



Review

Non-pharmacological strategies to delay cognitive decline

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ARTICLE INFO

Keywords:

Cognitive decline
Dementia
Non-pharmacological
Exercise
Ageing
Alzheimer's disease

ABSTRACT

Non-pharmacological preventive strategies to delay cognitive decline have become the focus of recent research. This review aims to discuss evidence supporting the use of physical and cognitive activity to reduce the risk of cognitive decline and dementia in later life. Both strategies are associated with better cognitive health in older adults. This positive effect seems stronger for middle-aged and older adults with normal cognition and less clear when cognitive impairment is present. Physical and cognitive activities have been linked to indirect and direct biological factors affecting brain health. Future research will need to explore details about type, intensity, duration and combination of interventions. An important aim is standardization between studies, as well as evidence of improved clinical outcomes and cost-effectiveness. Identifying strategies that succeed at sustaining improved lifestyle is necessary, and the use of modern technology could play a crucial role in this regard. In the meantime advice on physical and cognitive activities should be included when health advice is given to middle-aged and older adults.

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1. Introduction

Prevention of dementia has become a priority in many countries. Although we currently lack compelling evidence from clinical trials demonstrating that the clinical syndrome dementia can in fact be prevented by targeted strategies, many opinion leaders

are convinced that this is not an utopian dream, but a realistic goal that should be pursued [1]. Several large-scale trials designed to prevent dementia are currently under way, and their results should contribute to guide future policy and practice. Examples include the Finnish Geriatric Intervention Study to Prevent Cognitive Impairment and Disability (FINGER) [2], Multidomain Alzheimer Prevention study (MAPT) [3] and Prevention of Dementia by Intensive Vascular Care (preDIVA) [4].

Many publications on this topic have highlighted current knowledge gaps. During this phase of limited evidence and in the absence of effective pharmacological strategies to prevent dementia, a timely question is: *what role do non-pharmacological strategies*

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potentially play to support cognitive health in middle and older age with the more modest aim to delay rather than to prevent cognitive decline? By delaying cognitive decline by some years, many older individuals may reach the end of their natural lifespan before crossing the dementia threshold.

With professional and social media increasingly interested on topics related to cognitive decline and dementia, it is not surprising that medical and allied health clinicians in various settings, such as primary care, memory clinics, or other specialist and allied health clinics, are consulted about effective prevention strategies. This increased interest in the general population is a unique opportunity to build cognitive health literacy and encourage healthy lifestyle behaviour. This may be particularly important in middle aged community members as this seems to be a time period when modifiable risk factors increase the risk of cognitive decline in older age [5–7]. In parallel to this, health care providers are increasingly making the clinical judgement that giving information on this topic should be part of their recommendations and management plans.

The objective of this narrative review is to present targeted information derived from recent review publications on non-pharmacological strategies that could be used for informing middle aged and older individuals about how to better protect their cognitive health. For this review we have focused on physical and cognitive activities as two of the most significant protective factors [8].

2. Methods

A literature search was conducted for recent review publications (2004–2014) using the databases MEDLINE, PsycINFO, PubMed and Google Scholar. Search terms included prevention of dementia, cognitive decline, dementia, exercise, physical activity, motor activity, physical exertion, physical fitness, cognitive activity, cognitive stimulation, cognitive rehabilitation and cognitive training. The search was limited to humans, English language and aged. References listed in articles, including those published prior to 2004 were also followed up, if relevant for this review.

3. Results

3.1. Physical activity (PA)

Historical documents from China and Greece reveal that physical activity (PA) has been promoted as an integral part of a healthy lifestyle since ancient times. In the late nineteenth and early twentieth century early epidemiological studies reported a physical activity-related risk reduction for mortality and cardiovascular events [9]. PA can be defined as any body movement that results in increased energy expenditure. Most guidelines, including those for older adults, recommend at least 30 min of moderate-intensity PA on a minimum of 5 days/week [10]. There is a substantial body of evidence demonstrating that regular PA can reduce the risk of various medical conditions, such as cardiovascular disease, diabetes mellitus and depression. As all three of those conditions have been identified as important risk factors for dementia and Alzheimer's disease (AD) [8], one common hypothesis is that delayed cognitive decline could be achieved with PA [11–17]. Additionally PA is associated with decreased risk of cerebrovascular disease [18,19], which has been reported in many publications as increasing the risk of cognitive decline often via complex interactions with other underlying brain pathologies [20].

