


## Wirksamkeitsnachweise kognitiver Therapie eingesetzt bei leichten kognitiven Störungen (MCI)

## Proof of effectiveness of cognitive therapy used in mild cognitive impairments (MCI)

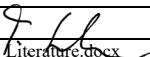
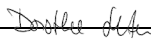
### Ersteller / Author

- Vollständigkeit und richtiger Inhalt
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## 1. Search in PubMed, search term "cognitive rehabilitation therapy computer mci" (91 results)

MCI-1. Ageing Res Rev. 2017 Nov;40:75-83. doi: 10.1016/j.arr.2017.09.003. Epub 2017 Sep 12.

**Positive effects of combined cognitive and physical exercise training on cognitive function in older adults with mild cognitive impairment or dementia: A meta-analysis.** Karssemeijer EGA(1), Aaronson JA(2), Bossers WJ(3), Smits T(4), Olde Rikkert MGM(1), Kessels RPC(5).

Combined cognitive and physical exercise interventions have potential to elicit cognitive benefits in older adults with mild cognitive impairment (MCI) or dementia. This meta-analysis aims to quantify the overall effect of these interventions on global cognitive functioning in older adults with MCI or dementia. Ten randomized controlled trials that applied a combined cognitive-physical intervention with cognitive function as an outcome measure were included. For each study effect sizes were computed (i.e., post-intervention standardized mean difference (SMD) scores) and pooled, using a random-effects meta-analysis. The primary analysis showed a small-to-medium positive effect of combined cognitive-physical interventions on global cognitive function in older adults with MCI or dementia (SMD[95% confidence interval]=0.32[0.17;0.47],  $p < 0.00$ ). A combined intervention was equally beneficial in patients with dementia (SMD=0.36[0.12;0.60],  $p < 0.00$ ) and MCI (SMD=0.39[0.15;0.63],  $p < 0.05$ ). In addition, the analysis showed a moderate-to-large positive effect after combined cognitive-physical interventions for activities of daily living (ADL) (SMD=0.65[0.09;1.21],  $p < 0.01$ ) and a small-to-medium positive effect for mood (SMD=0.27[0.04;0.50],  $p < 0.01$ ). These functional benefits emphasize the clinical relevance of combined cognitive and physical training strategies. Copyright © 2017 Elsevier B.V. All rights reserved. DOI: 10.1016/j.arr.2017.09.003 PMID: 28912076

MCI-2. BMC Geriatr. 2018 Sep 15;18(1):213. doi: 10.1186/s12877-018-0893-1.

**Technology-based cognitive training and rehabilitation interventions for individuals with mild cognitive impairment: a systematic review.** Ge S(1), Zhu Z(2)(3), Wu B(4)(5), McConnell ES(6)(7).

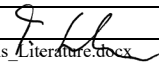
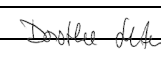
**BACKGROUND:** Individuals with mild cognitive impairment (MCI) are at heightened risk of developing dementia. Rapid advances in computing technology have enabled researchers to conduct cognitive training and rehabilitation interventions with the assistance of technology. This systematic review aims to evaluate the effects of technology-based cognitive training or rehabilitation interventions to improve cognitive function among individuals with MCI. **METHODS:** We conducted a systematic review using the following criteria: individuals with MCI, empirical studies, and evaluated a technology-based cognitive training or rehabilitation intervention. Twenty-six articles met the criteria. **RESULTS:** Studies were characterized by considerable variation in study design, intervention content, and technologies applied. The major types of technologies applied included computerized software, tablets, gaming consoles, and virtual reality. Use of technology to adjust the difficulties of tasks based on participants' performance was an important feature. Technology-based cognitive training and rehabilitation interventions had significant effect on global cognitive function in 8 out of 22 studies; 8 out of 18 studies found positive effects on attention, 9 out of 16 studies on executive function, and 16 out of 19 studies on memory. Some cognitive interventions improved non-cognitive symptoms such as anxiety, depression, and ADLs. **CONCLUSION:** Technology-based cognitive training and rehabilitation interventions show promise, but the findings were inconsistent due to the variations in study design. Future studies should consider using more consistent methodologies. Appropriate control groups should be designed to understand the additional benefits of cognitive training and rehabilitation delivered with the assistance of technology. DOI: 10.1186/s12877-018-0893-1 PMCID: PMC6139138 PMID: 30219036

**Conflict of interest statement:** ETHICS APPROVAL AND CONSENT TO PARTICIPATE: Not applicable. **CONSENT FOR PUBLICATION:** Not applicable. **COMPETING INTERESTS:** The authors declare that they have no competing interests. **PUBLISHER'S NOTE:** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

MCI-3. Trials. 2019 Aug 5;20(1):478. doi: 10.1186/s13063-019-3599-6.

**Effects of electroacupuncture combined with computer-based cognitive rehabilitation on mild cognitive impairment: study protocol for a pilot randomized controlled trial.** Kim JH(1)(2), Han JY(3), Park GC(4), Lee JS(5).

**BACKGROUND:** Mild cognitive impairment (MCI) is defined as an intermediate stage between normal aging and Alzheimer's disease (AD), and early and easily available interventions to delay the progress of MCI to AD are necessary. Feasible complementary and alternative therapies such as electroacupuncture (EA), exercise, and cognitive training have shown some beneficial effects on MCI and AD. Here we report the protocol for a randomized controlled trial of the efficacy and safety of EA combined with computer-based cognitive rehabilitation (EA-CCR) for the treatment of MCI. **METHODS:** The study will be a prospective, outcome assessor-blinded, parallel-arm, single-center (DongShin University Gwangju Korean Medicine Hospital, Republic of Korea), pilot randomized controlled clinical trial with a 1:1 allocation ratio. Participants with MCI will be randomized to a computer-based cognitive rehabilitation (CCR) or an EA-CCR group ( $n = 18$  each). The CCR group will receive RehaCom cognitive rehabilitation once (30 min) a day, 3 days per week (excluding Saturday and Sunday) for 8 weeks. The EA-CCR group will receive EA at Baihui (GV20), Sishencong (EX-HN1), Fengchi (GB20), and Shenting (GV24) in addition to RehaCom cognitive rehabilitation once (EA:30 min, CCR:30 min) a day, 3 days per week (excluding Saturday and Sunday) for 8 weeks. The primary outcome will be an improvement in

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cognitive function assessed using the Korean version of the Alzheimer's Disease Assessment Scale-cognitive subscale. Scores for the Korean version of the Montreal Cognitive Assessment scale, Center for Epidemiological Studies Depression Scale, Korean Activities of Daily Living scale, Korean Instrumental Activities of Daily Living scale, and European Quality of Life Five Dimension Five Level Scale will be recorded as secondary outcome measures. All scores will be recorded at baseline (before intervention), 8 weeks after the first intervention (i.e., at the end of the intervention), and 12 weeks after completion of the intervention. DISCUSSION: The study is expected to provide preliminary evidence regarding the efficacy, safety, and usefulness of EA-CCR for the treatment of MCI. TRIAL REGISTRATION: Korea Clinical Information Service, [cris.nih.go.kr](http://cris.nih.go.kr), KCT0003415 . Registered on 4 January 2019. Retrospectively registered, <http://cris.nih.go.kr> . DOI: 10.1186/s13063-019-3599-6 PMCID: PMC6683432 PMID: 31382998

MCI-4. Eur J Phys Rehabil Med. 2020 Feb;56(1):47-57. doi: 10.23736/S1973-9087.19.05899-4. Epub 2019 Oct 15. **Using virtual reality-based training to improve cognitive function, instrumental activities of daily living and neural efficiency in older adults with mild cognitive impairment.** Liao YY(1), Tseng HY(1), Lin YJ(2), Wang CJ(3), Hsu WC(4).


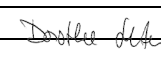
BACKGROUND: A combination of physical and cognitive training appears to be the effective intervention to improve cognitive function in older adults with mild cognitive impairment (MCI). Computing technology such as virtual reality (VR) may have the potential to assist rehabilitation in shaping brain health. However, little is known about the potential of VR-based physical and cognitive training designed as an intervention for cognition and brain activation in elderly patients with MCI. Moreover, whether a VR program designed around functional tasks can improve their instrumental activities of daily living (IADL) requires further investigation. AIM: This study investigated the effects of 12 weeks of VR-based physical and cognitive training on cognitive function, brain activation and IADL and compared the VR intervention with combined physical and cognitive training. DESIGN: A single-blinded randomized controlled trial. SETTING: Communities and day care centers in Taipei, Taiwan. POPULATION: Older adults with mild cognitive impairment. METHODS: Thirty-four community-dwelling older adults with MCI were randomized into either a VR-based physical and cognitive training (VR) group or a combined physical and cognitive training (CPC) group for 36 sessions over 12 weeks. Participants were assessed for their cognitive function (global cognition, executive function and verbal memory) and IADL at pre- and postintervention. Changes in prefrontal cortex activation during the global cognition test were also captured by functional near-infrared spectroscopy (NIRS) to identify the potential mediating pathway of the intervention. RESULTS: Both groups showed improved executive function and verbal memory (immediate recall). However, only the VR group showed significant improvements in global cognition ( $P < 0.001$ ), verbal memory (delayed recall,  $P = 0.002$ ), and IADL ( $P < 0.001$ ) after the intervention. The group  $\times$  time interaction effects further demonstrated that IADL were more significantly improved with VR training than with CPC training ( $P = 0.006$ ). The hemodynamic data revealed decreased activation in prefrontal areas after training ( $P = 0.0015$ ), indicative of increased neural efficiency, in the VR-trained subjects. CONCLUSIONS: VR-based physical and cognitive training improves cognitive function, IADL and neural efficiency in older adults with MCI. CLINICAL REHABILITATION IMPACT: VR training could be implemented for older adults with MCI. DOI: 10.23736/S1973-9087.19.05899-4 PMID: 31615196

MCI-5. Brain Sci. 2020 Dec 14;10(12):984. doi: 10.3390/brainsci10120984. **Cognitive Improvement Effects of Electroacupuncture Combined with Computer-Based Cognitive Rehabilitation in Patients with Mild Cognitive Impairment: A Randomized Controlled Trial.** Kim JH(1)(2), Han JY(3), Park GC(2), Lee JS(4).

This outcome assessor-blinded, randomized controlled clinical trial investigated the effects of electroacupuncture combined with computer-based cognitive rehabilitation (EA-CCR) on mild cognitive impairment (MCI). A per-protocol analysis was employed to compare the efficacy of EA-CCR to that of computer-based cognitive rehabilitation (CCR). Thirty-two patients with MCI completed the trial (EA-CCR group, 16; CCR group, 16). Patients received EA-CCR or CCR treatment once daily three days per week for eight weeks. Outcome (primary, ADAS-K-cog; secondary, MoCA-K, CES-D, K-ADL, K-IADL, and EQ-5D-5L) measurements were performed at baseline (week 0), at the end of the intervention (week 8), and at 12 weeks after completion of the intervention (week 20). Both groups showed significant changes in ADAS-K-cog score (EA-CCR,  $p < 0.001$ ; CCR,  $p < 0.001$ ) and MoCA-K (EA-CCR,  $p < 0.001$ ; CCR,  $p < 0.001$ ). Only the EA-CCR group had a significant change in CES-D ( $p = 0.024$ ). No significant differences in outcomes and in the results of a subanalysis based on age were noted between the groups. These results indicate that EA-CCR and CCR have beneficial effects on improving cognitive function in patients with MCI. However, electroacupuncture in EA-CCR showed no positive add-on effects on improving cognitive function, depression, activities of daily living, and quality of life in patients with MCI. DOI: 10.3390/brainsci10120984 PMCID: PMC7765117 PMID: 33327627 Conflict of interest statement: The authors declare no conflict of interest.

MCI-6. Medicine (Baltimore). 2018 Nov;97(45):e13007. doi: 10.1097/MD.00000000000013007. **A comparison of the effects between 2 computerized cognitive training programs, Bettercog and COMCOG, on elderly patients with MCI and mild dementia: A single-blind randomized controlled study.** Lee GJ(1)(2), Bang HJ(1)(3)(2), Lee KM(1)(3)(2), Kong HH(1)(2), Seo HS(1)(2), Oh M(1)(2), Bang M(1)(2).

BACKGROUND: A computerized cognitive rehabilitation program can be used to treat patients with mild cognitive impairment or dementia. We developed a new computerized cognitive rehabilitation program (Bettercog) that contained various treatment programs for cognitive training for mild cognitive impairment or dementia. This study was conducted to compare the clinical efficacy of Bettercog and computer-assisted cognitive rehabilitation (COMCOG) that has had

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clinical efficacy previously proven in patients with mild cognitive impairment or dementia. METHODS: Randomized, single-blind comparison pilot study of 20 elderly patients with cognitive decline-eight men and 12 women-with an average age of 74.3 years. Bettercog trains not only memory and attention but also orientation, calculation, executive function, language, comprehension, and spatiotemporal abilities. To retain subjects' interest, pictures, animations, and game elements were introduced. The subjects were divided into COMCOG and Bettercog groups by random assignment and underwent 12 sessions of a computerized cognitive rehabilitation program for three weeks. In a separate space, an independent clinical psychologist conducted the Seoul Neuropsychological Screening Battery 2nd edition (SNSB-II), Korean Mini-Mental State Examination (K-MMSE), Clinical Dementia Rating (CDR), and the Korean version of the Modified Barthel Index (K-MBI) before and after treatment. RESULTS: There was no significant difference between the two groups in baseline age, sex, illiteracy, years of education, and scores on the K-MMSE, CDR, SNSB-II, and K-MBI. In the posttreatment cognitive assessment, the K-MMSE scores of patients treated with Bettercog improved from  $19.2 \pm 3.9$  to  $21.3 \pm 4.0$  ( $P = .005$ ). In the memory domain of the SNSB-II, the percentile score improved from  $15.3 \pm 24.5$  to  $24.2 \pm 30.7$  ( $P = .026$ ). However, there was no statistically significant difference in the final K-MMSE, CDR, and SNSB-II scores between the two treatment groups. In both groups, K-MBI scores improved statistically significantly after treatment. CONCLUSIONS: Through this preliminary study, we verified that the newly developed computerized cognitive rehabilitation program is effective in improving cognitive function. However, 12 sessions are not enough to administer a variety of cognitive rehabilitation content to patients. It is, therefore, necessary to conduct a large-scale study using a computerized cognitive rehabilitation program that has various cognitive content. DOI: 10.1097/MD.000000000013007 PMID: PMC6250524 PMID: 30407291

MCI-7. J Med Internet Res. 2019 Aug 30;21(8):e12785. doi: 10.2196/12785.

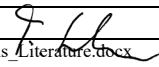
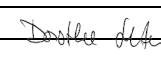
**Current State of Digital Biomarker Technologies for Real-Life, Home-Based Monitoring of Cognitive Function for Mild Cognitive Impairment to Mild Alzheimer Disease and Implications for Clinical Care: Systematic Review.** Piau A(1)(2), Wild K(2), Mattek N(2), Kaye J(2).

BACKGROUND: Among areas that have challenged the progress of dementia care has been the assessment of change in symptoms over time. Digital biomarkers are defined as objective, quantifiable, physiological, and behavioral data that are collected and measured by means of digital devices, such as embedded environmental sensors or wearables. Digital biomarkers provide an alternative assessment approach, as they allow objective, ecologically valid, and long-term follow-up with continuous assessment. Despite the promise of a multitude of sensors and devices that can be applied, there are no agreed-upon standards for digital biomarkers, nor are there comprehensive evidence-based results for which digital biomarkers may be demonstrated to be most effective. OBJECTIVE: In this review, we seek to answer the following questions: (1) What is the evidence for real-life, home-based use of technologies for early detection and follow-up of mild cognitive impairment (MCI) or dementia? And (2) What transformation might clinicians expect in their everyday practices? METHODS: A systematic search was conducted in PubMed, Cochrane, and Scopus databases for papers published from inception to July 2018. We searched for studies examining the implementation of digital biomarker technologies for mild cognitive impairment or mild Alzheimer disease follow-up and detection in nonclinic, home-based settings. All studies that included the following were examined: community-dwelling older adults (aged 65 years or older); cognitively healthy participants or those presenting with cognitive decline, from subjective cognitive complaints to early Alzheimer disease; a focus on home-based evaluation for noninterventional follow-up; and remote diagnosis of cognitive deterioration. RESULTS: An initial sample of 4811 English-language papers were retrieved. After screening and review, 26 studies were eligible for inclusion in the review. These studies ranged from 12 to 279 participants and lasted between 3 days to 3.6 years. Most common reasons for exclusion were as follows: inappropriate setting (eg, hospital setting), intervention (eg, drugs and rehabilitation), or population (eg, psychiatry and Parkinson disease). We summarized these studies into four groups, accounting for overlap and based on the proposed technological solutions, to extract relevant data: (1) data from dedicated embedded or passive sensors, (2) data from dedicated wearable sensors, (3) data from dedicated or purposive technological solutions (eg, games or surveys), and (4) data derived from use of nondedicated technological solutions (eg, computer mouse movements). CONCLUSIONS: Few publications dealt with home-based, real-life evaluations. Most technologies were far removed from everyday life experiences and were not mature enough for use under nonoptimal or uncontrolled conditions. Evidence available from embedded passive sensors represents the most relatively mature research area, suggesting that some of these solutions could be proposed to larger populations in the coming decade. The clinical and research communities would benefit from increasing attention to these technologies going forward. ©Antoine Piau, Katherine Wild, Nora Mattek, Jeffrey Kaye. Originally published in the Journal of Medical Internet Research (<http://www.jmir.org>), 30.08.2019. DOI: 10.2196/12785 PMID: PMC6743264 PMID: 31471958

MCI-8. Syst Rev. 2019 Sep 6;8(1):231. doi: 10.1186/s13643-019-1146-x.

**Computer-based cognitive interventions for mild cognitive impairment and dementia in older adults: protocol for a systematic review of published studies and meta-analysis.** Al Mahmud A(1), Slikboer R(2), Staggatt J(2), Bhar S(2).

BACKGROUND: A growing number of older adults experience mild cognitive impairment (MCI) and dementia. Recent technological advances allow for traditional cognitive interventions to be administered via computers and other devices. The aim of the proposed systematic review and meta-analyses is to determine the efficacy of computerised cognitive interventions for MCI and dementia in older adults. METHODS: We will systematically search electronic databases and reference lists to identify randomised controlled trials. We will include studies that examine the use of computer-based cognitive interventions for adults aged over 60 with MCI or dementia. Primarily outcomes are global and domain-specific

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cognitive function. Secondary outcomes are attitudes (usability, understandability, acceptability of the intervention), mood and quality of life. Risk of bias will be assessed. Finally, the summary effect sizes will be reported. **DISCUSSION:** This systematic review will summarise existing high-quality primary studies on computerised-cognitive interventions for MCI and dementia. Results from this review will provide the basis for future research in developing computer-based interventions for this population. **SYSTEMATIC REVIEW REGISTRATION:** PROSPERO CRD42016050236. DOI: 10.1186/s13643-019-1146-x PMCID: PMC6729043 PMID: 31492180  
 Conflict of interest statement: The authors declare that they have no competing interests.

MCI-9. Healthcare (Basel). 2020 Sep 11;8(3):335. doi: 10.3390/healthcare8030335.

**Virtual Reality-Based Cognitive-Motor Rehabilitation in Older Adults with Mild Cognitive Impairment: A Randomized Controlled Study on Motivation and Cognitive Function.** Park JS(1), Jung YJ(2), Lee G(3).

The purpose of this study was to investigate the effects of virtual reality-based cognitive-motor rehabilitation (VRCMR) on the rehabilitation motivation and cognitive function in older adults. This study enrolled 40 older adults with mild cognitive impairment (MCI), living in the community. The subjects were randomly assigned to a VRCMR group (n = 20) or a conventional cognitive rehabilitation (CCR) group (n = 20). The VRCMR group underwent VRCMR using MOTOCog, a computer recognition program, whereas the CCR group underwent conventional cognitive rehabilitation, which included puzzles, wood blocks, card play, stick construction activity, and maze activity. Both interventions were performed 30 min per day, 5 days/week, for 6 weeks. This study performed a cognitive assessment using the Montreal Cognitive Assessment (MoCA) scale, Trail Making Test A and B (TMT-A/B), and Digit Span Test forward and backward (DST-forward/backward). In addition, a 0-to-10 numeric rating self-report scale was used to assess interest and motivation during the rehabilitation training. After the intervention, the VRCMR group showed a significantly greater improvement in the MoCA (p = 0.045), TMT-A (p = 0.039), TMT-B (p = 0.040), and DST-forward (p = 0.011) scores compared to the CCR group, but not in the DST-backward score (p = 0.424). In addition, subjects in the experimental group had significantly higher interest (p = 0.03) and motivation (p = 0.03) than those in the control group. Cohen's d effect size was 0.4, 0.3, 0.35, 0.4, and 0.5 for the MoCA, TMT-A, TMT-B, DST-forward, and DST-backward tests, respectively. This study demonstrates that VRCMR enhances motivation for rehabilitation and cognitive function in older adults with MCI better than CCR. DOI: 10.3390/healthcare8030335 PMCID: PMC7551774 PMID: 32932997 Conflict of interest statement: The authors declare no conflict of interest.

MCI-10. Cogn Behav Neurol. 2019 Sep;32(3):172-178. doi: 10.1097/WNN.000000000000197.


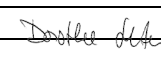
**Effects of a Mixed Reality-based Cognitive Training System Compared to a Conventional Computer-assisted Cognitive Training System on Mild Cognitive Impairment: A Pilot Study.** Park E(1)(2), Yun BJ(3), Min YS(1)(2), Lee YS(1)(4), Moon SJ(1), Huh JW(1)(4), Cha H(5), Chang Y(5)(6)(7), Jung TD(1)(4).

**BACKGROUND:** Mixed reality (MR) technology, which combines the best features of augmented reality and virtual reality, has recently emerged as a promising tool in cognitive rehabilitation therapy. **OBJECTIVE:** To investigate the effectiveness of an MR-based cognitive training system for individuals with mild cognitive impairment (MCI). **METHODS:** Twenty-one individuals aged 65 years and older who had been diagnosed with MCI were recruited for this study and were divided into two groups. Participants in the MR group (n=10, aged 70.5±4.2 years) received 30 minutes of training 3 times a week for 6 weeks using a newly developed MR-based cognitive training system. Participants in the control group (n=11, aged 72.6±5.3 years) received the same amount of training using a conventional computer-assisted cognitive training system. Both groups took the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD-K) both before and after intervention. To determine the effect of the intervention on cognitive function, we compared the difference in each group's CERAD-K scores. **RESULTS:** There was a statistically significant interaction between intervention (MR group vs control group) and time (before vs after intervention) as assessed by the Constructional Recall Test. The individuals with MCI who participated in the MR training showed significantly improved performance in visuospatial working memory compared with the individuals with MCI who participated in the conventional training. **CONCLUSION:** An MR-based cognitive training system can be used as a cognitive training tool to improve visuospatial working memory in individuals with MCI. DOI: 10.1097/WNN.000000000000197 PMID: 31517700

MCI-11. Health Inf Sci Syst. 2020 Nov 24;9(1):4. doi: 10.1007/s13755-020-00132-6. eCollection 2021 Dec.

**A method of VR-EEG scene cognitive rehabilitation training.** Tan W(1)(2), Xu Y(1), Liu P(1), Liu C(3), Li Y(1), Du Y(1), Chen C(4), Wang Y(3), Zhang Y(2)(5).

Virtual reality technology can intuitively provide patients of neuropsychological diseases with an almost real environment for cognitive rehabilitation training. In this paper, virtual reality technology is used to construct specific scenes that are universal and related to MCI patients to restore and train patients' scene memory cognitive ability to help patients strengthen or gradually restore scene memory cognitive ability. The construction of virtual reality scenes with different contents such as life, environment, transportation and tourism, real-time detection is carried out in combination with EEG signals of patients in different scenes. The experimental results of the analysis of EEG signals of patients shows that memory rehabilitation training is strengthened by using specific stimulation scenes. © Springer Nature Switzerland AG 2020. DOI: 10.1007/s13755-020-00132-6 PMCID: PMC7686436 PMID: 33269073  
 Conflict of interest statement: Conflict of interestThe authors declare that they have no conflict of interest.

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MCI-12. Arch Gerontol Geriatr. 2006 Nov-Dec;43(3):327-35. doi: 10.1016/j.archger.2005.12.003. Epub 2006 Jan 31.

**Outcomes of a computer-based cognitive rehabilitation program on Alzheimer's disease patients compared with those on patients affected by mild cognitive impairment.** Cipriani G(1), Bianchetti A, Trabucchi M.

