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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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1 Introduction

2 1. Behavioral variant frontotemporal dementia (bvFTD) and apathy

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

14 Traditionally, apathy has been viewed as a symptom indicating loss of interest or emotions.
15 In 1990, in a highly influential conceptual framework, Marin defined apathy as “diminished
16 motivation not attributable to diminished level of consciousness, cognitive impairment, or
17 emotional distress”.⁷ Marin (1991), in his paper entitled “Apathy: a neuropsychiatric syndrome”
18 introduced a major evolution of the concept of apathy. He suggested that neuropsychiatric disorders
19 also produce a syndrome of apathy and proposed diagnostic criteria for the syndrome of apathy
20 (i.e., a syndrome of primary motivational loss, that is loss of motivation not attributable to
21 emotional distress, intellectual impairment, or diminished level of consciousness) on the basis of its
22 distinction from the overt behavioral, cognitive, and emotional concomitants of goal-directed
23 behavior.⁸ However, according Marin (1991), both the symptom and the syndrome of apathy are of
24 conceptual interest. In 2001, Starkstein et al. operationalized Marin’s criteria into a set of diagnostic
25 criteria for apathy,⁹ and on the basis of Marin’s Apathy Evaluation Scale,¹⁰ they designed a
26 simplified 14-item scale (Starkstein Apathy Scale) that can be used with patients and caregivers.¹¹
27 In 2000, Stuss et al. argued that apathy cannot be clinically defined as a lack of motivation because
28 the assessment of motivation is problematic and usually requires inferences based on observations
29 of affect or behavior.¹² They suggested that apathy is best characterized in behavioral terms as “an
30 absence of responsiveness to stimuli - internal or external - as demonstrated by a lack of self-
31 initiated action”.¹² According to the authors, there are many advantages to this definition: (1) it
32 provides objective behavioral measurements; (2) apathy is not a singly definable state or a single

33 syndrome; and (3) apathy can be divided into separable types (states). Stuss’s conceptualization of
34 apathy states (apathetic behaviors) is derived from the model of frontal lobe function developed by
35 Stuss and colleagues.¹³ The authors emphasized: (i) emotional apathy, i.e., lack of concern and
36 limbic affective input as reward sensitivity; (ii) cognitive apathy, i.e., absence of initiated behavior
37 due to executive dysfunction as planning; and (iii) behavioral apathy, i.e., diminished self-initiated
38 actions).¹²

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

60 The assessment and measurement of apathy are crucial in clinical practice, as well as in
61 research settings. Apathy is commonly assessed using a variety of instruments, including diagnostic
62 criteria-based clinical interviews and validated assessment scales, based on patient (self-rated)
63 and/or informant reports.^{16,17} While many apathy scales are available, several limits have been
64 identified. First, these scales are biased by the subjective evaluation of the patient or his or her
65 relatives, and important differences in quotations can be noted between patients and caregivers,¹⁸

66 especially in neurological diseases with anosognosia, such as bvFTD. Second, the psychometric
67 properties of the scales can vary across different populations, and they provide only subjective
68 measurements of the patient's internal state, thoughts and past activities.¹⁷ Finally, although some
69 scales, such as the Dimensional Apathy Scale (DAS),¹⁹ aim to differentiate the different forms of
70 apathy, future research should address the ability to distinguish subtypes of apathy.

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

84 In line with these considerations, in a previous work,²² we built an ecological framework
85 under controlled conditions and a structured scenario (ECOCAPTURE, FRONTlab, ICM) designed
86 to identify and measure behavior and/or behavioral disorders to obtain objective and quantitative
87 measurements for assessing neuropsychiatric symptoms, such as apathy²² and disinhibition,²³ given
88 the limitations in measuring these behaviors using questionnaires and scales administered to
89 patients or caregivers. In this study, we used the ECOCAPTURE protocol to investigate behavior in
90 bvFTD patients under ecological conditions (a waiting room) while they freely explored a novel
91 environment, and we examined individuals performing a continuous stream of behavior (behavior
92 flow) over a 7-minute testing session (a part of the ECOCAPTURE scenario), in order to contribute
93 to the identification of apathy-like behaviors and thus the characterization of apathy.

94

95 **2. Direct behavioral observation and the ethological approach**

96 Ethology, the “biology of behavior”,²⁴ is a scientific discipline stemming from biology that
97 studies the behavior of animals in the natural environment. Human ethology, founded by Eibl-

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

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

120 Sampling decisions are another key point for behavioral data collection, especially with
121 regard to the scheduling of session onsets (e.g., a sample session might be scheduled to begin at a
122 predetermined time) or session terminations (e.g., after a fixed period). *Behavior continuous*
123 *sampling* means that the observer watches the subject and records each occurrence of a particular
124 behavior (and describes the context in which it occurs) for the entire duration of the sample
125 period.³³ The *behavior continuous sampling* method generates accurate frequency and duration data
126 through continuous recording, and it is considered the gold standard method.^{28,34} Another parameter
127 to consider in selecting a sampling method is the duration of the behavior (event or state); indeed,
128 behavior can be regarded either as instantaneous events or as states having an appreciable duration,
129 and this choice depends upon the questions about the behavior of interest.²⁸ Another parameter is
130 the desired scale of measurement (nominal, ordinal, interval, or ratio).³⁴ Thus, the observer records

131 the number of acts or the amount of time for which the behaviors are performed. An alternative
132 method is to record action patterns in the order in which they occur, creating a sequence of events to
133 produce a kinematic diagram. A kinematic diagram (or flow diagram or kinematic graph) provides
134 an excellent overview of behavioral sequences (i.e., the flow of the behavior)³⁵ and is useful for
135 illustrating transitions between behaviors.³²

136

137 **3. Toward a method with behavioral kinetics**

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

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

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

161 In the following, we illustrate some popular classifiers. Two series can be compared either
162 as a vector or by a distance measure (the Euclidian distance calculation to all points in the dataset),

163 but to compensate for potential localized misalignments between series, the classifiers use elastic
164 distance measures. For example, dynamic time warping (DTW, also called elastic matching) is an
165 effective method for measuring the similarity between two time series, which can vary in speed
166 (e.g., similarities in walking could be detected using DTW, even if one person was walking faster
167 than the other). In their review, Bagnall et al.³⁶ claimed that TSC papers in the datamining literature
168 have cited DTW as the benchmark for comparison. The nearest neighbor (NN) classifier assigns a
169 time series to the class of its closest neighbor in the feature space using Euclidian distance. One of
170 the most popular and traditional TSC approaches is the use of an NN classifier coupled with an
171 elastic distance function.³⁸

