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Research Paper

Title.

A temporal classification method based on behavior time series data in patients with behavioral variant of frontotemporal dementia and apathy.

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Introduction

1. Behavioral variant frontotemporal dementia (bvFTD) and apathy

Apathy is a common behavioral syndrome that occurs across a wide range of neurological and psychiatric disorders.[1,2] It is the most common neuropsychiatric syndrome (NPS) associated with behavioral variant frontotemporal dementia (bvFTD), but it is also highly prevalent in other neurodegenerative conditions.[2,3] BvFTD is an early-onset neurodegenerative disease resulting from frontotemporal lobar degeneration,[3] and it is characterized by a progressive deterioration of personality, social conduct and cognition.[4] BvFTD is a good model for studying apathy because apathy is one of the core features of bvFTD,[5] and it remains almost constant throughout the disease.[6] In 2011, the International bvFTD Criteria Consortium (FTDC) developed revised guidelines for the diagnosis of bvFTD, wherein bvFTD is a syndrome defined by a set of clinical (behavioral and cognitive) criteria: disinhibition, apathy/inertia, loss of empathy, perseverative/compulsive behaviors, hyperorality and a dysexecutive neuropsychological profile.[4]

Traditionally, apathy has been viewed as a symptom indicating loss of interest or emotions. In 1990, in a highly influential conceptual framework, Marin defined apathy as “diminished motivation not attributable to diminished level of consciousness, cognitive impairment, or emotional distress”.[7] Marin (1991), in his paper entitled “Apathy: a neuropsychiatric syndrome” introduced a major evolution of the concept of apathy. He suggested that neuropsychiatric disorders also produce a syndrome of apathy and proposed diagnostic criteria for the syndrome of apathy (i.e., a syndrome of primary motivational loss, that is loss of motivation not attributable to emotional distress, intellectual impairment, or diminished level of consciousness) on the basis of its distinction from the overt behavioral, cognitive, and emotional concomitants of goal-directed behavior.[8] However, according Marin (1991), both the symptom and the syndrome of apathy are of conceptual interest. In 2001, Starkstein et al. operationalized Marin’s criteria into a set of diagnostic criteria for apathy,[9] and on the basis of Marin’s Apathy Evaluation Scale,[10] they designed a simplified 14-item scale (Starkstein Apathy Scale) that can be used with patients and caregivers.[11] In 2000, Stuss et al. argued that apathy cannot be clinically defined as a lack of motivation because the assessment of motivation is problematic and usually requires inferences based on observations of affect or behavior.[12] They suggested that apathy is best characterized in behavioral terms as “an absence of responsiveness to stimuli - internal or external - as demonstrated by a lack of self-initiated action”.[12] According to the authors, there are many advantages to this definition: (1) it provides objective behavioral measurements; (2) apathy is not a singly definable state or a single syndrome; and (3) apathy can be divided into separable types (states). Stuss's conceptualization of apathy states (apathetic behaviors) is derived from the model of frontal lobe function developed by Stuss and colleagues.[13] The authors emphasized: (i) emotional apathy, i.e., lack of concern and limbic affective input as reward sensitivity; (ii) cognitive apathy, i.e., absence of initiated behavior due to executive dysfunction as planning; and (iii) behavioral apathy, i.e., diminished self-initiated actions).[12]

In 2006, in another influential theoretical framework, Levy and Dubois refined the definition of apathy to "the quantitative reduction of self-generated voluntary and purposeful behaviors".[14] Consequently, the authors argued that, first, apathy is an *observable state* that can subsequently be quantified; second, apathy is a pathology of voluntary action or goal-directed behavior (GDB); and third, the underlying mechanisms responsible for apathy are related to dysfunctions of the elaboration, execution or control of GDB.[14] Within neuroscience, GDB is understood as a set of related processes by which an internal state is translated, through action, into the attainment of a goal.[15] Levy and Dubois proposed an apathy model, partly aligned with previous conceptualizations, and they emphasized the multifactorial nature of apathy by defining three subtypes based on the impairment of distinct prefrontal cortex-basal ganglia circuits: (1) emotional-affective apathy refers to an inability to associate affective and emotional signals with ongoing and forthcoming behaviors and manifests as indifference or flat affect (unconcern); (2) cognitive apathy relates to impaired elaboration of plans for action; and (3) autoactivation apathy refers to difficulties in initiating the motor program necessary to complete the behavior.[14] Recently, the criteria for apathy were revised by an international consensus group.[2] The new diagnostic criteria propose that: (1) apathy is defined as "a quantitative reduction of goal-directed activity in comparison to the patient's previous level of functioning"; and (2) apathy is a persistent state, the symptoms of which should be observed in at least two of the following three dimensions: behavior/cognition; emotion (including both spontaneous emotions and emotions in response to the environment/others); and social interaction (including both spontaneous social initiative and environment/other-stimulated social interaction).[2]

The assessment and measurement of apathy are crucial in clinical practice, as well as in research settings. Apathy is commonly assessed using a variety of instruments, including diagnostic criteria-based clinical interviews and validated assessment scales, based on patient (self-rated) and/or informant reports.[16,17] While many apathy scales are available, several limits have been identified. First, these scales are biased by the subjective evaluation of the patient or his or her relatives, and important differences in quotations can be noted between patients and caregivers,[18] especially in neurological diseases with anosognosia, such as bvFTD. Second, the psychometric properties of the scales can vary across different populations, and they provide only subjective measurements of the patient's internal state, thoughts and past activities.[17] Finally, although some scales, such as the Dimensional Apathy Scale (DAS),[19] aim to differentiate the different forms of apathy, future research should address the ability to distinguish subtypes of apathy.

Thus, a challenging issue is the need to measure apathy objectively, reflecting the type of apathetic behavior (i.e., the form of apathy) investigated. To address this issue, direct behavioral observation in the natural environment or in simulated settings under more controlled conditions and structured scenarios, as well as behavioral sensing (sensor, video), is a promising method and tool. Burgess and Stuss,[20] reviewing fifty years of prefrontal cortex research and their impact on assessment, stated that "tests that mimic naturalistic situations may be just as effective in terms of time-effectiveness, discrimination power, specificity, sensitivity, and ease of administration (and sometimes perhaps more so) as those that do not".[20] The group of experts in the domain of apathy in brain disorders who revised the diagnostic criteria for apathy also suggested appropriate and updated tools that can be employed to assess apathy: (1) a number of clinical scales; and (2) new information and communications technologies (ICTs),[2] due to the emerging evidence that "new ICT approaches could provide clinicians with valuable additional information in terms of assessment, and therefore more accurate diagnosis of apathy".[21]

In line with these considerations, in a previous work,[22] we built an ecological framework under controlled conditions and a structured scenario (ECOCAPTURE, FRONTlab, ICM) designed to identify and measure behavior and/or behavioral disorders to obtain objective and quantitative measurements for assessing neuropsychiatric symptoms, such as apathy[22] and disinhibition,[23] given the limitations in measuring these behaviors using questionnaires and scales administered to patients or caregivers. In this study, we used the ECOCAPTURE protocol to investigate behavior in bvFTD patients under ecological conditions (a waiting room) while they freely explored a novel environment, and we examined individuals performing a continuous stream of behavior (behavior flow) over a 7-minute testing session (a part of the ECOCAPTURE scenario), in order to contribute to the identification of apathy-like behaviors and thus the characterization of apathy.

2. Direct behavioral observation and the ethological approach

Ethology, the "biology of behavior",[24] is a scientific discipline stemming from biology that studies the behavior of animals in the natural environment. Human ethology, founded by Eibl-

Eibesfeldt,[24,25] was established on the basis of classical zoo-ethology in connection with Lorenz's work,[26,27] and it has become an integral part of modern ethology. In our paper, the basic concepts, methods and tools related to ethology are used in relation to human ethology. The method of direct observation is the necessary link between laboratory research and "real-world" behavior and a key way to obtain more accurate, more objective information about behavior.[28] This method requires that the observer has a well-formulated research question and that he or her has a preliminary catalog of behaviors of interest called an ethogram. Ethograms are directories of species-typical behaviors observable under specific conditions, usually grouped into categories according to the type of behavior. Theoretically, in a specific category, all behaviors should be mutually exclusive (e.g., standing/sitting or activity/nonactivity): "Ethologists typically use two types of descriptions when constructing ethograms; *motor patterns* objectively describe physical movements made by the animal, while descriptions by consequence are *behaviors* defined in relation to the animal's environment".[29] Indeed, it is not the brain alone that produces behavior but rather its interaction with an even more complex and changing environment.[30]

The observer can consider behavior from different scales (for example, performing an activity is composed of a sequence of actions, including initiating the activity and maintaining the activity, or walking is a set of repetitive movements) and chooses the most effective scales of analysis to measure behavior. The complexity of behavior allows for many alternative segmentations depending on the level of information selected.[31] Thus, the behavior is broken up into units called behavior units or action patterns. Behaviors (or action patterns) are discrete, repeatable, and identifiable acts.[29] Once the behaviors of interest are defined, measurements are obtained in carefully selected and defined behavior units.[32]

Sampling decisions are another key point for behavioral data collection, especially with regard to the scheduling of session onsets (e.g., a sample session might be scheduled to begin at a predetermined time) or session terminations (e.g., after a fixed period). *Behavior continuous sampling* means that the observer watches the subject and records each occurrence of a particular behavior (and describes the context in which it occurs) for the entire duration of the sample period.[33] The *behavior continuous sampling* method generates accurate frequency and duration data through continuous recording, and it is considered the gold standard method.[28,34] Another parameter to consider in selecting a sampling method is the duration of the behavior (event or state); indeed, behavior can be regarded either as instantaneous events or as states having an appreciable duration, and this choice depends upon the questions about the behavior of interest.[28] Another parameter is the desired scale of measurement (nominal, ordinal, interval, or ratio).[34] Thus, the observer records the number of acts or the amount of time for which the behaviors are performed. An alternative method is to record action patterns in the order in which they occur, creating a sequence of events to produce a kinematic diagram. A kinematic diagram (or flow diagram or kinematic graph) provides an excellent overview of behavioral sequences (i.e., the flow of the behavior)[35] and is useful for illustrating transitions between behaviors.[32]

3. Toward a method with behavioral kinetics

As noted by Lehner, "Animals are always behaving. They perform a continuous stream of behavior from the moment when movement can first be detected in the embryo until their death".[32] In this study, instead of focusing on the behavioral sequence and/or the transitions between behaviors, our method tracked the flow of each specific behavior of interest and considered the temporal structure of behavioral data. Thus, each overt behavior was considered a signal (i.e., a set of values ordered by time) during a period of interest, the state changes of which could be analyzed. Since a signal is by definition a type of time series, the subjects' behavior data were transformed into behavior time series data. Therefore, in the rest of the paper, we use mathematical terms to describe the techniques and algorithms of mathematical time series analysis.

The objective of this paper is to present an approach considering behavioral kinetics to assess behavior in bvFTD patients and identify behavioral patterns contributing to the signature symptom of apathy. We aimed to construct a new behavior analysis method, called *ECOCAPTURE kinetics,* using temporal classification for behavior time series data analysis.