The aim of the present study is to evaluate the outcomes of a computer-based cognitive training on patients affected by Alzheimer's disease (AD) compared with the outcomes on patients affected by mild cognitive impairment (MCI), multiple system atrophy (MSA). Ten AD patients aged 74.1+/-5.6 years, with mini-mental state examination (MMSE) score at baseline of 23.9+/-2.4, and 10 MCI patients aged 70.6+/-6.0 years, with MMSE score of 28.0+/-1.4, attending our day-hospital of neurorehabilitation were selected for the study. Three MSA patients aged 69.0+/-9.5 years, MMSE scores 26.7+/-2.3 were selected from the same setting in order to have a different control group. Each patient attended two training programs and was evaluated according to cognitive and non-cognitive functions at baseline at the end of the second training program. The AD group showed a significant MMSE score improvement ( $p=0.010$ ). On the contrary, MMSE scores at baseline and at follow-up remained quite stable in the other two groups. AD patients also showed significant improvement in the areas of verbal production ( $p=0.036$ ) and executive functions ( $p=0.050$ ). MCI patients significantly improved in behavioral memory ( $p=0.017$ ;  $p=0.011$ ). No significant improvement was observed in MSA group. Our data seem to indicate that the same individualized rehabilitative intervention could have different effects according to patient's diagnosis. MCI and AD patients had significant improvements in global cognitive status and/or in specific cognitive areas. On the contrary, MSA patients did not benefit at all. DOI: 10.1016/j.archger.2005.12.003 PMID: 16451811

MCI-13. Restor Neurol Neurosci. 2018;36(2):207-213. doi: 10.3233/RNN-170754.

**Potential benefits of a cognitive training program in mild cognitive impairment (MCI).** Mendoza Laiz N(1), Del Valle Díaz S(1), Rioja Collado N(1), Gomez-Pilar J(2), Hornero R(2).

BACKGROUND: Dementia is a disease that is constantly evolving in older people. Its diverse symptoms appear with varying degrees of severity affecting the daily life of those who suffer from it. The rate in which dementia progresses depends on different aspects of the treatment, chosen to try to control and slow down the development of the illness. OBJECTIVE: The aim of this study is to assess the effectiveness of cognitive training through a Brain Computer Interface (BCI) and the NeuronUp platform in two age groups whose MMSE is between 18-23 MCI (mild dementia). METHOD: 32 subjects took part in the study. There were 22 subjects in Group 1 (61-69 years of age) and 10 subjects in Group 2 (70-81 years of age). The criterium for the selection of the groups was to identify the age range with greater improvements due to the training. In order to estimate neuropsychological performance, the subjects were evaluated with the Luria-DNA neuropsychological battery before and after training. This design enables us to evaluate five cognitive areas: visuospatial, spoken language, memory, intellectual processes and attention. RESULTS: After training, Group 1 showed significant improvements in almost all the variables measured when compared with Group 2. This reveals a significant increase in cognitive ability, the degree of which depends on the age. CONCLUSION: People with mild dementia may delay cognitive impairment with a suitable cognitive training program. DOI: 10.3233/RNN-170754 PMID: 29526855

MCI-14. Games Health J. 2020 Oct 15. doi: 10.1089/g4h.2020.0086. Online ahead of print.

**The Effectiveness of a Virtual Reality-Based Intervention on Cognitive Functions in Older Adults with Mild Cognitive Impairment: A Single-Blind, Randomized Controlled Trial.** Torpil B(1), Şahin S(2), Pekçetin S(1), Uyanık M(2).

Objective: Mild cognitive impairment (MCI) is a broad term for people at a stage between normal age-related cognitive decline and dementia, where cognitive problems are present but do not impair activities of daily living. This study aimed at evaluating the effectiveness of a virtual reality (VR)-based rehabilitation program on cognitive functions in MCI. Materials and Methods: Sixty-one older adults (25 men, 36 women) with MCI were randomized to the intervention group ( $n = 30$ ;  $70.12 \pm 2.57$  years) or control ( $n = 31$ ;  $70.30 \pm 2.73$  years) group. The intervention group received a VR (computer-generated interactive environments) intervention in addition to a conventional cognitive rehabilitation (CR) intervention, whereas the control group received only the CR intervention. Cognitive functions were assessed in both groups before and after the 12-week interventions by using the Loewenstein Occupational Therapy Cognitive Assessment-Geriatric. Results: Between-group comparisons revealed significantly greater improvements in orientation, visual-spatial perception, visuospatial organization, thinking operation, and attention/concentration functions in the VR group than in the control group ( $P < 0.001$  for all). Conclusion: Our results showed that 12 weeks of VR-based rehabilitation enhanced cognitive functions in older adults with MCI. Using VR applications in CR is recommended to improve cognitive functions of older adults with MCI. DOI: 10.1089/g4h.2020.0086 PMID: 33058735

MCI-15. Neuroimage Clin. 2019;22:101691. doi: 10.1016/j.nicl.2019.101691. Epub 2019 Jan 26.

**Computerized cognitive training for Chinese mild cognitive impairment patients: A neuropsychological and fMRI study.** Li BY(1), He NY(2), Qiao Y(1), Xu HM(2), Lu YZ(1), Cui PJ(3), Ling HW(2), Yan FH(4), Tang HD(5), Chen SD(6).

BACKGROUND: Computerized multi-model training has been widely studied for its effect on delaying cognitive decline. In this study, we designed the first Chinese-version computer-based multi-model cognitive training for mild cognitive impairment (MCI) patients. Neuropsychological effects and neural activity changes assessed by functional MRI were both evaluated. METHOD: MCI patients in the training group were asked to take training 3-4 times per week for 6 months.

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Neuropsychological and resting-state fMRI assessment were performed at baseline and at 6 months. Patients in both groups were continuously followed up for another 12 months and assessed by neuropsychological tests again. RESULTS: 78 patients in the training group and 63 patients in the control group accomplished 6-month follow-up. Training group improved 0.23 standard deviation (SD) of mini-mental state examination, while control group had 0.5 SD decline. Addenbrooke's cognitive examination-revised scores in attention ( $p = 0.002$ ) and memory ( $p = 0.006$ ), as well as stroop color-word test interference index ( $p = 0.038$ ) and complex figure test-copy score ( $p = 0.035$ ) were also in favor of the training effect. Difference between the changes of two groups after training was not statistically significant. The fMRI showed increased regional activity at bilateral temporal poles, insular cortices and hippocampus. However, difference between the changes of two groups after another 12 months was not statistically significant. CONCLUSIONS: Multi-model cognitive training help MCI patients to gained cognition benefit, especially in memory, attention and executive function. Functional neuroimaging provided consistent neural activation evidence. Nevertheless, after one-year follow up after last training, training effects were not significant. The study provided new evidence of beneficial effect of multi-model cognitive training. Copyright © 2019. Published by Elsevier Inc. DOI: 10.1016/j.nicl.2019.101691 PMID: 30708349

MCI-16. J Alzheimers Dis. 2019;71(2):541-548. doi: 10.3233/JAD-190631.

**Tracking Cognitive Performance in the General Population and in Patients with Mild Cognitive Impairment with a Self-Applied Computerized Test (Brain on Track).** Ruano L(1)(2)(3), Severo M(1)(2), Sousa A(3), Ruano C(4), Branco M(1)(3), Barreto R(5), Moreira S(6), Araújo N(1)(2), Pinto P(1)(2), Pais J(2), Lunet N(1)(2), Cruz VT(2)(6).

Repeated measurements could be helpful to identify patients with early cognitive decline. We compare the variation of cognitive performance over one year in patients with mild cognitive impairment (MCI) and healthy individuals using the Brain on Track self-applied computerized test (BoT). The study was initiated 30 patients with probable MCI and 377 controls from a population-based cohort, who performed the BoT test from home every three months for one year. The scores were compared using a linear mixed-effects model. All participants increased their scores in the first tests, after 120 days MCI patients started to decline, with a statistically significant higher rate. The area under the curve to detect MCI was 0.94. We identified a significant decline in cognitive performance over one year in patients with MCI using BoT and the test presented a high discriminative ability. DOI: 10.3233/JAD-190631 PMID: 31424407

MCI-17. Alzheimers Dement. 2014 Jan;10(1):10-7. doi: 10.1016/j.jalz.2013.01.011. Epub 2013 May 18.

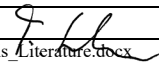
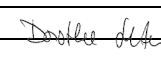
**Unobtrusive measurement of daily computer use to detect mild cognitive impairment.** Kaye J(1), Mattek N(2), Dodge HH(2), Campbell I(3), Hayes T(3), Austin D(3), Hatt W(4), Wild K(2), Jimison H(4), Pavel M(3).

BACKGROUND: Mild disturbances of higher order activities of daily living are present in people diagnosed with mild cognitive impairment (MCI). These deficits may be difficult to detect among those still living independently. Unobtrusive continuous assessment of a complex activity such as home computer use may detect mild functional changes and identify MCI. We sought to determine whether long-term changes in remotely monitored computer use differ in persons with MCI in comparison with cognitively intact volunteers. METHODS: Participants enrolled in a longitudinal cohort study of unobtrusive in-home technologies to detect cognitive and motor decline in independently living seniors were assessed for computer use (number of days with use, mean daily use, and coefficient of variation of use) measured by remotely monitoring computer session start and end times. RESULTS: More than 230,000 computer sessions from 113 computer users (mean age, 85 years; 38 with MCI) were acquired during a mean of 36 months. In mixed-effects models, there was no difference in computer use at baseline between MCI and intact participants controlling for age, sex, education, race, and computer experience. However, over time, between MCI and intact participants, there was a significant decrease in number of days with use ( $P = .01$ ), mean daily use (~1% greater decrease/month;  $P = .009$ ), and an increase in day-to-day use variability ( $P = .002$ ). CONCLUSIONS: Computer use change can be monitored unobtrusively and indicates individuals with MCI. With 79% of those 55 to 64 years old now online, this may be an ecologically valid and efficient approach to track subtle, clinically meaningful change with aging. Copyright © 2014 The Alzheimer's Association. Published by Elsevier Inc. All rights reserved. DOI: 10.1016/j.jalz.2013.01.011 PMID: 23688576

MCI-18. Neuropsychologia. 2012 Jul;50(8):1871-81. doi: 10.1016/j.neuropsychologia.2012.04.012. Epub 2012 Apr 21.

**Positive effects of computer-based cognitive training in adults with mild cognitive impairment.** Herrera C(1), Chambon C, Michel BF, Paban V, Alescio-Lautier B.

Considering the high risk for individuals with amnesic Mild Cognitive Impairment (A-MCI) to progress towards Alzheimer's disease (AD), we investigated the efficacy of a non-pharmacological intervention, that is, cognitive training that could reduce cognitive difficulties and delay the cognitive decline. For this, we evaluated the efficacy of a 12-week computer-based memory-attention training program based on recognition in subjects with A-MCI and compared their performances with those of A-MCI controls trained in cognitively stimulating activities. The effect of training was assessed by comparing outcome measures in pre- and post-tests 15 days before and after training. To evaluate the duration of training benefits, a follow-up test session was performed 6 months after memory and attention training or cognitively stimulating activities. Outcome measures showed that the trained group, compared to control group, improved episodic recall and recognition. Six months after training, scores remained at the level of the post-test. Since the training program was exclusively based on recognition, our results showed a generalization from recognition to recall processes, which are memory components that represent part of the core cognitive impairments in individuals at risk of converting to AD. Thus, cognitive training based on recognition holds promise as a preventive therapeutic method and

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could be proposed as a non-pharmacological early-intervention strategy. Future investigations need to focus on methodological constraints and delineating possible neuroplastic mechanisms of action. Copyright © 2012 Elsevier Ltd. All rights reserved. DOI: 10.1016/j.neuropsychologia.2012.04.012 PMID: 22525705

MCI-19. Eur J Nucl Med Mol Imaging. 2020 Feb;47(2):256-269. doi: 10.1007/s00259-019-04559-2. Epub 2019 Dec 7. **Brain metabolic signatures across the Alzheimer's disease spectrum.** Sala A(1)(2), Caprioglio C(1), Santangelo R(3), Vanoli EG(4), Iannaccone S(5), Magnani G(3), Perani D(6)(7)(8).

**PURPOSE:** Given the challenges posed by the clinical diagnosis of atypical Alzheimer's disease (AD) variants and the limited imaging evidence available in the prodromal phases of atypical AD, we assessed brain hypometabolism patterns at the single-subject level in the AD variants spectrum. Specifically, we tested the accuracy of [18F]FDG-PET brain hypometabolism, as a biomarker of neurodegeneration, in supporting the differential diagnosis of atypical AD variants in individuals with dementia and mild cognitive impairment (MCI). **METHODS:** We retrospectively collected N = 67 patients with a diagnosis of typical AD and AD variants according to the IWG-2 criteria (22 typical-AD, 15 frontal variant-AD, 14 logopenic variant-AD and 16 posterior variant-AD). Further, we included N = 11 MCI subjects, who subsequently received a clinical diagnosis of atypical AD dementia at follow-up (21 ± 11 months). We assessed brain hypometabolism patterns at group- and single-subject level, using W-score maps, measuring their accuracy in supporting differential diagnosis. In addition, the regional prevalence of cerebral hypometabolism was computed to identify the most vulnerable core regions. **RESULTS:** W-score maps pointed at distinct, specific patterns of hypometabolism in typical and atypical AD variants, confirmed by the assessment of core hypometabolism regions, showing that each variant was characterized by specific regional vulnerabilities, namely in occipital, left-sided, or frontal brain regions. ROC curves allowed discrimination among AD variants and also non-AD dementia (i.e., dementia with Lewy bodies and behavioral variant of frontotemporal dementia), with high sensitivity and specificity. Notably, we provide preliminary evidence that, even in AD prodromal phases, these specific [18F]FDG-PET patterns are already detectable and predictive of clinical progression to atypical AD variants at follow-up. **CONCLUSIONS:** The AD variant-specific patterns of brain hypometabolism, highly consistent at single-subject level and already evident in the prodromal stages, represent relevant markers of disease neurodegeneration, with highly supportive diagnostic and prognostic role. DOI: 10.1007/s00259-019-04559-2 PMID: 31811345

MCI-20. Am J Alzheimers Dis Other Demen. 2015 Feb;30(1):49-54. doi: 10.1177/1533317514545866. Epub 2014 Aug 7. **Using virtual reality for cognitive training of the elderly.** García-Betances RI(1), Jiménez-Mixco V(2), Arredondo MT(2), Cabrera-Umpiérrez MF(2).

There is a pressing demand for improving the quality and efficacy of health care and social support services needed by the world's growing elderly population, especially by those affected by mild cognitive impairment (MCI) and Alzheimer's disease (AD)-type early-stage dementia. Meeting that demand can significantly benefit from the deployment of innovative, computer-based applications capable of addressing specific needs, particularly in the area of cognitive impairment mitigation and rehabilitation. In that context, we present here our perspective viewpoint on the use of virtual reality (VR) tools for cognitive rehabilitation training, intended to assist medical personnel, health care workers, and other caregivers in improving the quality of daily life activities of people with MCI and AD. We discuss some effective design criteria and developmental strategies and suggest some possibly useful protocols and procedures. The particular innovative supportive advantages offered by the immersive interactive characteristics inherent to VR technology are discussed. © The Author(s) 2014. DOI: 10.1177/1533317514545866 PMID: 25107931

MCI-21. Front Neurol. 2020 Nov 27;11:583368. doi: 10.3389/fneur.2020.583368. eCollection 2020. **Analysis of Feasibility, Adherence, and Appreciation of a Newly Developed Tele-Rehabilitation Program for People With MCI and VCI.** Mosca IE(1), Salvadori E(1), Gerli F(1), Fabri L(1), Pancani S(1), Lucidi G(1), Lombardi G(1), Bocchi L(2), Pazzi S(3), Baglio F(1), Vannetti F(1), Sorbi S(1)(4), Macchi C(1)(5).

**Background:** Patients with Mild Cognitive Impairment (MCI) and Vascular Cognitive Impairment (VCI) are at a high risk of progressing to dementia. Recent guidelines indicate the importance of promoting multidimensional and multi-domain interventions to prevent further decline. Due to its growing effectiveness, comparable to conventional face-to-face interventions, the use of technology is gaining relevance. Tele-rehabilitation systems have the potential to engage patients in multi-dimensional activity programs and to guarantee a low-cost continuum of care through remote control. A possible limitation of such programs is represented by the lack of familiarization with technology and computers in elderly people. The purpose of this study is to describe the feasibility, adherence, and appreciation of the GOAL Tele-R system, administered by a web-application through remote control in patients with MCI/VCI. **Methods:** Feasibility of the Tele-R system was evaluated by means of distribution of patients' attrition along the study phases, controlling for potential systematic bias in drop-out rates due to the technological device. Adherence was evaluated analyzing drop-out rates and indexes of carried out activities. Patients' appreciation was analyzed through ad hoc satisfaction questionnaire items. **Results:** Out of 86 approached patients, 25 (29%) were not enrolled, 30 (35%) dropped-out after randomization, and 31 (36%) completed the study (standard care group n = 12, the tele-R group n = 19). Compared to the tele-R group, rates of drop-outs resulted significantly higher for the standard care group (34 vs. 62%, respectively, p = 0.029). Taking into account baseline characteristics, females resulted in a statistically significant higher rate of drop-outs compared to males (66 vs. 27%, respectively, p = 0.003). Overall adherence to the proposed activities was 84% (85% for cognitive module and 83% for physical activity module). Concerning satisfaction, participants provided a good mean level of appreciation (3.7 ± 0.8, range 1-5), a positive feedback for usability, and a subjective perception of cognitive,

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emotional, and physical benefits due to the training. Conclusion: The GOAL Tele-R system seems a feasible technological rehabilitation program, reaching an acceptable level of adherence and appreciation in patients with an MCI/VCI condition. Clinical Trial Registration: www.ClinicalTrials.gov, ID: NCT03383549 (registration date: 26/dec/2017). Copyright © 2020 Mosca, Salvadori, Gerli, Fabbri, Pancani, Lucidi, Lombardi, Bocchi, Pazzi, Baglio, Vannetti, Sorbi and Macchi. DOI: 10.3389/fneur.2020.583368 PMCID: PMC7728852 PMID: 33329326 Conflict of interest statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

MCI-22. Trials. 2018 Feb 12;19(1):100. doi: 10.1186/s13063-017-2371-z.

**The effectiveness of ICT-based neurocognitive and psychosocial rehabilitation programmes in people with mild dementia and mild cognitive impairment using GRADIOR and ehcoBUTLER: study protocol for a randomised controlled trial.** Vanova M(1)(2), Irazoki E(3)(4), García-Casal JA(3), Martínez-Abad F(5), Botella C(6)(7), Shiells KR(8), Franco-Martín MA(9)(4).

BACKGROUND: Cognitive rehabilitation is a highly individualised, non-pharmacological intervention for people with mild cognitive impairment (MCI) and dementia, which in recent years has also been developed for various IT platforms. METHODS: In this study, we aim to evaluate the effectiveness of the cognitive rehabilitation software GRADIOR in a multi-centre, single-blinded randomised controlled trial with people with MCI and mild dementia. A total of 400 people with MCI and mild dementia will be randomly allocated to one of four groups. This trial will compare the cognitive rehabilitation treatment using the GRADIOR programme with a psychosocial stimulation intervention (PSS) using the ehcoBUTLER platform, with a combined treatment consisting of GRADIOR and ehcoBUTLER, and with a group receiving treatment as usual during a period of 1 year. DISCUSSION: The outcomes of this clinical trial will be to determine any relevant changes in cognition, mood, quality of life, activities of daily living and quality of patient-carer relationship after 4 months and 1 year of intervention in a cross-sectional group comparison. Participants will be followed-up for 1 year to investigate potential long-term effects of the conducted treatments. TRIAL REGISTRATION: Current Controlled Trials ISRCTN, ID: 15742788 . Registered on 12 June 2017. DOI: 10.1186/s13063-017-2371-z PMCID: PMC5810083 PMID: 29433545

Conflict of interest statement: ETHICS APPROVAL AND CONSENT TO PARTICIPATE: The protocol was submitted for ethical approval in May 2017 to the Zamora Provincial Hospital Ethics Committee. Ethical approval was obtained on 17 May 2017. CONSENT FOR PUBLICATION: Not applicable COMPETING INTERESTS: We have read and understood BMC policy on declaration of interests and declare the following interests: MV and EI are paid members of INTRAS Foundation responsible for development and distribution of GRADIOR software. MV is a Marie Curie Early-Stage Researcher in the INDUCT project. MFM is a founder and director of INTRAS Foundation and a supervisor within the INDUCT project. JAGC is a former member of INTRAS Foundation and has no current competing interests. FMA and CB have no competing interests. PUBLISHER'S NOTE: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

MCI-23. Neuroimage Clin. 2019;23:101859. doi: 10.1016/j.nicl.2019.101859. Epub 2019 May 13.

**Diagnosis and prognosis of Alzheimer's disease using brain morphometry and white matter connectomes.** Wang Y(1), Xu C(2), Park JH(2), Lee S(3), Stern Y(4), Yoo S(5), Kim JH(6), Kim HS(7), Cha J(8); Alzheimer's Disease Neuroimaging Initiative.

Accurate, reliable prediction of risk for Alzheimer's disease (AD) is essential for early, disease-modifying therapeutics. Multimodal MRI, such as structural and diffusion MRI, is likely to contain complementary information of neurodegenerative processes in AD. Here we tested the utility of the multimodal MRI (T1-weighted structure and diffusion MRI), combined with high-throughput brain phenotyping-morphometry and structural connectomics-and machine learning, as a diagnostic tool for AD. We used, firstly, a clinical cohort at a dementia clinic (National Health Insurance Service-Ilsan Hospital [NHIS-IH]; N = 211; 110 AD, 64 mild cognitive impairment [MCI], and 37 cognitively normal with subjective memory complaints [SMC]) to test the diagnostic models; and, secondly, Alzheimer's Disease Neuroimaging Initiative (ADNI)-2 to test the generalizability. Our machine learning models trained on the morphometric and connectome estimates (number of features = 34,646) showed optimal classification accuracy (AD/SMC: 97% accuracy, MCI/SMC: 83% accuracy; AD/MCI: 97% accuracy) in NHIS-IH cohort, outperforming a benchmark model (FLAIR-based white matter hyperintensity volumes). In ADNI-2 data, the combined connectome and morphometry model showed similar or superior accuracies (AD/HC: 96%; MCI/HC: 70%; AD/MCI: 75% accuracy) compared with the CSF biomarker model (t-tau, p-tau, and Amyloid  $\beta$ , and ratios). In predicting MCI to AD progression in a smaller cohort of ADNI-2 (n = 60), the morphometry model showed similar performance with 69% accuracy compared with CSF biomarker model with 70% accuracy. Our comparisons of the classifiers trained on structural MRI, diffusion MRI, FLAIR, and CSF biomarkers showed the promising utility of the white matter structural connectomes in classifying AD and MCI in addition to the widely used structural MRI-based morphometry, when combined with machine learning. Copyright © 2019 The Authors. Published by Elsevier Inc. All rights reserved. DOI: 10.1016/j.nicl.2019.101859 PMCID: PMC6541902 PMID: 31150957

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MCI-24. *Alzheimers Res Ther.* 2019 Jan 10;11(1):4. doi: 10.1186/s13195-018-0464-x.

**Measuring instrumental activities of daily living in non-demented elderly: a comparison of the new performance-based Harvard Automated Phone Task with other functional assessments.** Marshall GA(1)(2), Aghjayan SL(3), Dekhtyar M(3), Locascio JJ(4), Jethwani K(5), Amariglio RE(3)(4), Czaja SJ(6), Loewenstein DA(6), Johnson KA(3)(4), Sperling RA(3)(4), Rentz DM(3)(4).

**BACKGROUND:** Impairment in instrumental activities of daily living (IADL) may occur in the earliest stages of mild cognitive impairment (MCI). However, there are few reliable measures of IADL in MCI or that have a sufficient range of scores in clinically normal (CN) elderly. The objective of this pilot study was to examine the convergent validity of a phone performance-based IADL instrument, the Harvard Automated Phone Task (APT), designed to measure the earliest IADL changes in Alzheimer's disease (AD), with other sensitive performance-based and subjective measures of everyday functional capacity among CN and MCI participants. **METHODS:** Twenty-nine CN and 17 MCI participants were administered the Harvard APT, the computer performance-based Czaja Functional Assessment Battery (CFAB), and the AD Cooperative Study ADL prevention instrument (ADCS ADL-PI) participant and study partner versions; in addition, 52 different CN and 7 MCI participants were administered the Harvard APT and the Subjective Study Partner and Participant-reported (SSPP) IADL scale. The Harvard APT was compared with the three other IADL assessments. **RESULTS:** In both CN and MCI, better performance on the Harvard APT was associated with better performance on the CFAB. In CN, better performance on the Harvard APT was associated with better ADCS ADL-PI participant-reported IADL, while in MCI better performance on the Harvard APT was associated with better ADCS ADL-PI study partner-reported IADL. Furthermore, in CN better performance on the Harvard APT was associated with better SSPP-IADL participant and study partner-reported IADL. **CONCLUSIONS:** In this small pilot study, the Harvard APT, a brief, self-administered, objective measure of IADL performance, appears to correlate well with other sensitive measures of everyday functioning, providing good preliminary convergent validity for this new measure. Moreover, it appears to perform well across both CN and MCI participants, which suggests that it is a promising measure of early, clinically meaningful functional change. This may not be the case as suggested in our small sample for subjective IADL scales that may perform differentially depending on the reporter (self vs. study partner) across the clinical spectrum possibly due to diminishing awareness of IADL difficulties in individuals who become cognitively impaired. Secondary prevention trials in AD have a great need for such ecologically valid and reliable measures of early IADL changes. DOI: 10.1186/s13195-018-0464-x PMCID: PMC6329044 PMID: 30630529

**Conflict of interest statement: ETHICS APPROVAL AND CONSENT TO PARTICIPATE:** The Partners Healthcare Institutional Review Board approved the study. Written informed consent was obtained from all participants prior to initiation of any study procedures in accordance with Institutional Review Board guidelines. **CONSENT FOR PUBLICATION:** Not applicable. **COMPETING INTERESTS:** Some of the authors have received research salary support from Eisai Inc. (GAM), Eli Lilly and Company (GAM, KAJ, RAS), Janssen Alzheimer Immunotherapy (DMR, GAM, KAJ, RAS), Genentech (GAM), Novartis (GAM), Avid Radiopharmaceuticals (KAJ, RAS), Navidea (KAJ), and Pfizer (KAJ). Additionally, DMR has served as a consultant for Eli Lilly, Neurotrack, Biogen, and Lundbeck Pharmaceuticals, GAM has served as a consultant for Grifols Shared Services North America, Inc. and Pfizer, KAJ has served as a consultant for Bayer, GE Healthcare, Janssen Alzheimer's Immunotherapy, Siemens Medical Solutions, Genzyme, Novartis, Biogen, Roche, ISIS Pharma, AZTherapy, GEHC, Lundberg, and Abbvie, and RAS has served as a consultant for AbbVie, Biogen, Bracket, Genentech, Lundbeck, Roche, and Sanofi. SJC and DAL have Intellectual Property for the CFAB, which is owned by the University of Miami and licensed to I-Function. SJC is also a Chief Scientific Officer of I-Function and an equity holder in I-Function. The remaining authors declare that they have no competing interests. **PUBLISHER'S NOTE:** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

MCI-25. *J Alzheimers Dis.* 2018;61(1):333-345. doi: 10.3233/JAD-170580.