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

180

181 **Materials and methods**

182 **1. The ECOCAPTURE ethological and ecological approach**

183 **1.1 The ECOCAPTURE paradigm**

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

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

201 **1.2 Cohort and ethics statement**

202 A cohort (ECOCAPTURE) of twenty patients with bvFTD (thirteen men and seven women)
203 and eighteen healthy controls participated in this research. This study is part of the clinical
204 observational study C16-87³⁹ sponsored by INSERM, the *French National Institute for Biomedical*
205 *Research*. It was granted approval by the local Ethics Committee (*Comité de Protection des*
206 *Personnes*, CPP) on May 17, 2017 (CPP 17-31), and was registered in a public clinical trial registry
207 (Clinicaltrials.gov: NCT03272230). All of the study participants gave their written informed
208 consent to participate, in line with French ethical guidelines. This study was performed in
209 accordance with the Declaration of Helsinki. Anonymity was preserved for all participants.

210 **1.3 The ECOCAPTURE scenario**

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

225 We hypothesized that the ECOCAPTURE scenario would be relevant to the study of apathy
226 because it favors the generation of GDB under contrasting conditions and offers many different

227 opportunities to investigate the patient's behavior. We showed in a previous study that the FP is
 228 favorable to the emergence of self-guided behavior and is conducive to exploratory behavior,
 229 allowing us to observe how the participant behaves when discovering a novel environment to which
 230 he or she should adapt.²² This study focuses on the analysis of the self-guided behavior that
 231 individuals develop to accomplish goals or activities during the 7-minute testing session FP. The
 232 GP, as well as the other phases intentionally contrived by the investigators of the ECOCAPTURE
 233 protocol (questionnaire to complete, sound stimuli), are beyond the scope of this paper.



234
 235 **Figure 1. The ECOCAPTURE ecological setting and scenario.**
 236 (A) The waiting room (PRISME, ICM) setup with different areas and specific objects that encourage a
 237 variety of activities. The waiting room has a surface area of 24 m² and is set up with several areas that
 238 encourage a variety of activities. The kitchen area is composed of kitchen furniture, food and drink, a cooler,
 239 a sink and an electric kettle. The sitting area is composed of a sofa with two cushions and two chairs. Games,
 240 such as a puzzle, Kapla, Sudoku, crosswords and a Rubik's cube, are scattered on a table in the center of the
 241 room. In one corner of the room, a furniture (4 drawer units) contains books and magazines, as well as
 242 candies. In the back of the room, a window with the blinds up overlooks the forecourt of the ICM building.
 243 (B) The 45-minute structured scenario ECOCAPTURE with phase onsets (after the examiner intervention)
 244 and phase terminations (after a fixed period). The scenario consists of five phases in the following order: a 7-
 245 minute free phase; a 7-minute free phase with eye-tracking glasses; a 7-minute sound stimulus phase
 246 (positive stimulus such as favorite music); a 10-minute guided phase (devoted to completing the
 247 questionnaire); and a 7-minute sound stimulus phase (negative stimulus such as crackling noise).

248

249 **1.4 The ECOCAPTURE ethogram**

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

267

268 **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.
	<i>Books and magazines</i>	Exploring books and magazines.
	<i>Furniture</i>	Exploring the furniture (4 drawer unit), opening the drawers.
	<i>Kitchen area</i>	Exploring the kitchen area (kitchen furniture, sink, cooler) and food and drink.
	<i>Games</i>	Exploring the games scattered on the table.
	<i>Outside window</i>	Standing by the window and looking outside.
	<i>Without apparent purpose</i>	Moving without apparent purpose.
	<i>Personal object</i>	Exploring or looking for a personal object (glasses, clothes).
	<i>Room</i>	Exploring miscellaneous objects in the room.
	<i>Door</i>	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.
<i>Reading</i>	Reading books or magazines or posters.
<i>Playing games</i>	Playing with games like the puzzle, Kapla, Sudoku, crosswords and the Rubik's Cube.
<i>Food and drink</i>	Food and drink related activities like eating, drinking and drink preparation.
<i>Tidying and cleaning</i>	Tidying the games or books and magazines. Cleaning the kitchen area.
<i>Tuning the radio</i>	Tuning the radio
<i>Space organization</i>	Carrying the tray with food and drink. Pushing or moving an object.
<i>Self-centered action</i>	Self-centered actions like taking on/off clothes, taking on/off glasses.
<i>Miscellaneous</i>	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).

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1.5 The ECOCAPTURE behavior sampling protocol

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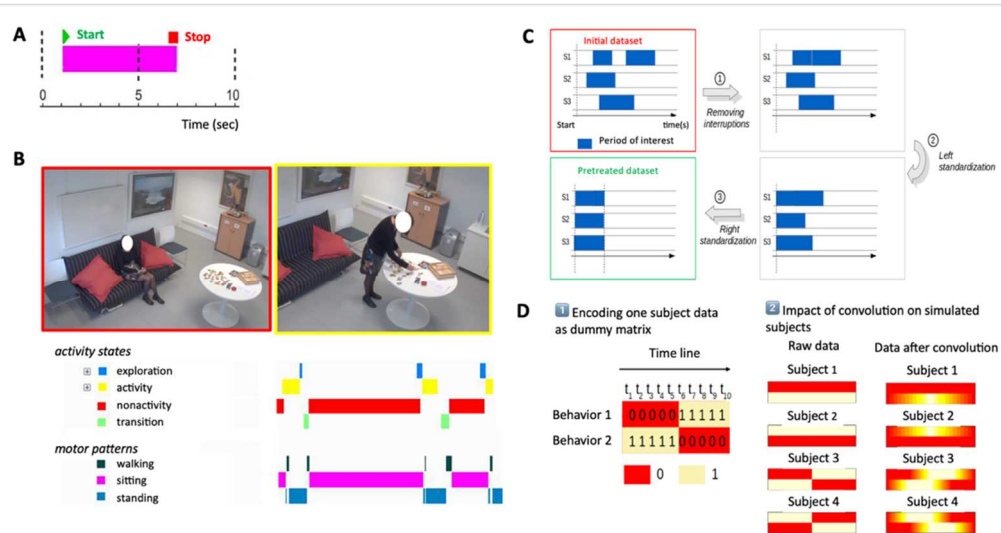
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Behavioral observations were collected through the continuous sampling method and based on the filmed material (videos), as well as the ECOCAPTURE ethogram (Table 1), by coders using a manual video annotation tool (The Observer XT®, NOLDUS Information 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



294

295 **Figure 2. The ECOCAPTURE 7-minute testing session and the preprocessing of the collected**
 296 **behavioral data.**

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

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2. Participants

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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.