Time series are encountered in many scientific domains, and a large number of time series classification (TSC) methods and algorithms have been proposed, which were reviewed in Bagnall et al.[36] and Ismail Fawaz et al.[37]. A classifier is an algorithm that maps the input data to a specific category (i.e., assigns a class label to a data input). TSC is different from the traditional classification problem because the attributes in a time series are ordered. Bagnall et al.[36] classified TSC algorithms into categories, depending on the strategy type based on the period studied (*whole series* or *intervals* of the series), the signal characteristics (the presence or absence of short patterns or their frequency count), the choice of distances (e.g., *elastic* distance measures) and the use of *model-based* algorithms for measuring similarities between series. Moreover, two or more of the above approaches could be combined into a single classifier.

In the following, we illustrate some popular classifiers. Two series can be compared either as a vector or by a distance measure (the Euclidian distance calculation to all points in the dataset), but to compensate for potential localized misalignments between series, the classifiers use elastic distance measures. For example, dynamic time warping (DTW, also called elastic matching) is an effective method for measuring the similarity between two time series, which can vary in speed (e.g., similarities in walking could be detected using DTW, even if one person was walking faster than the other). In their review, Bagnall et al.[36] claimed that TSC papers in the datamining literature have cited DTW as the benchmark for comparison. The nearest neighbor (NN) classifier assigns a time series to the class of its closest neighbor in the feature space using Euclidian distance. One of the most popular and traditional TSC approaches is the use of an NN classifier coupled with an elastic distance function.[38]

To develop our classifier, we retained a nonelastic Euclidian metric, combined with a convolutional approach aiming to take into account the neighborhood . We hypothesized that, after developing our new temporal classification method that inputs behavior time series data (subjects' behavior flow), we would classify bvFTD patients according to their behavioral kinetics and that these subgroups would be differentially associated with apathy and other neuropsychological features and thus would identify specific behavior patterns contributing to the behavioral signature of apathy. This approach can be extended to any behavioral study encoding time, and an R package is available as open-source software (OSS).

Materials and methods

1. The ECOCAPTURE ethological and ecological approach

1.1 The ECOCAPTURE paradigm

The ECOCAPTURE paradigm mimics a naturalistic situation (i.e., waiting comfortably in a waiting room), and the behavioral assessment of apathy in participants was driven by a 45-minute controlled scenario. The experiments took place on an experimental platform dedicated to the functional exploration of human behavior (PRISME, ICM core facility, Salpêtrière Hospital, Paris, France), which allowed us to assess behavior under ecological conditions. The platform was transformed into a furnished waiting room (Figure 1A) containing specific objects that provided opportunities to interact with the environment. The PRISME platform is equipped with a six-ceiling camera system (not hidden) covering the entire waiting room. Media Recorder® software (NOLDUS Information Technology, Wageningen, the Netherlands) enables synchronous video recordings from multiple cameras over the network. During the experiment, individuals' behavior was video-recorded, and their movement acceleration was measured using a wireless body sensor

(Move II® triaxial accelerometer, Movisens GmbH, Karlsruhe, Germany) worn on the right hip. An eye-tracking system (SMI Eye Tracking Glasses 2 Wireless, ®SensoMotoric Instruments, Teltow, Germany) was added to the multimodal recording system, and the subjects wore eye-tracking glasses for a 7-minute period during the 45-minute experimental session. The subjects were informed at the time of initial consent that their behavior would be tracked and recorded by video cameras located in the room.

1.2 Cohort and ethics statement

A cohort (ECOCAPTURE) of twenty patients with bvFTD (thirteen men and seven women) and eighteen healthy controls participated in this research. This study is part of the clinical observational study C16-87[39] sponsored by INSERM, the *French National Institute for Biomedical Research*. It was granted approval by the local Ethics Committee (*Comité de Protection des Personnes,* CPP) on May 17, 2017 (CPP 17-31), and was registered in a public clinical trial registry (Clinicaltrials.gov: NCT03272230). All of the study participants gave their written informed consent to participate, in line with French ethical guidelines. This study was performed in accordance with the Declaration of Helsinki. Anonymity was preserved for all participants.

1.3 The ECOCAPTURE scenario

The ECOCAPTURE paradigm of apathy assessment is driven by a 45-minute structured scenario. A general outline of the ECOCAPTURE scenario is schematically presented in Figure 1B. Outside of the waiting room, the examiner equipped the participant with an accelerometer, and then the participant was asked to wait in the room prior to the subsequent experimental tests. The subject was explicitly encouraged to make himself/herself comfortable and to enjoy the room, using the space, as well as the objects at his or her own convenience ("as if he/she was at home"). These guidelines were designed to promote the ecological validity of the behavior tracking method (i.e., how the research context is representative of the real-life situation in which individuals' behaviors were recorded). The scenario began with a phase called the *free phase* (FP), starting when the examiner left the room, with the subject left alone in the waiting room for a 7-minute period. Since no specific goal-directed activity was suggested by the examiner in this FP, the participants were mostly tested on their ability to self-initiate activities. This first phase (FP) was followed by several other phases, including a *guided phase* (GP) lasting 10 minutes, in which the participants were asked by the examiner to complete a questionnaire.

We hypothesized that the ECOCAPTURE scenario would be relevant to the study of apathy because it favors the generation of GDB under contrasting conditions and offers many different opportunities to investigate the patient's behavior. We showed in a previous study that the FP is favorable to the emergence of self-guided behavior and is conducive to exploratory behavior, allowing us to observe how the participant behaves when discovering a novel environment to which he or she should adapt.[22] This study focuses on the analysis of the self-guided behavior that individuals develop to accomplish goals or activities during the 7-minute testing session FP. The GP, as well as the other phases intentionally contrived by the investigators of the ECOCAPTURE protocol (questionnaire to complete, sound stimuli), are beyond the scope of this paper.

Figure 1. The ECOCAPTURE ecological setting and scenario.

(A) The waiting room (PRISME, ICM) setup with different areas and specific objects that encourage a variety of activities. The waiting room has a surface area of 24 m^2 and is set up with several areas that encourage a variety of activities. The kitchen area is composed of kitchen furniture, food and drink, a cooler, a sink and an electric kettle. The sitting area is composed of a sofa with two cushions and two chairs. Games, such as a puzzle, Kapla, Sudoku, crosswords and a Rubik's cube, are scattered on a table in the center of the room. In one corner of the room, a furniture (4 drawer units) contains books and magazines, as well as candies. In the back of the room, a window with the blinds up overlooks the forecourt of the ICM building. (B) The 45-minute structured scenario ECOCAPTURE with phase onsets (after the examiner intervention) and phase terminations (after a fixed period). The scenario consists of five phases in the following order: a 7-minute free phase; a 7-minute free phase with eye-tracking glasses; a 7-minute sound stimulus phase (positive stimulus such as favorite music); a 10-minute guided phase (devoted to completing the questionnaire); and a 7-minute sound stimulus phase (negative stimulus such as crackling noise).

1.4 The ECOCAPTURE ethogram

The ECOCAPTURE ethogram (Table 1) includes two behavioral categories: *motor patterns* and *activity states,* focusing on the self-directed behaviors exhibited by the subjects during the free phase. All of the behaviors included in each of these two categories are mutually exclusive (e.g., sitting and standing cannot occur concurrently, nor can activity and nonactivity). The *motor patterns* category describes the posture, as well as the body segment movements and locomotion, expressed by the observed individuals (e.g., sitting). The *activity states* category includes four behaviors: 1) **nonactivity**, a state in which the subject shows no apparent activity; 2) **activity**, a state in which the subject is engaged in an activity with sustained attention; 3) **exploration**, a state in which the subject explores the waiting room and various objects in the room; and 4) **transition,** focusing on the timing of transitions between states. Moreover, modifiers are used to strongly describe and identify the nature of the activity (*activity*), as well as the exploratory behavior (*exploration*). Each single behavior can have one and only one modifier attached. The modifiers correspond to items present in the environment (the waiting room) with which the subject could interact. For exploratory behavior, the modifier is indicative of the object of exploration (e.g., *kitchen area* or *books and magazines*). For the activity behavior, the modifier identifies a specific activity (e.g., *food and drink* related activity or *reading*). See the full detailed ECOCAPTURE apathy ethogram at Mendeley Data [Dataset].[40]

Table 1. The ECOCAPTURE ethogram of observed behaviors during the 7-minute free phase.

Behavior	*Modifier*	Description
MOTOR PATTERNS (posture, movement and locomotion)		
Lying		Subject lies down on the sofa. Subject is lying on the sofa.
Sitting		Subject sits on the sofa or on a chair. Subject is seated on the sofa or on a chair.
Standing		Subject stands. Subject is standing.
Walking		Subject walks and moves around the room. Subject moves at least two steps.
Out of view		Subject is out of sight because he or she left the waiting room (on his or her own initiative).
ACTIVITY STATES		
Nonactivity		Subject shows no apparent activity.
Exploration		**Subject explores the waiting room and objects in the room.**
	Books and magazines	Exploring books and magazines.
	Furniture	Exploring the furniture (4 drawer unit), opening the drawers.
	Kitchen area	Exploring the kitchen area (kitchen furniture, sink, cooler) and food and drink.
	Games	Exploring the games scattered on the table.
	Outside window	Standing by the window and looking outside.
	Without apparent purpose	Moving without apparent purpose.
	Personal object	Exploring or looking for a personal object (glasses, clothes).
	Room	Exploring miscellaneous objects in the room.
	Door	Going to the door.

Activity	**Subject is engaged in an activity, with sustained attention over a period of 10 seconds, for the specific reading and playing activities.**
Reading	Reading books or magazines or posters.
Playing games	Playing with games like the puzzle, Kapla, Sudoku, crosswords and the Rubik's Cube.
Food and drink	Food and drink related activities like eating, drinking and drink preparation.
Tidying and cleaning	Tidying the games or books and magazines. Cleaning the kitchen area.
Tuning the radio	Tuning the radio
Space organization	Carrying the tray with food and drink. Pushing or moving an object.
Self-centered action	Self-centered actions like taking on/off clothes, taking on/off glasses.
Miscellaneous	Opening or closing a window and the shutter.
Transition	A short-term state (a few seconds) from one state to another. Resuming a task following an interruption.
Out of view	Subject is out of sight because he or she left the waiting room (on his or her own initiative).