Based on systematic reviews and meta-analysis on risk factors for dementia and Alzheimer's disease (AD) published between 2005 and 2011, Barnes and Yaffe calculated the proportion of cases of AD that could be prevented if relevant risk factors could be eliminated.

For PA they estimated that approximately 13% of AD cases could be attributed to physical inactivity [8]. One of the systematic reviews incorporated in this calculation was based on 16 prospective studies and included 163,797 non-demented participants of which 3219 developed dementia at follow-up. The relative risks for the highest compared with lowest level of PA reported in this review were 0.72 (95% CI = 1.16–1.67) for dementia and 0.55 (95% CI = 0.36–0.84) for AD [21]. Other reviews, systematic and non-systematic, including those focusing on randomized controlled trials (RCTs) with non-demented participants, are consistent with these positive findings [22–27] including other dementia types such as vascular dementia [28]. However some reviews have reported mixed results [29–31].

There are fewer reviews in the literature investigating the potential cognitive benefits of PA for older adults who either have subjective memory complaints or do already experience some objective cognitive impairment, as for example mild cognitive impairment (MCI) in the absence of dementia. As the number of PA studies for this population is still limited and these reviews use either disparate inclusion criteria or mixed clinical samples, reported results are less consistent [32–35]. A number of studies have reported significant cognitive benefits mainly in the areas of attention, executive functions and memory [36–41], however, others have been negative [33,42,43].

3.2. Cognitive activity (CA)

The term cognitive activity (CA) should not be limited to cognitively stimulating leisure activities in middle and old age, but should also include cognitive activities in the context of life long learning, employment and volunteer work. Unemployment or underemployment in middle age is associated with an increased risk of cognitive decline in old age and intellectually stimulating work environments have been reported as showing protective potential [44–46].

Barnes and Yaffe [8] estimated that approximately 19% of AD cases could be attributed to cognitive inactivity or low educational attainment. This estimation was based on two systematic reviews and meta-analyses. The first publication included 22 longitudinal studies investigating various brain reserve markers (higher education, occupational attainment, intelligence and mentally stimulating leisure activities) in a total of 21,456 participants of whom 1733 developed dementia at follow-up and reported combined OR of 0.54 (95% CI = 0.49–0.59) [47]. The second paper included 13 cohort and six case-control studies investigating the association between low education and dementia or AD. The reported relative risks were 1.59 (95% CI = 1.26–2.01) for dementia and 1.80 (95% CI = 1.43–2.27) for AD [48].

Until recently, review papers investigating whether cognitive rehabilitation targeting memory could be of benefit for individuals with MCI were negative with only a very limited number of original studies available in the literature [49]. Most reviews published since then, however, have reported benefits [50]. For CA, in the context of secondary prevention interventions, a common typology is to distinguish the sub-groups cognitive stimulation (CS), cognitive training (CT) and cognitive rehabilitation (CR). CS aims to enhance cognitive and social functions, CT offers practising to improve specific tasks and CR focuses on improving everyday functioning. In a recent systematic review investigating the benefits for CS, CT and CR for participants with MCI or mild dementia, 11 out of 18 included studies using CS demonstrated significant improvements in cognitive function [51]. Only nine publications investigated whether the interventions had any impact on activities of daily living (ADLs) and no significant treatment differences were identified. A further 13 studies using CT and CR were reviewed and seven studies observed significant cognitive improvements. Benefits for ADLs were only found in one trial with MCI [52]. Additionally clinical significance

of the interventions was investigated with an approach similar to drug trial protocols. Only one trial with CS [53] and one trial with CT/CR [52] involving individuals with MCI demonstrated clinical significance. A recent study reviewed 11 RCTs of cognitive training interventions for people with mild to moderate dementia [49]. The quality of the trials was low to moderate and no effects were found on patient outcomes. One high quality trial found a positive effect on caregiver outcomes and improved activities of daily living in patients with dementia [54].