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

320

321 **2.1 Neuropsychological assessment**

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

337

338 **2.2 Behavioral disinhibition assessment**

339 In addition to cognitive disinhibition, we investigated behavioral disinhibition, using
340 behavioral disinhibitions metrics, as defined in another part of the ECOCAPTURE protocol, and
341 one of our previous studies.²³ We designed an ethogram of behaviors related to disinhibition in
342 bvFTD, according to the definitions of symptoms by Rascovsky et al.⁴ and to previous relevant
343 studies in the field.^{47,48} We proposed a list of 16 behaviors, divided in three disinhibition categories:
344 *compulsivity* (e.g., repetitive movements), *impulsivity* (e.g., inappropriate action), and *social*
345 *disinhibition* (e.g., familiar behavior towards investigator). See the complete ECOCAPTURE
346 ethogram at Mendeley Data⁴⁰. The number of times a behavior of interest occurs per video during
347 the 7-minute FP sample session was counted in each individual using The Observer (NOLDUS).
348 We summed the occurrences of behaviors within each disinhibition category to obtain the score of
349 *impulsivity*, *compulsivity*, and *social disinhibition*. These scores were then summed together to
350 obtain the global score of *disinhibition*.

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3. Statistical methods

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3.1 Overall

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3.2 Behaviors of interest

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3.3 Comparison of participants' demographic and neuropsychological scores

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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.

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**).

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

384 was set at $p < 0.05$. Characteristics for bvFTD and HC are presented as numbers (percentages) for
385 categorical variables and as the mean (range) and median [interquartile range] for continuous
386 variables, and standard deviations are noted for normally distributed variables.

387

388 **3.4 The statistical method ECOCAPTURE kinetics**

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

398

399 **Data preprocessing**

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

414

415 **Visualization with bandplots**

416 A bandplot is an appropriate tool for visualizing successive changes in subjects' state
417 behaviors across the period of interest. This type of diagram typically applies to a list of exclusive

418 state behaviors belonging to the same behavioral category of the ethogram. A specific color was
419 attributed to each behavior of the list. Then, each subject's ethogram data was represented by a
420 horizontal band with time as the abscissa, colored according to the related behavior manifested at
421 this specific timepoint. Two bandplots were computed through the analysis of the 7-minute FP,
422 adjusted after preprocessing alignment steps, to visualize the preprocessed behavioral data
423 (**behavior sequence** metric). The first was related to the value states (e.g., sitting, walking) from the
424 *motor patterns* behavioral category and is called in this paper the *motor bandplot*; the second was
425 related to the value states (e.g., exploration, nonactivity) from *the activity states* behavioral category
426 and is called in this paper the *activity bandplot*.

427

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

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

446

447 **Choice of a metric to compare two SBMs**

448 A first intuitive method consists of using Euclidean distance between the SBMs (individual
449 dummy matrices). However, with this approach, the distance between two subjects results from a
450 calculation of distance at each time point without considering potential relationships between two
451 successive time points. Consequently, the distance between two subjects exhibiting the same

452 behaviors at different timepoints will be 0, like the distance between two subjects manifesting
 453 different behaviors at all timepoints. This property was not relevant in the context of our study and
 454 constituted a methodological bias since we considered that two subjects exhibiting the same
 455 behaviors were closer than subjects manifesting different behaviors.

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

$$459 \quad (f * g)(n) = \sum_{m=-\infty}^{+\infty} f(m)g(n - m)$$

460 In our case, f was the binary signal for one given behavior (which can be noted as $f(t) =$
 461 $1_{Behavior}(t)$), while we chose g as a rectangular signal of unit height and width $2M$ $[-M, +M]$ (M
 462 being defined in the next section); thus, f and g sequences were padded with 0s (from left or right)
 463 to be defined on \mathbf{Z} , which led to:

$$464 \quad (f * g)(n) = \sum_{m=-M}^M f(n - m) = \sum_{m=-M}^M 1_{Behavior}(n - m)$$

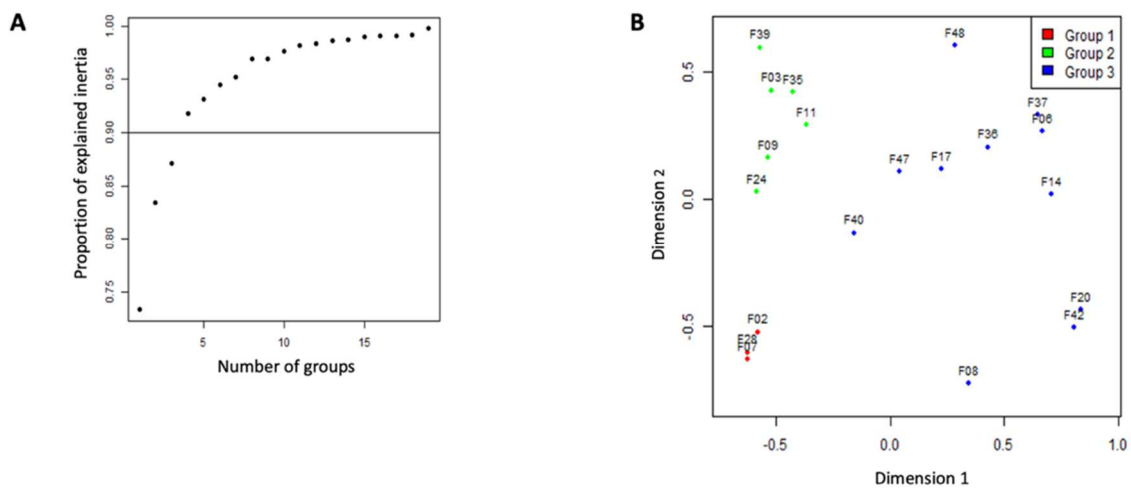
465
 466 Consequently, $f * g$ was the duration of behavior in the time window between $n-M$ and $n+M$.
 467 In other words, it consisted of calculating the duration of behaviors in a selected window moving
 468 across the timeline instead of calculating global frequencies. The size of the convolution window
 469 was chosen with $M = 200$ for a 400-second period. With this choice, all of the signals were covered
 470 by the convolution window. This size was also shown to maximize the discrimination between
 471 bvFTD and HC subjects (results not shown). Each line of the SMBs was convoluted according to
 472 this window, given a convoluted matrix. After convolution, the matrices were no longer composed
 473 of only 0 or 1 but of a duration of behavior in the neighborhood of the function. The final step
 474 consisted of using Euclidean distance on convoluted SMBs.