1.5 The ECOCAPTURE behavior sampling protocol

Behavioral observations were collected through the continuous sampling method and based on the filmed material (videos), as well as the ECOCAPTURE ethogram (Table 1), by coders using a manual video annotation tool (The Observer XT®, NOLDUS Information Technology, Wageningen, the Netherlands). In this study, we focused on the behavioral data collected during a 7-minute testing session, called in this paper the *7-minute FP* period, corresponding to the free phase, to capture all of the behaviors of interest (ethogram) and their durations (states). Behavior was labeled *State*, as defined by Lehner: "the behavior an individual, or group, is engaged in; an ongoing behavior".[34] Such behaviors, called *state behaviors,* have a start time and a stop time and take a period of time in such a way that allows us to calculate behavior duration (Figure 2A). The scale of measurement was an interval scale from 0 to 420, with units in seconds. For each specific behavior from the ethogram, a set of ECOCAPTURE metrics (dependent variables) were derived from the collected behavioral data to measure behavior in each participant: 1/ **behavior sequence** (a vector of structure of the type *state behavior* with the following members: start time, stop time and period of time) represents the sequence of a specific behavior during the 7-minute FP (Figure 2B); 2/ **behavior total duration** is the total duration of a behavior calculated by totaling the durations of all occurrences of the behavior, with metric values ranging from 0 to 420 sec.; and 3/ **behavior ratio** is the ratio of the total duration of a behavior to the total time of the sample session, providing the time allocated to the behavior during the 7-minute FP, interpreted as a percentage; 4/ **behavior occurrences** is the number of occurrences of a behavior during the 7-minute FP. These metrics allowed us to build **time budgets** for each participant (one per behavioral category as described in the ethogram). Time budgets are a key metric in ethology; the time budget lists the percentage of time that an individual spends performing each behavior or performing various activities.[35]

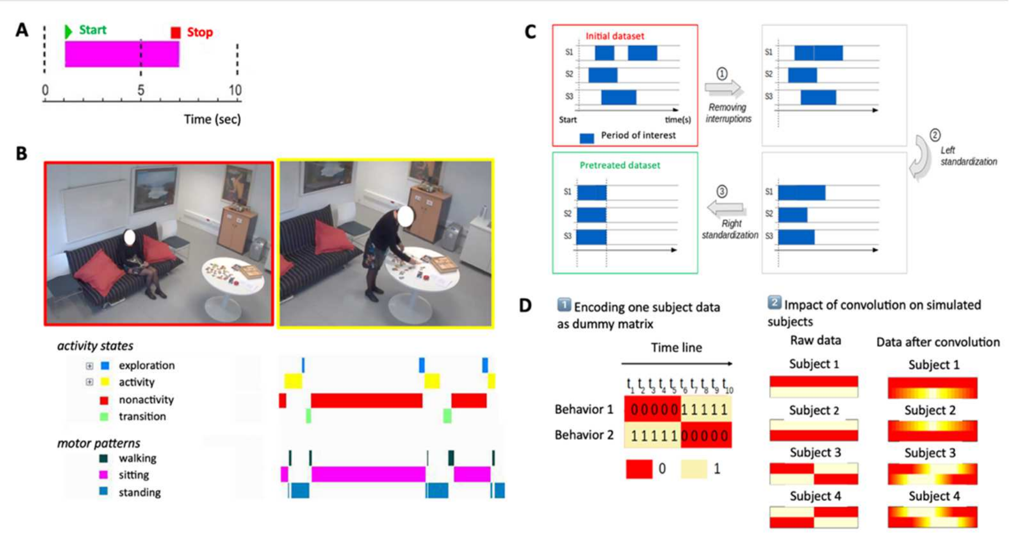

Figure 2. The ECOCAPTURE 7-minute testing session and the preprocessing of the collected behavioral data.
(A) *State behavior* has a start time and a stop time and takes a period of time (behavior duration). (B) ECOCAPTURE - Subject ethogram data resulting from behavior continuous sampling. Example of bvFTD patient ethogram data (The Observer XT®, NOLDUS). Sequence of each state behavior from the two categories: *activity states* (in red: *nonactivity*; in blue: *exploration*; in yellow: *activity – playing games*; in green: *transition*), and *motor patterns* (in dark green: *walking*; in magenta: *sitting*; in cyan: *standing*). (C) Example of alignment of the period of interest across three virtual subjects. (D) Visualization of a dummy matrix (1) and differences between convoluted and raw data (2).

2. Participants

A total of twenty bvFTD patients (see demographical details in Table 2) were recruited through neurological consultations at two AP-HP (Paris Public Hospitals) expert clinical sites: the national reference center on FTD at the *Institut de la Mémoire et de la Maladie d'Alzheimer* (IM2A) at the Pitié-Salpêtrière Hospital and at the Lariboisière Fernand-Widal Hospital. Diagnosis was established according to the International Consensus Diagnostic Criteria.[4] All of the patients met the inclusion criteria, with a Mini Mental State Examination score (MMSE)[41] between 20 and 30 used to determine general cognitive efficiency. Eighteen healthy controls (HCs) were recruited by public announcement and were required to score 27 out of 30 on the MMSE. HC subjects were matched to patients for age, gender and education level. Exclusion criteria for all of the participants included current or prior history of neurological disease other than bvFTD, psychiatric disease, and drug abuse.

The participants in the ECOCAPTURE cohort underwent the ECOCAPTURE paradigm and a comprehensive neuropsychological assessment.

2.1 Neuropsychological assessment

Traditional assessment of apathy severity was performed with the 14-item Starkstein Apathy Scale (SAS)[11], completed by the participants (SAS self-report questionnaire). The Frontal Assessment Battery (FAB)[42] was used to assess cognitive function, especially frontal and executive functions. The Mattis Dementia Rating Scale (MATTIS, DRS)[43], a widely used dementia screening instrument, exploring attention, initiation, perseveration, construction, conceptualization, and memory, was used to assess the individual's overall level of cognitive functioning. We used the Hospital Anxiety and Depression Scale self-administered questionnaire (HADS)[44] to screen for depressive symptoms and/or anxiety. The Hayling Sentence Completion Test (HSCT) examined the differing components of initiation and cognitive inhibition.[45] Participants were asked to complete sentences using the appropriate word (automatic condition, part A), and sentences using a completely unconnected word (inhibition condition, part B), as quickly as possible. The Hayling error score (HAYL_ERR, total error in HSCT part B) was the outcome measure of cognitive disinhibition. Additionally, we evaluated the changes in eating behavior and its disorders using the Eating Behavior Inventory (EBI)[46] investigating four domains of eating behaviors: eating habits, food preference, table manners, and swallowing problems.

2.2 Behavioral disinhibition assessment

In addition to cognitive disinhibition, we investigated behavioral disinhibition, using behavioral disinhibitions metrics, as defined in another part of the ECOCAPTURE protocol, and one of our previous studies.[23] We designed an ethogram of behaviors related to disinhibition in bvFTD, according to the definitions of symptoms by Rascovsky et al.[4] and to previous relevant studies in the field.[47,48] We proposed a list of 16 behaviors, divided in three disinhibition categories: *compulsivity* (e.g., repetitive movements), *impulsivity* (e.g., inappropriate action), and *social disinhibition* (e.g., familiar behavior towards investigator). See the complete ECOCAPTURE ethogram at Mendeley Data[40]. The number of times a behavior of interest occurs per video during the 7-minute FP sample session was counted in each individual using The Observer (NOLDUS). We summed the occurrences of behaviors within each disinhibition category to obtain the score of *impulsivity*, *compulsivity*, and *social disinhibition*. These scores were then summed together to obtain the global score of *disinhibition*.

3. Statistical methods

3.1 Overall

All of the statistical analyses were performed using R software (version 3.6.1, R Core Team 2019) in RStudio (version 1.2.5033). The main goal of our analyses was to assess differences between bvFTD patients and HCs and to stratify the bvFTD patients according to their behavioral kinetics extracted from video encoding. We developed a method called *ECOCAPTURE kinetics* to propose a clustering approach of individuals using their behavioral kinetics based on their ethogram behavioral data. It was essential as a prerequisite to collect the input behavioral data through behavior continuous sampling and based on an ethogram consisting of categories composed of mutually exclusive state behaviors. The proposed method *ECOCAPTURE kinetics* is quite different from those of the classical approach of sequencing behaviors, producing a kinematic diagram summarizing the likelihood of various behavioral sequences.

3.2 Behaviors of interest

The behavior of 20 bvFTD patients and 18 HCs was observed, and the behavioral data were collected during a single 7 minute testing session (7-minute FP) corresponding to the ECOCAPTURE scenario self-guided condition. We described exhaustively how subjects spent their time during the free phase and thus determined the behaviors of interest for this study (among the full range of behaviors recorded in the ECOCAPTURE ethogram), to which the method ECOCAPTURE kinetics was applied (i.e., tracking the flow of each specific behavior and analysis of state changes). To establish **time budgets** per group (bvFTD, HC), we first measured the percentage of time that each group (bvFTD patients and HC) spent on average performing each behavior from the category *activity states* and then performing various activities (as described by the set of modifiers related to the behavior *activity* in the ethogram, called **activity budget**).

3.3 Comparison of participants' demographic and neuropsychological scores

To compare the participants' demographics, we used Pearson's chi-square test for gender comparison (categorical variable) and the Mann–Whitney–Wilcoxon test for the quantitative variables (age, years of education). To compare the participants' neuropsychological scores (quantitative variables), we used the Mann–Whitney–Wilcoxon test. The Shapiro-Wilk test was used to test data normality and to indicate whether the data were parametric. The significance level was set at $p < 0.05$. Characteristics for bvFTD and HC are presented as numbers (percentages) for categorical variables and as the mean (range) and median [interquartile range] for continuous variables, and standard deviations are noted for normally distributed variables.

3.4 The statistical method ECOCAPTURE kinetics

The *ECOCAPTURE kinetics* method was designed to consider the time progression of each state behavior from the *activity states* and *motor pattern* categories, observed in each subject throughout the 7-minute FP. *ECOCAPTURE kinetics* are divided into five steps detailed in the following subsections. First, the data preprocessing aimed to align the data for all subjects, and the preprocessed dataset was visualized with colored bandplots. Then, the pretreated data were encoded in so-called *Subject's behavioral matrices* (SBMs), and a metric considering temporality was chosen. This metric is based on convolution principles. Finally, the bvFTD patients were classified according to the chosen metric, and the identified subgroups of patients were described and then characterized by behavioral curves and neuropsychological features.

Data preprocessing

In this study, behavioral data were collected during a period of interest (7-minute FP) that should be comparable across bvFTD patients (n = 20). Therefore, a three-step preprocessing method was applied (Figure 2C) to standardize all of the patients' sample sessions. Most of the time, periods of interest were uninterrupted (only one start and stop for a given period, i.e., the phase onset and phase termination according to the ECOCAPTURE scenario; see Figure 1B), but interruptions could also occur (several starts and stops for the same period, when a subject left the room for a moment, on his or her own initiative). In this case, the first preprocessing step consisted of removing the interruption duration(s) to obtain uninterrupted sequences. The second preprocessing step was a left standardization, causing all of the subjects to start at the same time. Indeed, the relative starting times of the period (from the start of video recording) could vary with subjects (longer time of instructions, etc.). The final step consisted of a right standardization, causing all subjects to stop the period at the same time. In this step, the minimal stop time was chosen. Figure 2C illustrates these three preprocessing (or alignment) steps. After this preprocessing, all of the subject data were comparable.

