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Mini Review

The Significance of Early Identification and Timely Intervention for People at Risk of Developing Alzheimer's Disease

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Abstract

People nowadays live long enough to experience various age-related diseases, among which is dementia due to Alzheimer's disease (AD), which has spurred massive demand for societal support and health care services. AD is a progressive brain disease that gradually causes increasing levels of cognitive impairment, particularly memory loss, and other substantial disabilities, placing huge emotional and financial burdens on caregivers and on medical and social care systems as the frequency of independent living and quality of life of the sufferers continue to decline. According to the most recent report from the World Health Organization (https://www.who.int/mental_health/neurology/ dementia/dementia_thematicbrief_epidemiology.pdf), the number of people living with dementia worldwide was estimated to be 47.47 million, and expected to reach 75.63 million in 2030 and 135.46 million in 2050. Each year, 3.6 million new cases of dementia were anticipated in Asia, 2.3 million in Europe, 1.2 million in the Americas, and 0.5 million in Africa. It was calculated based on data in 2010 that the approximate average survival period from the onset of dementia till death is 4.6 years.

Keywords: Alzheimer's disease; Dementia; Brain

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The Importance of Early Identification of Potential Risk for Developing AD

Currently, there is no known cure for AD. Given the non-curable nature of AD, it is particularly crucial that the illness is identified early to enable better symptom management and disease control. Better still, individuals who are at increased risk for later AD development could be treated even in the prodromal stage, so that their progression to AD could be delayed or prevented. Importantly, the cost of AD to society, the medical system and caregivers could be greatly reduced if early identification and treatment of AD can be achieved. Weimer and Sager [1] conducted a Monte-Carlo cost-benefit analysis based on estimates of parameters available in the medical literature, and showed that the early identification and treatment of AD have the potential to result in large positive net social benefits, as well as positive net savings for the state and federal government in the US. Geldmacher, et al. [2] examined the effect of treatment timing on risk of institutionalization of AD patients, and estimated the economic implications of earlier diagnosis and treatment initiation. They found that initiation of existing therapies at the earliest symptomatic onset was predicted to delay institutionalization by 91 days and reduce medical costs by USD 19,108 per institutionalized patient. Even after incorporating costs due to increased use of other medical services and drug costs incurred by earlier treatment, early intervention was still predicted to result in a net savings of USD 12,687 per patient, and over USD 1 billion in annual savings.

In the UK Barnett, et al. [3] tried to determine to what extent the timing of intervention in AD affected its cost-effectiveness. Using published data describing cognitive decline in the years prior to AD diagnosis, they modelled the effects on healthcare costs and quality-adjusted life years of hypothetical symptomatic and disease-modifying interventions. They found that a symptomatic treatment which could immediately improve cognition by one MMSE point and gradually reduce efficacy over 3 years would produce a peak net benefit when applied as early as 8 years prior to standard diagnosis. In this context, the net benefit was reduced by around 17% for every year that the intervention was delayed. On the other hand, for a disease-modifying intervention which was expected to halt cognitive decline for 1 year, the maximal economic benefits would occur if the intervention was applied 2 years prior to standard diagnosis. These results clearly indicate that the current diagnosis of AD, even in high-income, developed countries, is at least several years delayed relative to the optimal point of preventative or treatment benefits. Similarly, [4] computed the cost-effectiveness of assessing individuals presenting with subjective memory complaints early and contingently treating those receiving AD diagnosis with the cholinesterase inhibitor drug Donepezil. In comparison with a scenario without early assessment or pharmacological treatment, early assessment was estimated to reduce health care costs by GBP 3600 per patient, and societal costs by GBP 7750 per patient. Compared to drug treatment without early assessment, the savings was estimated to be GBP 2100 per patient in health care costs, and GBP 5700 in societal costs. The data thus speak to the urgent and pressing need for early AD identification and intervention, even in the relatively healthy or prodromal stage.

In a systematic review, Dubois, et al. [5] suggested that a timely AD diagnosis would potentially offer opportunities for early intervention, implementation of coordinated care plans, and better management of symptoms, improved patient safety, cost savings, and delay of institutionalization. Similarly, diagnosing and treating AD patients at an early stage is expected to improve the quality of life and reduce burdens for both the patient and the caregiver [4] given an early diagnosis offers the caregivers more opportunities to adapt to the caregiving role [6]. Better adaptation to the changes that characterize dementia then enables the caregivers to feel more competent in their job and experience less psychological issues. Early intervention may help caregivers in anticipating and accepting the future care role and transitions, and allow the caregivers to involve the patients during decision-making processes when this is still possible. As the levels of stress and burden are still relatively low in the pre-AD stage, the caregivers would have greater opportunities to prepare and empower themselves [6].

