalised and adapted care.

Author contributions

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Funding

Part of this work was funded by grants from the ENEDIS company (ERDF), 2015–2017; and from the foundation “Fondation pour la recherche médicale” FRM DEQ20150331725. The research leading to these results has received funding from the program “Investissements d’avenir” ANR-10-IAIHU-06.

Open practices

The study in this article earned Open Materials and Preregistered badges for transparent practices. Materials for the study are available at: <https://data.mendeley.com/datasets/mv8hndcd95/2>.

Declaration of competing interest

The authors report no competing interests.

Acknowledgements

Delphine Tanguy is supported by École Normale Supérieure Paris-Saclay. Raffaella Migliaccio is supported by France Alzheimer, Fondation Recherche Alzheimer, and Philippe Chatrier Foundations, and by Rosita Gomez association. Arabella Bouzigues is supported by Fondation Recherche Alzheimer.

Part of this work was carried out on the PRISME core facility of ICM. We gratefully acknowledge the scientific managers of the platform: Mathias PESSIGLIONE and Philippe FOSSATI, as well as the valuable assistance of Pierre LÉBOUCHER, Patrick KPEKOU, Pierre CANET, Gilles RAUTUREAU, and Karim NDIAYE for the setup and maintenance of the video and sensor-based data acquisition system. The authors acknowledge the support of all the patients and their relatives, as well as the healthy controls who agreed to participate in this study.

Appendix

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Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.cortex.2022.11.013>.

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