Visualization with bandplots

A bandplot is an appropriate tool for visualizing successive changes in subjects' state behaviors across the period of interest. This type of diagram typically applies to a list of exclusive state behaviors belonging to the same behavioral category of the ethogram. A specific color was attributed to each behavior of the list. Then, each subject's ethogram data was represented by a horizontal band with time as the abscissa, colored according to the related behavior manifested at this specific timepoint. Two bandplots were computed through the analysis of the 7-minute FP, adjusted after preprocessing alignment steps, to visualize the preprocessed behavioral data (**behavior sequence** metric). The first was related to the value states (e.g., sitting, walking) from the *motor patterns* behavioral category and is called in this paper the *motor bandplot*; the second was related to the value states (e.g., exploration, nonactivity) from *the activity states* behavioral category and is called in this paper the *activity bandplot*.

Extracting subjects' behavioral matrices (SBMs) from temporal behavior data

To apply our method to the ethogram data collected during the 7-minute FP (Figure 2B), we built high-dimensional time series matrices, one time series matrix per subject, in which each row corresponds to a specific behavior from the ECOCAPTURE ethogram. Our temporal approach was based on the discretization of time, which is the decomposition of the period time into n timepoints. For example, with a discretization of 1 second, if the time period lasts n seconds, the time is decomposed into n equidistant timepoints. Given one subject, every behavior occurs or not at each timepoint. This occurrence is encoded in a binary matrix with p (number of behaviors of interest) rows and n (number of timepoints) columns containing 1 if the behavior is realized at the time point or 0 otherwise. After discretizing the time into n time points, each subject's ethogram data were stored as p binary time series of size n, producing a matrix with indices of time (t) and behavior (b). The value of each specific metric **behavior sequence** was encoded as a binary vector (row of the matrix) to indicate the presence or absence of the related behavior. A given timepoint (t) and behavior (b), at which the behavior occurred was scored as 1 in the matrix cell (b, t), and when it did not occur was scored as 0. When the dataset is correctly pretreated, the sizes of these matrices are the same across subjects. These individual dummy matrices are called in this paper *Subject's behavioral matrices (SBMs)* and are composed of p binary vectors of size n. Establishing a distance between such matrices is required to allow for the classification of subjects considering temporality.

Choice of a metric to compare two SBMs

A first intuitive method consists of using Euclidean distance between the SBMs (individual dummy matrices). However, with this approach, the distance between two subjects results from a calculation of distance at each time point without considering potential relationships between two successive time points. Consequently, the distance between two subjects exhibiting the same behaviors at different timepoints will be 0, like the distance between two subjects manifesting different behaviors at all timepoints. This property was not relevant in the context of our study and constituted a methodological bias since we considered that two subjects exhibiting the same behaviors were closer than subjects manifesting different behaviors.

To address this issue, a convolution step was used for pretreatment of the data. Convolution is used to consider the neighborhood in imagery in convolutional neural networks and in signal theory. For discrete signals *f* and *g* and a given time n, its calculation equals:

$$(f * g)(n) = \sum_{m=-\infty}^{+\infty} f(m)g(n-m)$$

In our case, *f* was the binary signal for one given behavior (which can be noted as $f(t) = 1_{Behavior}(t)$), while we chose g as a rectangular signal of unit height and width 2M [-M, +M] (M being defined in the next section); thus, f and g sequences were padded with 0s (from left or right) to be defined on **Z**, which led to:

$$(f * g)(n) = \sum_{m=-M}^{M} f(n-m) = \sum_{m=-M}^{M} 1_{Behavior}(n-m)$$

Consequently, *f* * *g* was the duration of behavior in the time window between n-M and n+M. In other words, it consisted of calculating the duration of behaviors in a selected window moving across the timeline instead of calculating global frequencies. The size of the convolution window was chosen with M = 200 for a 400-second period. With this choice, all of the signals were covered by the convolution window. This size was also shown to maximize the discrimination between bvFTD and HC subjects (results not shown). Each line of the SMBs was convoluted according to this window, given a convoluted matrix. After convolution, the matrices were no longer composed of only 0 or 1 but of a duration of behavior in the neighborhood of the function. The final step consisted of using Euclidean distance on convoluted SMBs.

Figure 2D illustrates the interest of convolution: with the dataset without convolution, the Euclidean distance between Subjects 1 and 2 (having nothing in common) was the same as that between Subjects 3 and 4 (having the same behavior but at different timepoints). With the convoluted dataset, the distance between Subjects 3 and 4 was lower (6.32) than the distance between Subjects 1 and 2 (12.65) and even for a short time lower than the distance between Subjects 1 and 3 (7.07).

Patient clustering and characterization of the subgroups

From the distance matrix, a hierarchical classification was computed with the Ward D2 method. The number of clusters was determined visually based on the scree plot criterion by selecting the maximal number from which the gap in accumulated criteria can be seen as less important (Figure 3A). Then, multidimensional scaling (MDS) was used to visualize on a map the distances between the subjects with the groups assigned by the classification using the SMACOF R package[49]. To characterize the different groups, behavioral curves were computed. This procedure considers each behavior of interest separately. For each time point, the number of subjects exhibiting this behavior was calculated. Then, these numbers were plotted against time, and a curve was built per behavior (with potential smoothing). All behavioral curves are depicted on the same graph with one color per behavior. This procedure was inspired by the temporal dominance of sensations (TDS) curves in sensory analysis.[50] Finally, the Kruskal-Wallis test, followed by Dunn's pairwise test with Bonferroni's correction, was used to compare the neuropsychological scores between the groups. Boxplots were plotted to visually compare distributions in the groups of bvFTD patients and HCs.

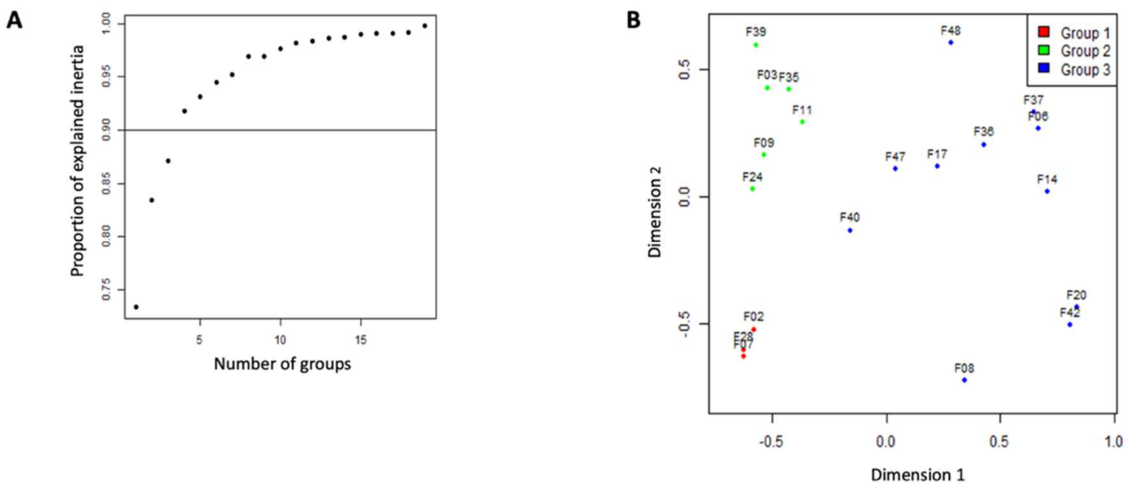

Figure 3. Patient clustering. (A) Explained cumulative inertia according to the number of groups. The black line indicates a limit of 90% of explained inertia, MDS results, Stress = 0.16. (B) MDS map of the bvFTD patients clustered in 3 groups.

Results

1. Intercoder reliability

Intercoder reliability was calculated in a subsample of eight observations. For this subsample, two different examiners coded the videos. All calculated Cohen's kappa coefficients were greater than 0.98, indicating close-to-perfect agreement between raters and therefore excellent interrater reliability.

2. Cohort characteristics and neuropsychological features

The bvFTD cohort (age range = 45-82 years old; mean = 65.8 years old) was composed of 7 women (35%) and 13 men, with the same level of education. The demographic characteristics are shown in Table 2. The participant groups did not differ in terms of age, education, or sex distribution.

The neuropsychological cognitive performance, severity of behavioral changes and emotional disorders of bvFTD patients and HCs are presented in Table 2 (see Shapiro-Wilk normality test data in Supplementary Table 1).

A significant difference was observed for the Starkstein Apathy Scale between the two groups (p = 1.1e-6), showing that bvFTD patients (SAS range = 7-25; mean = 15.35) were more apathetic than HCs. Higher SAS scores reflected increased endorsement of apathy in the bvFTD patients. Among the twenty bvFTD patients, fifteen were greater than or equal to the SAS pathological cutoff (14/42), while no HCs were greater than this threshold. The patients were also characterized by significant severity of depressive symptoms and anxiety as measured by the HAD.D (p = 3.3e-5) and the HAD.A (p = 0.005). The HADS is a screening tool using a severity cutoff for each subscale (HAD.D, HAD.A). A score of ≥ 11/21 is considered a clinically significant disorder, whereas a score between 8 and 10 suggests a mild disorder[44]. Regarding the HAD.D subscale, among the twenty bvFTD patients, five were greater than or equal to 8, including two patients greater than 10, while no HCs were greater than 3. Regarding the HAD.A subscale, among the twenty bvFTD patients, eleven were greater than or equal to 8, including four patients greater than 10, while only one HC was greater than 8. Moreover, the bvFTD patients presented a significant decrease in global cognitive efficiency, as revealed by the MMSE (p = 4.1e-7) and MATTIS (p = 1.4e-7), and sharp frontal syndrome, as revealed by the FAB (p = 2.9e-7). As expected, the bvFTD patients presented more cognitive disinhibition than the HCs, exhibiting an increased rate of response error (p = 1e-5). In the same way, bvFTD patients showed higher *compulsivity* (p = 0.013) and *social disinhibition* (p = 0.018) than HCs. A significant difference was also observed for the global score of *disinhibition* between the two groups (p = 0.006). Finally, bvFTD showed changes in eating behavior compared to the HCs (p =1e-6).

Table 2. Demographic characteristics, neuropsychological scores, and behavioral disinhibition metrics.

Data are shown as N (%), mean ± SD (range) or mean (range) and median [IQR]. *IQR* interquartile range, *SD* standard deviation, *YOE* years of education, *MMSE* Mini Mental State Examination, *FAB* Frontal Assessment Battery, *MATTIS* Mattis Dementia Rating Scale (DRS), *SAS* 14-item Starkstein Apathy Scale, *HAD* Hospital Anxiety and Depression Scale, *HAD.D* Depression, *HAD.A* Anxiety, *HAYL_ERR* Hayling error score (number of errors in part B) in the Hayling Sentence Completion Test (HSCT), *Impulsivity* number of occurrences of behaviors within the impulsivity category, *Compulsivity* number of occurrences of behaviors within the compulsivity category, *Social disinhibition* number of occurrences of behaviors within the social disinhibition category, *Disinhibition* global score of disinhibition, *EBI* Eating Behavior Inventory. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ for significant differences between the bvFTD and HC groups. • $p < 0.1$, for trend differences between the bvFTD and HC groups.