In order to achieve early and accurate diagnosis of AD, clinicians need to devise non-invasive and cost-effective screening tools that allow identification of individuals in the preclinical or early phases of AD, who would then receive more in-depth cognitive evaluation and dementia diagnostics [7]. It is likely that these tools are most effective if combining neuro-psychometric (e.g. episodic memory tests), clinical (e.g. subjective memory complaints), physiological (e.g. blood) and neurophysiological (e.g. EEG, MEG), radiological and other clinical measures [7]. The presence of additional brain pathologies such as alpha-synuclein inclusions, TDP-43 lesions, and VaD pathologies may also contribute to the various clinical features of AD patients. Importantly, changes to the A beta-Tau biomarkers were considered to occur before the manifestation of clinical symptoms, before or during the MCI stage [8], which could thus serve as important objective indices for preclinical or early-phase identification of AD.

Pressing Need for Timely Intervention

Accumulating evidence indicates that subtle losses of memory and other cognitive functions may be early prodromal signs for transitioning to AD. In this context, Amnesia mild cognitive impairment (a MCI), principally characterized by impairment in memory functions relative to age- and education-matched counterparts' mild cognitive impairment (MCI), is at particularly increased risk of subsequently converting to AD [9]. Since these individuals still have largely preserved cognitive and daily functioning, interventions on them might be particularly effective for symptom reduction and management.

Increasing research evidence has revealed the fact that the human brain retains the capacity to change in response to experience even until late adulthood. This implies that cognitive and mind training has the potential to ameliorate cognitive decline associated with pathological aging by inducing training-specific neuroplastic effects at both the neural and behavioural levels. Leung, et al. [10] examined the behavioural effects of a systematic thirteen-week cognitive training program on the attention and working memory of older adults who were at risk of cognitive decline. Findings clearly indicated training-induced improvement in auditory and visual-spatial attention and working memory. The training effect was specific to the experience provided. This pattern of findings is consistent with the prediction and the principle of experience-dependent neuroplasticity.

Kinsella, et al. [11] used a randomized-control design and included 52 participants with a MCI. The researchers found that memory rehabilitation training significantly improved prospective memory function, as well as knowledge and use of memory strategies. Jean, et al. [12] reviewed existing studies on the efficacy of cognitive intervention programmes on improving the cognitive functions of a MCI individuals. They concluded that 44% of all results showed statistically significant objective memory improvements following intervention, and 49% of all results showed significant after-intervention improvements in quality of life and affective measures. Chan, et al. [13] verified the efficacy of an eight-week Chinese calligraphy writing training course in improving attentional control and working memory for people with MCI. They observed that calligraphy writing, when compared with healthy controls, showed significant improvement in working memory and divided attention. This finding provides support to the idea that behavioural intervention such as an 8-week Chinese calligraphy writing training is useful for protecting specific cognitive functions in MCI.

Lee, et al. [14] administered a computerized errorless learning-based memory training programme to Chinese early-AD patients. Compared to a wait-list control group, the memory training improved the cognitive function of the patients. However, this study suffered from the very small sample size (<10 per group). In another study, the effect of 12-week cognitive rehabilitation was investigated in a sample of 201 mild AD patients, utilizing a randomized control design. While no significant intervention effect on everyday functioning was demonstrated, cognitive rehabilitation was found to improve quality of life and reduce depressive symptoms in female patients [15,16] also examined the clinical efficacy of cognitive rehabilitation in 69 early-stage AD patients who were concurrently receiving Acetylcholinesterase-inhibiting medication. Their intervention programme offered personalized contents about aids and strategies for achieving individually relevant goals, techniques to learn new information, practice in maintaining attention and concentration, and techniques for stress management. The results showed that cognitive rehabilitation significantly improved ratings of goal performance and satisfaction.

Research findings reported above supported the usefulness of preventive and early intervention for protecting against cognitive decline. Mowszowski, et al. [17] reviewed the existing literature on the beneficial effect of cognitive intervention in healthy older adults, individuals at risk for AD, and AD patients. They concluded that cognitive rehabilitation generally showed positive effects on improving cognition in healthy adults and at-risk individuals. It appears that early cognitive intervention in the healthy or preclinical phase may be more effective as a preventive measure than in the disease phase.

Conclusion

Due to the global trend of population aging, the prevalence of AD is rising rapidly worldwide, incurring huge costs and burdens for the society, medical system, caregivers, patients and their families. Convincing evidence supports the idea that early identification and preventive intervention for people at risk of developing AD can result in substantial reductions in costs and burdens at all scales. There is already an accumulated body of research indicating that these early interventions, particularly cognitive- and memory-based rehabilitation programmes, can improve cognitive functions and reduce the risk for progression to AD in at-risk MCI individuals.

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