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

481

482 Patient clustering and characterization of the subgroups

483 From the distance matrix, a hierarchical classification was computed with the Ward D2
 484 method. The number of clusters was determined visually based on the scree plot criterion by
 485 selecting the maximal number from which the gap in accumulated criteria can be seen as less
 486 important (Figure 3A). Then, multidimensional scaling (MDS) was used to visualize on a map the
 487 distances between the subjects with the groups assigned by the classification using the SMACOF R
 488 package⁴⁹. To characterize the different groups, behavioral curves were computed. This procedure
 489 considers each behavior of interest separately. For each time point, the number of subjects
 490 exhibiting this behavior was calculated. Then, these numbers were plotted against time, and a curve
 491 was built per behavior (with potential smoothing). All behavioral curves are depicted on the same
 492 graph with one color per behavior. This procedure was inspired by the temporal dominance of
 493 sensations (TDS) curves in sensory analysis.⁵⁰ Finally, the Kruskal-Wallis test, followed by Dunn's
 494 pairwise test with Bonferroni's correction, was used to compare the neuropsychological scores
 495 between the groups. Boxplots were plotted to visually compare distributions in the groups of
 496 bvFTD patients and HCs.
 497



498 **Figure 3. Patient clustering.** (A) Explained cumulative inertia according to the number of groups. The
 499 black line indicates a limit of 90% of explained inertia, MDS results, Stress = 0.16. (B) MDS map of the
 500 bvFTD patients clustered in 3 groups.
 501

502

503 Results

504 1. Intercoder reliability

505 Intercoder reliability was calculated in a subsample of eight observations. For this
 506 subsample, two different examiners coded the videos. All calculated Cohen's kappa coefficients

507 were greater than 0.98, indicating close-to-perfect agreement between raters and therefore excellent
508 interrater reliability.

509

510 **2. Cohort characteristics and neuropsychological features**

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

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

518 A significant difference was observed for the Starkstein Apathy Scale between the two
519 groups ($p = 1.1e-6$), showing that bvFTD patients (SAS range = 7-25; mean = 15.35) were more
520 apathetic than HCs. Higher SAS scores reflected increased endorsement of apathy in the bvFTD
521 patients. Among the twenty bvFTD patients, fifteen were greater than or equal to the SAS
522 pathological cutoff (14/42), while no HCs were greater than this threshold. The patients were also
523 characterized by significant severity of depressive symptoms and anxiety as measured by the
524 HAD.D ($p = 3.3e-5$) and the HAD.A ($p = 0.005$). The HADS is a screening tool using a severity
525 cutoff for each subscale (HAD.D, HAD.A). A score of $\geq 11/21$ is considered a clinically significant
526 disorder, whereas a score between 8 and 10 suggests a mild disorder⁴⁴. Regarding the HAD.D
527 subscale, among the twenty bvFTD patients, five were greater than or equal to 8, including two
528 patients greater than 10, while no HCs were greater than 3. Regarding the HAD.A subscale, among
529 the twenty bvFTD patients, eleven were greater than or equal to 8, including four patients greater
530 than 10, while only one HC was greater than 8. Moreover, the bvFTD patients presented a
531 significant decrease in global cognitive efficiency, as revealed by the MMSE ($p = 4.1e-7$) and
532 MATTIS ($p = 1.4e-7$), and sharp frontal syndrome, as revealed by the FAB ($p = 2.9e-7$). As
533 expected, the bvFTD patients presented more cognitive disinhibition than the HCs, exhibiting an
534 increased rate of response error ($p = 1e-5$). In the same way, bvFTD patients showed higher
535 *compulsivity* ($p = 0.013$) and *social disinhibition* ($p = 0.018$) than HCs. A significant difference was
536 also observed for the global score of *disinhibition* between the two groups ($p = 0.006$). Finally,
537 bvFTD showed changes in eating behavior compared to the HCs ($p = 1e-6$).

538

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

541 Data are shown as N (%), mean \pm SD (range) or mean (range) and median [IQR]. *IQR* interquartile range,
542 *SD* standard deviation, *YOE* years of education, *MMSE* Mini Mental State Examination, *FAB* Frontal
543 Assessment Battery, *MATTIS* Mattis Dementia Rating Scale (DRS), *SAS* 14-item Starkstein Apathy Scale,
544 *HAD* Hospital Anxiety and Depression Scale, *HAD.D* Depression, *HAD.A* Anxiety, *HAYL_ERR* Hayling
545 error score (number of errors in part B) in the Hayling Sentence Completion Test (HSCT), *Impulsivity*
546 number of occurrences of behaviors within the impulsivity category, *Compulsivity* number of occurrences of
547 behaviors within the compulsivity category, *Social disinhibition* number of occurrences of behaviors within
548 the social disinhibition category, *Disinhibition* global score of disinhibition, *EBI* Eating Behavior Inventory.
549 * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ for significant differences between the bvFTD and HC groups. • $p <$
550 0.1, for trend differences between the bvFTD and HC groups.