**Biological Factors Contributing to the Response to Cognitive Training in Mild Cognitive Impairment.** Peter J(1)(2), Schumacher LV(3), Landerer V(2), Abdulkadir A(1)(4), Kaller CP(5)(6), Lahr J(2), Klöppel S(1)(7).

In mild cognitive impairment (MCI), small benefits from cognitive training were observed for memory functions but there appears to be great variability in the response to treatment. Our study aimed to improve the characterization and selection of those participants who will benefit from cognitive intervention. We evaluated the predictive value of disease-specific biological factors for the outcome after cognitive training in MCI (n=25) and also considered motivation of the participants. We compared the results of the cognitive intervention group with two independent control groups of MCI patients (local memory clinic, n=20; ADNI cohort, n=302). The primary outcome measure was episodic memory as measured by verbal delayed recall of a 10-word list. Episodic memory remained stable after treatment and slightly increased 6 months after the intervention. In contrast, in MCI patients who did not receive an intervention, episodic memory significantly decreased during the same time interval. A larger left entorhinal cortex predicted more improvement in episodic memory after treatment and so did higher levels of motivation. Adding disease-specific biological factors significantly improved the prediction of training-related change compared to a model based simply on age and baseline performance. Bootstrapping with resampling (n=1000) verified the stability of our finding. Cognitive training might be particularly helpful in individuals with a bigger left entorhinal cortex as individuals who did not benefit from intervention showed 17% less volume in this area. When extended to alternative treatment options, stratification based on disease-specific biological factors is a useful step towards individualized medicine. DOI: 10.3233/JAD-170580 PMCID: PMC5734129 PMID: 29154279

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MCI-26. J Clin Med. 2019 Feb 9;8(2):224. doi: 10.3390/jcm8020224.

**Non-A $\beta$ -Dependent Factors Associated with Global Cognitive and Physical Function in Alzheimer's Disease: A Pilot Multivariate Analysis.** Pedrinolla A(1), Venturelli M(2)(3), Tamburin S(4), Fonte C(5)(6), Stabile AM(7), Galazzo IB(8), Ghinassi B(9), Venneri MA(10), Pizzini FB(11), Muti E(12), Smania N(13)(14), Di Baldassarre A(15), Naro F(10), Rende M(16), Schena F(17).

Recent literature highlights the importance of identifying factors associated with mild cognitive impairment (MCI) and Alzheimer's Disease (AD). Actual validated biomarkers include neuroimaging and cerebrospinal fluid assessments; however, we investigated non-A $\beta$ -dependent factors associated with dementia in 12 MCI and 30 AD patients. Patients were assessed for global cognitive function (Mini-Mental state examination-MMSE), physical function (Physical Performance Test-PPT), exercise capacity (6-min walking test-6MWT), maximal oxygen uptake (VO<sub>2</sub>max), brain volume, vascular function (flow-mediated dilation-FMD), inflammatory status (tumor necrosis factor- $\alpha$ , TNF- $\alpha$ , interleukin-6, -10 and -15) and neurotrophin receptors (p75NTR and Tropomyosin receptor kinase A -TrkA). Baseline multifactorial information was submitted to two separate backward stepwise regression analyses to identify the variables associated with cognitive and physical decline in demented patients. A multivariate regression was then applied to verify the stepwise regression. The results indicated that the combination of 6MWT and VO<sub>2</sub>max was associated with both global cognitive and physical function (MMSE = 11.384 + (0.00599  $\times$  6MWT) - (0.235  $\times$  VO<sub>2</sub>max)); (PPT = 1.848 + (0.0264  $\times$  6MWT) + (19.693  $\times$  VO<sub>2</sub>max)). These results may offer important information that might help to identify specific targets for therapeutic strategies (NIH Clinical trial identification number NCT03034746). DOI: 10.3390/jcm8020224 PMID: PMC6406356 PMID: 30744116 Conflict of interest statement: The authors declare that there is no conflict of interest.

MCI-27. Brain Sci. 2017 Sep 6;7(9):112. doi: 10.3390/brainsci7090112.

**Computer versus Compensatory Calendar Training in Individuals with Mild Cognitive Impairment: Functional Impact in a Pilot Study.** Chandler MJ(1), Locke DEC(2), Duncan NL(3), Hanna SM(4), Cuc AV(5), Fields JA(6), Hoffman Snyder CR(7), Lunde AM(8), Smith GE(9).

This pilot study examined the functional impact of computerized versus compensatory calendar training in cognitive rehabilitation participants with mild cognitive impairment (MCI). Fifty-seven participants with amnesic MCI completed randomly assigned calendar or computer training. A standard care control group was used for comparison. Measures of adherence, memory-based activities of daily living (mADLs), and self-efficacy were completed. The calendar training group demonstrated significant improvement in mADLs compared to controls, while the computer training group did not. Calendar training may be more effective in improving mADLs than computerized intervention. However, this study highlights how behavioral trials with fewer than 30-50 participants per arm are likely underpowered, resulting in seemingly null findings. DOI: 10.3390/brainsci7090112 PMID: PMC5615253 PMID: 28878146 Conflict of interest statement: The authors declare no conflict of interest. The funding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

MCI-28. J Alzheimers Dis. 2019;71(4):1071-1079. doi: 10.3233/JAD-190091.

**Research Use of Ecological Momentary Assessment for Adverse Event Monitoring Following Amyloid- $\beta$  Results Disclosure.** Mattos MK(1), Sereika SM(2), Beach SR(3), Kim H(4), Klunk WE(5), Knox M(4), Nadkarni NK(6), Parker LS(7), Roberts JS(8), Schulz R(9), Tamres L(4), Lingler JH(10).

As calls for transparency in human subjects research grow, investigators conducting Alzheimer's disease (AD) biomarker research are increasingly required to consider their ethical obligations regarding the return of AD biomarker test results to research participants. When disclosing these test results to potentially vulnerable participants, investigators may face unique challenges to identify adverse events, particularly psychological events. The purpose of this paper is to describe our research team's experience with developing and implementing a process for enhanced adverse event monitoring following the return of amyloid- $\beta$  (A $\beta$ ) imaging results to research participants with mild cognitive impairment (MCI). Ethical and logistical considerations are presented along with preliminary findings from an ongoing randomized controlled trial of A $\beta$  imaging results disclosure in MCI. Following receipt of amyloid imaging results, participants underwent 14 days of adverse event monitoring using ecological momentary assessment (EMA), a strategy to capture health, behaviors, and mood as they occur in participants' natural settings in real time. EMA telephone calls were placed at random during waking hours to screen for mood changes. Investigators were alerted for positive depression, anxiety, suicidal ideation screenings, or for two days of failed call attempts. Preliminary feasibility of twenty-four participants with MCI who participated in EMA mood assessments was successfully completed 83% (SD=0.4) of the time over 14 days with no alerts for anxiety or depression screening items. EMA, when used with standard adverse event monitoring, is a promising and novel approach to maximize early detection of negative psychological reactions following AD biomarker results disclosed in research settings. DOI: 10.3233/JAD-190091 PMID: PMC6839594 PMID: 31322563 Conflict of interest statement: Authors' disclosures available online (<https://www.j-alz.com/manuscript-disclosures/19-0091r2>).

MCI-29. J Alzheimers Dis. 2020;77(4):1545-1558. doi: 10.3233/JAD-191340.

**Utility of MemTrax and Machine Learning Modeling in Classification of Mild Cognitive Impairment.** Bergeron MF(1), Landset S(2), Zhou X(3)(4), Ding T(5), Khoshgoftaar TM(2), Zhao F(6), Du B(5), Chen X(7), Wang X(5), Zhong L(7), Liu X(7), Ashford JW(8)(9).

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**BACKGROUND:** The widespread incidence and prevalence of Alzheimer's disease and mild cognitive impairment (MCI) has prompted an urgent call for research to validate early detection cognitive screening and assessment. **OBJECTIVE:** Our primary research aim was to determine if selected MemTrax performance metrics and relevant demographics and health profile characteristics can be effectively utilized in predictive models developed with machine learning to classify cognitive health (normal versus MCI), as would be indicated by the Montreal Cognitive Assessment (MoCA). **METHODS:** We conducted a cross-sectional study on 259 neurology, memory clinic, and internal medicine adult patients recruited from two hospitals in China. Each patient was given the Chinese-language MoCA and self-administered the continuous recognition MemTrax online episodic memory test on the same day. Predictive classification models were built using machine learning with 10-fold cross validation, and model performance was measured using Area Under the Receiver Operating Characteristic Curve (AUC). Models were built using two MemTrax performance metrics (percent correct, response time), along with the eight common demographic and personal history features. **RESULTS:** Comparing the learners across selected combinations of MoCA scores and thresholds, Naïve Bayes was generally the top-performing learner with an overall classification performance of 0.9093. Further, among the top three learners, MemTrax-based classification performance overall was superior using just the top-ranked four features (0.9119) compared to using all 10 common features (0.8999). **CONCLUSION:** MemTrax performance can be effectively utilized in a machine learning classification predictive model screening application for detecting early stage cognitive impairment. DOI: 10.3233/JAD-191340 PMID: PMC7683062 PMID: 32894241 Conflict of interest statement: Authors' disclosures available online (<https://www.j-alz.com/manuscript-disclosures/19-1340r2>).

MCI-30. Aging Ment Health. 2014 Sep;18(7):838-46. doi: 10.1080/13607863.2014.899972. Epub 2014 Apr 4.

**The effects of a computer-based cognitive and physical training program in a healthy and mildly cognitive impaired aging sample.** González-Palau F(1), Franco M, Bamidis P, Losada R, Parra E, Papageorgiou SG, Vivas AB.

**OBJECTIVES:** The Long Lasting Memories (LLM) program concerns a newly integrated platform which combines cognitive exercises with physical activity within the context of advanced technologies. The main objective of this study was to present the preliminary results that determine the possible effectiveness of the LLM program in the improvement of cognitive functions and symptoms of depression in healthy elderly and subjects with mild cognitive impairment (MCI). **METHOD:** Fifty healthy and MCI subjects participated in the study. All of them received one hour's physical training and 35 minutes' cognitive training, 3 times a week, during the 12 weeks of the program. Before and after the intervention all participants were assessed using a battery of neuropsychological tests. **RESULTS:** The results showed a significant improvement after the LLM training in global cognitive function, in verbal memory, in attention, in episodic memory and symptoms of depression. **CONCLUSION:** This study indicates that LLM is a promising solution for older adults with and without cognitive impairment, maintaining their wellbeing with few professional and technical requirements. DOI: 10.1080/13607863.2014.899972 PMID: 24697325

MCI-31. Dement Geriatr Cogn Disord. 2004;18(2):138-44. doi: 10.1159/000079193. Epub 2004 Jun 18.

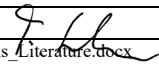
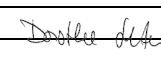
**Cognitive functioning after stroke: a one-year follow-up study.** Rasquin SM(1), Lodder J, Ponds RW, Winkens I, Jolles J, Verhey FR.

Cognitive disorders after stroke are one of the main causes of disability in daily activities. The main aim of this study was to investigate the frequency of post-stroke dementia, post-stroke mild cognitive impairment (MCI) and post-stroke amnesic MCI at different times after first-ever stroke; 196 patients were included in the study. In addition, cognitive disorders and their clinical course were studied. Frequency of post-stroke dementia was about 10% at all evaluation times; most patients had post-stroke MCI. Of the cognitive functions investigated, mental speed and calculation were most frequently affected. Performance on almost all cognitive tests was improved 6 and 12 months after stroke. Thus, while the frequency of post-stroke dementia is low, the frequency of post-stroke MCI is high, but improvement of cognitive function is possible.

MCI-32. JMIR Form Res. 2020 Jun 8;4(6):e16371. doi: 10.2196/16371.

**Feasibility of In-Home Sensor Monitoring to Detect Mild Cognitive Impairment in Aging Military Veterans: Prospective Observational Study.** Seelye A(1)(2)(3)(4), Leese MI(1), Dorociak K(1), Bouranis N(3)(4), Mattek N(3)(4), Sharma N(3)(4), Beattie Z(3)(4), Riley T(3)(4), Lee J(2)(4), Cosgrove K(3)(4), Fleming N(3)(4), Klinger J(1)(2), Ferguson J(1)(5), Lamberty GJ(1)(2), Kaye J(3)(4).

**BACKGROUND:** Aging military veterans are an important and growing population who are at an elevated risk for developing mild cognitive impairment (MCI) and Alzheimer dementia, which emerge insidiously and progress gradually. Traditional clinic-based assessments are administered infrequently, making these visits less ideal to capture the earliest signals of cognitive and daily functioning decline in older adults. **OBJECTIVE:** This study aimed to evaluate the feasibility of a novel ecologically valid assessment approach that integrates passive in-home and mobile technologies to assess instrumental activities of daily living (IADLs) that are not well captured by clinic-based assessment methods in an aging military veteran sample. **METHODS:** Participants included 30 community-dwelling military veterans, classified as healthy controls (mean age 72.8, SD 4.9 years; n=15) or MCI (mean age 74.3, SD 6.0 years; n=15) using the Clinical Dementia Rating Scale. Participants were in relatively good health (mean modified Cumulative Illness Rating Scale score 23.1, SD 2.9) without evidence of depression (mean Geriatrics Depression Scale score 1.3, SD 1.6) or anxiety (mean generalized anxiety disorder questionnaire 1.3, SD 1.3) on self-report measures. Participants were clinically assessed at baseline and 12 months later with health and daily function questionnaires and neuropsychological testing. Daily computer use, medication taking, and physical activity and sleep data were collected via passive computer monitoring software, an

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instrumented pillbox, and a fitness tracker watch in participants' environments for 12 months between clinical study visits. RESULTS: Enrollment began in October 2018 and continued until the study groups were filled in January 2019. A total of 201 people called to participate following public posting and focused mailings. Most common exclusionary criteria included nonveteran status 11.4% (23/201), living too far from the study site 9.4% (19/201), and having exclusionary health concerns 17.9% (36/201). Five people have withdrawn from the study: 2 with unanticipated health conditions, 2 living in a vacation home for more than half of the year, and 1 who saw no direct benefit from the research study. At baseline, MCI participants had lower Montreal Cognitive Assessment ( $P<.001$ ) and higher Functional Activities Questionnaire ( $P=.04$ ) scores than healthy controls. Over seven months, research personnel visited participants' homes a total of 73 times for technology maintenance. Technology maintenance visits were more prevalent for MCI participants ( $P=.04$ ) than healthy controls. CONCLUSIONS: Installation and longitudinal deployment of a passive in-home IADL monitoring platform with an older adult military veteran sample was feasible. Knowledge gained from this pilot study will be used to help develop acceptable and effective home-based assessment tools that can be used to passively monitor cognition and daily functioning in older adult samples. ©Adriana Seelye, Mira Isabelle Leese, Katherine Dorociak, Nicole Bouranis, Nora Mattek, Nicole Sharma, Zachary Beattie, Thomas Riley, Jonathan Lee, Kevin Cosgrove, Nicole Fleming, Jessica Klinger, John Ferguson, Greg John Lambert, Jeffrey Kaye. Originally published in JMIR Formative Research (<http://formative.jmir.org>), 08.06.2020. DOI: 10.2196/16371 PMCID: PMC7308933 PMID: 32310138 Conflict of interest statement: Conflicts of Interest: None declared.

MCI-33. Arch Gerontol Geriatr. 2020 Mar-Apr;87:103993. doi: 10.1016/j.archger.2019.103993. Epub 2019 Dec 3.

**The effect of severity of white matter hyperintensities on loss of functional independency in patients with mild cognitive impairment: A CREDOS-LTCI (clinical research center for dementia of South Korea-long term card insurance) study.** Cho HE(1), Choi SH(2), Sun Lim H(3), Kim JH(4), Kim HS(5).

OBJECTIVE: By combining data from the Clinical Research Center for Dementia of South Korea(CREDOS) study and long-term care insurance(LTCI), we aimed to assess whether the severity of white matter hyperintensity(WMH) predicted functional decline in cases of amnesic mild cognitive impairment(MCI). METHODS: WMH was evaluated in 3,569 patients with amnesic MCI using the visual rating scale developed for the CREDOS study. The participants were classified as having amnesic MCI with minimal WMH change(aMCI), with moderate WMH change(maMCI) and with severe WMH change(saMCI) according to the severity of the WMH measurements. A Kaplan-Meier survival probability estimate was used to compute median time from the diagnosis of MCI to LTCI enrollment for the three MCI groups. The effect of various risk factors of LTCI enrollment was evaluated using Cox's proportional hazards model, adjusted for covariates. RESULTS: As compared with aMCI cases, maMCI and saMCI patients required help with daily activities of living at a younger age. The saMCI and maMCI patients had higher risk of LTCI enrollment as compared with that of the aMCI patients. Younger patients( $\leq 65y$ ) with MCI had a 3.201 times higher risk of early LTCI enrollment than older patients( $> 65y$ ) did. High clinical dementia rating score and female sex were also risk factors of early LTCI enrollment. CONCLUSIONS: WMH predicted the rate of global functional decline and loss of independence in patients with MCI. The findings support the use of neuroimaging of WMH, in conjunction with biomarkers, as a tool in predicting functional decline in patients with MCI. Copyright © 2019. Published by Elsevier B.V. DOI: 10.1016/j.archger.2019.103993 PMID: 31851899

Conflict of interest statement: Declaration of Competing Interest The authors declare no conflicts of interest.

MCI-34. J Neuropsychiatry Clin Neurosci. 2011 Spring;23(2):149-54. doi: 10.1176/jnp.23.2.jnp149.


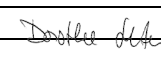
**Engaging in cognitive activities, aging, and mild cognitive impairment: a population-based study.** Geda YE(1), Topazian HM, Roberts LA, Roberts RO, Knopman DS, Pankratz VS, Christianson TJ, Boeve BF, Tangalos EG, Ivnik RJ, Petersen RC.

The authors investigated whether engaging in cognitive activities is associated with aging and mild cognitive impairment (MCI) in a cross-sectional study derived from an ongoing population-based study of normal cognitive aging and MCI in Olmsted County, MN. A random sample of 1,321 study participants ages 70 to 89 (N=1,124 cognitively normal persons, and N=197 subjects with MCI) were interviewed about the frequency of cognitive activities carried out in late life (within 1 year of the date of interview). Computer activities; craft activities, such as knitting, quilting, etc.; playing games; and reading books were associated with decreased odds of having MCI. Social activities, such as traveling, were marginally significant. Even though the point-estimates for reading magazines, playing music, artistic activities, and group activities were associated with reduced odds of having MCI, none of these reached statistical significance. The equally high prevalence of reading newspapers in both groups yielded no significant between-group difference. DOI: 10.1176/jnp.23.2.jnp149 PMCID: PMC3204924 PMID: 21677242

MCI-35. Mayo Clin Proc. 2012 May;87(5):437-42. doi: 10.1016/j.mayocp.2011.12.020.

**Computer activities, physical exercise, aging, and mild cognitive impairment: a population-based study.** Geda YE(1), Silber TC, Roberts RO, Knopman DS, Christianson TJ, Pankratz VS, Boeve BF, Tangalos EG, Petersen RC.

OBJECTIVE: To examine the association between computer use, physical exercise, aging, and mild cognitive impairment (MCI). PATIENTS AND METHODS: The Mayo Clinic Study of Aging is a population-based study of aging and MCI in Olmsted County, Minnesota. The study sample consists of a random sample of 926 nondemented individuals aged 70 to 93 years who completed self-reported questionnaires on physical exercise, computer use, and caloric intake within 1 year of the date of interview. The study was conducted from April 1, 2006, through November 30, 2008. An expert consensus panel classified each study participant as cognitively normal or having MCI on the basis of published criteria.

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RESULTS: Using a multivariable logistic regression model, we examined the impact of the presence during the study period of 2 lifestyle factors (physical exercise and computer use) after adjusting for a third lifestyle factor (caloric intake) on aging and MCI. We also adjusted for age, sex, education, medical comorbidity, and depression. The median daily caloric intake was significantly higher in participants with MCI than in controls (odds ratio, 1.04; 95% confidence interval, 1.02-1.06; P=.001). Participants who engaged in both moderate physical exercise and computer use had significantly decreased odds of having MCI (odds ratio [95% confidence interval], 0.36 [0.20-0.68]) compared with the reference group. In the interaction analyses, there was an additive interaction (P=.012) but not multiplicative interaction (P=.780). CONCLUSION: In this population-based sample, the presence of both physical exercise and computer use as assessed via survey was associated with decreased odds of having MCI, after adjustment for caloric intake and traditional confounders. Copyright © 2012 Mayo Foundation for Medical Education and Research. Published by Elsevier Inc. All rights reserved. DOI: 10.1016/j.mayocp.2011.12.020 PMID: 22560523

MCI-36. Am J Alzheimers Dis Other Demen. 2019 May;34(3):176-187. doi: 10.1177/1533317518813554. Epub 2018 Dec 5.

**A Comparative Single-Blind Randomized Controlled Trial With Language Training in People With Mild Cognitive Impairment.** Poptsi E(1), Lazarou I(1)(2), Markou N(1), Vassiloglou M(1), Nikolaidou E(1), Diamantidou A(1), Siatra V(1), Karathanassi E(1), Karakostas A(3), Zafeiropoulou FK(4), Tsiatsos T(3), Tsolaki M(1)(2).

BACKGROUND: Although cognitive training is effective for people with mild cognitive impairment (MCI), it is not clear which format is more effective. OBJECTIVE: To compare the effectiveness of the same language programs when carried out via computer, paper/pencil and orally in people with MCI. METHODS: Seventy-one participants with MCI were randomly classified in 3 experimental and 2 control groups. The experimental groups attended 48 sessions of language training for 6 months. The control groups attended either unstructured sessions or they were on waiting list. RESULTS: Mixed measures analysis of variance, at the follow-up, showed a significant cognitive abilities improvement among the experimental versus control groups. At the end of the language training, the 3 groups presented improvement in cognitive abilities and daily function, while the control groups remained at the same performance level. CONCLUSION: All 3 cognitive language training methods were equally significantly effective. DOI: 10.1177/1533317518813554 PMID: 30518237

MCI-37. J Alzheimers Dis. 2015;44(4):1333-47. doi: 10.3233/JAD-141260.

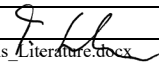
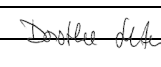
**Can a virtual reality cognitive training application fulfill a dual role? Using the virtual supermarket cognitive training application as a screening tool for mild cognitive impairment.** Zygouris S(1), Giakoumis D(2), Votis K(2), Doumpoulakis S(2), Ntovas K(1), Segkouli S(3), Karagiannidis C(4), Tzovaras D(2), Tsolaki M(5).

BACKGROUND: Recent research advocates the potential of virtual reality (VR) applications in assessing cognitive functions highlighting the possibility of using a VR application for mild cognitive impairment (MCI) screening. OBJECTIVE: The aim of this study is to investigate whether a VR cognitive training application, the virtual supermarket (VSM), can be used as a screening tool for MCI. METHODS: Two groups, one of healthy older adults (n = 21) and one of MCI patients (n = 34), were recruited from day centers for cognitive disorders and administered the VSM and a neuropsychological test battery. The performance of the two groups in the VSM was compared and correlated with performance in established neuropsychological tests. At the same time, the effectiveness of a combination of traditional neuropsychological tests and the VSM was examined. RESULTS: VSM displayed a correct classification rate (CCR) of 87.30% when differentiating between MCI patients and healthy older adults, while it was unable to differentiate between MCI subtypes. At the same time, the VSM correlates with various established neuropsychological tests. A limited number of tests were able to improve the CCR of the VSM when combined with the VSM for screening purposes. DISCUSSION: VSM appears to be a valid method of screening for MCI in an older adult population though it cannot be used for MCI subtype assessment. VSM's concurrent validity is supported by the large number of correlations between the VSM and established tests. It is considered a robust test on its own as the inclusion of other tests failed to improve its CCR significantly. DOI: 10.3233/JAD-141260 PMID: 25428251

MCI-38. Clin Gerontol. 2016 Oct-Dec;39(5):410-427. doi: 10.1080/07317115.2015.1120257. Epub 2016 Mar 2.