ECOCAPTURE Cohort	**bvFTD**	**HC**	**Group effect**	
	(*n* = 20)	**(*n* =18)**	**Chi²/Mann–Whitney–Wilcoxon test**	
Demographic information				
Male sex, N%	13 (65%)	8 (44%)		
Female sex, N%	7 (35%)	10 (56%)		
Gender (M/F)	13/7	8/10	$p = 0.34$	
Age (years)				
mean ± SD (range)	65.8 ± 8.78 (45, 82)	62.61 ± 7.24 (46, 71)		
median [IQR]	67 [61, 72.25]	64 [60.5, 67.5]	$p = 0.17$	
YOE (year)				
mean ± SD (range)	13.85 ± 4.78 (7, 22)	13.78 ± 2.21 (9, 17)		
median [IQR]	14.5 [9, 17]	14 [12, 15]	$p = 0.94$	
Neuropsychological data			***p* value**	**Comparison**
Cognitive and executive functions				
MMSE, /30				
mean ± SD (range)	24.05 ± 2.8 (20, 29)	29.39 ± 0.78 (28, 30)		
median [IQR]	23.5 [21.75, 26.25]	30 [29, 30]	$p = 4.1e-7$	bvFTD < HC ***
FAB, /18				
mean ± SD (range)	12.45 ± 3.41 (5, 16)	17.33 ± 0.84 (15, 18)		
median [IQR]	13.5 [11.5, 15]	17.5 [17, 18]	$p = 2.9e-7$	bvFTD < HC ***
MATTIS, /144				
mean ± SD (range)	119.5 ± 9.3 (104, 136)	142.17 ± 1.29 (139, 144)		
median [IQR]	119 [113, 125.5]	142 [141.25, 143]	$p = 1.4e-7$	bvFTD < HC ***
Apathy				
SAS, /42				
mean ± SD (range)	15.35 ± 4.78 (7, 25)	5.72 ± 3.08 (0, 12)		
median [IQR]	15.5 [13.75, 17]	6 [4, 7]	$p = 1.1e-6$	HC < bvFTD ***
Depression, Anxiety				
HAD.D, /21				
mean ± SD (range)	5.6 ± 3.4 (0, 12)	1.22 ± 1 (0, 3)		
median [IQR]	5 [3.5, 7.25]	1 [0.25, 2]	$p = 3.3e-5$	HC < bvFTD ***
HAD.A, /21				
mean ± SD (range)	7.85 ± 4.32 (1, 17)	4.22 ± 2.41 (0, 10)		
median [IQR]	8 [5.75, 10]	3.5 [3, 5.75]	$p = 0.005$	HC < bvFTD **
Cognitive disinhibition				
HAYL_ERR				
mean ± SD (range)	19.47 ± 14.42 (2, 45)	3.11 ± 2.56 (0, 8)		
median [IQR]	14 [8.5, 32]	2.5 [1, 5]	$p = 1e-5$	HC < bvFTD ***
Behavioral disinhibition data				
Disinhibition				
mean ± SD (range)	5.75 ± 8.02 (0, 31)	0.78 ± 1.56 (0, 6)		
median [IQR]	2.5 [0, 9]	0 [0, 1]	$p = 0.006$	HC < bvFTD **

Impulsivity mean ± SD (range) median [IQR]	 2.45 ± 5.36 (0, 20) 0 [0, 1.25]	 0.39 ± 1.15 (0, 4) 0 [0, 0]	 *p* = 0.099	 HC < bvFTD ˙
Compulsivity mean ± SD (range) median [IQR]	 2.3 ± 4.03 (0, 13) 0 [0, 2.25]	 0.11 ± 0.47 (0, 2) 0 [0, 0]	 *p* = 0.013	 HC < bvFTD *
Social disinhibition mean ± SD (range) median [IQR]	 1 ± 1.21 (0, 5) 1 [0, 1.25]	 0.28 ± 0.57 (0, 2) 0 [0, 0]	 *p* = 0.018	 HC < bvFTD *
Eating behavior data				
EBI, /32 mean ± SD (range) median [IQR]	 13.25 ± 6.03 (1, 22) 13 [10.75, 17. 5]	 1.33 ± 1.91 (0, 7) 0.5 [0, 2]	 *p* = 1e-6	 HC < bvFTD ***

3. Behaviors of interest and time budgets

The behaviors of interest were selected based on the time budgets of the bvFTD patients and the HCs. Figure 4A shows the **time budget** in the bvFTD and HC groups. The bvFTD patients spent more time inactive (13%) than the controls (2%). Both groups spent a large proportion of time on activities (up to 60% in bvFTD and 69% in HC). Figure 4B shows the **activity budget** in each group. In the bvFTD patients, the time spent on activities was divided between playing games (34%), reading (34%), and food and drink related activities (28%). The remaining 3% of time was spent on various activities as described in the ethogram (e.g., self-centered action). The HCs spent most of their time on similar activities as the bvFTD patients. We retained nine behaviors of interest, which are presented in Table 3.

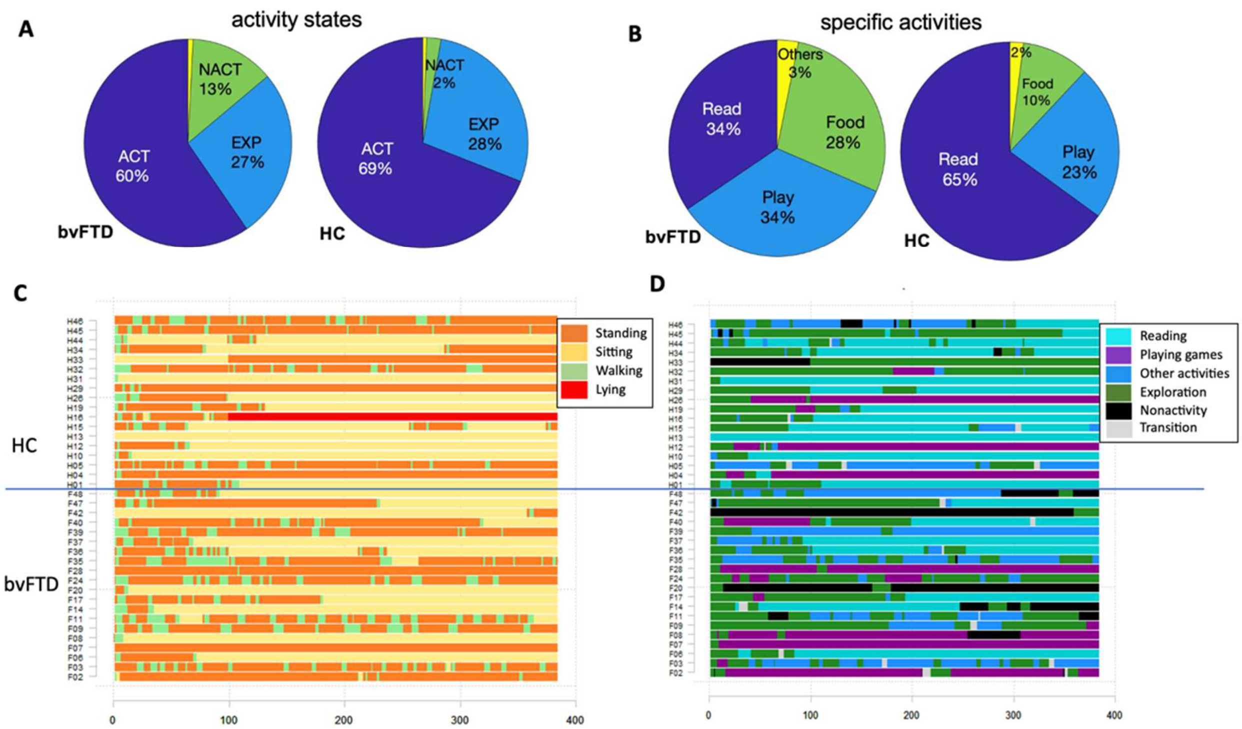

Figure 4. Subjects' behavior data are presented as time budgets and bandplots.
(A) Time budgets for activity (ACT), exploration (EXP) and nonactivity (NACT) in bvFTD patients and HCs. (B) Time budgets for reading (Read), playing games (Play), food and drink related activities (Food), and other activities (Others) as described in the EOCAPTURE ethogram in bvFTD patients and HCs. (C) Bandplots for motor states of the bvFTD patients (bottom) and HCs (top). (D) Bandplots for activity states of the bvFTD patients (bottom) and HCs (top).

Table 3. Behaviors of interest, on which the method *ECOCAPTURE kinetics* is applied (i.e., tracking the flow of each specific behavior and analysis of state changes).

Behavior	*Modifier*	Description
ACTIVITY STATES		
1 - Nonactivity		Subject shows no apparent activity.
2 – Exploration		Subject explores the waiting room and objects in the room.
Activity		Subject is engaged in an activity.
	3 - Reading	Reading books or magazines or posters.
	4 - Playing games	Playing with games like the puzzle, Kapla, Sudoku, crosswords and the Rubik's Cube.
	5 - Other activities	All other activities including the food and drink related activities.
MOTOR PATTERNS (posture, movement and locomotion)		
6 - Lying		Subject lies down on the sofa. Subject is lying on the sofa.
7 - Sitting		Subject sits on the sofa or on a chair. Subject is seated on the sofa or on a chair.
8 - Standing		Subject stands. Subject is standing.
9 - Walking		Subject walks and moves around the room. Subject moves at least two steps.

4. Bandplots

Preprocessing alignment steps applied to the analysis of the 7-minute FP resulted in an adjusted period of interest lasting approximately 400 sec. The *motor bandplot* (Figure 4C) and the *activity bandplot* (Figure 4D) were computed through this analysis for a 400-second period. Each bandplot is split vertically into two sub-bandplots: the 20 bottom rows correspond to the bvFTD patients, while the 18 top rows correspond to the HCs. These visual resources allow us to visualize the raw data and identify the sequence of behaviors of interest (Table 3) for each subject. Each row represents the motor behavioral patterns (in the *motor bandplot*) and the activity behavioral patterns (in the *activity bandplot*) for a particular subject. For example, the first row of the HC *motor bandplot* (Figure 4C) shows orange and green band sequences throughout the 400-second period, thus reporting that this subject exhibited these related state behaviors (standing and walking, respectively) at these corresponding start times and for a period of time (band length).

Figures 4C and 4D show several interesting features of and behavioral patterns in the *motor* and *activity bandplots*. In the *motor bandplot*, the patients show a high prevalence of walking and standing sequences (orange and green bands, respectively) until the end of the 400-second period, compared to the HCs, in whom several walking and standing sequences appear narrower on the left of the timeline (i.e., the very first minutes of the analysis of the 400-second period) and are followed by a long sitting position (yellow section). In the *activity bandplot*, the temporal organization of activity reveals a specific pattern that is widely present in the HCs, in which a short exploration time (green band) is followed by a long-term activity (Reading or Playing games, or Other activities, including mainly Food and drink related activities). Compared to the HC bandplot, the bvFTD bandplot shows more large black bands (nonactivity) and a higher prevalence of blue bands (Other activities, including mainly Food and drink related activities) and overall presents a more heterogeneous behavioral pattern.

