International Psychogeriatrics (2019), 31:7, 913–916 © International Psychogeriatric Association 2019
doi:10.1017/S1041610219001121

EDITORIAL

Cognitive decline in older adults: applying multiple perspectives to develop novel prevention strategies

Cognitive decline among older adults encompasses the range of subclinical decline, mild cognitive impairment (MCI), and Alzheimer-type dementia. In 2015, 47 million people worldwide were estimated to have dementia, and the prevalence is expected to triple by 2050 (Baumgart *et al.*, 2015). Alzheimer's disease is the fifth most-common cause of death among adults 65 years and older in the United States, although this may be an underestimate, as dementia often leads to health conditions that are considered direct causes of death. Examples of these associated conditions include swallowing disorders and immobility, which increase the risk for potentially fatal pneumonia in older adults (Alzheimer's Association, 2019). Given the gravity of these outcomes, combined with the finding that only 5% to 15% of people with MCI progress to Alzheimer's disease in a given year (Mitchell and Shiri-Feshki, 2008; Petersen, 2011), modifying potential risk factors through prevention strategies is of high importance. Consequently, there has been a growing body of research on identifying at-risk older adults and developing effective prevention strategies for those at risk of dementia.

Previous research has identified a number of potentially modifiable risk factors, including midlife obesity and hypertension, current smoking status, and diabetes, along with factors that decrease risk, such as years of formal education, diet, and participation in cognitive training activities (Baumgart *et al.*, 2015). Two recent systematic reviews reported insufficient evidence in the current literature for two other prevention strategies: physical activity (Brasure *et al.*, 2018) and pharmacological interventions (Fink *et al.*, 2018). Additionally, although a number of risk factors have been identified, applying those findings to specific individuals has proven rather complicated (Mukadam, 2018), necessitating continued work to develop risk identification procedures and prevention strategies with clinical utility.

Harnessing multiple theoretical perspectives and methodological approaches will increase our ability to better characterize risk factors of dementia development and identify effective means of prevention. This issue of *International Psychogeriatrics* includes several articles that focus on cognitive decline, particularly Alzheimer's and other dementias, from three different but potentially impactful perspectives: examination of internet use as a prevention strategy (Berner *et al.*, 2019); artificial intelligence as a mechanism to identify individual-level risk of Alzheimer's disease conversion (Grassi *et al.*, 2018a); and lastly, based on a mouse model, re-invigoration of IGF-2 as a potential preventative agent (Xia *et al.*, 2019). Each of these papers is accompanied by thoughtful commentaries by Moxley and Czaja (2019), Graham and Depp (2019), and O'Hara and Hallmayer (2019), respectively.

The notion of "prescribing" social media to improve cognitive outcomes may seem counterintuitive, given that studies of internet use in younger populations commonly report on its potential downsides such as greater psychopathology, problematic alcohol use, self-injurious behavior, and impaired sleep (Elhai *et al.*, 2017; Hale and Guan, 2015; Ko *et al.*, 2008, 2009; Lam *et al.*, 2009). For older adults, however, internet engagement could be a beneficial preventative agent slowing cognitive decline in some people. Berner *et al.*'s (2019) well-powered study of older adults in Sweden and the Netherlands found that self-reported internet use at baseline was associated with less cognitive decline, controlling for baseline cognitive functioning. This paper offers a hopeful implication that internet use could be a potentially helpful preventive strategy for older adults. This possibility is particularly exciting given that internet use is an easy and appealing intervention for many older adults who may struggle to access other prevention options, including those with significant mobility limitations or those who live in areas with low healthcare access. Internet use has exploded among older adults over the past few years, with 53% of adults 65 and older using the internet compared to 22% in 2004 (Chang *et al.*, 2015). If internet use is demonstrated in future research to slow cognitive decline, we may see population-wide impact without resorting to highly structured dissemination tactics.

Berner and colleagues (2019) hypothesized that internet use would provide a challenging and engaging cognitive context that may facilitate learning and active use of other cognitive facilities. The brain remains plastic in later life, and targeted cognitive engagement can help improve cognitive function and associated outcomes even among older adults

with significant mental health issues (e.g., Thomas *et al.*, 2018). In Moxley and Czaja's (2019) commentary, the authors principally argue for social connectivity as the primary mediator of change, specifically mentioning that social connectivity via the internet may decrease loneliness, increase sense of purpose, and provide more accessible methods of connecting to others. Social isolation and loneliness are common among older adults, and are associated with worse cognitive functioning (Boss *et al.*, 2015). If social connectivity is the primary mediator for the internet's effect on cognition in older adults, this may also provide support for continued development of social engagement-based interventions for older adults.