**Cognitive Training Program to Improve Working Memory in Older Adults with MCI.** Hyer L(1)(2)(3), Scott C(1), Atkinson MM(1), Mullen CM(1)(2), Lee A(1)(2), Johnson A(2)(3), Mckenzie LC(1)(2).

OBJECTIVES: Deficits in working memory (WM) are associated with age-related decline. We report findings from a clinical trial that examined the effectiveness of Cogmed, a computerized program that trains WM. We compare this program to a Sham condition in older adults with Mild Cognitive Impairment (MCI). METHODS: Older adults (N = 68) living in the community were assessed. Participants reported memory impairment and met criteria for MCI, either by poor delayed memory or poor performance in other cognitive areas. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS, Delayed Memory Index) and the Clinical Dementia Rating scale (CDR) were utilized. All presented with normal Mini Mental State Exams (MMSE) and activities of daily living (ADLs). Participants were randomized to Cogmed or a Sham computer program. Twenty-five sessions were completed over five to seven weeks. Pre, post, and follow-up measures included a battery of cognitive measures (three WM tests), a subjective memory scale, and a functional measure. RESULTS: Both intervention groups improved over time. Cogmed significantly outperformed Sham on Span Board and exceeded in subjective memory reports at follow-up as assessed by the Cognitive Failures Questionnaire (CFQ). The Cogmed group demonstrated better performance on the Functional Activities Questionnaire (FAQ), a measure of adjustment and far transfer, at follow-up. Both groups, especially Cogmed,

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enjoyed the intervention. CONCLUSIONS: Results suggest that WM was enhanced in both groups of older adults with MCI. Cogmed was better on one core WM measure and had higher ratings of satisfaction. The Sham condition declined on adjustment. DOI: 10.1080/07317115.2015.1120257 PMID: 29471774

MCI-39. *Curr Alzheimer Res.* 2019;16(6):483-494. doi: 10.2174/1567205016666190506141733.

**Connected Speech Deficit as an Early Hallmark of CSF-defined Alzheimer's Disease and Correlation with Cerebral Hypoperfusion Pattern.** Mazzon G(1), Ajčević M(1)(2), Cattaruzza T(1), Menichelli A(3), Guerriero M(3), Capitanio S(4), Pesavento V(3), Dore F(4), Sorbi S(2)(5), Manganotti P(1), Marini A(6)(7).

BACKGROUND: Diagnosis of prodromal Alzheimer's disease (AD) still represents a hot topic and there is a growing interest for the detection of early and non-invasive biomarkers. Although progressive episodic memory impairment is the typical predominant feature of AD, communicative difficulties can be already present at the early stages of the disease. OBJECTIVE: This study investigated the narrative discourse production deficit as a hallmark of CSFdefined prodromal AD and its correlation with cerebral hypoperfusion pattern. METHODS: Narrative assessment with a multilevel procedure for discourse analysis was conducted on 28 subjects with Mild Cognitive Impairment (15 MCI due to AD; 13 MCI non-AD) and 28 healthy controls. The diagnostic workup included CSF AD biomarkers. Cerebral hypoperfusion pattern was identified by SPECT image processing. RESULTS: The results showed that the discourse analysis of global coherence and lexical informativeness indexes allowed to identify MCI due to AD from MCI non-AD and healthy subjects. These findings allow to hypothesize that the loss of narrative efficacy could be a possible early clinical hallmark of Alzheimer's disease. Furthermore, a significant correlation of global coherence and lexical informativeness reduction with the SPECT hypoperfusion was found in the dorsal aspect of the anterior part of the left inferior frontal gyrus, supporting the hypothesis that this area has a significant role in communicative efficacy, and in particular, in semantic selection executive control. CONCLUSION: This study contributes to the understanding of the neural networks for language processing and their involvement in prodromal Alzheimer's disease. It also suggests an easy and sensitive tool for clinical practice that can help identifying individuals with prodromal Alzheimer's disease. Copyright© Bentham Science Publishers; For any queries, please email at epub@benthamscience.net. DOI: 10.2174/1567205016666190506141733 PMID: 31057108

MCI-40. *J Alzheimers Dis.* 2011;26 Suppl 3(Suppl 3):349-57. doi: 10.3233/JAD-2011-0009.

**Cognitive training changes hippocampal function in mild cognitive impairment: a pilot study.** Rosen AC(1), Sugiura L, Kramer JH, Whitfield-Gabrieli S, Gabrieli JD.

A randomized pilot experiment examined the neural substrates of response to cognitive training in participants with mild cognitive impairment (MCI). Participants performed exercises previously demonstrated to improve verbal memory and an active control group performed other computer activities. An auditory-verbal fMRI task was conducted before and after the two-month training program. Verbal memory scores improved significantly and left hippocampal activation increased significantly in the experimental group (gains in 5 of 6 participants) relative to the control group (reductions in all 6 participants). Results suggest that the hippocampus in MCI may retain sufficient neuroplasticity to benefit from cognitive training. DOI: 10.3233/JAD-2011-0009 PMID: 21971474

MCI-41. *J Alzheimers Dis.* 2017;56(2):447-452. doi: 10.3233/JAD-160995.

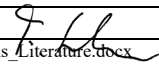
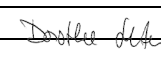
**Investigating Simulated Driving Errors in Amnesic Single- and Multiple-Domain Mild Cognitive Impairment.** Hird MA(1)(2), Vesely KA(1)(2), Fischer CE(1)(3), Graham SJ(4)(5), Naglie G(6)(7)(8), Schweizer TA(1)(9)(10).

The areas of driving impairment characteristic of mild cognitive impairment (MCI) remain unclear. This study compared the simulated driving performance of 24 individuals with MCI, including amnesic single-domain (sd-MCI, n=11) and amnesic multiple-domain MCI (md-MCI, n=13), and 20 age-matched controls. Individuals with MCI committed over twice as many driving errors (20.0 versus 9.9), demonstrated difficulty with lane maintenance, and committed more errors during left turns with traffic compared to healthy controls. Specifically, individuals with md-MCI demonstrated greater driving difficulty compared to healthy controls, relative to those with sd-MCI. Differentiating between different subtypes of MCI may be important when evaluating driving safety. DOI: 10.3233/JAD-160995 PMID: 27983557

MCI-42. *Clin Rehabil.* 2018 Feb;32(2):213-222. doi: 10.1177/0269215517719951. Epub 2017 Jul 20.

**Does cognition-specific computer training have better clinical outcomes than non-specific computer training? A single-blind, randomized controlled trial.** Park JH(1), Park JH(2).

OBJECTIVE: The purpose of this study was to investigate differences between non-specific computer training (NCT) and cognition-specific computer training (CCT). DESIGN: Randomized controlled experimental study. SETTING: Local community welfare center. SUBJECTS: A total of 78 subjects with mild cognitive impairment (MCI) were randomly assigned to the NCT ( n = 39) or CCT group ( n = 39). INTERVENTION: The NCT group underwent NCT using Nintendo Wii for improving functional performance, while the CCT group underwent CCT using CoTras for improving function of the cognitive domain specifically. Subjects in both groups received 30-minute intervention three times a week for 10 weeks. MAIN MEASURES: To identify effects on cognitive function, the Wechsler Adult Intelligence Scale (WAIS) digit span subtests, Rey Auditory Verbal Learning Test (RAVLT), Trail Making Test-Part B (TMT-B), Rey-Osterrieth Complex Figure Test, and Modified Taylor Complex Figure (MTCF) were used. Health-related quality of life (HRQoL) was assessed

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using the Short-Form 36-item questionnaire. RESULTS: After 10 weeks, the WAIS subtests (digit span forward:  $0.48 \pm 0.08$  vs.  $0.12 \pm 0.04$ ; digit span backward:  $0.46 \pm 0.09$  vs.  $0.11 \pm 0.04$ ) and HRQoL (vitality:  $9.05 \pm 1.17$  vs.  $2.69 \pm 1.67$ ; role-emotional:  $8.31 \pm 1.20$  vs.  $4.15 \pm 0.71$ ; mental health:  $11.62 \pm 1.63$  vs.  $6.95 \pm 1.75$ ; bodily pain:  $4.21 \pm 2.17$  vs.  $0.10 \pm 0.38$ ) were significantly higher in the NCT group ( $P < 0.05$ ). CONCLUSION: NCT was superior to CCT for improving cognitive function and HRQoL of elderly adults with MCI. DOI: 10.1177/0269215517719951 PMID: 28726492

MCI-43. J Prev Alzheimers Dis. 2014 Dec;1(3):143-150. doi: 10.14283/jpad.2014.27.

**A patient-centered analysis of enrollment and retention in a randomized behavioral trial of two cognitive rehabilitation interventions for Mild Cognitive Impairment.** Locke DE(1), Greenaway MC(2), Duncan N(3), Fields JA(4), Cuc AV(1), Snyder CH(5), Hanna S(4), Lunde A(4), Smith GE(4).

BACKGROUND: A major potential barrier for studying behavioral interventions for patients with Mild Cognitive Impairment (MCI) is the willingness and ability of people to enroll in and adhere to behavioral interventions, especially when the intervention involves dyads of patients with MCI and support partners. Details regarding recruitment strategies and processes (such as number of dyads screened) are often missing from reports of behavioral trials. In addition, reports do not detail the reasons a potentially eligible candidate opts out of participation in a research study.

OBJECTIVE: To describe the challenges and successes of enrollment and retention in a behavioral trial for persons with MCI and their care partners, and to better understand barriers to participation from the patient's point of view. DESIGN: Multi-site, randomized trial. SETTING: Major medical centers. PARTICIPANTS: Our accrual target for the study was 60 participants. Potential candidates were patients presenting to memory evaluation clinics whose resulting clinical diagnosis was MCI. A total of 200 consecutive potential candidates were approached about participating in the study across the three sites. INTERVENTION: Detailed recruitment and retention data of a randomized trial comparing two behavioral interventions (memory notebook training versus computer training) provided in two separate training time frames (10 days versus 6 weeks). MEASUREMENTS: Structured interview with those declining to participate in the trial. RESULTS: Overall recruitment 37% with a range of 13%-72% across sites. Overall retention 86% with a range of 74%-94% across sites. CONCLUSION: The primary barriers to enrollment from the patient's perspective were distance to the treatment center and competing comprehensive behavioral programming. However, retention data suggest that those dyads who enroll in behavioral programs are highly committed. DOI: 10.14283/jpad.2014.27 PMID: 27398353

MCI-44. Neuropsychologia. 2019 Jun;129:372-378. doi: 10.1016/j.neuropsychologia.2019.04.023. Epub 2019 May 4.

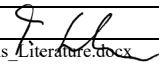
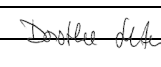
**Poor awareness of IADL deficits is associated with reduced regional brain volume in older adults with cognitive impairment.** Steward KA(1), Kennedy R(2), Erus G(3), Nasrallah IM(3), Wadley VG(2).

Performance of instrumental activities of daily living (IADLs) can become compromised in older adults with mild cognitive impairment (MCI). Patients' level of insight into their everyday functioning varies both amongst individuals and across domains assessed, with some individuals exhibiting complete unawareness of deficits. The current cross-sectional study examined the neuroanatomical substrates of self-awareness in order to help explain the variability in this phenomenon in older adults across a continuum of cognitive impairment. Eighty-five participants (ages 54-88, mean age = 73 years, 57% female, 89% Caucasian) diagnosed with MCI or mild probable dementia underwent structural magnetic resonance imaging. Level of self-awareness was assessed by calculating the discrepancy between objective and subjective performance across six IADLs (Financial Management, Driving, Grocery Shopping, Nutrition Evaluation, Medication Management, and Telephone Use). Over-estimation of current abilities occurred in 13-31% of the sample depending on which IADL was evaluated. Poor awareness was significantly related to reduced volume in the bilateral medial prefrontal cortex, middle and posterior cingulate cortex, right insular cortex, and cerebellum. No associations were found with total white matter lesion load. These findings were broadly consistent across all functional domains assessed, supporting the theory that cortical midline and cerebellar structures are involved in self-referential processing across a variety of different cognitive and behavioral skills. Longitudinal studies are needed to confirm this association. Copyright © 2019 Elsevier Ltd. All rights reserved. DOI: 10.1016/j.neuropsychologia.2019.04.023 PMID: 31059694

MCI-45. BMJ Open. 2019 Sep 24;9(9):e031937. doi: 10.1136/bmjopen-2019-031937.

**Developing assistive robots for people with mild cognitive impairment and mild dementia: a qualitative study with older adults and experts in aged care.** Law M(1), Sutherland C(2), Ahn HS(2), MacDonald BA(2), Peri K(3), Johanson DL(1), Vajsakovic DS(1), Kerse N(4), Broadbent E(5).

OBJECTIVES: This research is part of an international project to design and test a home-based healthcare robot to help older adults with mild cognitive impairment (MCI) or early dementia. The aim was to investigate the perceived usefulness of different daily-care activities for the robot, developed from previous research on needs. DESIGN: Qualitative descriptive analysis using semistructured interviews. Two studies were conducted. In the first study, participants watched videos of a prototype robot performing daily-care activities; in the second study, participants interacted with the robot itself. SETTING: Interviews were conducted at a university and a retirement village. PARTICIPANTS: In study 1, participants were nine experts in aged care and nine older adults living in an aged care facility. In study 2, participants were 10 experts in aged care. RESULTS: The themes that emerged included aspects of the robot's interactions, potential benefits, the appearance, actions and humanness of the robot, ways to improve its functionality and technical issues. Overall, the activities were perceived as useful, especially the reminders and safety checks, with possible benefits of companionship, reassurance and reduced caregiver burden. Suggestions included

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personalising the robot to each individual, simplifying the language and adding more activities. Technical issues still need to be fixed. CONCLUSION: This study adds to knowledge about healthcare robots for people with MCI by developing and testing a new robot with daily-care activities including safety checks. The robot was seen to be potentially useful but needs to be tested with people with MCI. © Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ. DOI: 10.1136/bmjopen-2019-031937 PMCID: PMC6773341 PMID: 31551392

MCI-46. Gerontology. 2019;65(2):155-163. doi: 10.1159/000492177. Epub 2018 Sep 10.

**Perceived Stress and Mild Cognitive Impairment among 32,715 Community-Dwelling Older Adults across Six Low- and Middle-Income Countries.** Koyanagi A(1)(2), Oh H(3), Vancampfort D(4)(5), Carvalho AF(6)(7), Veronese N(8), Stubbs B(9)(10)(11), Lara E(12)(13).

BACKGROUND: Perceived stress may be a modifiable risk factor for mild cognitive impairment (MCI) and ultimately dementia, but studies on this topic from low- and middle-income countries (LMICs) are lacking. OBJECTIVE: We assessed the association between perceived stress and MCI in six LMICs (China, Ghana, India, Mexico, Russia, and South Africa) using nationally representative data. METHODS: Cross-sectional, community-based data on individuals aged ≥50 years from the World Health Organization's Study on Global Ageing and Adult Health were analyzed. The definition of MCI was based on the National Institute on Ageing-Alzheimer's Association criteria. A perceived stress score (range 0 [lowest stress] to 10 [highest stress]) was computed based on two questions from the Perceived Stress Scale. Multivariable logistic regression analysis was conducted to assess the association between perceived stress and MCI. RESULTS: The mean (SD) age of the 32,715 participants was 62.1 (15.6) years and 51.7% were females. After adjustment for potential confounders including depression, in the overall sample, a one-unit increase in the perceived stress score was associated with a 1.14 (95% CI = 1.11-1.18) times higher odds for MCI. The association was similar among those aged 50-64 and ≥65 years. Countrywise analysis showed that there was a moderate level of between-country heterogeneity in this association (I<sup>2</sup> = 59.4%), with the strongest association observed in Russia (OR = 1.33, 95% CI = 1.15-1.55). CONCLUSION: If our study results are confirmed in prospective studies, addressing perceived stress may have an impact in reducing the risk for MCI and subsequent dementia in LMICs. © 2018 S. Karger AG, Basel. DOI: 10.1159/000492177 PMCID: PMC6409159 PMID: 30199870  
Conflict of interest statement: Conflicts of interest None.

MCI-47. Mol Neurobiol. 2016 Dec;53(10):7228-7236. doi: 10.1007/s12035-015-9610-7. Epub 2015 Dec 21.

**Neuroprotective Effects of Electroacupuncture on an Animal Model of Bilateral Common Carotid Artery Occlusion.** Yang EJ(1), Cai M(1), Lee JH(2).

Mild cognitive impairment (MCI) is considered as an intermediate zone between normal aging and dementia. The most prominent feature of MCI is an isolated mild decline in memory, whereas other cognitive functions remain intact. The symptoms of vascular cognitive impairment (VCI) range from MCI to dementia, and an animal model of VCI has been established in a gerbil by transient bilateral common carotid artery occlusion (BCCAO). In the current study, we set out to investigate whether electroacupuncture (EA) could improve memory in gerbils with BCCAO-induced MCI. Animals were randomly divided into two groups: sham-operated group (n = 17) and a model group that was subdivided into BCCAO, n = 17, and EA-treated BCCAO, n = 28. Gerbils were treated with EA at KI3 or GV20 four times every other day using a set of electrical stimulus pulses (1 mA, 2 Hz) that were applied for 20 min. For investigation of cognitive function, we performed a Y-maze test and Western blotting to identify the expression of neuroinflammatory proteins. EA treatment at KI3 ("Taegye" acupoint) improved cognitive function and reduced the expression of neuroinflammatory proteins including ionized calcium-binding adaptor molecule 1, toll-like receptor 4, tumor necrosis factor alpha, and phospho-extracellular signal-regulated kinase in the hippocampus of gerbils that had undergone BCCAO. Furthermore, using micro-positron emission tomography/computed tomography, we demonstrated that EA treatment increased glucose metabolism in the hippocampus of these animals. The present study highlights the neuroprotective effect of EA treatment against BCCAO-induced memory dysfunction, neuroinflammation, and glucose metabolism. Our findings suggest that EA, which has previously been used in complementary and alternative medicine, might also be considered as a therapy that can improve memory and reduce neuroinflammation associated with dementia. DOI: 10.1007/s12035-015-9610-7 PMID: 26687230

MCI-48. Neurobiol Aging. 2019 Apr;76:9-17. doi: 10.1016/j.neurobiolaging.2018.12.001. Epub 2018 Dec 13.

**Neuroimaging findings and clinical trajectories of Lewy body disease in patients with MCI.** Massa F(1), Arnaldi D(2), De Cesari F(1), Girtler N(3), Brugnolo A(3), Grazzini M(1), Bauckneht M(4), Meli R(1), Morbelli S(4), Pardini M(2), Sambucetti G(4), De Carli F(5), Tiraboschi P(6), Nobili F(7).

Elderly patients with mild cognitive impairment (MCI) may develop a Lewy body disease; their neuroimaging features at presentation are largely unknown. We present an intriguing group of 13 patients with MCI preceding (2.9 ± 1.9 years) parkinsonism (MCI-P), and eventually dementia 4.6 ± 1.6 years later (6 patients), whereas 7 patients remained dementia free after 4.7 ± 2.7 years. Neuropsychological tests, dopamine transporter (DAT) single photon emission computed tomography, and 18F-fluorodeoxyglucose positron emission tomography were compared with healthy controls and with cognitively normal patients with Parkinson's disease (PD-MOT). Compared to controls, MCI-P but not PD-MOT showed significant posterior temporo-parieto-occipital hypometabolism. Basal ganglia DAT uptake was similar between MCI-P and PD-MOT. Patients who converted to dementia were older, tended to have higher movement disorder society-unified Parkinson's disease rating scale scores and developed at least another clinical core feature fulfilling the criteria

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for probable dementia with Lewy bodies (DLB). Concurrent impairment of Corsi span and semantic verbal fluency, or of temporal lobe hypometabolism at baseline and reduced putamen-to-caudate ratio on DAT-SPECT at parkinsonism onset, both predicted ( $p < 0.001$ ) the evolution to dementia. The constructs of Park cognitive subtype and prodromal Lewy body dementia partially overlap; functional imaging and neuropsychology may help in characterizing the patients and in tracking the risk toward dementia. Copyright © 2018 Elsevier Inc. All rights reserved. DOI: 10.1016/j.neurobiolaging.2018.12.001 PMID: 30611093

MCI-49. Clin Interv Aging. 2018 Sep 17;13:1787-1798. doi: 10.2147/CIA.S157324. eCollection 2018.

**Development and assessment of a web-based intervention for educating older people on strategies promoting healthy cognition.** Vanoh D(1)(2), Ishak IH(1), Shahar S(1), Manaf ZA(1), Ali NM(3), Noah SAM(4).

**BACKGROUND:** The increase in the population of aging people has increased the occurrence of cognitive decline leading to predemented stage of dementia, ie, mild cognitive impairment (MCI). The cognitive tools that are web-based have been proven to be useful in decreasing the risk of MCI. Thus, in the present study, an education tool that is web-based, called WESIHAT 2.0©, had been created to educate elderly people about precautionary strategies against MCI.

**METHODOLOGY:** WESIHAT 2.0 was devised in a senior-friendly style, which includes touch screen, greater font size, larger icons, and employed multimedia components of text, images, and videos. The components employed in WESIHAT 2.0 were a screening tool called TUA-WELLNESS, 10 guides for memory improvement, health diary, and guide for a healthy menu. This application assessed a group of 73 candidates consisting of elderly people, health professionals, caregivers, and information technology (IT) professionals for 1 month. **RESULTS:** All the elderly people, caregivers, and 75% of IT and health professionals were satisfied with the subject matter of WESIHAT 2.0. About more than half of the elderly people, caregivers, and IT and health professionals had given a consensus on the comprehensive ease of the terminologies, sentences, images, table, and advice related to diet included in the web application. Proposals for improvements of the web portal included suggestions such as using smaller sentences, using greater font size, adding more images, and avoiding the use of unfamiliar terminologies. **CONCLUSION:** WESIHAT 2.0 is a suitable tool for educating older people about the lifestyle modification strategies to slower progression to cognitive impairment, with regard to the significance of expert advice. DOI: 10.2147/CIA.S157324 PMCID: PMC6152600 PMID: 30271134  
Conflict of interest statement: Disclosure The authors report no conflicts of interest in this work.

MCI-50. J Am Geriatr Soc. 2007 Oct;55(10):1534-40. doi: 10.1111/j.1532-5415.2007.01386.x.

**Early cognitive change in the general population: how do different definitions work?** Stephan BC(1), Matthews FE, McKeith IG, Bond J, Brayne C; Medical Research Council Cognitive Function and Aging Study.

**OBJECTIVES:** To explore the application of existing classifications of mild cognitive impairment (MCI) and associated states in a large population sample. **DESIGN:** Prospective cohort study, baseline phase (cross-sectional analysis). **SETTING:** Large-scale multicenter study in the United Kingdom. **PARTICIPANTS:** Thirteen thousand four individuals aged 65 and older from the Medical Research Council Cognitive Function and Aging Study. From this, a subsample of 2,640 individuals was selected and completed a more-detailed cognitive assessment. **MEASUREMENTS:** Information on sociodemographic status, general health, cognitive impairment (measured using the Mini-Mental State Examination), and functional ability was collected in a structured interview at baseline. The Geriatric Mental State Automated Geriatric Examination for Computer-Assisted Taxonomy and the Cambridge Cognitive Examination were used in assessment to determine cognitive status. Using a systematic literature review to collect all symptom classifications for nonnormal dementia states, these were then operationalized retrospectively. Each participant was classified according to each. **RESULTS:** Population prevalence estimates were variable (range 0.1-42%), reflecting differences in the focus and content of each state. Limited overlap existed between states such that many individuals were concurrently classified as normal and impaired. This highlights the heterogeneity in classification as captured using different definitions. **CONCLUSION:** Classification of cognitively impaired and cognitively normal individuals is dependent on the way criteria are defined and operationalized. Each classification captures a unique group of individuals, with little concordance. Given the importance of early detection of dementia and the calls for screening, and recruitment into pharmacological trials of cognitively impaired individuals, there is an urgent need for an agreed-upon standard MCI case definition to use as a criterion standard. DOI: 10.1111/j.1532-5415.2007.01386.x PMID: 17908056

MCI-51. J Alzheimers Dis. 2017;58(4):1175-1187. doi: 10.3233/JAD-161282.

**Frequency-Dependent Changes in the Amplitude of Low-Frequency Fluctuations in Mild Cognitive Impairment with Mild Depression.** Li Y(1)(2), Jing B(3), Liu H(3), Li Y(4), Gao X(2), Li Y(2), Mu B(1), Yu H(5), Cheng J(6), Barker PB(7), Wang H(1), Han Y(1)(8)(9)(10)(11).

