Exploring the eye dynamics and rest-activity rhythm and patterns of individuals living with dementia in home settings.
Assessment of ability to interact with the environment and its implications for goal-directed behaviors.

Context and scientific justification
As age stands out as the primary risk factor for most forms of dementia, the growing elderly population implies a rise in prevalence in the number of individuals affected by dementia. Dementia is characterized by cognitive deficits alongside behavioral and psychological symptoms of dementia (BPSD). The majority of individuals with dementia will develop BPSD during their disease [1]. Alzheimer's disease (AD) and behavioral variant frontotemporal dementia (bvFTD) are two forms of dementia that very often are accompanied by severe BPSD. Among these BPSD, apathy is the most prevalent and disabling non-cognitive symptom of dementia, affecting up to 60% of AD and 84% of bvFTD patients [2]. Apathy, defined as the quantitative reduction of voluntary goal-directed behaviors [3], is also indicative of cognitive decline and predicts a loss of autonomy in activities of daily life (ADL). There is also a heavy burden on caregivers of patients living with dementia that is associated with BPSD presence and intensity [4]. However, diagnosing BPSD, such as apathy, remains challenging, as it heavily relies on the introspective capacity of individuals through questionnaires, given that these patients commonly present anosognosia. As such, to accurately measure apathy, we require a more reliable way of characterizing behavior. Actigraphy studies have started exploring the capabilities of mobile technologies (e.g., sensors), which provide objective, frequent, real-world assessments of individuals [5]. **Among these emerging technologies, eye tracking stands out as a promising tool that can provide an additional perspective on ocular dynamics and patient's behavior. This, in turn, can reveal their ability to navigate and engage with the environment, showcasing efficient and tailored goal-directed behaviors.** Generally, studies of people's behavior in home settings consider the accelerometer-measured rest–activity rhythm (RAR), its patterns and amplitude as relevant clinical biomarkers [6]. RAR is one of the most prominent outputs of the circadian system since circadian disruption impacts sleep, health, and well-being. Complementary, qualitative and subjective reports are collected using ecological momentary assessment (EMA). EMA involves repeated sampling of subjects' current behaviors and experiences in real-time, in natural environments [7], using questionnaires and diaries, often integrated within a mobile application.

Hypothesis: Combining novel multimodal sensing, ecological momentary assessment, and cerebral imaging with machine learning models will allow the development of a toolbox for objective monitoring and quantification/characterization of apathy in bvFTD and AD, within the natural home environment.

Scientific questions
(1) How can robust apathy detection and quantification be achieved and individualized for diverse individuals living with dementia, using sensors (accelerometer, eye-tracking) and EMA? **(2)** How do these behavioral and physiological markers correlate with cerebral imaging to identify the neural basis of apathy?

Scientific objectives
Objective 1: Monitoring objective markers of apathy using continuous multimodal sensing. Sensors, featuring accelerometers, seamlessly enable continuous measurement of the rest–activity patterns in large populations without disruption to individual daily routines [7]. Crucial to health, rest–activity patterns encompass fundamental human behaviors such as physical activity, sleep, and RAR. The ongoing advancements in monitoring these patterns not only ensure a comprehensive understanding of daily life but also pave the way for exploring the association of behavioral markers of apathy, including activity level, sleep quality, and emotional arousal. **The additional incorporation of eye-tracking technology is expected to provide clarity on these markers of apathy and broader behavioral disorders such as exploration deficit and, more generally, a lack of interaction with the environment.** Previous research by the host team in a laboratory setting highlighted the exploration deficit as a marker of apathy in bvFTD [8] and demonstrated that apathetic patients have a decrease in eye saccade frequency, which is reflective of their exploration deficit [9]. Utilizing eye-tracking technology, our study will deeply investigate the ocular dynamics that are unique to specific forms of apathy within the natural home environment. Our study will be unique because it will be the first study to explore these eye dynamics in their natural environment, potentially paving the road for the utilization of eye movements in the diagnostic process. By deepening our understanding of these disorders, our focus shifts to unraveling their impact on purposeful behavior, especially the absence of exploratory behavior. Our current proposal seeks to elucidate the intricate ways in which these disorders culminate in a decline of the patient's autonomy in ADL - **an outcome commonly termed dependence, which is a public health concern.**

__Objective 2:__ **Developing an automated analysis approach for extracting personalized digital biomarkers of apathy.** With this data, we hypothesize that we can extract objective digital biomarkers that can differentiate between episodes with and without apathy and models that quantify the severity of apathy. Those analytic approaches need to be personalized based on the data of the individual patient.

__Objective 3:__ **Clarify the neural bases of apathy - and its various forms - in bvFTD and MA.** The final objective will focus on presenting neuroimaging evidence pertinent to apathy, specifically striving to pinpoint the functional neural networks affected. **Connectivity and functional networks are impacted by bvFTD, and AD.** Large-scale brain network analysis has been widely used to understand brain dysfunction across neurologic disorders. Among the large-scale brain networks, the dorsal attention network (DAN) is centered on the frontal eye field (FEF) and intraparietal sulcus (IPS) and is involved in goal-directed top-down attention/behavior [10]. Because of these implications, there is an interest in merging the sensor-based data with the supplementary cerebral data to better precise the behavioral profile of the patient. **These results will also allow us to explore the link between the functional networks and apathy and goal-directed behavior, contributing to the existing literature exploring how connectivity networks are impacted by bvFTD and AD.**

Suitability of the project for the ICM - Information on the role of each supervisor and the scientific expertise provided: Since 2017, the FrontLAB at ICM has been leading the ECOCAPTURE research program (PIs: Dr. Bénédicte Batrancourt, Pr. Richard Levy), focusing on assessing apathy and disinhibition in ecological conditions using video and sensors [8, 9, 11, 12]. In 2022, this project expanded its investigation to at-home settings with ECOCAPTURE@HOME; utilizing wrist-worn sensors, the study aims to identify behavior markers of apathy through sensor-based data collected over a 28-day period [13]. The ECOCAPTURE@HOME study plans to recruit a total of 60 dyads (the patient and their partner) between 40 and 85 years old divided into three groups: bvFTD, AD, and healthy controls (HC). Both Dr. Batrancourt and Pr. Levy have extensive expertise with research into BPSD of dementia. We firmly believe that to be able to optimize the prevention and treatment of these symptoms, we first need to identify objective and quantifiable tools to measure them. In this way, we present a relevant collaboration for this study. Specifically, Dr. Batrancourt is a research engineer with expertise in measuring behavior using sensors under ecological conditions. Pr. Levy is a clinical neurologist with expertise in apathy in dementia. Pr. Levy is also the director of the Behavioral Neuropsychiatry Unit (UNPC), and of the Institute of Memory and Alzheimer's Disease (IM2A), Pitié-Salpêtrière Hospital, Paris.

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