4. Conclusions

With the increasing number of systematic and non-systematic reviews investigating the potential benefits of PA and CA, the evidence is mounting that both these non-pharmacological strategies are associated with better cognitive health outcomes for older adults. This finding is stronger for participants with normal cognition and less clear for participants with subjective cognitive complaints or mild cognitive impairment. Research with animal models and, more recently, research with humans have produced a growing body of evidence about potential underlying biological mechanisms explaining the protective effects of PA and CA on brain health. For PA, indirect effects on the body such as risk reduction of vascular and metabolic disease and mitigation of the negative effects from chronic stress, oxidation and inflammation have been described [55]. For both PA and CA additional direct effects on the brain, such as increased neurogenesis, enhanced brain plasticity and reduced build up of AD specific amyloid load, have been suggested [55–58].

This research field, especially when it comes to randomized controlled trials, is still in its infancy and, not surprisingly, there are many unanswered questions. Next to the challenge that future trials should aim to optimize methods with better standardization for inclusion criteria, interventions and outcome variables, more emphasis must be given to clinical significance, person-centred approaches and health economic evaluation to generate meaningful evidence relevant to future guidelines, policies and community programmes [51]. For both, PA and CA, more evidence needs to be gathered to compare different types, durations and intensities of interventions. This is required for the development of clinical practice guidelines and recommendations for specific sub-populations. Aerobic exercise and resistance training seem to be the most effective types of PA for protecting cognitive health and the intensity should be at least moderate. Durations of 6 months and longer are more effective than shorter durations [26]. General PA guidelines to improve health outcomes for older adults suggest a combination of different types of PA, but it is unclear if this would also increase the benefits for cognitive health. Combining PA and CA interventions should be investigated in future trials, but selection of the control intervention needs to be carefully considered to avoid contamination by social engagement factors [59,60]. Long term follow-up of RCTs should be conducted where feasible to learn more about which cognitive areas show the highest long term benefits from targeted interventions. For example in the recent publication of the 10 year follow-up of the cognitive training ACTIVE trial with healthy older community members, reasoning and speed showed long term benefits whereas memory did not [61]. In parallel to these challenges, more research is needed to determine which strategies are most effective at motivating middle aged and older individuals to tackle behaviour change and to successfully maintain those changes [62]. The rapidly increasing use of computers and Internet by seniors offers unprecedented opportunities to use modern information and communication technology in combination with smart consumer electronics for the delivery, guidance, monitoring and reinforcement of CA and PA. The advantages of these novel technologies include overcoming of

geographical or mobility-related barriers, high level of individualization, immediate feedback to participants, online monitoring and incorporation of behavioural strategies to ensure continued interest and programme retention [63,64]. Additionally attitudes about ageing are considered to have an important influence on cognitive health outcomes, and the hypothesis that individuals with negative attitudes are less motivated to contemplate behaviour change needs to be investigated further [65]. Should this hypothesis be confirmed, future research would need to investigate whether targeted educational programmes can significantly improve attitudes about ageing. More specifically, attitudes and preferences of middle aged and older individuals in relation to PA and CA to support cognitive health need to be taken into account when translating targeted non-pharmacological interventions into the community environment. A recent qualitative study determined via structured focus groups with older adults with normal cognition, memory complaints, MCI or mild dementia that depending on the clinical group preferences varied significantly. Healthier groups emphasized the need to feel challenged by the programme, whereas those with cognitive impairment focussed more on safety and accessibility [66]. Practical recommendation by health care providers to middle aged and older community members with or without MCI who contemplate an increase in PA and CA should start with giving information, including current knowledge limitations, tailored to the personal situation and medical history. Potential barriers preventing behavioural changes should be explored, highlighting the need for safety and pointing out suitable guidelines. Most importantly, this topic needs to be revisited at each subsequent appointment, as individuals often need time and repetition of information to move towards contemplating and attempting behaviour change [26]. A future ideal scenario is that educating community members about positive behaviour to support cognitive health is as commonly and regularly attempted as promoting strategies to protect cardio- and cerebrovascular health.

Contributors

All authors have contributed equally to this manuscript and have approved the final version.

Competing interests

None declared.

Funding

KJA is funded by NHMRC fellowship #1002560.

Provenance and peer review

Commissioned; externally peer reviewed.

