Alzheimer's Disease (AD) Detect & Prevent – presymptomatic AD detection and prevention

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Abstract: Alzheimer's disease (AD) is a major cause of the rapidly growing and crushing aging challenge that threatens to economically undermine today's healthcare system. AD prevalence will grow to over 100 million cases in 2050. AD is incurable but can be prevented. Therefore, the most viable solution may be to detect very early signs of AD (presymptomatically) in citizens-at-risk and to intervene in time to reduce AD risk or prevent it entirely. The present project will refine and validate two breakthrough innovations for AD detection and AD prevention and commercialize them as a one-stop digital medical device, named 'AD Detect & Prevent'. The first innovation is a highly sensitive cognitive assessment method recently pioneered by a group of researchers that has been shown to detect subtle presymptomatic stage cognitive decline specific to AD. This will be integrated with the second innovation – a digital AD prevention programme delivered on an award-winning computerized cognitive training and rehabilitation platform (app + web) that uses high intensity immersive and adaptive 'neurogames' and audio-based therapy for behavioural intervention, designed for strengthening core cognitive functions, building cognitive reserve, changing lifestyle and thus reducing the overall AD risk in individuals. The detection and prevention methods will undergo vigorous scientific validation, and the ambition is to create and become the global standard of care for precise presymptomatic detection of AD and effective AD prevention.

Keywords*: Alzheimer's disease, presymptomatic, detection, prevention*

Introduction

To date, AD is incurable. However, scientific studies indicate that 1/3 of all AD cases could be prevented if effective interventions happen before disease onset (Barnes et al., 2009). This is significant because a 5-year onset delay could result in 41% lower prevalence by 2050 (Zissimopoulos, Crimmins, & St.Clair, 2014). Therefore, timely detection of AD is key. However, the main challenge in early AD detection today is that current methods are unable to detect the earliest signs of cognitive changes that are so subtle that both the individual and standardized clinical neuropsychological assessments are unable to pick up before the symptomatic phase, thus delaying detection by decades (Rajan, Wilson, Weuve, Barnes, & Evans, 2015). The present project discovered groundbreaking innovations to address these challenges of AD and aims to deliver an integrated AD solution that offers presymptomatic detection and effective prevention.

In respect of presymptomatic AD detection, recently, a group of researchers at the University of Oxford developed a set of highly sensitive cognitive tests of working memory (WM, one of the first cognitive domains to be affected in early-stage AD) that can identify individuals highly susceptible to developing AD but are currently free of clinical symptoms (Liang et al., 2016). These cognitive detection tests will be gamified and further validated in the present project. In the short term, this detection method can be used in high-risk population segments where the need is the most acute. If this detection method is applied to high AD risk individuals and the aging population at scale in the long term, it could hold a tremendous potential for enabling prevention and slowing the progression of AD in early-stage patients.

In terms of presymptomatic AD prevention, a well-established, novel and innovative digital platform designed for computerized cognitive training and neurorehabilitation has been shown to be able to create significant cognitive and behavioural improvements in various population segments. It could be an effective way to prevent or delay AD onset since scientific studies have documented the great potential for preventing AD using these methods (Paillard, Rolland, & de Souto Barreto, 2015; Shah, 2013).

Integrating presymptomatic AD detection and prevention into a specialized ‘AD Detect-Prevent’ solution that targets populations-at-risk and elderlies could have a massive impact on the population-wide outlook for AD trajectory (Zissimopoulos et al., 2014). In practice, offering the solution in an easily accessible and user-friendly digital app and web format makes it highly scalable.

The integrated ‘AD Detect-Prevent’ solution will subsequently undergo empirical and clinical validation. Three vigorous behavioural and neuroimaging studies are designed to examine the precision and validity of the AD detection tool, and the efficacy of the AD prevention programme.

Description of design proposal

Scientifically, at the heart of the proposed AD solution is a 'graded' cognitive assessment test named the 'what was where' task (Figure 1) (Liang et al., 2016). It is based on the principle that humans experience the world in a 'graded' rather than dichotomous manner. The 'graded' model and method of assessing WM has received much solid scientific support and demonstrated that it is a more sensitive indicator of AD than standardized clinical tests. When gamified and integrated into a well-established digital platform, this assessment method will become universally available and offers an affordable and validated tool to aid presymptomatic AD detection.

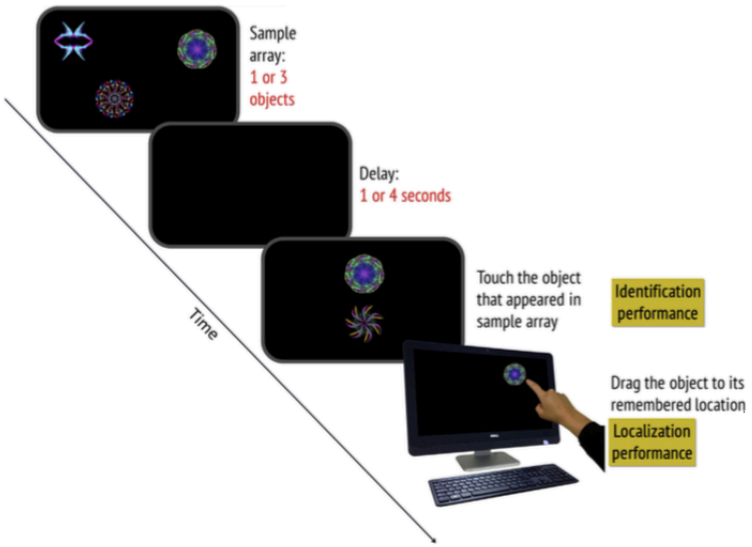

Figure 1 The 'what was where' task where one or three fractals are presented on a touchscreen, after a variable delay one of the items returns with a foil. Participants touch the item they recall and drag it to its remembered location. Using this task, researchers discovered that while performance on item identification and location recall was comparable, misbinding errors/swaps were increased in asymptomatic carriers of amyloid precursor protein gene mutation compared to age-matched controls without the gene mutation. Reprinted from "Visual short-term memory binding deficit in familial Alzheimer's disease", by Liang, Y., Pertzov, Y., Nocholas, J. M., Henley, S. M. D., Crutch, S., Woodward, F., Husain, M. (2016), *Cortex, 78,* 150-164.

The technical product foundation of the proposed solution is a digital platform, designed for cognitive training and rehabilitation. The platform uses high intensity immersive, personalized neurogames and audio-based digital therapy for behavioural modifications, and it is designed to strengthen core cognitive functions, build cognitive reserve and change unhealthy lifestyle. These activities are packaged into easy-to-follow programmes and a highly intuitive user interface (Figure 2). During the project, the 'graded' cognitive assessment methods will be gamified and integrated into the digital platform. Based on each user's assessment outcome, a tailored AD prevention programmes will subsequently be offered. They are highly personalized

and intensive, exercise multiple cognitive domains simultaneously, are highly motivating and engaging, and are continuously adaptive as training progresses.

Figure 2 Illustrations of the digital platform based on which the integrated AD detection and prevention solution will be delivered.

Complementary data description

Complementary data submitted consists of illustrations of the digital platform and its existing neurogames.

Technical information for exhibition

The solution to be exhibited at the conference will be presented on a tablet (even though the solution is also available on smartphones and via the web).

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