**BACKGROUND:** Depression is a potential marker of preclinical Alzheimer's disease (AD). However, little is known about the abnormal characteristics revealed by resting-state functional magnetic resonance imaging (rs-fMRI) in mild cognitive impairment (MCI) subjects with depressive symptoms (MCI-d). **OBJECTIVE:** The study was to examine whether abnormalities in amplitudes of low-frequency oscillation occurred in MCI-d and tried to find the possible spectrum showed higher recognition ability to the diagnosis by utilizing functional MRI (fMRI). **METHODS:** The amplitude of low-frequency fluctuation (ALFF) and fractional ALFF (fALFF) within full frequency (0.01-0.1Hz), slow-5 (0.01-0.027Hz), and slow-4 (0.027-0.073Hz) were computed using resting-state fMRI data of 27 MCI without depressive symptoms, 19 MCI-d, and 32 well-matched healthy controls (HC). Analysis of covariance was performed on ALFF and fALFF among MCI, MCI-d, and HC groups. **RESULTS:** Several brain regions showed significant differences in ALFF and fALFF within full frequency, slow-5, and slow-4 bands among three groups. Importantly, receiver operating characteristic analysis

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revealed that the ALFF values in the full frequency band in the left parahippocampal gyrus and the left precuneus, Slow 5 value in ALFF in the left inferior frontal gyrus, and Slow 4 value in ALFF in the left precuneus could effectively differentiate MCI-d from MCI patients. CONCLUSION: In this study, we found that several changes in special brain regions are associated with MCI and MCI-d patients. And the differences depend on the studied frequency bands of rs-fMRI data. The affective network and the default-mode network might be damaged simultaneously in MCI-d patients. DOI: 10.3233/JAD-161282 PMID: 28550250

MCI-52. PLoS One. 2017 Jul 24;12(7):e0181883. doi: 10.1371/journal.pone.0181883. eCollection 2017.

**Virtual daily living test to screen for mild cognitive impairment using kinematic movement analysis.** Seo K(1), Kim JK(2), Oh DH(3)(4), Ryu H(2), Choi H(5).

Questionnaires or computer-based tests for assessing activities of daily living are well-known approaches to screen for mild cognitive impairment (MCI). However, questionnaires are subjective and computerized tests only collect simple performance data with conventional input devices such as a mouse and keyboard. This study explored the validity and discriminative power of a virtual daily living test as a new diagnostic approach to assess MCI. Twenty-two healthy controls and 20 patients with MCI were recruited. The virtual daily living test presents two complex daily living tasks in an immersive virtual reality environment. The tasks were conducted based on subject body movements and detailed behavioral data (i.e., kinematic measures) were collected. Performance in both the proposed virtual daily living test and conventional neuropsychological tests for patients with MCI was compared to healthy controls. Kinematic measures considered in this study, such as body movement trajectory, time to completion, and speed, classified patients with MCI from healthy controls,  $F(8, 33) = 5.648, p < 0.001, \eta^2 = 0.578$ . When both hand and head speed were employed in conjunction with the immediate free-recall test, a conventional neuropsychological test, the discrimination power for screening MCI was significantly improved to 90% sensitivity and 95.5% specificity (cf. the immediate free-recall test alone has 80% sensitivity and 77.3% specificity). Inclusion of the kinematic measures in screening for MCI significantly improved the classification of patients with MCI compared to the healthy control group, Wilks' Lambda = 0.451,  $p < 0.001$ . DOI: 10.1371/journal.pone.0181883 PMCID: PMC5524295 PMID: 28738088

Conflict of interest statement: Competing Interests: The authors have declared that no competing interests exist.

MCI-53. J Alzheimers Dis. 2016;52(2):713-7. doi: 10.3233/JAD-160079.

**Less Daily Computer Use is Related to Smaller Hippocampal Volumes in Cognitively Intact Elderly.** Silbert LC(1)(2), Dodge HH(1)(3)(4), Lahna D(1), Promjunyakul NO(1), Austin D(1)(3), Mattek N(1)(3), Erten-Lyons D(1)(2), Kaye JA(1)(3)(2).

BACKGROUND: Computer use is becoming a common activity in the daily life of older individuals and declines over time in those with mild cognitive impairment (MCI). The relationship between daily computer use (DCU) and imaging markers of neurodegeneration is unknown. OBJECTIVE: The objective of this study was to examine the relationship between average DCU and volumetric markers of neurodegeneration on brain MRI. METHODS: Cognitively intact volunteers enrolled in the Intelligent Systems for Assessing Aging Change study underwent MRI. Total in-home computer use per day was calculated using mouse movement detection and averaged over a one-month period surrounding the MRI. Spearman's rank order correlation (univariate analysis) and linear regression models (multivariate analysis) examined hippocampal, gray matter (GM), white matter hyperintensity (WMH), and ventricular cerebral spinal fluid (vCSF) volumes in relation to DCU. A voxel-based morphometry analysis identified relationships between regional GM density and DCU. RESULTS: Twenty-seven cognitively intact participants used their computer for 51.3 minutes per day on average. Less DCU was associated with smaller hippocampal volumes ( $r=0.48, p=0.01$ ), but not total GM, WMH, or vCSF volumes. After adjusting for age, education, and gender, less DCU remained associated with smaller hippocampal volume ( $p=0.01$ ). Voxel-wise analysis demonstrated that less daily computer use was associated with decreased GM density in the bilateral hippocampi and temporal lobes. CONCLUSIONS: Less daily computer use is associated with smaller brain volume in regions that are integral to memory function and known to be involved early with Alzheimer's pathology and conversion to dementia. Continuous monitoring of daily computer use may detect signs of preclinical neurodegeneration in older individuals at risk for dementia. DOI: 10.3233/JAD-160079 PMCID: PMC4866889 PMID: 26967228

MCI-54. PLoS One. 2014 Jan 15;9(1):e85441. doi: 10.1371/journal.pone.0085441. eCollection 2014.

**Connectivity features for identifying cognitive impairment in presymptomatic carotid stenosis.** Lin CJ(1), Tu PC(2), Chern CM(3), Hsiao FJ(4), Chang FC(5), Cheng HL(6), Tang CW(7), Lee YC(8), Chen WT(9), Lee IH(3).

Severe asymptomatic stenosis of the internal carotid artery (ICA) leads to increased incidence of mild cognitive impairment (MCI) likely through silent embolic infarcts and/or chronic hypoperfusion, but the brain dysfunction is poorly understood and difficult to diagnose. Thirty cognitively intact subjects with asymptomatic, severe ( $\geq 70\%$ ), unilateral stenosis of the ICA were compared with 30 healthy controls, matched for age, sex, cardiovascular risk factors and education level, on a battery of neuropsychiatric tests, voxel-based morphometry of magnetic resonance imaging (MRI), diffusion tensor imaging and brain-wise, seed-based analysis of resting-state functional MRI. Multivariate regression models and multivariate pattern classification (support vector machines) were computed to assess the relationship between connectivity measures and neurocognitive performance. The patients had worse dizziness scores and poorer verbal memory, executive function and complex visuo-spatial performance than controls. Twelve out of the 30 patients (40%) were considered to have MCI. Nonetheless, the leukoaraiosis Sheltens scores, hippocampal and brain volumes were not different between groups. Their whole-brain mean fractional anisotropy (FA) was significantly reduced and regional functional connectivity (Fc) was significantly impaired in the dorsal attention network (DAN), frontoparietal

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network, sensorimotor network and default mode network. In particular, the Fc strength at the insula of the DAN and the mean FA were linearly related with attention performance and dizziness severity, respectively. The multivariate pattern classification gave over 90% predictive accuracy of individuals with MCI or severe dizziness. Cognitive decline in stroke-free individuals with severe carotid stenosis may arise from nonselective widespread disconnections of long-range, predominantly interhemispheric non-hippocampal pathways. Connectivity measures may serve as both predictors for cases at risk and therapeutic targets for mitigating vascular cognitive impairment. DOI: 10.1371/journal.pone.0085441 PMCID: PMC3893296 PMID: 24454868

Conflict of interest statement: Competing Interests: The authors have declared that no competing interests exist.

MCI-55. Aging Ment Health. 2018 Dec;22(12):1666-1677. doi: 10.1080/13607863.2017.1381946. Epub 2017 Oct 11.

**Communication technology adoption among older adult veterans: the interplay of social and cognitive factors.** Leone C(1), Lim JSL(1), Stern A(1), Charles J(2), Black S(3)(4), Baecker R(1).

OBJECTIVES: InTouch is an electronic communication platform designed to be accessible by computer-naive seniors. The present study explored the process of adoption and use of the application by seniors with and without mild cognitive impairment (MCI) through the lens of Social Cognitive Theory (SCT). METHOD: We studied adoption and use of InTouch for social communication over a 12-week period in a 475-bed Veteran's care facility at Sunnybrook Health Sciences Centre in Toronto, Canada. Eleven older adult veterans participated, six of whom had MCI, as indicated by their Montreal Cognitive Assessment score. Veterans were partnered with volunteers, each was provided with an iPad with the InTouch application. Qualitative data were collected through interviews, field notes, and direct observation. Quantitative data were collected from data logging of the software and medical charts. Data types and sources were triangulated and examined through the lens of SCT. RESULTS: A total of 2361 messages (102 videos, 359 audios, 417 photos, 1438 texts) were sent by 10 of the 11 veterans over the 12-week study period. There was no apparent difference in extent of adoption or use, between participants with and without MCI. Participants used various resources and techniques to learn, provided that they felt motivated to connect with others using the app. CONCLUSION: This pilot illustrates both the accessibility of InTouch and the promise of using extrinsic motivators such as social bonding to promote learning in institutionalized older adults with and without cognitive impairment, whose intrinsic motivation and self-efficacy may well be suffering. DOI: 10.1080/13607863.2017.1381946 PMID: 29019416

MCI-56. Neuropsychology. 2010 May;24(3):327-35. doi: 10.1037/a0018015.

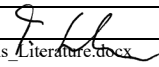
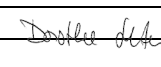
**Prospective memory functioning in mild cognitive impairment.** Costa A(1), Perri R, Serra L, Barban F, Gatto I, Zabberoni S, Caltagirone C, Carlesimo GA.

OBJECTIVE: The present study aimed to investigate prospective memory (PM) in persons with mild cognitive impairment (MCI). METHOD: Twenty individuals with MCI (10 with an amnesic profile and 10 with a dysexecutive profile of cognitive impairment) and 20 control subjects (CS) were recruited. In the PM tasks, subjects had to execute three actions after 20 min had elapsed (time-based condition) or after a timer rang (event-based condition). Separate scores were computed for correct recall of the intention to perform the actions (prospective component) and for correct execution of the actions (retrospective component). RESULTS: Although individuals with MCI were less accurate than CS in both prospective (Cohen's d ranged from 1.04 to 2.23) and retrospective (Cohen's d ranged from 0.81 to 1.06) components of the experimental task, they were significantly more impaired in the former than the latter component (Cohen's d = 0.42). Moreover, the deficit in the prospective component of the time-based task was particularly evident in MCI participants presenting with a dysexecutive impairment in respect to amnesic MCI individuals (Cohen's d = 0.99). CONCLUSIONS: Results of the present study show that the ability of subjects with MCI to comply effectively with a planned delayed intention is impaired and suggest that dysexecutive disorders are likely responsible for this deficit. DOI: 10.1037/a0018015 PMID: 20438210

MCI-57. BMC Psychiatry. 2018 Sep 24;18(1):308. doi: 10.1186/s12888-018-1886-5.

**The Erlangen test of activities of daily living in persons with mild dementia or mild cognitive impairment (ETAM) - an extended validation.** Book S(1), Luttenberger K(2), Stemmler M(3), Meyer S(4), Graessel E(2).

BACKGROUND: The ability to perform activities of daily living (ADLs) is a central marker in the diagnosis and progression of the dementia syndrome. ADLs can be identified as basic ADLs (BADLs), which are fairly easy to perform, or instrumental ADLs (IADLs), which involve more complex activities. Presently, the only performance-based assessment of IADL capabilities in persons with cognitive impairment is the Erlangen Test of Activities of Daily Living in Persons with Mild Dementia or Mild Cognitive Impairment (ETAM). The aim of the present study was to revalidate the ETAM in persons with mild cognitive impairment (MCI) or mild dementia and to analyze its application to persons with moderate dementia. METHODS: We used baseline data from a cluster randomized controlled trial involving a sample of 443 users of 34 day-care centers in Germany. We analyzed groups of persons with MCI, mild dementia, and moderate dementia, categorized on the basis of the Mini-Mental State Examination (MMSE) and the Montreal Cognitive Assessment (MoCA). An item analysis was performed, and new discriminant validities were calculated. We computed a confirmatory factor analysis (CFA) to examine the postulated theoretical model of the ETAM with all six items loading on a single IADL factor. This was the first time that the ETAM's sensitivity to change was analyzed after a time period of 6 months. RESULTS: The overall sample scored on average 17.3 points (SD = 7.2) on the ETAM (range: 0-30 points). Persons with MCI scored on average 23.2 points, persons with mild dementia scored 18.4 points, and persons with moderate dementia scored 12.9 points,  $p < .001$  (ANOVA). The item analysis yielded good difficulty indices and discrimination powers. The CFA indicated a good fit between the model and the observed data. After 6 months, both the ETAM score

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at baseline and the change in MMSE score (t0-t1) were significant predictors of the ETAM score at t1. CONCLUSIONS: The ETAM is a valid and reliable instrument for assessing IADL capabilities in persons with MCI or mild dementia. It is sensitive to changes in cognitive abilities. The test parameters confirm its application to persons with moderate dementia. TRIAL REGISTRATION: Identifier: ISRCTN16412551 (Registration date: 30 July 2014, registered retrospectively). DOI: 10.1186/s12888-018-1886-5 PMCID: PMC6154426 PMID: 30249231

Conflict of interest statement: CONSENT FOR PUBLICATION: Not applicable. COMPETING INTERESTS: The authors declare that they have no competing interests. PUBLISHER'S NOTE: Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

MCI-58. Neurology. 2016 Aug 9;87(6):595-600. doi: 10.1212/WNL.0000000000002950. Epub 2016 Jul 6.

**Type 2 diabetes mellitus is associated with brain atrophy and hypometabolism in the ADNI cohort.** Li W(1), Risacher SL(2), Huang E(2), Saykin AJ(2); Alzheimer's Disease Neuroimaging Initiative.

OBJECTIVE: We investigated type 2 diabetes mellitus (T2DM) as a risk factor for brain atrophy and glucose hypometabolism in older adults with or at risk of cognitive impairment. METHODS: Participants with the T2DM were identified from the Alzheimer's Disease Neuroimaging Initiative (ADNI-1/GO/2 cohorts). Analysis of covariance models were used to compare participants with and without T2DM, controlling for potential confounding factors. RESULTS: Whole brain volume and whole brain [(18)F]-fluorodeoxyglucose (FDG) uptake were significantly different as a function of T2DM status, independent of baseline clinical diagnosis. On post hoc analysis, a lower whole brain volume was seen in participants with both mild cognitive impairment (MCI) and T2DM (n = 76) compared with participants who had MCI but not T2DM (n = 747; p = 0.009). Similarly, mean FDG uptake in gray matter and white matter was lower in participants with both MCI and T2DM (n = 72) than in participants with MCI without T2DM (n = 719; p = 0.04). Subsequent regional analysis revealed that the decreased FDG uptake in participants with both MCI and T2DM was mainly manifested in 3 brain regions: frontal lobe, sensory motor cortex, and striatum. CONCLUSIONS: T2DM may accelerate cognition deterioration in patients with MCI by affecting glucose metabolism and brain volume. © 2016 American Academy of Neurology. DOI: 10.1212/WNL.0000000000002950 PMCID: PMC4977372 PMID: 27385744

MCI-59. Alzheimers Res Ther. 2017 Jun 6;9(1):39. doi: 10.1186/s13195-017-0264-8.


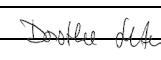
**Efficacy of the Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training (USMART) program among patients with mild cognitive impairment: a randomized controlled crossover trial.** Han JW(1), Son KL(2), Byun HJ(1), Ko JW(1), Kim K(3), Hong JW(1), Kim TH(1), Kim KW(4)(5).

BACKGROUND: Spaced retrieval training (SRT) is a nonpharmacological intervention for mild cognitive impairment (MCI) and dementia that trains the learning and retention of target information by recalling it over increasingly long intervals. We recently developed the Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training (USMART) program as a convenient, self-administered tablet-based SRT program. We also demonstrated the utility of USMART for improving memory in individuals with MCI through an open-label uncontrolled trial. METHODS: This study had an open-label, single-blind, randomized, controlled, two-period crossover design. Fifty patients with MCI were randomized into USMART-usual care and usual care-USMART treatment sequences. USMART was completed or usual care was provided biweekly over a 4-week treatment period with a 2-week washout period between treatment periods. Primary outcome measures included the Word List Memory Test, Word List Recall Test (WLRT), and Word List Recognition Test. Outcomes were measured at baseline, week 5, and week 11 by raters who were blinded to intervention type. An intention-to-treat analysis and linear mixed modeling were used. RESULTS: Of 50 randomized participants, 41 completed the study (18% dropout rate). The USMART group had larger improvements in WLRT score (effect size = 0.49, p = 0.031) than the usual care group. There were no significant differences in other primary or secondary measures between the USMART and usual care groups. Moreover, no USMART-related adverse events were reported. CONCLUSIONS: The 4-week USMART modestly improved information retrieval in older people with MCI, and was well accepted with minimal technical support. TRIAL REGISTRATION: ClinicalTrials.gov NCT01688128 . Registered 12 September 2012. DOI: 10.1186/s13195-017-0264-8 PMCID: PMC5461696 PMID: 28587629

MCI-60. Alzheimers Dement. 2018 Feb;14(2):187-194. doi: 10.1016/j.jalz.2017.07.756. Epub 2017 Oct 26.

**Weekly observations of online survey metadata obtained through home computer use allow for detection of changes in everyday cognition before transition to mild cognitive impairment.** Seelye A(1), Mattek N(2), Sharma N(2), Riley T(2), Austin J(2), Wild K(2), Dodge HH(3), Lore E(2), Kaye J(4).

INTRODUCTION: Subtle changes in instrumental activities of daily living often accompany the onset of mild cognitive impairment (MCI) but are difficult to measure using conventional tests. METHODS: Weekly online survey metadata metrics, annual neuropsychological tests, and an instrumental activity of daily living questionnaire were examined in 110 healthy older adults with intact cognition (mean age = 85 years) followed up for up to 3.6 years; 29 transitioned to MCI during study follow-up. RESULTS: In the baseline period, incident MCI participants completed their weekly surveys 1.4 hours later in the day than stable cognitively intact participants, P = .03, d = 0.47. Significant associations were found between earlier survey start time of day and higher memory (r = -0.34; P < .001) and visuospatial test scores (r = -0.37; P < .0001). Longitudinally, incident MCI participants showed an increase in survey completion time by 3 seconds per month for more than the year before diagnosis compared with stable cognitively intact participants (β = 0.12, SE = 0.04, t = 2.8; P = .006). DISCUSSION: Weekly online survey metadata allowed for detection of changes in everyday cognition before transition to MCI. Published by Elsevier Inc. DOI: 10.1016/j.jalz.2017.07.756 PMCID: PMC5803336 PMID: 29107052

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Beurteilung Qualität / Validität hoch / mittel / gering	Beurteilung Relevanz relevant / nicht relevant	Beurteilung Gewichtung hoch / mittel / gering
mittel	nicht relevant	

MCI-61. Neurology. 2011 Feb 15;76(7):652-9. doi: 10.1212/WNL.0b013e31820ce6a5.

**Global clinical dementia rating of 0.5 in MCI masks variability related to level of function.** Chang YL(1), Bondi MW, McEvoy LK, Fennema-Notestine C, Salmon DP, Galasko D, Hagler DJ Jr, Dale AM; Alzheimer's Disease Neuroimaging Initiative.

**OBJECTIVE:** To evaluate whether ratings on Clinical Dementia Rating (CDR) items related to instrumental activities of daily living (IADL) are associated with cognitive or brain morphometric characteristics of participants with mild cognitive impairment (MCI) and global CDR scores of 0.5. **METHODS:** Baseline cognitive and morphometric data were analyzed for 283 individuals with MCI who were divided into 2 groups (impaired and intact) based on their scores on the 3 CDR categories assessing IADL. Rates of progression to Alzheimer disease (AD) over 2 years were also compared in the 2 groups. **RESULTS:** The impaired IADL MCI group showed a more widespread pattern of gray matter loss involving frontal and parietal regions, worse episodic memory and executive functions, and a higher percentage of individuals progressing to AD than the relatively intact IADL MCI group. **CONCLUSIONS:** The results demonstrate the importance of considering functional information captured by the CDR when evaluating individuals with MCI, even though it is not given equal weight in the assignment of the global CDR score. Worse impairment on IADL items was associated with greater involvement of brain regions beyond the mesial temporal lobe. The conventional practice of relying on the global CDR score as currently computed underutilizes valuable IADL information available in the scale, and may delay identification of an important subset of individuals with MCI who are at higher risk of clinical decline. DOI: 10.1212/WNL.0b013e31820ce6a5 PMCID: PMC3053336 PMID: 21321338

MCI-62. Front Psychol. 2017 Jul 25;8:1243. doi: 10.3389/fpsyg.2017.01243. eCollection 2017.


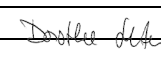
**Recommendations for the Use of Serious Games in Neurodegenerative Disorders:** 2016 Delphi Panel. Manera V(1)(2), Ben-Sadoun G(1), Aalbers T(3), Agopyan H(4), Askenazy F(1)(5)(6), Benoit M(1)(6)(7), Bensamoun D(1)(7), Bourgeois J(1)(5), Bredin J(4), Bremond F(2), Crispim-Junior C(2), David R(1)(6)(8), De Schutter B(9), Ettore E(8), Fairchild J(10)(11), Foulon P(12), Gazzaley A(13), Gros A(1)(8), Hun S(5), Knoefel F(14)(15)(16), Olde Rikkert M(17), Phan Tran MK(2), Politis A(18), Rigaud AS(19)(20), Sacco G(1)(8), Serret S(1)(5), Thümmler S(1)(4)(5), Welter ML(21)(22)(23)(24), Robert P(1)(6)(8).

The use of Serious Games (SG) in the health domain is expanding. In the field of neurodegenerative disorders (ND) such as Alzheimer's disease, SG are currently employed both to support and improve the assessment of different functional and cognitive abilities, and to provide alternative solutions for patients' treatment, stimulation, and rehabilitation. As the field is quite young, recommendations on the use of SG in people with ND are still rare. In 2014 we proposed some initial recommendations (Robert et al., 2014). The aim of the present work was to update them, thanks to opinions gathered by experts in the field during an expert Delphi panel. Results confirmed that SG are adapted to elderly people with mild cognitive impairment (MCI) and dementia, and can be employed for several purposes, including assessment, stimulation, and improving wellbeing, with some differences depending on the population (e.g., physical stimulation may be better suited for people with MCI). SG are more adapted for use with trained caregivers (both at home and in clinical settings), with a frequency ranging from 2 to 4 times a week. Importantly, the target of SG, their frequency of use and the context in which they are played depend on the SG typology (e.g., Exergame, cognitive game), and should be personalized with the help of a clinician. DOI: 10.3389/fpsyg.2017.01243 PMCID: PMC5524915 PMID: 28790945

MCI-63. Psychiatry Investig. 2014 Jan;11(1):52-8. doi: 10.4306/pi.2014.11.1.52. Epub 2014 Jan 21.

**Development of the ubiquitous spaced retrieval-based memory advancement and rehabilitation training program.** Han JW(1), Oh K(1), Yoo S(2), Kim E(2), Ahn KH(3), Son YJ(3), Kim TH(1), Chi YK(1), Kim KW(4).