References

- [1] Smith DA, Yaffe K. Dementia (including Alzheimer's disease) can be prevented: statement supported by international experts. *J Alzheimer's Dis* 2014;38:699–703.
- [2] Kivipelto M, Solomon A, Ahtiluoto S, et al. The Finnish geriatric intervention study to prevent cognitive impairment and disability (FINGER): study design and progress. *Alzheimer's Dement* 2013;9:657–65.
- [3] Carrie I, Van Kan GA, Gillette-Guyonnet S, et al. Recruitment strategies for preventive trials. The MAPT study (multidomain Alzheimer preventive trial). *J Nutr Health Aging* 2012;16(4):355–9.
- [4] Richard E, Van den Heuvel E, Moll van Charante EP, et al. Prevention of dementia by intensive vascular care (PreDIVA): a cluster randomized trial in progress. *Alzheimer Dis Assoc Disord* 2009;23(3):198–204.
- [5] Sabia S, Nabi H, Kivimaki M, et al. Health behaviors from early to late midlife as predictors of cognitive function: the Whitehall II study. *Am J Epidemiol* 2009;170:428–37.

- [6] Qiu C. Preventing Alzheimer's disease by targeting vascular risk factors: hope and gap. *J Alzheimer's Dis* 2012;32:721–31.
- [7] Anstey KJ, Cherbuin N, Herath PM. Development of a new method for assessing global risk of Alzheimer's disease for use in population health approaches to prevention. *Prev Sci* 2013;14:411–21.
- [8] Barnes DE, Yaffe C. The projected effect of risk factor reduction on Alzheimer's disease prevalence. *Lancet Neurol* 2011;10:819–28.
- [9] McAuley D. A history of physical activity, health and medicine. *J R Soc Med* 1994;87:32–5.
- [10] US Department of Health and Human Services. Physical activity and health. A Report of the Surgeon General. GA, USA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion; 1996.
- [11] Taylor RS, Brown A, Ebrahim S, et al. Exercise-based rehabilitation for patients with coronary heart disease: systematic review and meta-analysis of randomized, controlled trials. *Am J Med* 2004;116:682–92.
- [12] Lindstrom J, Ilanne-Parikka P, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet* 2006;368:1673–9.
- [13] Sjösten N, Kivilä S-L. The effects of physical exercise on depressive symptoms among the aged: a systematic review. *Int J Geriatr Psychiatry* 2006;21:410–8.
- [14] Warburton DER, Nicol CD, Bredin SSD. Health benefits of physical activity: the evidence. *CMAJ* 2006;174:801–9.
- [15] Daley A. Exercise and depression: a review of reviews. *J Clin Psychol Med Settings* 2008;15:140–7.
- [16] Heran BS, Chen JM, Ebrahim S, et al. Exercise-based cardiac rehabilitation for coronary heart disease. *Cochrane Database Syst Rev* 2011;2011:CD001800.
- [17] Almeida OP, Khan KM, Hankey GJ, et al. 150 minutes of vigorous physical activity per week predicts survival and successful ageing: a population-based 11-year longitudinal study of 12,201 older Australian men. *Br J Sports Med* 2014;48:220–5.
- [18] Lee CD, Folsom AR, Blair SN. Physical activity and stroke risk: a meta-analysis. *Stroke* 2003;34:2475–81.
- [19] Huerta JM, Chirlaque MD, Tormo MJ, et al. Physical activity and risk of cerebrovascular disease in the European Prospective Investigation into Cancer and Nutrition-Spain Study. *Stroke* 2013;44:111–8.
- [20] Vermeer SE, Prins ND, den Heijer T, et al. Silent brain infarcts and the risk of dementia and cognitive decline. *N Engl J Med* 2003;348:1215–22.
- [21] Hamer M, Chida Y. Physical activity and risk of neurodegenerative disease: systematic review of prospective evidence. *Psychol Med* 2009;39:3–11.
- [22] Colcombe S, Kramer AF. Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychol Sci* 2003;14:125–30.
- [23] Rolland Y, Abellan van Kan G, Vellas B. Physical activity and Alzheimer's disease: from prevention to therapeutic perspectives. *J Am Med Dir Assoc* 2008;9:390–405.
- [24] Sofi F, Valecchi D, Bacci D, et al. Physical activity and risk of cognitive decline: a meta-analysis of prospective studies. *J Intern Med* 2010;269:107–17.
