Multimodal monitoring of cognitive and behavioural changes in patients living with dementia - Optimising the creation of a global therapeutic home environment

Context and scientific justification: According to the World Health Organization (WHO), there are currently more than 55 million people living with dementia. With the demographic shifts in the global population, marked by both growth and ageing, the number of new cases of dementia is predicted to increase exponentially. Dementia has devastating impacts on patients and their families as well as a negative economic effect. The economic burden was accounted for in 2019 to reach 1.3 trillion US dollars, half of which was paid by caregivers [1]. Dementia is responsible for major disabilities in everyday life [2] and negatively impacts patients' autonomy. **This loss of autonomy largely stems from Behavioural and Psychological Symptoms in Dementia (BPSD)** including apathy, depression, anxiety, delusions, hallucinations, disinhibition, sleep-wake cycle disturbances, and other inappropriate behaviours [3]. Over 90% of all dementia patients display BPSD over the course of their illness [3], which in turn are associated with cognition deficits and progression of disease [4]. Loss of motivation, or apathy, contributes significantly to caregiver burden [3, 5], and has a negative impact on prognosis, institutionalisation, and poorer life expectancy [4]. Despite mounting interest in BPSD in dementia, **we currently lack reliable approaches to accurately quantify the nature and extent of these changes, and to evaluate the clinical staging of these disturbances in the home setting.** The most common cause of dementia is Alzheimer's disease (AD), followed by frontotemporal dementia (FTD) [6]. In this project, we focus on **two BPSD symptoms – apathy and anhedonia - which are directly linked to a motivation deficit that significantly impacts patients' autonomy.** Apathy involves reduced voluntary goal-directed behaviour [7] while anhedonia is characterised by a decreased ability to experience and to pursue pleasure [8]. Assessment of patients' behaviour via a carer report is often subjective. Laboratory settings provide more objective and detailed information but their methodology is often divorced from everyday scenarios in which these behaviours manifest. Studies examining apathy and anhedonia at home are extremely scant or nonexistent. We recently demonstrated that BPSDs can be assessed in a more natural environment like the patient's home using remote monitoring [9]. Our proposed study, part of the ECOCAPTURE@CARE project, aims to monitor patients, track BPSD evolution and provide vital insights for symptom management.

Hypothesis: Combining behavioural sensing and environmental sensing, and ecological momentary assessment, with machine learning models, we will develop a toolbox for: 1/ objective monitoring and quantification/characterisation of behavioural changes in individuals; 2/ facilitate goal-directed behaviours in activities of daily living (ADLs). Ultimately the data collected will be used to improve patients' autonomy and caregiver self-efficacy, and extend ageing in place.

Scientific questions : 1/ How do we as a global community deliver quality care to people with dementia both in the home and aged care setting? **2/** How can we accurately quantify the nature and extent of BPSD across different clinical stages of dementia? **3/** How can we facilitate patients' goal-directed behaviours in activities of daily living, and improve caregivers' self-efficacy? **4/** What will be the outcomes of the ECOCAPTURE@CARE project? What will be the positive impacts for the patient, the global care community, and the society?

Scientific objectives:

Objective 1: Continuous, behavioural and environmental sensing to characterise and differentiate apathy and anhedonia. The ECOCAPTURE@CARE project will span two sites: Paris and Sydney uniting two major centres of FTD research, Paris Brain Institute (ICM) in Paris and Brain and Mind Centre in Sydney, to develop novel strategies to assess apathy and anhedonia. The first objective is to implement analyses to characterise and differentiate apathy and anhedonia from multimodal sensor-based data (body-worn and in-home sensors) and Ecological Momentary Assessment (EMA). The main outcomes will include: 1/ Improved characterisation of BPSD at the individual patient level, 2/ Measures and the control of responses to novel events or medication,3/ Evaluation of the effectiveness of our proposed global therapeutic home environment.

Objective 2. Setting up and optimising the creation of a global therapeutic home environment, providing non-pharmacological intervention (NPI) for apathy and anhedonia. As of today, there are no effective treatments for dementia nor for apathy and anhedonia. The ECOCAPTURE@CARE project will tackle this issue by designing a novel therapeutic program and environment at home. We will adopt a two-tiered approach: **1/ modifying the non-human environment,** by proposing an adapted environment (structured and simplified environment with presence of visual, light, sound indicators, etc.) to facilitate goal-directed behaviours and autonomy. The operational objective is to reduce reactive behaviours and to allow subjects to interact more easily with their environment to carry out activities of

daily living; **2/ modifying the human environment** by training the caregivers to improve their awareness and responses to behavioural disturbances. We will test intervention effects on patients' autonomy in ADLs and caregivers' quality of life and sense of burden.

Objective 3. Set up an online platform where BPSD information is housed to give access to families and the care community to disease information for monitoring and detecting changes across the disease trajectory. The realisation of this study requires the identification of a comprehensive database of valuable information about the patient. Thanks to this database and using machine learning techniques, we can personalise intervention approaches tailored to the individual, and predict long-term prognosis. This platform can also give caregivers key information to interpret and respond to patients' behaviours.