5. Patient clustering and kinetics profiles

The classification of the bvFTD patients provided the graphics of accumulated inertia presented in Figure 3A. Following a scree plot criterion, 3 groups were selected. The three subgroups of bvFTD patients were represented using MDS based on the obtained distance matrix (Figure 3B). The three subgroups contained three (Group 1), six (Group 2) and eleven (Group 3) patients. Figure 5A shows the kinetics in the three subgroups of bvFTD patients and HCs.

Group 1 consisted of three patients standing and playing games during the 400-second FP. Group 2 comprised six patients alternating exploration and activities, other than reading and playing games, and therefore essentially food and drink related activities, mostly standing (but sitting and walking patterns occur as well). The time diagram throughout the 400-second FP presented different types of waves. Concerning the motor pattern, the standing behavior signal had higher values and peaks, with a relatively low amplitude, since the walking signal had lower values, with a gradually decreased amplitude. Concerning the activity pattern, the activity signal and the exploration signals crossed several times. The exploration signal began with the highest value ($n = 6$), while the activity signal began with the lowest ($n = 0$). Subsequently, the exploration signal decreased until $t = 200$ sec and then increased until almost the end, while the activity signal increased from $t = 0$ sec to $t = 200$ sec and then decreased.

Group 3 consisted of eleven patients mainly sitting and reading or who were not active. The behavioral kinetics of Group 3 showed several interesting features. First, the exploration signal began with a very high value ($n = 10$), but unlike Group 2, the exploration signal gradually decreased until $t = 400$ sec, reaching very low values (1 or 0) from $t = 240$ seconds. The reading activity signal began with the lowest value ($n = 0$) and gradually increased until $t = 250$ seconds, when the waveform signal was flat (n = 6). The two signals crossed only once, at t = 100 sec. Second, the nonactivity signal, the waveform of which was flat from the beginning, stood out as the second highest signal (2 < n <= 5) after the reading signal. Third, concerning the motor pattern, the sitting signal rapidly increased (from n = 1 to 8) until t = 120 sec and was maintained at a high level (from n = 8 to 11) until the end, with a flat waveform. The walking and standing signals gradually decreased and reached low values (n = 0 or 1) from t = 100 sec and (0 < n <= 2) from t = 100 sec, respectively. Finally, the Group 3 and HC time diagrams were very close, especially with regard to the exploration and reading signals. However, in the HCs compared to the bvFTD Group 3, the inactivity signal had a very low level (0 <= n <=1), and the standing signal maintained a high level during the whole 400-second period, close to that of the sitting signal.

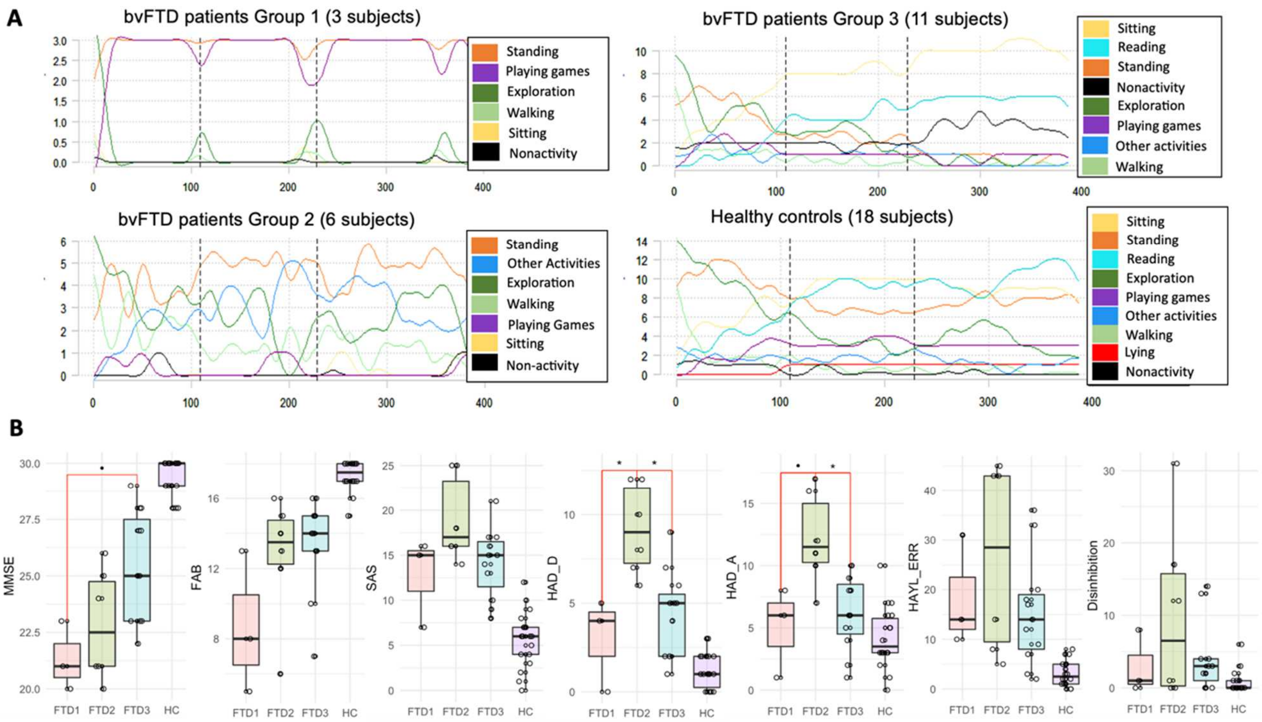

Figure 5. Behavioral kinetics and neuropsychological features of the three bvFTD groups. (A) Kinetics in the 3 selected groups of bvFTD patients and in the HC group. The time diagrams include the signal throughout the 400-second FP for each behavior manifested in a particular group. (B) Distribution of MMSE, FAB, SAS, HAD.D, HAD.A, HAYL_ERR scores (neuropsychological data) and Disinhibition global score (behavioral *disinhibition data*) in the selected subgroups of bvFTD patients (FTD1, FTD2, FTD3) and HC.

6. Neuropsychological profiles of the bvFTD patient subgroups

We compared the selected bvFTD subgroups (called in the rest of the paper FTD1, FTD2, FTD3) with demographic, neuropsychological scores, and behavioral disinhibition metrics (Table 4). Three neuropsychological variables showed significant differences (with a p value less than 0.05) or trend differences (with a p value less than 0.1): MMSE (cognitive impairment), HAD.D (depression) and HAD.A (anxiety). No significant groups differences were found in overall level of cognitive functioning (MATTIS) nor in executive performance (FAB). No significant difference was observed in cognitive disinhibition (HAYL_ERR) between the three groups of patients, nor in behavioral disinhibition (impulsivity, compulsivity, social disinhibition). There was no statistical difference in eating behavior (EBI) between the three groups of patients.

However, as seen previously, the whole bvFTD patients significantly differed from the HCs. Indeed, the bvFTD patients were more apathetic on SAS (p = 1.1e-6) and characterized by severity of depressive symptoms on HAD.D (p = 3.3e-5) and anxiety on HAD.A (p = 0.005). They presented a global cognitive impairment on MMSE (p = 4.1e-7) and MATTIS (p = 1.4e-7), as well as executive deficits on FAB (p = 2.9e-7). The bvFTD patients manifested cognitive disinhibition on HAYL_ERR (p = 1e-5) as well as behavioral disinhibition on ECOCAPTURE (p = 0.006). Moreover, they showed changes in eating behavior on EBI (p =1e-6).

The FTD2 group seemed to be more apathetic (not significant) than the other groups (Figure 5B), and although the statistical test was not significant, FTD2 has a higher average score (mean = 19) than FTD1 (mean = 12.67) and FTD3 (mean = 14.09) on the SAS. Among the six FTD2 patients, all were greater than or equal to the SAS pathological cutoff (14/42), which was not the case for FTD1 and FTD3. Moreover, FTD2 was more depressed (FTD2 > FTD1, p = 0.024; FTD2 > FTD3, p = 0.018) on the HAD.D and anxious on the HAD.A than the other groups (FTD2 > FTD3, p = 0.024; FTD2 > FTD1, p = 0.055). Regarding the HAD.D subscale, among the six FTD2 patients, four were greater than or equal to 8, including two patients greater than 10, while among the three FTD1 patients, all were less than 8, and among the eleven FTD3 patients, only one was greater than 8. Regarding the HAD.A subscale, among the six FTD2 patients, four were greater than or equal to 10, while among the three FTD1 patients, all were less than or equal to 8, and among the eleven FTD3 patients, only one was greater than 8. Although no significant difference was observed in cognitive disinhibition, nor in behavioral disinhibition, between the three groups of patients, FTD2 has a higher average score (mean = 26.33) than FTD1 (mean = 18.33) and FTD3 (mean = 15.07) on the HAYL_ERR (Figure 5). In the same way, FTD2 has a higher average score (mean = 10.17) than FTD1 (mean = 3) and FTD3 (mean = 4.09) on the disinhibition global score (Figure 5), as well as on impulsivity and compulsivity categories. However, we noted that social disinhibition is almost homogeneous among all patients.

We also showed that FTD3 patients had higher cognitive capacity (i.e., MMSE score) than the others (FTD3 > FTD1, $p = 0.067$; FTD3 > FTD2, not significant) while being among the least depressed (FTD3 < FTD2, $p = 0.018$) and anxious patients (FTD3 < FTD2, $p = 0.024$). Regarding the MMSE, among the eleven FTD3 patients, seven were greater than or equal to 25, while all three FTD1 patients were less than 25, and among the six FTD2 patients, only two were greater than 25. The results were consistent for the executive functioning (FAB); among the eleven FTD3 patients, seven were greater than or equal to 14, while all three FTD1 patients were less than 14, and among the six FTD2 patients, only two were greater than or equal to 14. These findings underscore two poles: a cognitive and executive pole (MMSE, FAB) and a behavioral pole (SAS, HAD.D, HAD.A).

Table 4. Demographic and neuropsychological characteristics in the three selected subgroups, and behavioral disinhibition metrics.