551

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

Impulsivity mean \pm SD (range) median [IQR]	2.45 \pm 5.36 (0, 20) 0 [0, 1.25]	0.39 \pm 1.15 (0, 4) 0 [0, 0]	$p = 0.099$	HC < bvFTD *
Compulsivity mean \pm SD (range) median [IQR]	2.3 \pm 4.03 (0, 13) 0 [0, 2.25]	0.11 \pm 0.47 (0, 2) 0 [0, 0]	$p = 0.013$	HC < bvFTD *
Social disinhibition mean \pm SD (range) median [IQR]	1 \pm 1.21 (0, 5) 1 [0, 1.25]	0.28 \pm 0.57 (0, 2) 0 [0, 0]	$p = 0.018$	HC < bvFTD *
<i>Eating behavior data</i>				
EBI, /32 mean \pm SD (range) median [IQR]	13.25 \pm 6.03 (1, 22) 13 [10.75, 17.5]	1.33 \pm 1.91 (0, 7) 0.5 [0, 2]	$p = 1e-6$	HC < bvFTD ***

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3. Behaviors of interest and time budgets

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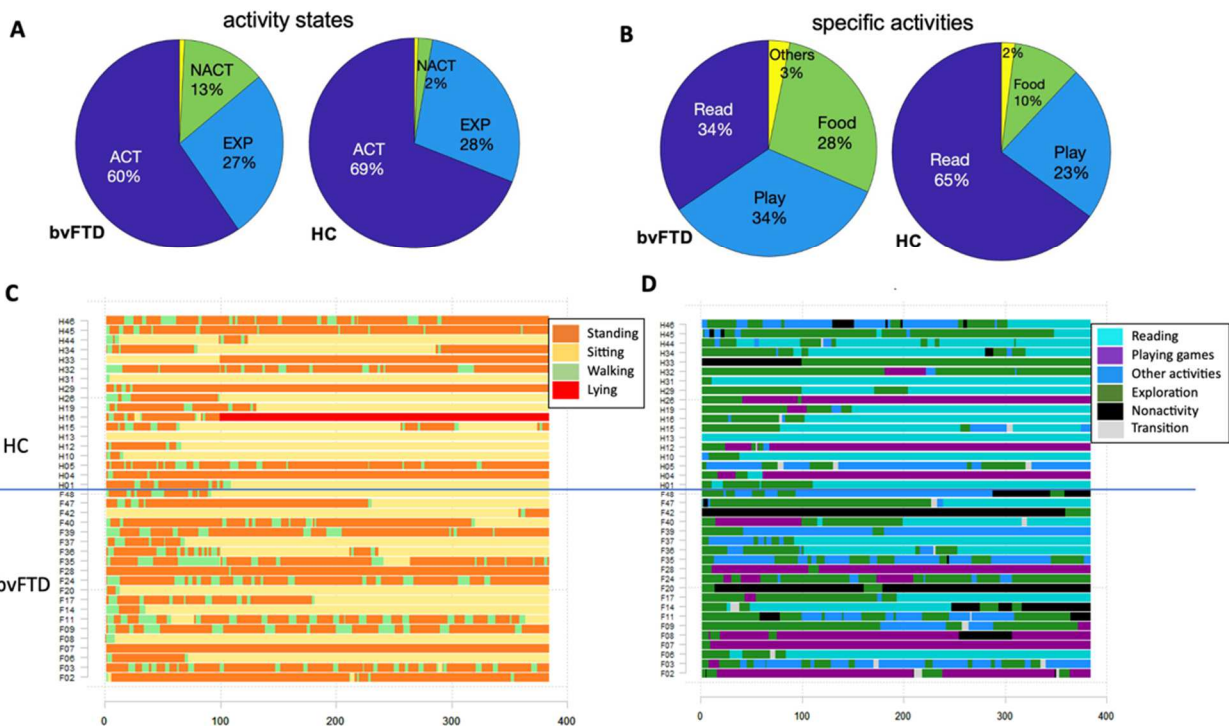
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The behaviors of interest were selected based on the time budgets of the bvFTD patients and the HCs. Figure 4A shows the **time budget** in the bvFTD and HC groups. The bvFTD patients spent more time inactive (13%) than the controls (2%). Both groups 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.



564

565

566 **Figure 4. Subjects' behavior data are presented as time budgets and bandplots.**

567 (A) Time budgets for activity (ACT), exploration (EXP) and nonactivity (NACT) in bvFTD patients and
 568 HCs. (B) Time budgets for reading (Read), playing games (Play), food and drink related activities (Food),
 569 and other activities (Others) as described in the EOCAPTURE ethogram in bvFTD patients and HCs. (C)
 570 Bandplots for motor states of the bvFTD patients (bottom) and HCs (top). (D) Bandplots for activity states of
 571 the bvFTD patients (bottom) and HCs (top).

572

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

575

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.

576

577 **4. Bandplots**

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

589 Figures 4C and 4D show several interesting features of and behavioral patterns in the *motor*
 590 and *activity bandplots*. In the *motor bandplot*, the patients show a high prevalence of walking and

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

601

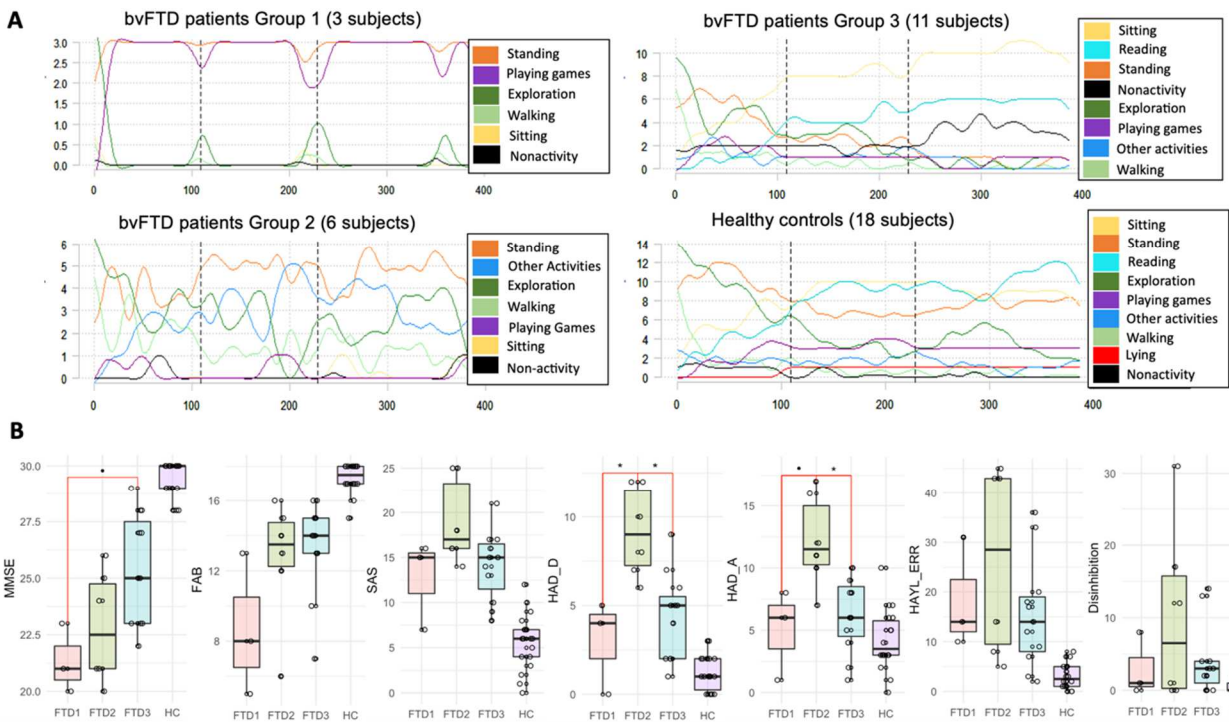
602 **5. Patient clustering and kinetics profiles**