Suitability of the project for the Paris Brain Institute (ICM) and the University of Sydney. Information on the role of each supervisor and the scientific expertise provided. Since 2017, the FrontLAB at ICM has led the ECOCAPTURE research program (PIs: Dr. Bénédicte Batrancourt, Pr. Richard Levy), focusing on assessing apathy and disinhibition in ecological conditions using video and sensors [9, 13]. Expanding its investigation to at-home settings with ECOCAPTURE@HOME, the study aims to identify behaviour markers of apathy and disinhibition through sensor-based data collected over a 28-day period [10]. Simultaneously, the MIND lab (Director: Pr. Muireann Irish) in the Frontier research group at Sydney specialises in the assessment of anhedonia in dementia. The MIND group was the first to demonstrate that anhedonia is an early and prominent feature in FTD [11, 12] with major impacts on patients' autonomy. Both Dr. Bénédicte Batrancourt and Pr. Muireann Irish have extensive expertise with research into BPSD. We believe that identifying monitoring tools is crucial for optimising BPSD prevention and treatment. Our collaboration represents a significant step toward this goal. Specifically, Dr. Bénédicte Batrancourt is a research engineer with expertise in measuring behaviour using sensors, and digital biomarkers of BPSD; Pr. Muireann Irish is Professor of Cognitive Neuroscience specialising in the cognitive and behavioural changes in dementia. She is an NHMRC Professorial Fellow, the director of the MIND research group, and the past president of the Australasian Cognitive Neuroscience Society. The student candidate, Julie Behenska is Sorbonne Université graduate with a master's degree in Integrative biology and physiology, specialised in behavioural and cognitive neuroscience. During her last internship, she studied motivational disturbances in FTD within the MIND research group.

References

1. Organization, World Health. WHO. WHO Dementia. [Online] March 15, 2023. https://www.who.int/news-room/fact-sheets/detail/dementia.
2. Piguet O., Hornberger M., Mioshi E., Hodges J. R., Behavioural-variant frontotemporal dementia: Diagnosis, clinical staging, and management. 2, 2011, The Lancet Neurology, Vol. 10, pp. 162–172.
3. Cerejeira J., Lagarto L., Mukaetova-Ladinska E., Behavioral and Psychological Symptoms of Dementia. 3, 2012, Frontiers in Neurology, Vol. 7, p. 73.
4. Ismail Z., …, Miller D., Lyketsos C. G., Neuropsychiatric symptoms as early manifestations of emergent dementia: Provisional diagnostic criteria for mild behavioral impairment. Alzheimer's & Dementia (2015).
5. Wong C. C., Wallhagen M. I., The impact of patient behavioral symptoms on the physical and mental health of family caregivers. 1, 2012, Dem Geriat Cogn Dis, Vol. 2, pp. 516-28.
6. Fieldhouse J.L.P., et al., Clinical Phenotypes of Behavioral Variant Frontotemporal Dementia by Age at Onset. 2021, Journal of Alzheimer's Disease, pp. 1-10.
7. Levy R., Dubois, B., Apathy and the Functional Anatomy of the Prefrontal Cortex-Basal Ganglia Circuits. 7, 2006, Cerebral Cortex, Vol. 16, pp. 916–928.
8. Husain M., Roiser, J. P., Neuroscience of apathy and anhedonia: A transdiagnostic approach. 8, 2018, Nature Reviews Neuroscience, Vol. 19, pp. 470–484.
9. **Batrancourt B**, Lecouturier K, …, Rametti-Lacroux A, Dubois B, Levy R., Exploration Deficits Under Ecological Conditions as a Marker of Apathy in Frontotemporal Dementia. s.l. : Front Neurol, 2019.
10. Godefroy V., Levy R., …, **Batrancourt B.**, ECOCAPTURE@HOME: Protocol for the Remote Assessment of Apathy and Its Everyday-Life Consequences. 15, 2021, Int J Environ Res Public Health, Vol. 18, p. 7824.
11. Shaw S. R., …, Piguet O., Whitton A. E., **Irish M.**, Anhedonia in semantic dementia—exploring right hemispheric contributions to the loss of pleasure. 8, 2021, Brain Sciences, Vol. 11, p. 998.
12. Shaw S. R., …, Piguet O., Ahmed R. M., Whitton A. E., **Irish M**., Uncovering the prevalence and neural substrates of anhedonia in frontotemporal dementia. 5, 2021, Brain, Vol. 144, pp. 1551–1564.
13. Tanguy, D., **Batrancourt, B.**, …, Levy, R., Migliaccio, R., ECOCAPTURE study group. (2022). An ecological approach to identify distinct neural correlates of disinhibition in frontotemporal dementia. Neuroimage Clin.