- [25] Lautenschlager NT, Cox K, Cyarto EV. The influence of exercise on brain ageing and dementia. *Biochim Biophys Acta* 2012;1822:474–81.
- [26] Lautenschlager NT. Physical activity and cognition in older adults with mild cognitive impairment and dementia. *Neurodegener Dis Manag* 2013;3(3):211–8.
- [27] Sodergren M. Lifestyle predictors of healthy ageing in men. *Maturitas* 2013;75:113–7.
- [28] Aarsland D, Sardaahae FS, Anderssen S, et al. Is physical activity a potential preventive factor for vascular dementia? A systematic review. *Aging Ment Health* 2010;14:386–95.
- [29] Angevaren M, Aufdemkampe G, Verhaar HJ, et al. Physical activity and enhanced fitness to improve cognitive function in older people without known cognitive impairment. *Cochrane Database Syst Rev* 2008;3:CD005381.
- [30] Smith PJ, Blumenthal JA, Babyak MA. Effects of the dietary approaches to stop hypertension diet, exercise, and caloric restriction on neurodegeneration in overweight adults with high blood pressure. *Hypertension* 2010;55:1331–8.
- [31] Snowden M, Steinman L, Mochan K, et al. Effect of exercise on cognitive performance in community-dwelling older adults: review of international trials and recommendations for public health practice and research. *JAGS* 2011;59:704–16.
- [32] Heyn P, Beatrix CA, Ottenbacher KJ. The effects of exercise training on elderly persons with cognitive impairment and dementia: a meta-analysis. *Arch Phys Med Rehabil* 2004;85:1694–704.
- [33] Van Uffelen JG, Chinapaw MJ, van Mechelen W, et al. Waling or vitamin B for cognition in older adults with mild cognitive impairment? A randomized controlled trial. *Br J Sports Med* 2008;42:344–51.
- [34] Ahlskog JE, Geda YE, Graff-Radford N, et al. Physical exercise as a preventative or disease-modifying treatment of dementia and brain aging. *Mayo Clin Proc* 2011;86(9):876–84.
- [35] Gates N, Singh MAF, Sachdev PS, et al. The effect of exercise training on cognitive function in older adults with mild cognitive impairment: a meta-analysis of randomized controlled trials. *Am J Geriatr Psychiatry* 2013;21(11):1086–97.
- [36] Busse AI, Filho WJ, Magaldi RM, et al. Effects of resistance training exercise on cognitive performance in elderly individuals with memory impairment: results of a controlled trial. *Einstein* 2008;6(4):402–7.
- [37] Lautenschlager NT, Cox KL, Flicker L, et al. Effects of physical activity on cognitive function in older adults at risk for Alzheimer's disease. *JAMA* 2008;300(9):1027–37.
- [38] Baker LD, Frank LL, Foster-Schubert K, et al. Effects of the aerobic exercise on mild cognitive impairment: a controlled trial. *Arch Neurol* 2010;67(10):71–9.
- [39] Muscari A, Giannoni C, Pierpaoli L, et al. Chronic endurance exercise training prevents aging-related cognitive decline in healthy older adults: a randomized controlled trial. *Int J Geriatr Psychiatry* 2010;25:1055–64.
- [40] Lam LC, Chau RC, Wong BM, et al. Interim follow-up of a randomized controlled trial comparing Chinese style mind body (tai chi) and stretching exercises on cognitive function in subjects at risk of progressive cognitive decline. *Int J Geriatr Psychiatry* 2011;26:733–40.
- [41] Nagamatsu LS, Handy TC, Hsu CL, et al. Resistance training promotes cognitive and functional brain plasticity in seniors with probable mild cognitive impairment. *Arch Intern Med* 2012;172(8):666–8.
- [42] Scherder EJA, Van Paasschen J, Deijen JB, et al. Physical activity and executive functions in the elderly with mild cognitive impairment. *Aging Ment Health* 2005;9(9):272–80.
- [43] Varela S, Ayan C, Cancela JM, et al. Effects of two different intensities of aerobic exercise on elderly people with mild cognitive impairment: a randomized pilot study. *Clin Rehabil* 2011;26(5):442–50.
- [44] Finkel D, Andel R, Gatz M, et al. The role of occupational complexity in trajectories of cognitive aging before and after retirement. *Psychol Aging* 2009;24:563–73.