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

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

619 Group 3 consisted of eleven patients mainly sitting and reading or who were not active. The
620 behavioral kinetics of Group 3 showed several interesting features. First, the exploration signal
621 began with a very high value ($n = 10$), but unlike Group 2, the exploration signal gradually
622 decreased until $t = 400$ sec, reaching very low values (1 or 0) from $t = 240$ seconds. The reading
623 activity signal began with the lowest value ($n = 0$) and gradually increased until $t = 250$ seconds,

624 when the waveform signal was flat ($n = 6$). The two signals crossed only once, at $t = 100$ sec.
 625 Second, the nonactivity signal, the waveform of which was flat from the beginning, stood out as the
 626 second highest signal ($2 < n \leq 5$) after the reading signal. Third, concerning the motor pattern, the
 627 sitting signal rapidly increased (from $n = 1$ to 8) until $t = 120$ sec and was maintained at a high level
 628 (from $n = 8$ to 11) until the end, with a flat waveform. The walking and standing signals gradually
 629 decreased and reached low values ($n = 0$ or 1) from $t = 100$ sec and ($0 < n \leq 2$) from $t = 100$ sec,
 630 respectively. Finally, the Group 3 and HC time diagrams were very close, especially with regard to
 631 the exploration and reading signals. However, in the HCs compared to the bvFTD Group 3, the
 632 inactivity signal had a very low level ($0 \leq n \leq 1$), and the standing signal maintained a high level
 633 during the whole 400-second period, close to that of the sitting signal.
 634



635
 636 **Figure 5. Behavioral kinetics and neuropsychological features of the three bvFTD groups.**
 637 (A) Kinetics in the 3 selected groups of bvFTD patients and in the HC group. The time diagrams include the
 638 signal throughout the 400-second FP for each behavior manifested in a particular group. (B) Distribution of
 639 MMSE, FAB, SAS, HAD.D, HAD.A, HAYL_ERR scores (neuropsychological data) and Disinhibition
 640 global score (behavioral *disinhibition data*) in the selected subgroups of bvFTD patients (FTD1, FTD2,
 641 FTD3) and HC.

642

643

6. Neuropsychological profiles of the bvFTD patient subgroups

644 We compared the selected bvFTD subgroups (called in the rest of the paper FTD1, FTD2,
645 FTD3) with demographic, neuropsychological scores, and behavioral disinhibition metrics (Table
646 4). Three neuropsychological variables showed significant differences (with a p value less than
647 0.05) or trend differences (with a p value less than 0.1): MMSE (cognitive impairment), HAD.D
648 (depression) and HAD.A (anxiety). No significant groups differences were found in overall level of
649 cognitive functioning (MATTIS) nor in executive performance (FAB). No significant difference
650 was observed in cognitive disinhibition (HAYL_ERR) between the three groups of patients, nor in
651 behavioral disinhibition (impulsivity, compulsivity, social disinhibition). There was no statistical
652 difference in eating behavior (EBI) between the three groups of patients.

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

660 The FTD2 group seemed to be more apathetic (not significant) than the other groups (Figure
661 5B), and although the statistical test was not significant, FTD2 has a higher average score (mean =
662 19) than FTD1 (mean = 12.67) and FTD3 (mean = 14.09) on the SAS. Among the six FTD2
663 patients, all were greater than or equal to the SAS pathological cutoff (14/42), which was not the
664 case for FTD1 and FTD3. Moreover, FTD2 was more depressed (FTD2 > FTD1, $p = 0.024$;
665 FTD2 > FTD3, $p = 0.018$) on the HAD.D and anxious on the HAD.A than the other groups
666 (FTD2 > FTD3, $p = 0.024$; FTD2 > FTD1, $p = 0.055$). Regarding the HAD.D subscale, among the
667 six FTD2 patients, four were greater than or equal to 8, including two patients greater than 10,
668 while among the three FTD1 patients, all were less than 8, and among the eleven FTD3 patients,
669 only one was greater than 8. Regarding the HAD.A subscale, among the six FTD2 patients, four
670 were greater than or equal to 10, while among the three FTD1 patients, all were less than or equal to
671 8, and among the eleven FTD3 patients, only one was greater than 8. Although no significant
672 difference was observed in cognitive disinhibition, nor in behavioral disinhibition, between the
673 three groups of patients, FTD2 has a higher average score (mean = 26.33) than FTD1 (mean =
674 18.33) and FTD3 (mean = 15.07) on the HAYL_ERR (Figure 5). In the same way, FTD2 has a
675 higher average score (mean = 10.17) than FTD1 (mean = 3) and FTD3 (mean = 4.09) on the
676 disinhibition global score (Figure 5), as well as on impulsivity and compulsivity categories.
677 However, we noted that social disinhibition is almost homogeneous among all patients.