Data are shown as min-max (mean) or N. *YOE Years of Education, MMSE* Mini Mental State Examination, *FAB* Frontal Assessment Battery, *MATTIS* Mattis Dementia Rating Scale (DRS), *SAS* the 14-item Starkstein Apathy Scale, *HAD* Hospital Anxiety and Depression scale, *HAD.D* Depression, *HAD.A* Anxiety, *HAYL_ERR* Hayling error score (number of errors in part B) in the Hayling Sentence Completion Test (HSCT). *Impulsivity* number of occurrences of behaviors within the impulsivity category, *Compulsivity* number of occurrences of behaviors within the compulsivity category, *Social disinhibition* number of occurrences of behaviors within the social disinhibition category, *Disinhibition* global score of disinhibition, *EBI* Eating Behavior Inventory. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ for significant differences between the bvFTD groups. • $p < 0.1$, for trend differences between the bvFTD groups.

bvFTD patients	**FTD1**	**FTD2**	**FTD3**	**Group effect**	
N	**3**	**6**	**11**	**Chi²/Kruskal-Wallis test**	
Demographic information					
Gender (M/F)	1/2	4/2	8/3	$p = 0.45$	
Age (years)	57-70 (62.67)	58-72 (65)	45-82 (67.09)	$p = 0.31$	
Years of education	9-22 (17.67)	8-17 (12)	7-20 (13.82)	$p = 0.28$	
				***p* value**	**Comparison**
Neuropsychological data					
Cognitive functions					
MMSE, /30	20-23 (21.33)	20-26 (22.83)	22-29 (25.45)	0.035 *	FTD3 > FTD1, $p = 0.067$ •
FAB, /18	5-13 (8.67)	6-16 (12.67)	7-16 (13.36)	0.14	
MATTIS, /144	113-127 (119.67)	104-135 (120.5)	106-136 (118.91)	0.954	
Apathy					
SAS, /42	7-16 (12.67)	14-25 (19)	8-21 (14.09)	0.12	
Depression, Anxiety					
HAD.D, /21	0-5 (3)	6-12 (9.17)	1-9 (4.36)	0.007 **	FTD2 > FTD1, $p = 0.024$ * FTD2 > FTD3, $p = 0.018$ *
HAD.A, /21	1-8 (5)	7-17 (12.17)	1-10 (6.27)	0.013 *	FTD2 > FTD3, $p = 0.024$ * FTD2 > FTD1, $p = 0.055$ •

Cognitive disinhibition					
HAYL_ERR	10-31 (18.33)	5-45 (26.33)	2-36 (15.7)	0.561	
Behavioral disinhibition data					
Disinhibition	0-8 (3)	0-31 (10.17)	0-14 (4.09)	0.776	
Impulsivity	0-1 (0.33)	0-20 (5.17)	0-13 (1.55)	0.508	
Compulsivity	0-7 (2.33)	0-13 (4)	0-9 (1.36)	0.703	
Social disinhibition	0-1 (0.33)	0-2 (1)	0-5 (1.18)	0.495	
Eating behavior data					
EBI, /32	9-22 (13.67)	2-22 (14.5)	1-21 (12.45)	0.61	

Discussion

Here, we provide a method to explore a subject's behavior under ecological settings (a waiting room) in order to contribute to the identification of apathy-like behaviors and thus the characterization of apathy.

in the sense that apathy can be defined as the quantitative reduction of self-generated goal-directed behaviors[14] and characterized in behavioral terms as "an absence of responsiveness to stimuli - internal or external - as demonstrated by a lack of self-initiated action".[12] We design a framework to analyze temporal behavior data during a 7-minute period and use a temporal classification method for behavior time series data analysis. Our results show that bvFTD patients can be classified according to their behavioral kinetics. We do not pretend, at this stage of investigation, that the obtained subgroups show apathy as a multifaceted construct or that the three bvFTD subgroups match the dissociable forms of apathy or domains widely emphasized in the literature. Nevertheless, it remains relevant to further investigate each bvFTD group regarding functional markers of apathetic states. There is evidence in the literature of the multidimensional nature of apathy. Although there has been debate, most experts now consider apathy to be a syndrome and a multifaceted construct divided into separable types of apathy (emotional-affective/motivational, cognitive, autoactivation/behavioral) related to changes in a complex cerebral network of subcortical and cortical territories. However, the identification and characterization of the different components (or different forms of apathy or apathy states) remain open questions in neuroscience. Recently, Dickson & Husain (2022) argued that existing frameworks are not based on empirical evidence of clearly dissociable domains of apathy, but rather on the authors' conceptualizations from the prior literature or observations of patients with neurological conditions[51], and thus the different apathy scales have been constructed, often reflecting the theoretical dimensions of the syndrome that investigators subscribe to. In their opinion, although there is evidence for behavioral and emotional domains of apathy, the contention that there might be a separate dimension of cognitive or executive apathy is far less robust.[51]

In this discussion, we attempt to further characterize each bvFTD group according to manifested apathetic behaviors while considering apathy to be secondary to different neurological and psychiatric disorders (here, bvFTD) and as such "often considered to incorporate some of the features of the related disorder or syndrome".[12]

First, our study shows that the bvFTD patients and HCs behaved differently during the 7 minutes spent in the waiting room. The motor and activity bandplots highlight differences in the way in which the bvFTD patients and HCs organize their motor and activity behavior sequences. Bandplots are an interesting opportunity to visualize all of the raw data synthetically and capture the sequential behavior patterns exhibited by both the bvFTD patients and HCs throughout the period of interest. In the HCs, the temporal organization of activity seemed to reveal a specific pattern in which a short time of exploratory behavior concurrent with walking and standing is followed by a long-term activity (in a sitting position). In the bvFTD patients, the sequence of behaviors seemed to be more erratic and less regular, globally characterized by consecutive walking and standing occurrences until the end of the period, as well as nonactivity, providing a more heterogeneous bandplot. These observed behavioral patterns are consistent with the findings from our previous study,[22] which reported an exploration deficit in bvFTD patients. In this previous work, we analyzed the behavioral data in 14 bvFTD patients and 14 HCs during the 7-minute FP sample session decomposed into three subsample periods. In our analysis, we were interested in measuring how long each behavior from the ethogram (Table 1) lasted in patients versus healthy controls. We showed that, during the very first minutes, when they discovered the room, the bvFTD patients manifested more inactivity and less exploratory behavior than the HC group. Therefore, in the context of facing a new environment, the HCs first explored it and then engaged in sustained activities; in contrast, the bvFTD patients were mostly characterized by inactivity and delayed exploration (they eventually explored this new place, but in a more irregular way than the HCs and several times throughout the free phase). Hence, exploratory behavior deficits under ecological conditions could be a marker of apathy in bvFTD. Moreover, it is interesting to note that exploratory behavior is of considerable interest to many scientists from different domains. First, there is evidence of links between exploration and the environment: "exploration encompasses a wide spectrum of behaviors that are concerned with gathering information about the environment";[52] and exploratory behaviors in mammals have been considered reactions to novel settings.[53] Second, many studies have focused on exploratory behavior throughout the lifespan: 1/in humans, exploration dominates behavior for the first 9 months of life,[54] while 2/ there is a reduction in exploration with aging,[55] and 3/ aging causes a significant decline in open field exploration in rats.[56]

Second, our study confirms that bvFTD patients do not form a homogeneous group and shows that bvFTD patients manifest different behavior patterns under similar conditions. Indeed, our classification ECOCAPTURE kinetics method applied to bvFTD patients allows us to further characterize temporal patterning and, in particular, to investigate behavioral heterogeneity in the group of bvFTD patients. Interestingly, three subgroups of bvFTD patients were identified with different behavioral kinetics and neuropsychological profiles.

FTD1 is a very small group (n = 3) but has the remarkable feature of constituting a group of patients who are similar to one another in respect to their kinetics profile (i.e., activity and motor behaviors). The FTD1 apathetic profile could be inferred from the following elements and the observed patients' behavior features. 1) The patients did not respond appropriately to the people (the examiner's guidelines) and external stimulation around them. Indeed, they were directly involved in an activity (playing games) without considering the environment or without taking the time to explore the room a little beforehand. It is important to note that the table on which the games were placed was located at the entrance of the room, which is one of the first areas of the room with which the subject can interact. Thus, the FTD1 patients presented a deficit in exploration. 2) The FTD1 patients exhibited self-initiated behavior (playing games); and 3) they played games during the whole free phase (the 400-second period). One can thus deduce that the FTD1 patients manifested perseverative activity with an inability to escape from it and shift among other behaviors and activities. This behavior disorder is consistent with the set of core diagnostic criteria for bvFTD, which include perseverative behavior.[4] 4) FTD1 patients present severe cognitive and executive impairment while they do not report themselves as anxious, depressed or apathic. This result is intuitive to suggest that cognitive impairment might be related to the patients' incapacity for rating themselves for behavioral and emotional disorders; therefore, these patients might be more apathetic than they reported. In this case, the caregivers' ratings are lacking to further characterize the severity of apathy. At the level of executive functions, the responses are those that require flexibility, selection, and so on, controlling the more automatic behaviors. When patients present severe cognitive impairment, the outcome is impaired behavior or the absence of behavior.[12] Here, FTD1 was characterized more by a disorder of executive cognitive functioning than by an absence or disorder of self-initiated behavior. Several studies in patients with dementia have shown a significant association between executive dysfunction and more severe apathy.[57]

FTD2 was a group of six patients alternating between activity and exploration, mostly standing (but sitting and walking patterns occurred as well). The FTD2 apathetic profile could be inferred from the following elements and observed patients' behavior features. 1) These patients manifested essentially food and drink related activities, without reading and playing very little. The high prevalence of food and drink related activities is consistent with numerous studies that have shown that bvFTD patients usually have hyperphagia.[58,59] 2) Interestingly, exploration occurred until the end of the free phase, as if the subject could not initiate or maintain an activity (other than food and drink related activity). This form of exploratory behavior can be considered aimless wandering (nonfocused walking with little or no goal) and points to a lack of self-initiated activity in FTD2. Thus, FTD2 can be characterized by disorders related to decreased spontaneous goal-directed behavior, which could correspond either to emotional/affective apathy or to autoactivation/behavioral apathy.[12,14] These goal-directed behavior impairments, such as manifested in aimless exploration, are consistent with the insight provided by behavioral disinhibition measures collected during the ECOCAPTURE testing session. Indeed, FTD2 has a higher average score (no significant) than the others groups on impulsivity and compulsivity. Disinhibition disorders may limit the person's ability to focus on a goal, initiate an activity and sustain it. Interestingly, during the 7-minute FP, FTD2 exhibited the two main types of behavioral disturbances which have been distinguished in bvFTD patients: apathetic and disinhibited manifestation.[3,4,60] 3) Interestingly, the previous behavioral metrics were consistent with the neuropsychological data. Indeed, the FTD2 patients were more apathetic (not significant) on SAS and more depressed and anxious than the other groups (significant). Apathy, depression and anxiety were explored with self-rating scales. Although self-reported data are often discussed as having methodological bias (especially concerning apathy), considering the lack of insight into bvFTD, here, it is interesting to have these three measurements targeting behavior collected in the same way. 4) The FTD2 patients presented severe cognitive disorders (MMSE, mean = 22.83) but moderate executive impairment (FAB, mean = 12.67). It is remarkable to note how much the behavioral and cognitive profile of the FTD2 patients seems to match with the established criteria for bvFTD[4]: apathy (ECOCAPTURE, SAS), cognitive disinhibition (HAYL_ERR), behavioral disinhibition (ECOCAPTURE) and especially impulsivity and compulsivity, global cognitive impairment (MMSE, MATTIS) and executive deficits (FAB), changes in eating behaviour (EBI), and finally a behavior dominated by food or beverage seeking behavior (ECOCAPTURE).

If the clinical picture of bvFTD appears clearly amongst these patients, interpretation of apathy-like behaviors remains remain less obvious. More generally, characterization of apathy remains an open question in neuroscience. Dickson & Husain (2022) highlighted evidence for behavioral and emotional blunting domains of apathy, but questioned the existence of a separate domain of cognitive or executive apathy (i.e., the inclusion of an executive dysfunction as a dimension of apathy)[51]: "Is cognitive apathy a reduction of goal-directed thoughts, or is it more to do with specific problems of executive ability"?