- [45] Marqué JC, Duarte LR, Bessières P, et al. Higher mental stimulation at work is associated with improved cognitive functioning in both young and older workers. *Ergon* 2010;53:1287–301.
- [46] Leist AK, Glymour MM, Mackenbach JP, et al. Time away from work predicts later cognitive function: differences by activity during leave. *Ann Epidemiol* 2014;23:455–62.
- [47] Valenzuela MJ. Brain reserve and the prevention of dementia. *Curr Opin Psychiatry* 2008;21:296–302.
- [48] Caamano-Isorna F, Corral M, Montes-Martinez A, Takkouche B. Education and dementia: a meta-analytic study. *Neuroepidemiology* 2006;26:226–32.
- [49] Martin M, Clare L, Altgassen AM, et al. Cognition-based interventions for healthy older people and people with mild cognitive impairment. *Cochrane Database Syst Rev* 2011;19(1):1–51.
- [50] Hampstead BM, Gillis MM, Stringer AY. Cognitive rehabilitation of memory for mild cognitive impairment: a methodological review and model for future research. *JINS* 2014;19:1–17.
- [51] Kurz AF, Leucht S, Lautenschlager NT. The clinical significance of cognition-focused interventions for cognitively impaired older adults: A systematic review of randomized controlled trials. *Int Psychogeriatr* 2011;23(9):1364–75.
- [52] Tsolaki M, Kounti F, Agogiatou C, et al. Effectiveness of nonpharmacological approaches in patients with mild cognitive impairment. *Neurodegener Dis* 2011;8(3):138–45.
- [53] Haight BK, Gibson F, Michel Y. The Northern Ireland life review/life storybook project for people with dementia. *Alzheimer's Dement* 2006;2:56–8.
- [54] Bahar-Fuchs A, Clare L, Woods B. Cognitive training and cognitive rehabilitation for mild to moderate Alzheimer's disease and vascular dementia. *Cochrane Database Syst Rev* 2013;1–70.
- [55] Barnes DE, Lautenschlager NT. Physical activity and cognitive aging. In: Yaffe K, editor. *Chronic medical diseases and cognitive aging. Toward a healthy body and brain*. Oxford: Oxford University Press; 2013. p. 171–96, 314 pages. ISBN: 978-0-19-979355-6.
- [56] Liang KY, Mintun MA, Fagan AM, et al. Exercise and Alzheimer's disease biomarkers in cognitively normal older adults. *Ann Neurol* 2010;68:311–8.
- [57] Landau SM, Marks SM, Mormino EC, et al. Association of lifetime cognitive engagement and low β -amyloid deposition. *Arch Neurol* 2012;69(5):623–9.
- [58] Brown BM, Peiffer JJ, Taddei K, et al. Physical activity and amyloid- β plasma and brain levels: results from the Australian imaging, biomarkers and lifestyle study of ageing. *Mol Psychiatry* 2013;18:875–81.
- [59] Barnes DE, Santos-Modesitt W, Poelke G, et al. The Mental Activity and eXercise (MAX) trial: are randomized controlled trial to enhance cognitive function in older adults. *JAMA Intern Med* 2013;173(9):797–804.
- [60] Lautenschlager NT, Cox KL. "Can participation in mental and physical activity protect cognition in old age?" [commentary]. *JAMA Intern Med* 2013;173(9):805–6.
- [61] Rebok GW, Ball K, Guey LT, et al. Ten-year effects of the advanced cognitive training for independent and vital elderly cognitive training trial on cognition and everyday functioning in older adults. *J Am Geriatr Soc* 2014;62:16–24.
- [62] Clare L, Hindle JW, Jones IR, et al. The AgeWell study of behavior change to promote health and wellbeing in later life: study protocol for a randomized controlled trial. *Trials* 2012;13:115.
- [63] Kueider AM, Parisi JM, Gross AL, et al. Computerized cognitive training with older adults: a systematic review. *PLOS ONE* 2012;7(7):e40588.
- [64] Gell NM, Rosenberg DE, Demiris G, et al. Patterns of technology use among older adults with and without disabilities. *Gerontologist* 2013. <http://dx.doi.org/10.1093/geront/gnt166>.
- [65] Levy BR, et al. Association between positive age stereotypes and recovery from disability in older persons. *JAMA* 2012;308:1972–3.
- [66] Chong T, Doyle C, Cyarto E, et al. Physical activity program preferences and perspectives of older adults with and without cognitive impairment. *Asia-Pac Psychiatry* 2014;6:179–90.