**OBJECTIVE:** The Ubiquitous Spaced Retrieval-based Memory Advancement and Rehabilitation Training (USMART) program was developed by transforming the spaced retrieval-based memory training which consisted of 24 face-to-face sessions into a self-administered program with an iPad app. The objective of this study was to evaluate the feasibility and efficacy of USMART in elderly subjects with mild cognitive impairment (MCI). **METHODS:** Feasibility was evaluated by checking the satisfaction of the participants with a 5-point Likert scale. The efficacy of the program on cognitive functions was evaluated by the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Neuropsychological Assessment Battery before and after USMART. **RESULTS:** Among the 10 participants, 7 completed both pre- and post-USMART assessments. The overall satisfaction score was 8.0±1.0 out of 10. The mean Word List Memory Test (WLMT) scores significantly increased after USMART training after adjusting for age, educational levels, baseline Mini-Mental Status Examination scores, and the number of training sessions (pre-USMART, 16.0±4.1; post-USMART, 17.9±4.5; p=0.014, RM-ANOVA). The magnitude of the improvements in the WLMT scores significantly correlated with the number of training sessions during 4 weeks (r=0.793; p=0.033). **CONCLUSION:** USMART was effective in improving memory and was well tolerated by most participants with MCI, suggesting that it may be a convenient and cost-effective alternative for the cognitive rehabilitation of elderly subjects with cognitive impairments. Further studies with large numbers of participants are necessary to examine the relationship between the number of

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training sessions and the improvements in memory function. DOI: 10.4306/pi.2014.11.1.52 PMID: PMC3942552 PMID: 24605124 64. J Am Geriatr Soc. 2013 Dec;61(12):2111-9. doi: 10.1111/jgs.12552. Prevalence of and potential risk factors for mild cognitive impairment in community-dwelling residents of Beijing. Li X, Ma C, Zhang J, Liang Y, Chen Y, Chen K, Wang J, Zhang Z, Wang Y; Beijing Ageing Brain Rejuvenation Initiative. OBJECTIVES: To estimate the prevalence of mild cognitive impairment (MCI) in Beijing, China, and to explore the potential protective and risk factors for MCI. DESIGN: Population-based survey. SETTING: The Beijing Ageing Brain Rejuvenation Initiative (BABRI). PARTICIPANTS: Participants randomly recruited from BABRI (N=1,211). MEASUREMENTS: Participants underwent a battery of neuropsychological examinations to determine cognitive function and answered a series of personal questions. The prevalence of MCI and its subtypes were computed using Petersen's criteria. Influencing factors for MCI were estimated based on participant medical history, lifestyle, diet, and leisure activities. RESULTS: One thousand twenty (aged >55, mean 63.9±6.6; 36.7% male) subjects completed the neuropsychological tests. The overall prevalence of MCI was 15.7%, with single-domain amnesic, multiple-domain amnesic, and nonamnesic subtype prevalences of 6.4%, 3.7%, and 5.6%, respectively. Eight hundred sixty-four subjects were used for the case-control analysis. Hypertension, diabetes mellitus, and cerebrovascular disease were found to be associated with MCI. Healthy diet and greater involvement in physical, intellectual, and social activities were associated with a lower risk of MCI. CONCLUSION: The prevalence of MCI was compatible with that found in previous published reports, and the information on the epidemiology of MCI, especially risk factors, may help to explore therapeutic strategies and preventive approaches to delay conversion to dementia. © 2013, Copyright the Authors Journal compilation © 2013, The American Geriatrics Society. DOI: 10.1111/jgs.12552 PMID: 24479143

MCI-65. Scand J Occup Ther. 2015 May;22(3):196-206. doi: 10.3109/11038128.2014.982172. Epub 2015 Jan 12. **Amount and type of everyday technology use over time in older adults with cognitive impairment.** Hedman A(1), Nygård L, Almkvist O, Kottorp A.


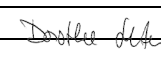
OBJECTIVES: This two-year study examined everyday technology (ET) use in older adults with mild cognitive impairment (MCI) testing five predefined theoretical assumptions regarding factors potentially influencing the amount of ET used in everyday life. METHODS: Data from 37 participants with MCI were collected at inclusion, six, 12, and 24 months, on the type and amount of ET used and how difficult this was, activity involvement, and cognitive and diagnostic status. These variables were, together with age group (55-64, 65-74, or 75-84 years) and educational level, analysed in a mixed-linear-effect model. RESULTS: A significant decrease in the overall amount of ET used was found over time, but the number of users of specific ETs both decreased and increased. Increasing perceived difficulty in ET use, less activity involvement, decreasing cognitive status, and belonging to the oldest age group significantly decreased ET use. Two years after inclusion 42% of the participants had converted to dementia, but neither change in diagnostic status nor length of education contributed significantly to the predictive model. CONCLUSION: Over time, a decreasing use of ET was shown in this sample with MCI. This process was influenced by several aspects important to consider in occupational therapy intervention planning. DOI: 10.3109/11038128.2014.982172 PMID: 25580938

MCI-66. Phys Sportsmed. 2019 Feb;47(1):21-26. doi: 10.1080/00913847.2018.1527647. Epub 2018 Oct 8. **Experimental effects of exercise on memory function among mild cognitive impairment: systematic review and meta-analysis.** Loprinzi PD(1), Blough J(2), Ryu S(2), Kang M(2).

OBJECTIVE: The objective of this study was to evaluate the experimental effects of exercise on memory function among adults with mild cognitive impairment (MCI). METHODS: A systematic review and meta-analysis were employed. Studies were identified using electronic databases, including PubMed, PsychInfo, SPORTDiscus, and Google Scholar. To be eligible for inclusion, studies had to employ an experimental design, be conducted in humans (no animal models) with mild cognitive impairment, include an exercise intervention arm (either acute exercise or chronic training), and measure memory function (any type) as the outcome measure. Comprehensive Meta-Analysis software was used to compute the standardized mean difference effect size (Cohen's d) and 95% CI using a random-effects model. RESULTS: In total, 11 studies met our criteria, contributing to 20 effect size estimates. Among the 20 effect size estimates, 13 contributed to a short-term memory recall, with 7 contributing to a delayed/long-term memory recall. The overall weighted mean effect size was  $d = 0.30$  (95% CI: 0.16-0.44;  $P < 0.001$ ), indicating a small to medium effect of exercise on improving memory function. For the moderation analysis, there was no evidence of a moderation effect for recall duration ( $Q = 0.004$ ,  $df(1)$ ,  $P = 0.95$ ), as exercise (vs. control) demonstrated both short-term ( $d = 0.31$ ; 95% CI: 0.14-0.47;  $P < 0.001$ ) and long-term memory ( $d = 0.29$ ; 95% CI: 0.06-0.53;  $P = 0.013$ ) benefits. CONCLUSION: Current evidence suggests that exercise may help to improve memory function among those with MCI. Safe and progressive forms of exercise should be promoted among MCI patients. DOI: 10.1080/00913847.2018.1527647 PMID: 30246596

MCI-67. Front Physiol. 2018 Mar 14;9:169. doi: 10.3389/fphys.2018.00169. eCollection 2018. **Impact of Nitric Oxide Bioavailability on the Progressive Cerebral and Peripheral Circulatory Impairments During Aging and Alzheimer's Disease.** Venturelli M(1), Pedrinolla A(2), Boscolo Galazzo I(3), Fonte C(1)(4), Smania N(1)(4), Tamburin S(1), Muti E(5), Crispoltoni L(6), Stabile A(6), Pistilli A(6), Rende M(6), Pizzini FB(7), Schena F(1).

Advanced aging, vascular dysfunction, and nitric oxide (NO) bioavailability are recognized risk factors for Alzheimer's disease (AD). However, the contribution of AD, per se, to this putative pathophysiological mechanism is still unclear. To better answer this point, we quantified cortical perfusion with arterial spin labeling (PVC-CBF), measured ultrasound internal carotid (ICA), and femoral (FA) artery blood flow in a group of patients with similar age (~78 years) but different cognitive impairment (i.e., mild cognitive impairment MCI, mild AD-AD1, moderate AD-AD2, and severe AD-

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AD3) and compared them to young and healthy old (aged-matched) controls. NO-metabolites and passive leg-movement (PLM) induced hyperemia were used to assess systemic vascular function. Ninety-eight individuals were recruited for this study. PVC-CBF, ICA, and FA blood flow were markedly (range of 9-17%) and significantly (all  $p < 0.05$ ) reduced across the spectrum from YG to OLD, MCI, AD1, AD2, AD3 subjects. Similarly, plasma level of nitrates and the values of PLM were significantly reduced (range of 8-26%;  $p < 0.05$ ) among the six groups. Significant correlations were retrieved between plasma nitrates, PLM and PVC-CBF, CA, and FA blood flow. This integrative and comprehensive approach to vascular changes in aging and AD showed progressive changes in NO bioavailability and cortical, extracranial, and peripheral circulation in patients with AD and suggested that they are directly associated with AD and not to aging. Moreover, these results suggest that AD-related impairments of circulation are progressive and not confined to the brain. The link between cardiovascular and the central nervous systems degenerative processes in patients at different severity of AD is likely related to the depletion of NO. DOI: 10.3389/fphys.2018.00169 PMID: 29593548

MCI-68. Arch Gerontol Geriatr. 2014 Sep-Oct;59(2):457-61. doi: 10.1016/j.archger.2014.06.003. Epub 2014 Jun 25.  
**Early identification of cognitive impairment and dementia: Results from four years of the community consultation center.** Ishiwata A(1), Kitamura S(2), Nomura T(3), Nemoto R(4), Ishii C(4), Wakamatsu N(5), Katayama Y(6).


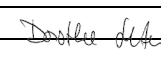
The community consultation center was established as the core facility for a project entitled "Community Support Network for Citizens with Mild Cognitive Impairment (MCI) and Dementia." This study reports on our center's activity and user outcomes. Users consulted with medical staff regarding their memory problems and were self-screened using a touch-panel computer assisted screening tool (TPST). Dementia was suspected when the TPST score was 12 points or below, and the Mini-Mental State Examination (MMSE) was conducted by our onsite clinical psychologists, which served as the gold standard. All reports were provided to user's primary care physicians, or a nearby medical institute if users did not have a primary care physician. Patient outcomes were obtained from participating medical institutes. Informed consent was obtained for all users. In the four-year period, 2802 users visited the center. Of them, 1565 registered (men/women=519/1046; mean age, 74 years). Of 1354 people who used TPST, 622 (45.9%) scored 12 points or below. 409 confirmed diagnoses from the medical institutes revealed MCI in 11.2%, Alzheimer's disease in 37.1%, and vascular dementia in 8.0%. Among the 207 users who had no primary care physicians at consultation, 43 (20.8%) were diagnosed with MCI or dementia. Approximately half of the users who took the TPST were suspected of dementia following interview by a clinical psychologist. Both MCI and dementia were confirmed by the medical institutes in 59.6% of users. We conclude that our consultation center plays a pivotal role in early diagnosis of MCI and dementia. Copyright © 2014 Elsevier Ireland Ltd. All rights reserved. DOI: 10.1016/j.archger.2014.06.003 PMID: 25022712

MCI-69. Scand J Occup Ther. 2009;16(4):216-26. doi: 10.3109/11038120802684299.  
**Perceived difficulty in everyday technology use among older adults with or without cognitive deficits.** Rosenberg L(1), Kottorp A, Winblad B, Nygård L.

This study's purpose was comparing perceived relevance of and difficulty in use of everyday technology such as remote controls, cell phones, and microwave ovens, in older adults with/without cognitive deficits. Three groups included 157 participants; 34 had mild-stage dementia, 30 had mild cognitive impairment (MCI), and 93 lacked known cognitive impairments. Data were collected in structured interviews with the Everyday Technology Use Questionnaire (ETUQ). Analyses revealed that participants with no known cognitive deficits (Group 3) considered a higher proportion of technologies relevant to their life situation than participants with mild-stage dementia (Group 1) and those with MCI (Group 2). Furthermore, participants with no known cognitive deficits reported the lowest mean level of perceived difficulty in everyday technology use, followed by those with MCI and those with mild-stage dementia. All three groups differed significantly ( $p < 0.01$ ;  $p < 0.001$ ) in perceived difficulty using technology, indicating that measurement of perceived difficulty in everyday technology use may sensitively detect changes resulting from MCI/dementia. Findings indicate that perceived difficulty in using everyday technology increases in people with MCI and is accentuated in mild-stage dementia. This calls for increased attention to these issues when assessing functional ability in daily activities of older adults with possible MCI/dementia, and for further research. DOI: 10.3109/11038120802684299 PMID: 19148847

MCI-70. Neuropsychol Rehabil. 2012;22(6):809-35. doi: 10.1080/09602011.2012.691044. Epub 2012 Jun 19.  
**Training of attentional control in mild cognitive impairment with executive deficits: results from a double-blind randomised controlled study.** Gagnon LG(1), Belleville S.

This study evaluated the efficacy of a cognitive intervention for attentional control in older adults with mild cognitive impairment (MCI) with an executive deficit. It also sought to verify if the benefits of training generalised to primary and secondary outcome measures. Participants ( $n = 24$ ) were randomly assigned to a training programme or active control condition. The experimental group completed a computer-based training programme involving Variable Priority (VP) coordination of both components of a dual task, to which was added a self-regulatory strategy designed to augment meta-cognition. The active control group performed Fixed Priority (FP) training: rote practice of the same dual task involving a visual detection task combined with an alpha-arithmetic task. Six one-hour training sessions were held three times a week for two weeks. Participants were tested pre- and post-training to detect improvement and transfer effects. Both groups improved on the visual detection and alpha-arithmetic tasks completed in focused attention, but only participants receiving VP training significantly improved their dual-task cost in accuracy for the visual detection task. As for transfer effects, both FP and VP training produced improvements on select outcome measures: focused attention, speed of processing, and switching abilities. No reliable advantage for generalisability of VP over FP training was found.

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Overall, these findings indicate that cognitive intervention may improve attentional control in persons with MCI and an executive deficit. DOI: 10.1080/09602011.2012.691044 PMID: 22712452

MCI-71. Neuroimage. 2016 Jan 1;124(Pt A):997-1008. doi: 10.1016/j.neuroimage.2015.10.002. Epub 2015 Oct 13.  
**Patterns of effective connectivity during memory encoding and retrieval differ between patients with mild cognitive impairment and healthy older adults.** Hampstead BM(1), Khoshnoodi M(2), Yan W(3), Deshpande G(4), Sathian K(5).

Previous research has shown that there is considerable overlap in the neural networks mediating successful memory encoding and retrieval. However, little is known about how the relevant human brain regions interact during these distinct phases of memory or how such interactions are affected by memory deficits that characterize mild cognitive impairment (MCI), a condition that often precedes dementia due to Alzheimer's disease. Here we employed multivariate Granger causality analysis using autoregressive modeling of inferred neuronal time series obtained by deconvolving the hemodynamic response function from measured blood oxygenation level-dependent (BOLD) time series data, in order to examine the effective connectivity between brain regions during successful encoding and/or retrieval of object location associations in MCI patients and comparable healthy older adults. During encoding, healthy older adults demonstrated a left hemisphere dominant pattern where the inferior frontal junction, anterior intraparietal sulcus (likely involving the parietal eye fields), and posterior cingulate cortex drove activation in most left hemisphere regions and virtually every right hemisphere region tested. These regions are part of a frontoparietal network that mediates top-down cognitive control and is implicated in successful memory formation. In contrast, in the MCI patients, the right frontal eye field drove activation in every left hemisphere region examined, suggesting reliance on more basic visual search processes. Retrieval in the healthy older adults was primarily driven by the right hippocampus with lesser contributions of the right anterior thalamic nuclei and right inferior frontal sulcus, consistent with theoretical models holding the hippocampus as critical for the successful retrieval of memories. The pattern differed in MCI patients, in whom the right inferior frontal junction and right anterior thalamus drove successful memory retrieval, reflecting the characteristic hippocampal dysfunction of these patients. These findings demonstrate that neural network interactions differ markedly between MCI patients and healthy older adults. Future efforts will investigate the impact of cognitive rehabilitation of memory on these connectivity patterns. Published by Elsevier Inc. DOI: 10.1016/j.neuroimage.2015.10.002 PMID: 26458520


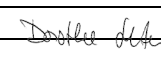
MCI-72. PLoS One. 2014 Jun 18;9(6):e100303. doi: 10.1371/journal.pone.0100303. eCollection 2014.  
**A nationwide survey of mild cognitive impairment and dementia, including very mild dementia, in Taiwan.** Sun Y(1), Lee HJ(2), Yang SC(2), Chen TF(3), Lin KN(4), Lin CC(5), Wang PN(6), Tang LY(2), Chiu MJ(7).

An increasing population of dementia patients produces substantial societal impacts. We assessed the prevalence of mild cognitive impairment (MCI) and all-cause dementia, including very mild dementia (VMD), in Taiwan. In a nationwide population-based cross-sectional survey, participants were selected by computerized random sampling from all 19 Taiwan counties and were enrolled between December 2011 and March 2013. Cases were identified through in-person interviews based on the National Institute on Aging-Alzheimer's Association clinical criteria. Demographic data and histories involving mental status and function in daily living were collected. The principal objective assessments were the Taiwanese Mental Status Examination and Clinical Dementia Rating. In all, 10,432 people aged 65 years or older (mean age 76.2 ± 6.7, 52.3% women) were interviewed. The age-adjusted prevalence of all-cause dementia was 8.04% (95% CI 7.47-8.61), including a 3.25% (95% CI 2.89-3.61) prevalence of VMD; that of MCI was 18.76% (95% CI 17.91-19.61). Women had a higher prevalence than men of both all-cause dementia (9.71% vs. 6.36%) and MCI (21.63% vs. 15.57%). MCI affects a considerable portion of the population aged 65 and above in Taiwan. The inclusion of VMD yields dementia prevalence rates higher than those previously reported from Taiwan. Old age, female gender, and a low educational level are significant associated factors. DOI: 10.1371/journal.pone.0100303 PMID: 24940604

Conflict of interest statement: Competing Interests: The authors have declared that no competing interests exist.

MCI-73. Int Psychogeriatr. 2014 Nov 3:1-7. doi: 10.1017/S1041610214002269. Online ahead of print.  
**Development of a computerized tool for the chinese version of the montreal cognitive assessment for screening mild cognitive impairment.** Yu K(1), Zhang S(2), Wang Q(1), Wang X(3), Qin Y(4), Wang J(1), Li C(5), Wu Y(1), Wang W(1), Lin H(1).

**ABSTRACT** Background: The Montreal Cognitive Assessment (MoCA) is used for screening mild cognitive impairment (MCI), and the Beijing version (MoCA-BJ) is widely used in China. We aimed to develop a computerized tool for MoCA-BJ (MoCA-CC). Methods: MoCA-CC used person-machine interaction instead of patient-to-physician interaction; other aspects such as the scoring system did not differ from the original test. MoCA-CC, MoCA-BJ and routine neuropsychological tests were administered to 181 elderly participants (MCI = 96, normal controls [NC] = 85). Results: A total of 176 (97.24%) participants were evaluated successfully by MoCA-CC. Cronbach's  $\alpha$  for MoCA-CC was 0.72. The test-retest reliability (retesting after six weeks) was good (intraclass correlation coefficient = 0.82;  $P < 0.001$ ). Significant differences were observed in total scores ( $t = 9.38, P < 0.001$ ) and individual item scores ( $t = 2.18-8.62, P < 0.05$ ) between the NC and MCI groups, except for the score for "Naming" ( $t = 0.24, P = 0.81$ ). The MoCA-CC total scores were highly correlated with the MoCA-BJ total scores ( $r = 0.93, P < 0.001$ ) in the MCI participants. The area under receiver-operator curve for the prediction of MCI was 0.97 (95% confidence interval = 0.95-1.00). At the optimal cut-off score of 25/26, MoCA-CC demonstrated 95.8% sensitivity and 87.1% specificity. Conclusion: The MoCA-CC tool

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developed here has several advantages over the paper-pencil method and is reliable for screening MCI in elderly Chinese individuals, especially in the primary clinical setting. It needs to be validated in other diverse and larger populations. DOI: 10.1017/S1041610214002269 PMID: 25362894

MCI-74. J Neuropsychiatry Clin Neurosci. 2005 Winter;17(1):98-105. doi: 10.1176/jnp.17.1.98.

**Self-administered screening for mild cognitive impairment: initial validation of a computerized test battery.** Tornatore JB(1), Hill E, Laboff JA, McGann ME.

The Computer-Administered Neuropsychological Screen for Mild Cognitive Impairment (CANS-MCI), a computer administered, scored, and interpreted touch screen battery was evaluated for its ability to detect mild cognitive impairment. Subjects were three hundred ten community-dwelling elders who enrolled in an National Institute on Aging (NIA)-funded study. One-month test-retest reliability correlations were all significant ( $p < 0.05$ - $p < 0.001$ ). Concurrent validity correlations were all significant ( $p < 0.001$ ). A high level of diagnostic validity was attained relative to the Weschler Memory Scale-Revised (WMS-R) LMS-II test ( $p < 0.001$ ). Confirmatory factor analysis supported a three-factor model indicating the tests measure the intended cognitive dimensions of memory, language/spatial fluency, and executive function/mental control. Goodness-of-fit indicators were strong (Bentler Comparative Fit Index=0.99; Root Mean Square Error of Approximation=0.055). Initial validation analyses indicate that the CANS-MCI shows promise of being a reliable, valid screening tool in determining whether more intensive testing for early cognitive impairment is warranted. DOI: 10.1176/jnp.17.1.98 PMID: 15746489

MCI-75. Alzheimers Res Ther. 2015 Dec 29;7:80. doi: 10.1186/s13195-015-0162-x.

**Conversion of mild cognitive impairment patients in Alzheimer's disease: prognostic value of Alpha3/Alpha2 electroencephalographic rhythms power ratio.** Moretti DV(1).

**INTRODUCTION:** The increase in electroencephalogram (EEG) alpha3/alpha2 frequency power ratio has been demonstrated as a biomarker characteristic of subjects with mild cognitive impairment (MCI) who will develop Alzheimer's disease (AD). **METHODS:** Seventy-four adult subjects with MCI underwent clinical and neuropsychological evaluation, EEG recording, and high-resolution 3D magnetic resonance imaging (MRI). This group has been evaluated after a three years follow-up. Twenty-seven of these subjects underwent perfusion single-photon emission computed tomography (SPECT) evaluation also. Increasing alpha3/alpha2 power ratio, was computed for each subject. Differences in EEG markers, cortical thickness, brain perfusion among the groups were estimated. **RESULTS:** In the higher alpha3/alpha2 frequency power ratio group, greater memory impairment was correlated with greater cortical atrophy and lower perfusional rate in the temporo-parietal cortex. After a follow-up of three years, these patients converted in AD. **CONCLUSION:** High EEG upper/low alpha power ratio was associated with cortical thinning and lower perfusion in the temporo-parietal lobe. Moreover, atrophy and lower perfusion rate were both significantly correlated with memory impairment in MCI subjects. The increase of EEG upper/low alpha frequency power ratio could be useful for identifying individuals at risk for progression to AD dementia and may be of value in the clinical context. DOI: 10.1186/s13195-015-0162-x PMID: 26715588

MCI-76. Clin Interv Aging. 2016 Jul 6;11:897-912. doi: 10.2147/CIA.S103313. eCollection 2016.

**Electroencephalography-driven approach to prodromal Alzheimer's disease diagnosis: from biomarker integration to network-level comprehension.** Moretti DV(1).

Decay of the temporoparietal cortex is associated with prodromal Alzheimer's disease (AD). Additionally, shrinkage of the temporoparietal cerebral area has been connected with an increase in  $\alpha_3/\alpha_2$  electroencephalogram (EEG) power ratio in prodromal AD. Furthermore, a lower regional blood perfusion has been exhibited in patients with a higher  $\alpha_3/\alpha_2$  proportion when contrasted with low  $\alpha_3/\alpha_2$  proportion. Furthermore, a lower regional blood perfusion and reduced hippocampal volume has been exhibited in patients with higher  $\alpha_3/\alpha_2$  when contrasted with lower  $\alpha_3/\alpha_2$  EEG power ratio. Neuropsychological evaluation, EEG recording, and magnetic resonance imaging were conducted in 74 patients with mild cognitive impairment (MCI). Estimation of cortical thickness and  $\alpha_3/\alpha_2$  frequency power ratio was conducted for each patient. A subgroup of 27 patients also underwent single-photon emission computed tomography evaluation. In view of  $\alpha_3/\alpha_2$  power ratio, the patients were divided into three groups. The connections among cortical decay, cerebral perfusion, and memory loss were evaluated by Pearson's r coefficient. Results demonstrated that higher  $\alpha_3/\alpha_2$  frequency power ratio group was identified with brain shrinkage and cutdown perfusion inside the temporoparietal projections. In addition, decay and cutdown perfusion rate were connected with memory shortfalls in patients with MCI. MCI subgroup with higher  $\alpha_3/\alpha_2$  EEG power ratio are at a greater risk to develop AD dementia. DOI: 10.2147/CIA.S103313 PMID: 27462146

MCI-77. J Alzheimers Dis. 2017;58(3):735-746. doi: 10.3233/JAD-170024.

**Chinese Calligraphy Writing for Augmenting Attentional Control and Working Memory of Older Adults at Risk of Mild Cognitive Impairment: A Randomized Controlled Trial.** Chan SCC(1)(2), Chan CCH(1)(2), Derbie AY(1)(2), Hui I(1)(2), Tan DGH(1)(2), Pang MYC(2), Lau SCL(1)(2), Fong KNK(2).

**BACKGROUND:** Nonpharmacological intervention for individuals with mild cognitive impairment (MCI) needs further investigation. **OBJECTIVE:** Test efficacy of an eight-week Chinese calligraphy writing training course in improving attentional control and working memory. **METHODS:** Ninety-nine participants with MCI were randomized into the eight-week calligraphy writing (n=48) or control (tablet computer) training (n=51). Outcomes of the interventions were

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attentional control, working memory, visual scan and processing speed. They were measured at baseline, post-training, and six-month follow-up. RESULTS: Calligraphy writing, when compared with control, significantly improved working memory as reflected from DST-Backward sequence ( $p=0.009$ ) and span scores ( $p=0.002$ ), and divided attention as reflected from CTT2 ( $p<0.001$ ), and at the post-training. The unique improvement in working memory (span:  $p<0.001$ ; sequence:  $p=0.008$ ) of the intervention group was also found at follow-up when comparing with those at baseline. Changes in the other outcome measures were not statistically significant. CONCLUSION: The findings provide support that Chinese calligraphy writing training for eight weeks using a cognitive approach would improve working memory and to a lesser extent attentional control functions of patients with early MCI. They also demonstrate the usefulness of using mind-and-body practice for improving specific cognitive functions. DOI: 10.3233/JAD-170024 PMID: 28482639

MCI-78. Int J Med Inform. 2017 Sep;105:136-142. doi: 10.1016/j.ijmedinf.2017.06.001. Epub 2017 Jun 16. **Barriers to technology use among older heart failure individuals in managing their symptoms after hospital discharge.** Nguyen L(1), Keshavjee K(2), Archer N(3), Patterson C(4), Gwadry-Sridhar F(5), Demers C(6).