In studies comparing younger and older adults, one must consider the possibility that many observed differences between the two age groups are at least partly a result of cohort effects rather than aging effects. Could the process of learning new technology and discovering the internet's avenues to connect with others be a critical contributor to slowing cognitive decline? If so, it is possible that future generations in which most people have been using the internet and other technology for much of their adult lives may not see the same benefit. However, given the fast pace of technological advances, new technology will always offer opportunities for cognitive challenges and new social connections. As Moxley and Czaja (2019) suggest, future studies examining differences in cognitive decline based on how older adults use the internet will help delineate how personalized internet use can contribute to better cognition with aging.

Xia and colleagues (2019) revitalized a tried-and-true methodological approach, by studying IGF-2 in mice to better understand the impact of inflammation on cognition, and particularly, the potential to use anti-inflammatory agents to prevent neuronal degeneration. For decades, inflammation has been a major target of research and interventions related to cognitive decline, and, as O'Hara and Hallmayer (2019) emphasize, returning to well-known theories and methodologies is an underrated but useful research agenda. Continued use of well-developed, useful theories and models can significantly contribute to the literature, as illustrated by Xia *et al.*'s work.

Developing effective prevention strategies is a critical component of slowing cognitive decline among older adults. At the same time, identifying older adults most at risk of decline is necessary for impactful dissemination of preventive interventions. A number of potential predictors of cognitive decline have been identified, but a clinically useful method of identifying at-risk individuals is still in process. Grassi *et al.*'s work (2018a) advances that progression by describing the validation process of their previously developed machine learning approach (Grassi *et al.*, 2018b), which aims to identify individuals with MCI who are more likely to convert to Alzheimer's disease within the next three years. Their machine learning technique showed a high level of predictive power.

Graham and Depp's (2019) thoughtful commentary highlights the strengths of this approach, including use of clinical predictors in the model and their strong prediction results, while also cautioning about the need to replicate these results in other samples. Machine learning's capability for complexity can at times be a double-edged sword, as predictors that fit one population perfectly may increase error in another population. In this respect, a strength of Berner *et al.*'s paper (2019) is mirrored in a limitation of Grassi *et al.*'s (2018a): specifically, that Berner *et al.* collected data from two countries, increasing the generalizability of their findings, while Grassi *et al.*'s work was limited to one American city. International data collection is a way forward for public health research, and increased international collaborations via large consortia and open science 'accelerators' provides a path for researchers to increase their impact.

Like Graham and Depp (2019), we also view Grassi *et al.*'s paper (2018a) with a combination of excitement and caution. Machine learning provides an avenue to increase complexity of models, allowing for a way to integrate many predictors into a single calculation of risk. However, in order for these approaches to be practical for clinical use, these models must incorporate only the data that can be feasibly collected in usual care settings. Grassi *et al.* (2018a) include some sources of data that are likely to be feasible in many clinics, but accessibility for different data sources will vary by clinic. Using as many easy pieces of data (e.g., demographic data, quick and easy to collect clinical data) will increase ultimate uptake and utility. Graham and Depp (2019) also expressed the need for these approaches to improve interpretability, given the so-called 'black box' nature of machine learning – i.e. it doesn't tell us how it arrived at a specific conclusion. Ultimately, machine learning approaches like Grassi *et al.*'s (2018a) are promising and innovative, but their clinical impact is yet to be determined.

Overall, identification of high-risk individuals and prevention strategies should be major goals for research on cognitive decline in older adults. This issue adds to a growing body of literature that informs machine learning-driven identification methods and accessible prevention strategies. Future work will benefit from consideration of diverse methods, particularly by integrating classical methods with forward-thinking innovations. This will allow for the development of a clinically useful

https://doi.org/10.1017/S1041610219001121 Published online by Cambridge University Press

toolkit that assists healthcare providers in identifying older adults at high risk of cognitive decline and facilitates implementation of preventive strategies in healthcare and at home. The studies presented here indicate that this type of toolkit is in development, and benefits to older adults will only continue to increase in the near future.

Funding

This work was supported, in part, by the National Institute of Mental Health T32 Geriatric Mental Health Program (grant MH019934 to DVJ [PI]), and an R01 grant (R01MH094151-01 to DVJ [PI]), and the Sam and Rose Stein Institute for Research on Aging, University of California San Diego.

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