Furthermore, the link between apathy and other disorders is a key point, largely debated in the literature, under several neurological and/or psychiatric conditions and especially in bvFTD.[61,62] In their review about "the nosological position of apathy in clinical practice", Starkstein and Leentjen[63] argued in favor of links between apathy and cognitive impairment, as well as between apathy and depression, and they noted that the syndrome of apathy is most frequent among individuals with neurological disorders and some degree of cognitive impairment and depression. Although apathy can occur in the absence of depression, most studies have shown that a considerable proportion of patients exhibit both apathy and depression,[64] and it is known that depression and apathy usually occur together in neurodegenerative diseases.[65] Our findings are in line with studies and confirm that it is important to continue to investigate and understand links between apathy and depression, as well as between apathy and cognitive impairment.

FTD3 was composed of eleven patients mainly sitting throughout the free phase. The duration of the sitting position was the main common point among all of the FTD3 patients. However, while sitting, some patients read while others were inactive; thus, the group was heterogeneous regarding the level of activity. Surprisingly, all of the FTD3 patients presented another common point, which was relatively preserved and executive cognitive functioning, regardless of the activity level. Indeed, the FTD3 patients presented only mild cognitive and executive impairments, and they had higher cognitive capacity than other patients (FTD3 > FTD1, $p = 0.067$; FTD3 > FTD2, not significant), as well as lower cognitive disinhibition (not significant) than other patients. Moreover, the FTD3 patients rated themselves as apathetic but not depressed or anxious, and they were among the least depressed (FTD3 < FTD2, $p = 0.018$) and anxious patients (FTD3 < FTD2, $p = 0.024$). On this common neuropsychological basis, two different behaviors appeared. First, some FTD3 patients initiated and maintained reading activity for the duration of the free phase. These patients are those (among all 20 patients) whose behavior came closest to the HCs. Indeed, they exhibited the specific behavioral pattern highlighted in HCs in our previous study, in which we showed that, in the context of facing a new environment, HCs first explored it and then engaged in sustained activities [22]. FTD3 neuropsychological features confirm the proximity between FTD3 patients and HCs. Second, the other FTD3 patients sat and exhibited no activity. The key feature of apathy in these FTD3 patients without activity appeared to be relatively preserved cognitive functioning, but an absence of self-initiated activity led to a supposition of flat affect (unconcern) and could correspond to emotional/affective apathy.

Limitations

The present study has some limitations. First, the number of patients was limited; thus, the results remain exploratory. Further studies on a larger sample of bvFTD patients are needed. If confirmed in a larger sample of patients, this method of classification according to the behavior kinetics of individuals with apathy might identify behavioral patterns contributing to the signature symptom of apathy. Second, the behavioral data were collected from the filmed material (videos) by coders using a manual video annotation tool, and this process was very time consuming. Third, the behavioral data collection was based on an ethogram that consisted of the whole set of behaviors exhibited by individuals during a specific period under study. While an exhaustive census of all manifested behaviors might be an objective process, it is not the case when classifying them into specific behavioral categories and especially choosing the behavior units (i.e., level of behavior segmentation) and the most effective scales of analysis to measure behavior. Fourth, regarding the assessment of apathy, caregivers' ratings are lacking to better characterize the severity of apathy and manage the patients' subjectivity and anosognosia. The caregiver's version of the apathy scale should be added to the neuropsychological assessment in future studies. Fifth, regarding the assessment of depression and anxiety, we used the Hospital Anxiety and Depression Scale, which is a screening tool for use in nonpsychiatric patients to identify those with emotional distress,[66] but the HADS is not an interview instrument designed for the diagnosis of depression or anxiety disorders. Thus, the presence of depressive or anxiety symptoms might not be underpinned by a major depressive or anxiety disorder, and when scores >= 10, we cannot conclude that a comorbid depression or anxiety disorder exists without a diagnostic scale; therefore, we only report the number of patients with a score greater than the threshold. To further investigate the links between apathy and depression or anxiety, an interview instrument designed for diagnosis should be added to the neuropsychological assessment in future studies. Sixth, activities of daily living (ADL) as well as instrumental activities of daily living (IADLs) measures might clarify the behavioral profile of these studied patients. The Clinical Dementia Rating scale (CDR)[67] should be added to the neuropsychological assessment in future studies.

Finally, regarding the proposed classification method, we chose a strategy based on distance analysis with convolution, but alternatives could also be considered. For example, Levenshtein's distance is used in genomics, or the Hamming distance between two strings of equal length is used in information theory. These distances (and others) are also available in the *eccptrk* R package and could also be used by the reader on his or her own data. In addition to the choice of distance, other methods of classification could be selected as parameters. Since this paper presents a proof of concept, the related R package was built as flexibly as possible and included customization of convolution parameters (such as window size), various distances and classification algorithms.

Another conceptual approach (not developed in the paper) could have been based on Markov chains to work on the probability of transitions between two behaviors[68,69] and it could be interesting to compare this approach to ours.

4. Perspectives and conclusion

This paper presents a methodology to classify subjects according to their behaviors across time, considering the kinetics (and not only the state durations), and it offers free tools to visualize these behavioral kinetics (curves and bandplots). In the ECOCAPTURE study, the method applied to bvFTD patients showed the existence of three groups of patients and allowed us to investigate the key features of apathetic behaviors manifested in each of the groups, as well as the links between apathy and depression or between apathy and cognitive impairment.

The same type of approach could be conducted to answer other problematics in the ECOCAPTURE project or in any other research study addressing the issue of measuring behavior. For example, other phases (guided) could be analyzed instead of the free phase for bvFTD subject classification; thus, it would allow us to investigate dissociations between self-initiated behaviors and externally guided behaviors. We could further study the behavioral signature of apathy by focusing on other pathologies since apathy is secondary to different neurological and psychiatric disorders. Subjects with other neurological and/or psychiatric pathologies (e.g., depression or Alzheimer's disease) could also be classified according to their behaviors with this strategy. The choice to consider the behavior as a signal opens the door to data fusion, integrating sensor-based data, and particularly the intensity of the acceleration throughout the period studied. Over the past two decades, technological advances in sensing and mobile computing have provided researchers with new ways to collect behavioral data at a fine temporal scale both in and out of the laboratory.[70] Indeed, the use of a 3D accelerometer has been well established for assessing subjects' movements during activities (i.e., actigraphy). In Liu et al.,[71] we described the method and the preliminary results in patients with bvFTD (n=14) matched to HCs (n=14). This actigraphy study aimed to retain some metrics leading to differentiation between patients and control subjects. The data recorded were acceleration in three mutually orthogonal directions with a sample rate of 64 Hz and based on the video analysis during the free phase and the guided phase. We fixed thresholds to determine the amount of time during which the subject showed the fastest acceleration. We showed that, during the guided phase, acceleration in the bvFTD patients was significantly lower than that in the HCs. Furthermore, any other problem of classification according to behavior recorded across time could be conducted with this approach. The approach could easily be adapted to ethograms in animal observation or other human behavioral experimentations. Such approaches could also be applicable to scientific fields other than behavioral studies for classifying subjects, such as sensory analysis or marketing (for evaluating the behavior of consumers across time during the viewing of an advertisement). The attributes would no longer be behaviors but sensory attributes (such as sweet, salted, etc.) or emotions (sad, happy, interested, etc.). These examples of applications are not exhaustive, and we are convinced that the extensive use of recording videos in every scientific field will lead to an increased use of these types of methods. Finally, the clinical applicability seems realistic and feasible, like a rapid clinical test or a path to early diagnosis of apathy, through a short scenario of a few minutes that would take place in a waiting room before the neurological consultation. Moreover this paradigm could be used also in clinical trials and especially to measure change in behavior after therapeutic intervention. Cognitive impairments and behavioral disorders (such as apathy, disinhibition, anxiety, stress, etc.) may be treated with pharmacological interventions as well as a variety of non-pharmacological interventions (NPI). Systematic and literature reviews have identified evidence-based nonpharmacological practices (multisensory stimulation, receptive music therapy, cognitive stimulation) to address these disorders. However, It is still not known what mechanisms are being targeted, but this is necessary to tailor these interventions accordingly and individually to increase the effectiveness of these treatments. Apathy is often targeted with NPI. This paradigm could be used to measure changes in behavior after NPI. What is relevant to determine is whether and to what extent the therapeutical intervention is efficient to reduce apathy and reinforce goal-directed behaviors. Since, complex behaviors and their disorders (e.g., distinction between cognitive and behavioral apathy) are extremely difficult to capture through questionnaires, the most robust way to assess and characterize behaviors (e.g., apathetic-like behaviors) might be through the integration of three tools and approaches: 1) an ethological approach in natural settings and/or lab settings for observation and characterization of behaviors based on detailed ethograms, 2) passive behavioral sensing to collect sensor-based physiological data (e.g., heart rate, skin conductance, acceleration) using wearable sensors, 3) interview and neuropsychological assessment to collect active and subjective data through scales and questionnaire in patients as well as their caregivers (e.g., patient's apathy level, dyadic interaction) .

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Competing interests

The authors report no competing interests.

Data and code availability statement

The preprocessed data (behavioral data coded from video), the ECOCAPTURE metrics (number of occurrences and/or total duration of each behavior during the *7-minute FP* period), and the neuropsychological data that support the findings of this study are available on Mendeley Data [dataset][72] . The ECOCAPTURE ethograms (coding scheme) used for behavioral coding from video are available on Mendeley Data [dataset][40].

All of the functions of the proposed statistical method based on behavioral kinetics were implemented in the dedicated R package *eccptrk* (Ecocapture kinetics) and are available on GitLab [dataset][73]. The R code required to reproduce the results of the paper is also available on GitLab. Therefore, the procedures can be replicated on other datasets.

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Credit Author Statement

Bénédicte Batrancourt: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Data curation, Writing - Original Draft, Visualization, Supervision, Project administration. **Caroline Peltier:** Methodology, Software, Validation, Formal analysis, Data curation, Writing - Original Draft, Visualization. **François-Xavier Lejeune:** Methodology, Software, Validation, Formal analysis, Data curation, Writing - Original Draft, Visualization. **Richard Levy:** Conceptualization, Methodology, Investigation, Resources, Writing - Review &

Editing, Funding acquisition, Supervision, Project administration. **Frédéric Marin:** Writing - Review & Editing, Methodology. **Lars G. T. Jorgensen:** Writing - Review & Editing. **Guilhem Carle:** Resources, Writing - Review & Editing. **Delphine Tanguy:** Resources, Writing - Review & Editing. **Valérie Godefroy:** Data curation, Writing - Review & Editing. **Armelle Rametti-Lacroux:** Resources, Data curation, Writing - Review & Editing. **Raffaella Migliaccio:** Resources, Writing - Review & Editing. **David Bendetowicz:** Resources, Writing - Review & Editing. **Emmanuel Cognat:** Resources, Writing - Review & Editing. **Stéphanie Bombois:** Resources, Writing - Review & Editing.

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