BACKGROUND: In North America, heart failure (HF) is the leading cause for hospital readmission. Supportive technology, such as computers and tablets, could potentially assist patients with self-care to manage their condition after hospital discharge; however, older individuals have difficulties in adopting technology to manage their condition. METHOD: This study used a mixed methods design to identify barriers to technology use in HF self-care. In the qualitative phase, semi-structured interviews were conducted with 18 HF patients and 10 informal caregivers or care partners (CP). In the quantitative phase, five questionnaires were administered to 15 patients and 8 CP: Montreal Cognitive Assessment; Short Literacy Survey and Subjective Numeracy Scale; Self-Care of HF Index; Knowledge Assessment Questionnaire; and Patient Activation Measure. RESULTS: In the qualitative phase, five themes emerged regarding engagement in self care and technology use: knowledge level of HF; level of willingness to ask questions related to HF; confidence level in making health-related decisions individually; level of technology usage in daily activities; and self-recording of health measurements. Quantitative analysis found that most HF patients had mild cognitive impairment (MCI), adequate health numeracy levels to understand and manage their health condition, high confidence levels in managing their condition and willingness to engage in self-care. There was variation in willingness to adopt technology. CONCLUSION: Patients were willing to engage in HF self-care however they relied on CPs who were more willing to ask questions about HF. Technology tools may assist in HF self-care, but they must be tailored for use among older individuals. Copyright © 2017 Elsevier B.V. All rights reserved. DOI: 10.1016/j.ijmedinf.2017.06.001 PMID: 28750907

MCI-79. J Am Med Dir Assoc. 2017 Dec 1;18(12):1099.e1-1099.e4. doi: 10.1016/j.jamda.2017.08.019. Epub 2017 Sep 30. **Homecare Robots to Improve Health and Well-Being in Mild Cognitive Impairment and Early Stage Dementia: Results From a Scoping Study.** Darragh M(1), Ahn HS(2), MacDonald B(2), Liang A(1), Peri K(3), Kerse N(4), Broadbent E(5).

OBJECTIVES: This scoping study is the first step of a multiphase, international project aimed at designing a homecare robot that can provide functional support, track physical and psychological well-being, and deliver therapeutic intervention specifically for individuals with mild cognitive impairment. DESIGN: Observational requirements gathering study. PARTICIPANTS AND SETTINGS: Semistructured interviews were conducted with 3 participant groups: (1) individuals with memory challenges, mild cognitive impairment (MCI), or mild dementia (patients;  $n = 9$ ); (2) carers of those with MCI or dementia (carers;  $n = 8$ ); and (3) those with expertise in MCI or dementia research, clinical care, or management (experts;  $n = 16$ ). Interviews took place at the university, at dementia care facilities or other workplaces, at participant's homes, or via skype (experts only). MEASUREMENTS: Semistructured interviews were conducted, transcribed, and reviewed. RESULTS: Several key themes were identified within the 4 topics of: (1) daily challenges, (2) safety and security, (3) monitoring health and well-being, and (4) therapeutic intervention. CONCLUSIONS: A homecare robot could provide both practical and therapeutic benefit for the mildly cognitively impaired with 2 broad programs providing routine and reassurance; and tracking health and well-being. The next phase of the project aims to program homecare robots with scenarios developed from these results, integrate components from project partners, and then test the feasibility, utility, and acceptability of the homecare robot. Copyright © 2017 AMDA – The Society for Post-Acute and Long-Term Care Medicine. Published by Elsevier Inc. All rights reserved. DOI: 10.1016/j.jamda.2017.08.019 PMID: 28974463

MCI-80. Dement Geriatr Cogn Dis Extra. 2016 Dec 15;6(3):568-579. doi: 10.1159/000453546. eCollection 2016 Sep-Dec. **Generalization of Context-Specific Training in Individuals with Mild Cognitive Impairment: An Event-Related Potential Study.** Chan SC(1), Lam TL(1), Fong KN(2), Pang MY(2), Chan CC(1).

BACKGROUND: This study examined the neural processes associated with the generalization of the effect of context-specific (CS) training to noncontextual situations among individuals with mild cognitive impairment (MCI). METHODS: Fourteen and 16 participants with MCI were randomly allocated to a Chinese calligraphy writing (CW) training or a control group, respectively. The CW participants learned how to write Chinese strokes in a semicursive style to construct characters, tapping on working memory functions. The control group, on the other hand, learned how to use a tablet computer without emphasis on working memory functions. They then performed two 2-back tasks with CS semicursive strokes and non-context-specific (NCS) digits. Event-related electroencephalogram signals were concurrently recorded. RESULTS: The CW participants had a significantly shorter reaction time in the CS than in the NCS task ( $p < 0.05$ ). They showed significantly longer latency in working memory updating ( $N200$ ;  $t_{Sub}>11</Sub> = 4.70$ ,  $p = 0.05$ ) and shorter latency in the evaluation of visual representation ( $P300$ ;  $t_{Sub}>12</Sub> = 4.67$ ;  $p = 0.05$ ) than the control

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group when performing the 2-back CS task. Shorter P300 latency was also revealed in the 2-back NCS task ( $t_{<Sub>12</Sub>} = 5.15, p = 0.041$ ), suggesting a possible generalization of the training effect among the CW participants. **CONCLUSION:** The results suggest that CS working memory is likely to be generalized to NCS domains among individuals with MCI. Future research should extend the scope of the generalization and apply it beyond experimental conditions. DOI: 10.1159/000453546 PMCID: PMC5260610 PMID: 28203246

MCI-81. J Nutr Health Aging. 2013 Jan;17(1):64-71. doi: 10.1007/s12603-012-0381-9.

**The advanced activities of daily living: a tool allowing the evaluation of subtle functional decline in mild cognitive impairment.** De Vriendt P(1), Gorus E, Cornelis E, Bautmans I, Petrovic M, Mets T.

**OBJECTIVES:** Assessment of advanced activities of daily living (a-ADL) can be of interest in establishing the diagnosis of Alzheimer's disease (AD) in an earlier stage, since these activities demand high cognitive functioning and are more responsive to subtle changes. In this study we tested a new a-ADL tool, developed according to the International Classification of Functioning, Disability and Health (ICF). The a-ADL tool is based on the total number of activities performed (TNA) by a person and takes each subject as his own reference. It distinguishes a total disability index (a-ADL-DI), a cognitive disability index (a-ADL-CDI), and a physical disability index (a-ADL-PDI), with lower score representing more independency. We explored whether these indices allow distinction between cognitively healthy persons, patients with Mild Cognitive Impairment (MCI) and patients with mild AD. **METHODS:** Participants were on average 80 years old (SD 4.6; 66-90), were community dwelling, and were diagnosed as (1) cognitively healthy subjects (n=26); (2) patients with MCI (n = 17), or (3) mild AD (n = 25), based upon extensive clinical evaluation and a set of global, cognitive, mood and functional assessments. The a-ADL-tool was not part of the clinical evaluation. **RESULTS:** The a-ADL-CDI was significantly different between the three groups ( $p < .01$ ). The a-ADL-DI was significantly different between MCI and AD ( $p < .001$ ). The tool had good psychometrical properties (inter-rater reliability; agreement between patient and proxy; correlations with cognitive tests). Although the sample size was relatively small, ROC curves were computed for the a-ADL-DI and a-ADL-CDI with satisfactory and promising results. **CONCLUSION:** The a-ADL-CDI and a-ADL-DI might offer a useful contribution to the identification and follow up of patients with mild cognitive disorders in an older population. DOI: 10.1007/s12603-012-0381-9 PMID: 23299382

MCI-82. J Neuroeng Rehabil. 2021 Jan 4;18(1):2. doi: 10.1186/s12984-020-00764-5.

**Dynamic changes of region-specific cortical features and scalp-to-cortex distance: implications for transcranial current stimulation modeling.** Lu H(1)(2), Li J(3), Zhang L(4), Chan SSM(3), Lam LCW(3); Open Access Series of Imaging Studies.

**BACKGROUND:** Transcranial current stimulation in rehabilitation is a fast-growing field featured with computational and biophysical modeling. Cortical features and scalp-to-cortex distance (SCD) are key variables for determining the strength and distribution of the electric field, yet longitudinal studies able to capture these dynamic changes are missing. We sought to investigate and quantify the ageing effect on the morphometry and SCD of left primary motor cortex (M1) and dorsolateral prefrontal cortex (DLPFC) in normal ageing adults and mild cognitive impairment (MCI) converters. **METHODS:** Baseline, 1-year and 3-year follow-up structural magnetic resonance imaging scans from normal ageing adults (n = 32), and MCI converters (n = 22) were drawn from the Open Access Series of Imaging Studies. We quantified the changes of the cortical features and SCDs of left M1 and DLPFC, including grey matter volume, white matter volume, cortical thickness, and folding. Head model was developed to simulate the impact of SCD on the electric field induced by transcranial current stimulation. **RESULTS:** Pronounced ageing effect was found on the SCD of left DLPFC in MCI converters. The SCD change of left DLPFC from baseline to 3-year follow-up demonstrated better performance to discriminate MCI converters from normal ageing adults than the other morphometric measures. The strength of electric field was consequently decreased with SCD in MCI converters. **CONCLUSION:** Ageing has a prominent, but differential effect on the region-specific SCD and cortical features in older adults with cognitive impairments. Our findings suggest that SCD, cortical thickness, and folding of the targeted regions could be used as valuable imaging markers when conducting transcranial brain stimulation in individuals with brain atrophy. DOI: 10.1186/s12984-020-00764-5 PMCID: PMC7784346 PMID: 33397402 Conflict of interest statement: The authors declare that they have no competing interests.

MCI-83. Curr Alzheimer Res. 2018;15(9):848-855. doi: 10.2174/1567205015666180427122746.

**Semantic Intrusions and Failure to Recover From Semantic Interference in Mild Cognitive Impairment: Relationship to Amyloid and Cortical Thickness.** Curiel RE(1), Loewenstein DA(1)(2), Rosselli M(3), Penate A(2), Greig-Custo MT(2), Bauer RM(4)(5), Guinjoan SM(6), Hanson KS(7), Li C(8), Lizarraga G(8), Barker WW(2), Torres V(3), DeKosky S(4), Adjouadi M(8), Duara R(2)(4)(9).

**BACKGROUND:** Accumulating evidence indicates that the failure to recover from the effects of proactive semantic interference [frPSI] represents an early cognitive manifestation of preclinical Alzheimer's disease. A limitation of this novel paradigm has been a singular focus on the number of targets correctly recalled, without examining co-occurring semantic intrusions [SI] that may highlight specific breakdowns in memory. **OBJECTIVES:** We focused on SI and their relationship to amyloid load and regional cortical thickness among persons with amnesic mild cognitive impairment (aMCI). **METHODS:** Thirty-three elders diagnosed with aMCI underwent F-18 florbetaben amyloid PET scanning with MRI scans of the brain. We measured the correlation of SI elicited on cued recall trials of the Loewenstein-Acevedo Scales for Semantic Interference and Learning [LASSI-L] with mean cortical amyloid load and regional cortical thickness in AD prone regions. **RESULTS:** SI on measures sensitive to frPSI was related to greater total amyloid load and lower overall cortical thickness [CTH]. In particular, SI were highly associated with reduced CTh in the left entorhinal cortex [ $r = -.71$ ;

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$p < .001$ ] and left medial orbital frontal lobe [ $r = -.64$ ;  $p < .001$ ]; together accounting for 66% of the explained variability in regression models. **CONCLUSION:** Semantic intrusions on measures susceptible to frPSI related to greater brain amyloid load and lower cortical thickness. These findings further support the hypothesis that frPSI, as expressed by the percentage of intrusions, may be a cognitive marker of initial neurodegeneration and may serve as an early and distinguishing test for preclinical AD that may be used in primary care or clinical trial settings. Copyright© Bentham Science Publishers; For any queries, please email at [epub@benthamscience.org](mailto:epub@benthamscience.org). DOI: 10.2174/1567205015666180427122746 PMID: 29701153

Conflict of interest statement: CONFLICT OF INTEREST The authors declare no conflict of interest, financial or otherwise.

MCI-84. Dement Geriatr Cogn Disord. 2009;27(4):301-9. doi: 10.1159/000204915. Epub 2009 Mar 2.

**Use of the virtual action planning supermarket for the diagnosis of mild cognitive impairment: a preliminary study.** Werner P(1), Rabinowitz S, Klinger E, Korczyn AD, Josman N.

**BACKGROUND:** Although executive functioning (EF) was found to be associated with cognitive deterioration, the majority of the tests for assessing EF lack ecological validity. **AIMS:** To examine the feasibility and the validity of the virtual action planning supermarket (VAP-S) for the diagnosis of patients with mild cognitive impairment (MCI). **METHODS:** Thirty MCI patients (mean age = 69.5 years) were compared to 30 healthy elderly persons (mean age = 69.2 years) in their performance of the VAP-S. **RESULTS:** Significant differences were found between the groups in the majority of the measures of the VAP-S. The combination of the MMSE and the trajectory duration provided the best predictive classification for the groups. **CONCLUSION:** MCI patients have EF deficits, and the VAP-S is a viable tool to assess EF deficits in patients with MCI and healthy elderly. DOI: 10.1159/000204915 PMID: 19252401

MCI-85. Clin Interv Aging. 2014 May 8;9:801-11. doi: 10.2147/CIA.S56435. eCollection 2014.

**Acceptance of an assistive robot in older adults: a mixed-method study of human-robot interaction over a 1-month period in the Living Lab setting.** Wu YH(1), Wrobel J(1), Cornuet M(1), Kerhervé H(1), Damnée S(1), Rigaud AS(1).

**BACKGROUND:** There is growing interest in investigating acceptance of robots, which are increasingly being proposed as one form of assistive technology to support older adults, maintain their independence, and enhance their well-being. In the present study, we aimed to observe robot-acceptance in older adults, particularly subsequent to a 1-month direct experience with a robot. **SUBJECTS AND METHODS:** Six older adults with mild cognitive impairment (MCI) and five cognitively intact healthy (CIH) older adults were recruited. Participants interacted with an assistive robot in the Living Lab once a week for 4 weeks. After being shown how to use the robot, participants performed tasks to simulate robot use in everyday life. Mixed methods, comprising a robot-acceptance questionnaire, semistructured interviews, usability-performance measures, and a focus group, were used. **RESULTS:** Both CIH and MCI subjects were able to learn how to use the robot. However, MCI subjects needed more time to perform tasks after a 1-week period of not using the robot. Both groups rated similarly on the robot-acceptance questionnaire. They showed low intention to use the robot, as well as negative attitudes toward and negative images of this device. They did not perceive it as useful in their daily life. However, they found it easy to use, amusing, and not threatening. In addition, social influence was perceived as powerful on robot adoption. Direct experience with the robot did not change the way the participants rated robots in their acceptance questionnaire. We identified several barriers to robot-acceptance, including older adults' uneasiness with technology, feeling of stigmatization, and ethical/societal issues associated with robot use. **CONCLUSION:** It is important to destigmatize images of assistive robots to facilitate their acceptance. Universal design aiming to increase the market for and production of products that are usable by everyone (to the greatest extent possible) might help to destigmatize assistive devices. DOI: 10.2147/CIA.S56435 PMID: 24855349

MCI-86. Aging Ment Health. 2014;18(3):340-5. doi: 10.1080/13607863.2013.832731. Epub 2013 Sep 9.

**Using a screening tool to evaluate potential use of e-health services for older people with and without cognitive impairment.** Malinowsky C(1), Nygård L, Kottorp A.

**OBJECTIVES:** E-health services are increasingly offered to provide clients with information and a link to healthcare services. The aim of this study is to investigate the perceived access to and the potential to use technologies important for e-health services among older adults with mild cognitive impairment (MCI) or mild Alzheimer's disease (AD) and controls. **METHOD:** The perceived access to and perception of difficulty in the use of everyday technology (such as cell phones, coffee machines, computers) was investigated in a sample of older adults ( $n = 118$ ) comprising three subsamples: adults with MCI ( $n = 37$ ), with mild AD ( $n = 37$ ), and controls ( $n = 44$ ) using the Everyday Technology Use Questionnaire (ETUQ). The use of seven technologies important for e-health services was specifically examined for each subsample and compared between the subsamples. **RESULTS:** The findings demonstrated that the older adults in all subsamples perceive access to e-health technologies and potentially would use them competently in several e-health services. However, among persons with AD a lower proportion of perceived access to the technology was described, as well as for persons with MCI. **CONCLUSION:** To make the benefits of e-health services available and used by all clients, it is important to consider access to the technology required in e-health services and also to support the clients' capabilities to understand and use the technologies. Also, the potential use of the ETUQ to explore the perceived access to and competence in using e-health technologies is a vital issue in the use of e-health services. DOI: 10.1080/13607863.2013.832731 PMID: 24548108

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MCI-87. Clin Interv Aging. 2012;7:539-49. doi: 10.2147/CIA.S36297. Epub 2012 Dec 4.

**Detection of activities of daily living impairment in Alzheimer's disease and mild cognitive impairment using information and communication technology.** Sacco G(1), Joumier V, Darmon N, Dechamps A, Derreumaux A, Lee JH, Piano J, Bordone N, Konig A, Teboul B, David R, Guerin O, Bremond F, Robert P.

**BACKGROUND:** One of the key clinical features of Alzheimer's disease (AD) is impairment in daily functioning. Patients with mild cognitive impairment (MCI) also commonly have mild problems performing complex tasks. Information and communication technology (ICT), particularly techniques involving imaging and video processing, is of interest in order to improve assessment. The overall aim of this study is to demonstrate that it is possible using a video monitoring system to obtain a quantifiable assessment of instrumental activities of daily living (IADLs) in AD and in MCI. **METHODS:** The aim of the study is to propose a daily activity scenario (DAS) score that detects functional impairment using ICTs in AD and MCI compared with normal control group (NC). Sixty-four participants over 65 years old were included: 16 AD matched with 10 NC for protocol 1 (P1) and 19 MCI matched with 19 NC for protocol 2 (P2). Each participant was asked to undertake a set of daily tasks in the setting of a "smart home" equipped with two video cameras and everyday objects for use in activities of daily living (8 IADLs for P1 and 11 for P2, plus 4 temporal execution constraints). The DAS score was then computed from quantitative and qualitative parameters collected from video recordings. **RESULTS:** In P1, the DAS score differentiated AD (DAS(AD,P1) = 0.47, 95% confidence interval [CI] 0.38-0.56) from NC (DAS(NC,P1) = 0.71, 95% CI 0.68-0.74). In P2, the DAS score differentiated MCI (DAS(MCI,P2) = 0.11, 95% CI 0.05-0.16) and NC (DAS(NC,P2) = 0.36, 95% CI 0.26-0.45). **CONCLUSION:** In conclusion, this study outlines the interest of a novel tool coming from the ICT world for the assessment of functional impairment in AD and MCI. The derived DAS scores provide a pragmatic, ecological, objective measurement which may improve the prediction of future dementia, be used as an outcome measurement in clinical trials and lead to earlier therapeutic intervention. DOI: 10.2147/CIA.S36297 PMID: PMC3526878 PMID: 23271900

MCI-88. J Alzheimers Dis. 2017;56(1):89-105. doi: 10.3233/JAD-161004.

**Comparison of Model-Based Indices of Cerebral Autoregulation and Vasomotor Reactivity Using Transcranial Doppler versus Near-Infrared Spectroscopy in Patients with Amnesic Mild Cognitive Impairment.** Marmarelis VZ(1), Shin DC(1), Tarumi T(2), Zhang R(2).

We recently introduced model-based "physiomarkers" of dynamic cerebral autoregulation and CO<sub>2</sub> vasomotor reactivity as an aid for diagnosis of early-stage Alzheimer's disease (AD) [1], where significant impairment of dynamic vasomotor reactivity (DVR) was observed in early-stage AD patients relative to age-matched controls. Milder impairment of DVR was shown in patients with amnesic mild cognitive impairment (MCI) using the same approach in a subsequent study [2]. The advocated approach utilizes subject-specific data-based models of cerebral hemodynamics to quantify the dynamic effects of resting-state changes in arterial blood pressure and end-tidal CO<sub>2</sub> (the putative inputs) upon cerebral blood flow velocity (the putative output) measured at the middle cerebral artery via transcranial Doppler (TCD). The obtained input-output models are then used to compute model-based indices of DCA and DVR from model-predicted responses to an input pressure pulse or an input CO<sub>2</sub> pulse, respectively. In this paper, we compare these model-based indices of DVR and DCA in 46 amnesic MCI patients, relative to 20 age-matched controls, using TCD measurements with their counterparts using Near-Infrared Spectroscopy (NIRS) measurements of blood oxygenation at the lateral prefrontal cortex in 43 patients and 22 age-matched controls. The goal of the study is to assess whether NIRS measurements can be used instead of TCD measurements to obtain model-based physi biomarkers with comparable diagnostic utility. The results corroborate this view in terms of the ability of either output to yield model-based physi biomarkers that can differentiate the group of aMCI patients from age-matched healthy controls. DOI: 10.3233/JAD-161004 PMID: PMC5240580 PMID: 27911329

MCI-89. Front Psychol. 2021 Jan 18;11:614920. doi: 10.3389/fpsyg.2020.614920. eCollection 2020.

**The Italian Version of the Test Your Memory (TYM-I): A Tool to Detect Mild Cognitive Impairment in the Clinical Setting.** Barulli MR(1), Piccininni M(1)(2), Brugnolo A(3)(4), Musarò C(1), Di Dio C(1), Capozzo R(1), Tortelli R(1)(5), Lucca U(6), Logroscino G(1)(7).

The Test Your Memory (TYM) is a brief self-administered, cognitive screening test, currently used in several settings. It requires minimal administrator supervision and the computation of the final test score takes approximately 2 min. We assessed the discrimination ability of the Italian version of the TYM (TYM-I) in detecting Mild Cognitive Impairment (MCI) in clinical setting. TYM-I was administered to 94 MCI patients and 134 healthy controls. The clinical diagnosis of MCI was considered as the gold standard. An extended formal neuropsychological test battery was used to define MCI subtypes. Receiver Operating Characteristic (ROC) analyses were conducted to find the optimal cut-off and measure discrimination ability of TYM-I in detecting MCI. TYM-I had a similar area under the curve (AUC = 0.85) point estimate as Mini Mental State Examination (MMSE) (AUC = 0.83). A TYM-I score lower or equal to 36 was found to be optimal cut off to detect MCI. The TYM-I showed the highest discrimination ability among individuals aged more than 70 and high educational level (AUC = 0.89). The amnesic MCI subtype patients, compared to non-amnesic MCI patients, had worse performance in recall, orientation and visuospatial abilities TYM-I subscores. The TYM-I is a valid screening test in detecting cognitive dysfunction, easily carried out in clinical practice. The TYM-I subscores may allow to identify amnesic and non-amnesic MCI subtypes. Copyright © 2021 Barulli, Piccininni, Brugnolo, Musarò, Di Dio, Capozzo, Tortelli, Lucca and Logroscino. DOI: 10.3389/fpsyg.2020.614920 PMID: PMC7848116 PMID: 33536981 Conflict of interest statement: The authors declare that the research was conducted in the absence of any commercial or financial

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relationships that could be construed as a potential conflict of interest. The reviewer AL declared a shared affiliation, with no collaboration, with one of the authors GL to the handling editor at the time of the review.

MCI-90. Neuroimage Clin. 2014 Nov 18;7:34-42. doi: 10.1016/j.nicl.2014.11.007. eCollection 2015.

**Volume of interest-based [18F]fluorodeoxyglucose PET discriminates MCI converting to Alzheimer's disease from healthy controls. A European Alzheimer's Disease Consortium (EADC) study.** Pagani M(1), De Carli F(2), Morbelli S(3), Öberg J(4), Chincarini A(5), Frisoni GB(6), Galluzzi S(7), Pernecky R(8), Drzezga A(9), van Berckel BN(10), Ossenkoppele R(10), Didic M(11), Guedj E(12), Brugnolo A(13), Picco A(13), Arnaldi D(13), Ferrara M(13), Buschiazio A(3), Sambuceti G(3), Nobili F(13).

An emerging issue in neuroimaging is to assess the diagnostic reliability of PET and its application in clinical practice. We aimed at assessing the accuracy of brain FDG-PET in discriminating patients with MCI due to Alzheimer's disease and healthy controls. Sixty-two patients with amnesic MCI and 109 healthy subjects recruited in five centers of the European AD Consortium were enrolled. Group analysis was performed by SPM8 to confirm metabolic differences. Discriminant analyses were then carried out using the mean FDG uptake values normalized to the cerebellum computed in 45 anatomical volumes of interest (VOIs) in each hemisphere (90 VOIs) as defined in the Automated Anatomical Labeling (AAL) Atlas and on 12 meta-VOIs, bilaterally, obtained merging VOIs with similar anatomo-functional characteristics. Further, asymmetry indexes were calculated for both datasets. Accuracy of discrimination by a Support Vector Machine and the AAL VOIs was tested against a validated method (PALZ). At the voxel level SPM8 showed a relative hypometabolism in the bilateral precuneus, and posterior cingulate, temporo-parietal and frontal cortices. Discriminant analysis classified subjects with an accuracy ranging between .91 and .83 as a function of data organization. The best values were obtained from a subset of 6 meta-VOIs plus 6 asymmetry values reaching an area under the ROC curve of .947, significantly larger than the one obtained by the PALZ score. High accuracy in discriminating MCI converters from healthy controls was reached by a non-linear classifier based on SVM applied on predefined anatomo-functional regions and inter-hemispheric asymmetries. Data pre-processing was automated and simplified by an in-house created Matlab-based script encouraging its routine clinical use. Further validation toward nonconverter MCI patients with adequately long follow-up is needed. DOI: 10.1016/j.nicl.2014.11.007 PMID: 25610765

MCI-91. Br J Clin Psychol. 2011 Nov;50(4):425-34. doi: 10.1111/j.2044-8260.2010.02004.x. Epub 2011 Feb 21.