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

688

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

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

700

bvFTD patients	FTD1	FTD2	FTD3	Group effect	
N	3	6	11	Chi ² /Kruskal-Wallis test	
<i>Demographic information</i>					
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)	$p = 0.28$	
				<i>p</i> value	Comparison
<i>Neuropsychological data</i>					
<i>Cognitive functions</i>					
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	
<i>Apathy</i>					
SAS, /42	7-16 (12.67)	14-25 (19)	8-21 (14.09)	0.12	
<i>Depression, Anxiety</i>					
HAD.D, /21	0-5 (3)	6-12 (9.17)	1-9 (4.36)	0.007 **	FTD2 > FTD1, $p = 0.024$ * FTD2 > FTD3, $p = 0.018$ * FTD2 > FTD3, $p = 0.024$ * FTD2 > FTD1, $p = 0.055$ •
HAD.A, /21	1-8 (5)	7-17 (12.17)	1-10 (6.27)	0.013 *	

<i>Cognitive disinhibition</i> HAYL_ERR	10-31 (18.33)	5-45 (26.33)	2-36 (15.7)	0.561	
<i>Behavioral disinhibition data</i>					
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	
<i>Eating behavior data</i>					
EBI, /32	9-22 (13.67)	2-22 (14.5)	1-21 (12.45)	0.61	

701

702

703 Discussion

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

707 in the sense that apathy can be defined as the quantitative reduction of self-generated goal-
708 directed behaviors¹⁴ and characterized in behavioral terms as “an absence of responsiveness to
709 stimuli - internal or external - as demonstrated by a lack of self-initiated action”.¹² We design a
710 framework to analyze temporal behavior data during a 7-minute period and use a temporal
711 classification method for behavior time series data analysis. Our results show that bvFTD patients
712 can be classified according to their behavioral kinetics. We do not pretend, at this stage of
713 investigation, that the obtained subgroups show apathy as a multifaceted construct or that the three
714 bvFTD subgroups match the dissociable forms of apathy or domains widely emphasized in the
715 literature. Nevertheless, it remains relevant to further investigate each bvFTD group regarding
716 functional markers of apathetic states. There is evidence in the literature of the multidimensional
717 nature of apathy. Although there has been debate, most experts now consider apathy to be a
718 syndrome and a multifaceted construct divided into separable types of apathy (emotional-
719 affective/motivational, cognitive, autoactivation/behavioral) related to changes in a complex
720 cerebral network of subcortical and cortical territories. However, the identification and
721 characterization of the different components (or different forms of apathy or apathy states) remain
722 open questions in neuroscience. Recently, Dickson & Husain (2022) argued that existing
723 frameworks are not based on empirical evidence of clearly dissociable domains of apathy, but rather
724 on the authors' conceptualizations from the prior literature or observations of patients with
725 neurological conditions⁵¹, and thus the different apathy scales have been constructed, often
726 reflecting the theoretical dimensions of the syndrome that investigators subscribe to. In their
727 opinion, although there is evidence for behavioral and emotional domains of apathy, the contention
728 that there might be a separate dimension of cognitive or executive apathy is far less robust.⁵¹

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

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

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

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

793 FTD2 was a group of six patients alternating between activity and exploration, mostly
794 standing (but sitting and walking patterns occurred as well). The FTD2 apathetic profile could be
795 inferred from the following elements and observed patients' behavior features. 1) These patients
796 manifested essentially food and drink related activities, without reading and playing very little. The

797 high prevalence of food and drink related activities is consistent with numerous studies that have
798 shown that bvFTD patients usually have hyperphagia.^{58,59} 2) Interestingly, exploration occurred
799 until the end of the free phase, as if the subject could not initiate or maintain an activity (other than
800 food and drink related activity). This form of exploratory behavior can be considered aimless
801 wandering (nonfocused walking with little or no goal) and points to a lack of self-initiated activity
802 in FTD2. Thus, FTD2 can be characterized by disorders related to decreased spontaneous goal-
803 directed behavior, which could correspond either to emotional/affective apathy or to
804 autoactivation/behavioral apathy.^{12,14} These goal-directed behavior impairments, such as manifested
805 in aimless exploration, are consistent with the insight provided by behavioral disinhibition measures
806 collected during the ECOCAPTURE testing session. Indeed, FTD2 has a higher average score (no
807 significant) than the others groups on impulsivity and compulsivity. Disinhibition disorders may
808 limit the person's ability to focus on a goal, initiate an activity and sustain it. Interestingly, during
809 the 7-minute FP, FTD2 exhibited the two main types of behavioral disturbances which have been
810 distinguished in bvFTD patients: apathetic and disinhibited manifestation.^{3,4,60} 3) Interestingly, the
811 previous behavioral metrics were consistent with the neuropsychological data. Indeed, the FTD2
812 patients were more apathetic (not significant) on SAS and more depressed and anxious than the
813 other groups (significant). Apathy, depression and anxiety were explored with self-rating scales.
814 Although self-reported data are often discussed as having methodological bias (especially
815 concerning apathy), considering the lack of insight into bvFTD, here, it is interesting to have these
816 three measurements targeting behavior collected in the same way. 4) The FTD2 patients presented
817 severe cognitive disorders (MMSE, mean = 22.83) but moderate executive impairment (FAB, mean
818 = 12.67). It is remarkable to note how much the behavioral and cognitive profile of the FTD2
819 patients seems to match with the established criteria for bvFTD⁴: apathy (ECOCAPTURE, SAS),
820 cognitive disinhibition (HAYL_ERR), behavioral disinhibition (ECOCAPTURE) and especially
821 impulsivity and compulsivity, global cognitive impairment (MMSE, MATTIS) and executive
822 deficits (FAB), changes in eating behaviour (EBI), and finally a behavior dominated by food or
823 beverage seeking behavior (ECOCAPTURE).

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

831 Furthermore, the link between apathy and other disorders is a key point, largely debated in
832 the literature, under several neurological and/or psychiatric conditions and especially in bvFTD.^{61,62}
833 In their review about “the nosological position of apathy in clinical practice”, Starkstein and
834 Leentjen⁶³ argued in favor of links between apathy and cognitive impairment, as well as between
835 apathy and depression, and they noted that the syndrome of apathy is most frequent among
836 individuals with neurological disorders and some degree of cognitive impairment and depression.
837 Although apathy can occur in the absence of depression, most studies have shown that a
838 considerable proportion of patients exhibit both apathy and depression,⁶⁴ and it is known that
839 depression and apathy usually occur together in neurodegenerative diseases.⁶⁵ Our findings are in
840 line with studies and confirm that it is important to continue to investigate and understand links
841 between apathy and depression, as well as between apathy and cognitive impairment.

842 FTD3 was composed of eleven patients mainly sitting throughout the free phase. The
843 duration of the sitting position was the main common point among all of the FTD3 patients.
844 However, while sitting, some patients read while others were inactive; thus, the group was
845 heterogeneous regarding the level of activity. Surprisingly, all of the FTD3 patients presented
846 another common point, which was relatively preserved and executive cognitive functioning,
847 regardless of the activity level. Indeed, the FTD3 patients presented only mild cognitive and
848 executive impairments, and they had higher cognitive capacity than other patients (FTD3 > FTD1, p
849 = 0.067; FTD3 > FTD2, not significant), as well as lower cognitive disinhibition (not significant)
850 than other patients. Moreover, the FTD3 patients rated themselves as apathetic but not depressed or
851 anxious, and they were among the least depressed (FTD3 < FTD2, p = 0.018) and anxious patients
852 (FTD3 < FTD2, p = 0.024). On this common neuropsychological basis, two different behaviors
853 appeared. First, some FTD3 patients initiated and maintained reading activity for the duration of the
854 free phase. These patients are those (among all 20 patients) whose behavior came closest to the
855 HCs. Indeed, they exhibited the specific behavioral pattern highlighted in HCs in our previous
856 study, in which we showed that, in the context of facing a new environment, HCs first explored it
857 and then engaged in sustained activities [22]. FTD3 neuropsychological features confirm the
858 proximity between FTD3 patients and HCs. Second, the other FTD3 patients sat and exhibited no
859 activity. The key feature of apathy in these FTD3 patients without activity appeared to be relatively
860 preserved cognitive functioning, but an absence of self-initiated activity led to a supposition of flat
861 affect (unconcern) and could correspond to emotional/affective apathy.

862

863 **Limitations**

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

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

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

901

902 **4. Perspectives and conclusion**

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

909 The same type of approach could be conducted to answer other problematics in the
910 ECOCAPTURE project or in any other research study addressing the issue of measuring behavior.
911 For example, other phases (guided) could be analyzed instead of the free phase for bvFTD subject
912 classification; thus, it would allow us to investigate dissociations between self-initiated behaviors
913 and externally guided behaviors. We could further study the behavioral signature of apathy by
914 focusing on other pathologies since apathy is secondary to different neurological and psychiatric
915 disorders. Subjects with other neurological and/or psychiatric pathologies (e.g., depression or
916 Alzheimer's disease) could also be classified according to their behaviors with this strategy. The
917 choice to consider the behavior as a signal opens the door to data fusion, integrating sensor-based
918 data, and particularly the intensity of the acceleration throughout the period studied. Over the past
919 two decades, technological advances in sensing and mobile computing have provided researchers
920 with new ways to collect behavioral data at a fine temporal scale both in and out of the laboratory.⁷⁰
921 Indeed, the use of a 3D accelerometer has been well established for assessing subjects' movements
922 during activities (i.e., actigraphy). In Liu et al.,⁷¹ we described the method and the preliminary
923 results in patients with bvFTD (n=14) matched to HCs (n=14). This actigraphy study aimed to
924 retain some metrics leading to differentiation between patients and control subjects. The data
925 recorded were acceleration in three mutually orthogonal directions with a sample rate of 64 Hz and
926 based on the video analysis during the free phase and the guided phase. We fixed thresholds to
927 determine the amount of time during which the subject showed the fastest acceleration. We showed
928 that, during the guided phase, acceleration in the bvFTD patients was significantly lower than that
929 in the HCs. Furthermore, any other problem of classification according to behavior recorded across
930 time could be conducted with this approach. The approach could easily be adapted to ethograms in

931 animal observation or other human behavioral experimentations. Such approaches could also be
932 applicable to scientific fields other than behavioral studies for classifying subjects, such as sensory
933 analysis or marketing (for evaluating the behavior of consumers across time during the viewing of
934 an advertisement). The attributes would no longer be behaviors but sensory attributes (such as
935 sweet, salted, etc.) or emotions (sad, happy, interested, etc.). These examples of applications are not
936 exhaustive, and we are convinced that the extensive use of recording videos in every scientific field
937 will lead to an increased use of these types of methods. Finally, the clinical applicability seems
938 realistic and feasible, like a rapid clinical test or a path to early diagnosis of apathy, through a short
939 scenario of a few minutes that would take place in a waiting room before the neurological
940 consultation. Moreover this paradigm could be used also in clinical trials and especially to measure
941 change in behavior after therapeutic intervention. Cognitive impairments and behavioral disorders
942 (such as apathy, disinhibition, anxiety, stress, etc.) may be treated with pharmacological
943 interventions as well as a variety of non-pharmacological interventions (NPI). Systematic and
944 literature reviews have identified evidence-based nonpharmacological practices (multisensory
945 stimulation, receptive music therapy, cognitive stimulation) to address these disorders. However, It
946 is still not known what mechanisms are being targeted, but this is necessary to tailor these
947 interventions accordingly and individually to increase the effectiveness of these treatments. Apathy
948 is often targeted with NPI. This paradigm could be used to measure changes in behavior after NPI.
949 What is relevant to determine is whether and to what extent the therapeutical intervention is
950 efficient to reduce apathy and reinforce goal-directed behaviors. Since, complex behaviors and their
951 disorders (e.g., distinction between cognitive and behavioral apathy) are extremely difficult to
952 capture through questionnaires, the most robust way to assess and characterize behaviors (e.g.,
953 apathetic-like behaviors) might be through the integration of three tools and approaches: 1) an
954 ethological approach in natural settings and/or lab settings for observation and characterization of
955 behaviors based on detailed ethograms, 2) passive behavioral sensing to collect sensor-based
956 physiological data (e.g., heart rate, skin conductance, acceleration) using wearable sensors, 3)
957 interview and neuropsychological assessment to collect active and subjective data through scales
958 and questionnaire in patients as well as their caregivers (e.g., patient's apathy level, dyadic
959 interaction) .

960

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969

970 **Competing interests**

971 The authors report no competing interests.

972

973 **Data and code availability statement**

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

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

983

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990

991 **Credit Author Statement**

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1006

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