**A naturalistic study of prospective memory function in MCI and dementia.** Thompson CL(1), Henry JD, Withall A, Rendell PG, Brodaty H.

OBJECTIVE. Naturalistic measures of prospective memory (PM) show less age-related decline than laboratory measures. We investigated whether a naturalistic measure of PM differentiates between normal ageing, mild cognitive impairment (MCI), and dementia. METHOD. Ninety-eight older adults agreed to perform a time-based PM task in their everyday lives. RESULTS. Despite a self-selection bias in task acceptance, dementia participants performed more poorly relative to both the MCI and control group. Performance on the naturalistic PM task showed good convergent validity with both a cognitive screening measure and a laboratory PM assessment. CONCLUSIONS. PM difficulties are experienced in the everyday lives of people with dementia and are related to laboratory-based assessments but do not appear to be evident on a naturalistic task for those with MCI. ©2011 The British Psychological Society. DOI: 10.1111/j.2044-8260.2010.02004.x PMID: 22003951

## 2. Search in PubMed, search term "RehaCom" (29 results)

**The HeadApp developers are also the RehaCom developers. HeadApp is based on the same operating principle, the same methods were used, but on a modernized basis. Therefore, the scientific studies and proof of effectiveness can be transferred.**

RehaCom-1. Appl Neuropsychol Adult. 2020 May 5:1-11. doi: 10.1080/23279095.2020.1747070. Online ahead of print.

**RehaCom rehabilitation training improves a wide-range of cognitive functions in multiple sclerosis patients.** Naeni Davarani M(1), Arian Darestani A(1), Hassani-Abharian P(2)(3), Vaseghi S(3)(4), Zarrindast MR(3)(5)(6), Nasehi M(4).

Multiple sclerosis (MS) is a chronic neurodegenerative disease that impairs cognitive performance. Attention, response control, working memory, and processing speed are highly impaired in MS. On the other hand, RehaCom is a computerized software that improves cognitive dysfunctions. In this study, we aimed to investigate the effect of RehaCom on attention, response control, processing speed, working memory, visuospatial skills, and verbal/non-verbal executive functions in MS patients. Sixty patients were selected randomly and divided into control (n = 30) and experimental (n = 30) groups. Integrated Auditory Visual-2 (IVA-2), Paced Auditory Serial Addition Test (PASAT), Symbol Digit Modalities Test (SDMT), Judgment of Line Orientation (JLO) and The Delis-Kaplan Executive Function System (DKEFS) were used to assess cognitive functions. Patients in the experimental group were treated by RehaCom for 5 weeks (two 60-min sessions per week). Cognitive performance of all patients in both groups was assessed at weeks 5 and 10 (post-test and follow-up stages, respectively). The results showed that RehaCom treatment improved all studied cognitive functions at the post-test stage. This effect also remained at the follow-up stage for some cognitive functions.

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In conclusion, treatment with RehaCom may have significant therapeutic effects on cognitive dysfunctions in MS patients. DOI: 10.1080/23279095.2020.1747070 PMID: 32368936

RehaCom-2. Psychiatry Res. 2019 Nov;281:112563. doi: 10.1016/j.psychres.2019.112563. Epub 2019 Sep 7.

**Computerized cognitive remediation therapy, REHACOM, in first episode of schizophrenia: A randomized controlled trial.** García-Fernández L(1), Cabot-Ivorra N(2), Rodríguez-García V(3), Pérez-Martín J(4), Dompablo M(5), Pérez-Gálvez B(6), Rodríguez-Jimenez R(7).

Patients with schizophrenia show cognitive impairments that have been linked to poor social functioning. Computerized cognitive remediation therapy has shown to be effective in improving both cognition and functioning in chronic schizophrenia, but relatively little is known about how these approaches improve cognition and functioning when applied to early stages of psychosis. Eighty-six participants with a first episode of psychosis, undergoing a specific program for early stages of schizophrenia, undertook either the REHACOM computerized cognitive remediation intervention (n = 36), or an active control condition (n = 50) consisting in 24 one-hour sessions addressed twice a week. Clinical features, cognition and functioning were assessed at baseline, post-treatment and six months after finishing the intervention. A significant progressive improvement in neurocognition and functioning was globally shown with no differences observed between the experimental and control group at post training or follow up. All cognitive domains but Social Cognition improved between 0.5 and 1 S.D. through the study period. The computerized cognitive remediation therapy REHACOM has not proved to be effective on improving cognition nor functioning compared to controls in outpatients with a first episode of schizophrenia. Copyright © 2019 Elsevier B.V. All rights reserved. DOI: 10.1016/j.psychres.2019.112563 PMID: 31525673 [Indexed for MEDLINE]

RehaCom-3. J Clin Neurosci. 2020 Jan;71:101-107. doi: 10.1016/j.jocn.2019.08.114. Epub 2019 Sep 5.

**Efficacy of RehaCom cognitive rehabilitation software in activities of daily living, attention and response control in chronic stroke patients.** Veisi-Pirkooi S(1), Hassani-Abharian P(2), Kazemi R(3), Vaseghi S(4), Zarrindast MR(5), Nasehi M(6).

BACKGROUND: Our world is unfortunately facing a huge number of stroke. Attention, response control and activities of daily living (ADL) are important cognitive functions affected by stroke. In line with this explanation, we aimed to investigate the effect of RehaCom rehabilitation software on ADL, attention and response control in chronic stroke patients with damage to middle and anterior cerebral arteries. METHOD: For selecting participants, among chronic stroke patients who referred to our special rehabilitation clinic for patients with stroke, fifty patients selected. Participants were assigned to control (n = 25) and experimental (n = 25) groups. The experimental group was compared with the control group before and after using RehaCom (ten 45-min sessions in five weeks). RESULTS: There is a significant enhancement in ADL, attention and response control scores in the experimental group compared with the control group. In fact, treatment with RehaCom significantly improved the score of all studied variables in chronic stroke patients. CONCLUSIONS: In conclusion, RehaCom cognitive rehabilitation software has improvement effect on ADL, attention and response control in patients with chronic stroke. Our study reveals a new information about the efficacy of computerized training in the rehabilitation of stroke patients. Copyright © 2019. Published by Elsevier Ltd. DOI: 10.1016/j.jocn.2019.08.114 PMID: 31495655 [Indexed for MEDLINE]

Conflict of interest statement: Declaration of Competing Interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

RehaCom-4. Ann Rehabil Med. 2020 Apr;44(2):142-150. doi: 10.5535/arm.2020.44.2.142. Epub 2020 Apr 29.

**Influence of RehaCom Therapy on the Improvement of Manual Skills in Multiple Sclerosis Subjects.**

Pawlukowska W(1)(2), Dobrowolska N(1), Szylińska A(1), Koziarska D(2), Meller A(2), Rotter I(1), Nowacki P(2).

Author information: (1)Department of Medical Rehabilitation and Clinical Physiotherapy, Pomeranian Medical University, Szczecin, Poland. (2)Department of Neurology, Pomeranian Medical University, Szczecin, Poland.

OBJECTIVE: To assess the influence of cognitive therapy, in combination with cognitive software, on manual dexterity in individuals with multiple sclerosis (MS). METHODS: The Nine-Hole Peg Test (NHPT) was used to establish the eligibility of individuals with MS for testing and to assess their upper limb performance. In addition to standard upper limb rehabilitation, 20 participants received RehaCom-based visual-motor therapy, administered three times a week in 20-minute routines. RESULTS: A significant relationship was found between the use of manual therapy that utilized the cognitive function platform and the improvement of the non-dominant hand (p=0.037). Compared to controls, the experimental group scored higher on the NHPT, when using the dominant hand (p=0.007). All members of the experimental group, aged ≤60 years, needed considerably less time to do the NHPT with the dominant hand (p=0.008). CONCLUSION: Application of manual therapy using the cognitive function platform improves performance of the hand. However, further research is needed to analyze the correlation between cognitive function and motor performance in patients with MS. DOI: 10.5535/arm.2020.44.2.142 PMID: 32392653 Conflict of interest statement: No potential conflict of interest relevant to this article was reported.

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RehaCom-5. J Clin Neurosci. 2020 Feb;72:93-97. doi: 10.1016/j.jocn.2020.01.007. Epub 2020 Jan 11.

**The therapeutic effect of treatment with RehaCom software on verbal performance in patients with multiple sclerosis.** Arian Darestani A(1), Naeeni Davarani M(1), Hassani-Abharian P(2), Zarrindast MR(3), Nasehi M(4).

Multiple sclerosis (MS) is characterized by central nervous system lesions that lead to neurological dysfunctions including fatigue, depression and anxiety. MS is affecting almost 2.3 million people around the world, with the significant highest prevalence in the North America. MS also affects different cognitive abilities, such as attention, memory and executive functions. Furthermore, a significant impairment in verbal fluency and naming abilities in patients with MS has been reported. RehaCom, is a software that has improvement effects on cognitive functions. The goal of this research is to investigate the effect of treatment with RehaCom on verbal performance in patients with MS. To select the participants, 60 patients with MS who referred to our clinic were chosen randomly and divided into Control (n = 30) and Experimental (n = 30) groups. The participants in the experimental group were treated by RehaCom software for 10 sessions during 5 weeks (2 sessions per week and each session was 1 h). Controlled Oral Word Association Test (COWAT) and California Verbal Learning Test - Second Edition (CVLT-II), were used to assess verbal performance (verbal fluency, and verbal learning and memory) at weeks 0 (baseline), 5 (post-test) and 10 (follow-up). The results showed that, treatment with RehaCom improved verbal performance in patient with MS, at both post-test and follow-up stages. In conclusion, treatment with RehaCom cognitive rehabilitation software can improve verbal fluency, and verbal learning and memory in patient with MS, possibly by affecting the brain regions involved in language performance. Copyright © 2020 Elsevier Ltd. All rights reserved. DOI: 10.1016/j.jocn.2020.01.007 PMID: 31937503 [Indexed for MEDLINE]

Conflict of interest statement: Declaration of Competing Interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

RehaCom-6. J Am Med Dir Assoc. 2016 Dec 1;17(12):1114-1122. doi: 10.1016/j.jamda.2016.07.021. Epub 2016 Aug 31.


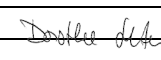
**Clinical Efficacy of Acupuncture Treatment in Combination With RehaCom Cognitive Training for Improving Cognitive Function in Stroke: A 2 × 2 Factorial Design Randomized Controlled Trial.** Jiang C(1), Yang S(2), Tao J(2), Huang J(1), Li Y(2), Ye H(3), Chen S(1), Hong W(1), Chen L(4).

OBJECTIVE: The aim of this study was to identify the clinical efficacy of acupuncture in combination with RehaCom cognitive training in poststroke patients with cognitive dysfunction. METHODS/DESIGN: This study was a 2 × 2 factorial design randomized controlled trial comparing acupuncture, computer-assisted cognitive rehabilitation, and the usual treatment by per-protocol analysis. The trial was completed by 204 stroke patients, including 49 patients in a control group, 52 patients in an acupuncture treatment group, 51 patients in a RehaCom training group, and 52 patients in an acupuncture combined with RehaCom group. All of the patients accepted basic treatment and health education. The interventions continued for 12 weeks (30 minutes per day, 5 days per week). The relative cognitive and functional outcomes were measured at baseline and 12 weeks (at the end of intervention) using the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), and Functional Independence Measure (FIM) scales. RESULTS: After 12 weeks of treatment, the functional statuses of the patients in each of the 4 groups showed varying degrees of improvement. Multiple comparisons of the changes in the MMSE, MoCA, and FIM scores indicated that acupuncture combined with RehaCom cognitive training (ACR) had enhanced therapeutic effects on the functional statuses of the stroke patients (P < .05). In addition, ACR had similar therapeutic effects on the functional statuses of the stroke patients according to each of the assessment scales applied (P $\Delta$ change value MMSE = 0.399, P $\Delta$ MoCA = 0.794, P $\Delta$ FIM = 0.862). The interaction effect values between acupuncture and RehaCom training (acceptance or nonacceptance) were as follows:  $\Delta$ MMSE: F = 6.251, P = .013;  $\Delta$ MoCA: F = 4.991, P = .027; and  $\Delta$ FIM: F = 6.317, P = .013. Further, the main effect values for acupuncture and RehaCom training were both significant (P < .05). CONCLUSIONS: There is an interaction effect in the treatment of stroke patients using ACR. The use of acupuncture in combination with RehaCom training has better therapeutic effects on the functional statuses of poststroke patients than the use of either treatment alone, demonstrating the clinical significance of this combination therapy. Copyright © 2016 AMDA – The Society for Post-Acute and Long-Term Care Medicine. Published by Elsevier Inc. All rights reserved. DOI: 10.1016/j.jamda.2016.07.021 PMID: 27592180 [Indexed for MEDLINE]

RehaCom-7. Psychiatr Pol. 2013 Mar-Apr;47(2):213-23.

**[The efficacy of cognitive neurorehabilitation with RehaCom program in schizophrenia patients].** [Article in Polish] Mak M(1), Tybura P, Bieńkowski P, Karakiewicz B, Samochowicz J.

Schizophrenic patients present cognitive dysfunctions which are currently regarded to be one of endophenotypical markers predisposing to schizophrenia. This indicates neurostructural changes underlying schizophrenia, which can be treated as a neurodegenerative and neurodeveloping disease. AIM: The purpose of this study was to assess the possibility of neuropsychological rehabilitation in schizophrenia. METHODS: 41 participants and 40 control subjects were randomly selected and did not show differences in gender, age and illness duration. Both groups had the diagnosis of paranoid schizophrenia according to ICD-10 criteria and were treated with antipsychotic drugs. Cognitive functions were checked with Wisconsin Card Sorting Test (WCST), Trail Making Test (TMT), and Stroop Color -Word Interference Test (SCWT) in the beginning and in the end of the experiment. In the research group each patient was trained with the rehabilitation programs that focused on attention and concentration and topological memory. This group was compared with the control group that was not trained with RehaCom. RESULTS: RehaCom procedures apparently can be useful in neuropsychological rehabilitation of cognitive dysfunctions in patients with diagnosed schizophrenia. Every participant from the research group showed a significant improvement in the training programs, especially in

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attention/concentration procedure. The analysis of parameters obtained in the neuropsychological tests showed some improvement in neuropsychological assessment in both groups. **CONCLUSIONS:** Cognitive rehabilitation produces moderate improvement in cognitive functioning. A comprehensive treatment using also new technologies supporting pharmacological treatments and other therapies should result in increased cognitive functioning and as a consequence improvement of quality of patient's life. PMID: 23888756 [Indexed for MEDLINE]

RehaCom-8. Ann Agric Environ Med. 2013;20(1):77-81.

**The efficacy of cognitive rehabilitation with RehaCom programme in schizophrenia patients. The role of selected genetic polymorphisms in successful cognitive rehabilitation.** Mak M(1), Samochowicz J, Tybura P, Bieńkowski P, Karakiewicz B, Zaremba Pechmann L, Mroczek B.

**INTRODUCTION:** Schizophrenic patients present cognitive dysfunctions which are regarded to be one of endophenotypical markers predisposing to schizophrenia. Currently, schizophrenia can be treated as a neurodegenerative and neurodeveloping disease with genetic background. **OBJECTIVE:** Assessment of the possible positive effect of neuropsychological rehabilitation in schizophrenia, in patients presenting cognitive dysfunctions. An additional aim was to verify the hypothesis that some genetic polymorphisms can be a prognostic factor for success in neuropsychological rehabilitation. **MATERIAL AND METHODS:** 41 participants and 40 control subjects were randomly selected. Both groups had the diagnosis of paranoid schizophrenia. Cognitive functions were checked with the Wisconsin Card Sorting Test, Trail Making Test, and Stroop Test at the beginning and end of the experiment. In the research group, each patient trained with the rehabilitation programme RehaCom, whereas the control group did not receive such training. Genes COMT rs4680 and BDNF rs6265 were analysed in the genetic part of study. **RESULTS:** RehaCom procedures appear to be useful in the neuropsychological rehabilitation of cognitive dysfunctions in patients diagnosed with schizophrenia. The research group showed a moderate improvement in the training programmes. Analysis of parameters obtained in the neuropsychological tests showed a slight improvement in both groups. At the present time, analysis of the polymorphisms of genes cannot be treated as a prognostic factor for the success of neuropsychological rehabilitation because statistical analyses showed few dependences with little statistical significance. **CONCLUSIONS:** Cognitive rehabilitation produces moderate improvement in cognitive functioning. PMID: 23540216 [Indexed for MEDLINE]

RehaCom-9. MEDICC Rev. 2012 Oct;14(4):32-5. doi: 10.1590/s1555-79602012000400007. **Clinical impact of RehaCom software for cognitive rehabilitation of patients with acquired brain injury.** Fernández E(1), Bringas ML, Salazar S, Rodríguez D, García ME, Torres M.

We describe the clinical impact of the RehaCom computerized cognitive training program instituted in the International Neurological Restoration Center for rehabilitation of brain injury patients. Fifty patients admitted from 2008 through 2010 were trained over 60 sessions. Attention and memory functions were assessed with a pre- and post-treatment design, using the Mini-Mental State Examination, Wechsler Memory Scale and Trail Making Test (Parts A and B). Negative effects were assessed, including mental fatigue, headache and eye irritation. The program's clinical usefulness was confirmed, with 100% of patients showing improved performance in trained functions. DOI: 10.1590/s1555-79602012000400007 PMID: 23154316 [Indexed for MEDLINE]

RehaCom-10. Mult Scler Relat Disord. 2020 Jan 7;39:101932. doi: 10.1016/j.msard.2020.101932. Online ahead of print. **Do Secondary Progressive Multiple Sclerosis patients benefit from Computer- based cognitive neurorehabilitation? A randomized sham controlled trial.** Messinis L(1), Kosmidis MH(2), Nasios G(3), Konitsiotis S(4), Ntoskou A(5), Bakirtzis C(6), Grigoriadis N(6), Patrikelis P(7), Panagiotopoulos E(5), Gourzis P(8), Malefaki S(9), Papathanasopoulos P(10).

**BACKGROUND:** Cognitive impairment is common in multiple sclerosis (MS), but deficits tend to be more pronounced in progressive MS, negatively impacting daily functional capacity. Despite this, most cognitive rehabilitation (CR) interventions to date have focused on relapsing-remitting MS (RRMS). Moreover, information on the efficacy of CR in progressive MS is limited and controversial. The present study investigated the efficacy of a home based, computer assisted cognitive rehabilitation (HBCACR) intervention (RehaCom™ software) exclusively in a Secondary Progressive Multiple Sclerosis (SPMS) sample. **METHODS:** This was a randomized, multi site, sham controlled trial. Thirty six (36) individuals with SPMS, naïve to the RehaCom software, with cognitive deficits were randomized to the treatment (IG; n= 19) or control group condition (CG; n=17). Treatment with the RehaCom modules consisted of 24 domain and task specific, 45 minute session's over an 8-week period, three sessions per week, applied by each patient at home. The CG completed non specific computer based activities at home with the same frequency and duration. Primary cognitive outcome measures included the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery, and secondary outcome measures for depression (BDI-FS), fatigue (MFIS), and quality of life (EuroQol EQ-5D) visual analogue scale (VAS). **RESULTS:** The two groups were well matched on demographic and clinical characteristics, cognitive reserve and severity of cognitive deficits at baseline assessment. At post treatment assessment the IG group showed significant improvements with large effect sizes; in verbal learning [z = -4.759, p <.0005, g = 2.898], visuospatial memory [z = -3.940, p <.0005, g = 1.699] and information processing speed [z= -4.792, p <.0005, g = 2.980], compared with the sham control group. We also found significant between group differences on physical [z=- 3.308, p = .001, g= -.604], cognitive [z = -4.011, p <.0005, g = -1.654], psychosocial [z= 3.308, p = .010, g = -.940], and general fatigue impact [z= -2.623, p = .008, g = -.519], depression severity [z = -2.730, p = .006, g = -.519], and quality of life [z= -4.239, p <.0005, g = -1.885] in favor of the treated group. **CONCLUSION:** These data provide the

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first evidence supporting the efficacy of computer based restorative cognitive rehabilitation applied at home exclusively in SPMS patients, suggesting that adaptive neuroplasticity may occur after functional cognitive training in progressive MS. Improved cognitive functioning in combination with mood augmentation appear to have ameliorated fatigue, which impacted daily functioning activity and culminated in improved health related quality of life. Copyright © 2020 Elsevier B.V. All rights reserved. DOI: 10.1016/j.msard.2020.101932 PMID: 31927200

RehaCom-11. BMC Complement Altern Med. 2014 Aug 7;14:290. doi: 10.1186/1472-6882-14-290.

**The synergistic effect of acupuncture and computer-based cognitive training on post-stroke cognitive dysfunction: a study protocol for a randomized controlled trial of 2 × 2 factorial design.** Yang S, Ye H, Huang J, Tao J, Jiang C, Lin Z, Zheng G, Chen L(1).

**BACKGROUND:** Stroke is one of the most common causes of cognitive impairment. Up to 75% of stroke survivors may be considered to have cognitive impairment, which severely limit individual autonomy for successful reintegration into family, work and social life. The clinical efficacy of acupuncture with Baihui (DU20) and Shenting (DU24) in stroke and post-stroke cognitive impairment has been previously demonstrated. Computer-assisted cognitive training is part of conventional cognitive rehabilitation and has also shown to be effective in improvement of cognitive function of affected patients. However, the cognitive impairment after stroke is so complexity that one single treatment cannot resolve effectively. Besides, the effects of acupuncture and RehaCom cognitive training have not been systematically compared, nor has the possibility of a synergistic effect of combination of the two therapeutic modalities been evaluated. Our primary aim of this trial is to evaluate the synergistic effect of acupuncture and RehaCom cognitive training on cognitive dysfunction after stroke. **METHOD/DESIGN:** A randomized controlled trial of 2 × 2 factorial design will be conducted in the Rehabilitation Hospital Affiliated to Fujian University of Traditional Chinese Medicine. A total of 240 patients with cognitive dysfunction after stroke who meet the eligibility criteria will be recruited and randomized into RehaCom training group, acupuncture group, a combination of both or control group in a 1:1:1:1 ratio. All patients will receive conventional treatment. The interventions will last for 12 weeks (30 min per day, Monday to Friday every week). Evaluations will be conducted by blinded assessors at baseline and again at 4, 8 and 12 weeks. Outcome measurements include mini-mental state examination (MMSE), Montreal cognitive assessments (MoCA), functional independence measure scale (FIM) and adverse events. **DISCUSSION:** The results of this trial are expected to clarify the synergistic effect of acupuncture and RehaCom cognitive training on cognitive dysfunction after stroke. Furthermore, to confirm whether combined or alone of acupuncture and RehaCom cognitive training, is more effective than conventional treatment in the management of post-stroke cognitive dysfunction. **TRIAL REGISTRATION:** Chinese Clinical Trial Registry: ChiCTR-TRC-13003704. DOI: 10.1186/1472-6882-14-290 PMCID: PMC4133058 PMID: 25099775 [Indexed for MEDLINE]

RehaCom-12. Tunis Med. 2009 Oct;87(10):660-3.

**[Cognitive remediation therapy in schizophrenia: a case report]. [Article in French]** Dellagi L(1), Ben Azouz O, Johnson I, Kebir O, Amado I, Tabbane K.

**BACKGROUND:** Despite progress in chemo-therapeutics, schizophrenia remains a chronic disease with occurrence of residual symptoms and drug resistance in 60% of the cases. Besides, cognitive impairment is frequent and highly correlated to social dysfunction seen in patients with schizophrenia. Several cognitive remediation programs have been elaborated. REHACOM is one of such programs. Aim of the study is to evaluate through a case control the efficiency of REHACOM towards cognitive functions. **METHODS:** This program has been administered to a patient suffering from undifferentiated schizophrenia which was ameliorated after drug therapy considering positive symptoms but still was complaining from cognitive deficits causing social withdrawal. **RESULTS:** After following the remediation program, the patient was ameliorated considering its negative symptoms as attested by an amelioration of the PANSS negative score and considering its cognitive performances on memory, attention and executive functions. We have also noticed an improvement in his self-esteem and his quality of life. **CONCLUSION:** This first trial of a cognitive remediation program among our patients suffering from schizophrenia using REHACOM was encouraging. Enlarging its use and designing controlled studies will be the next step of our study. PMID: 20187353 [Indexed for MEDLINE]

RehaCom-13. Trials. 2019 Aug 5;20(1):478. doi: 10.1186/s13063-019-3599-6.

**Effects of electroacupuncture combined with computer-based cognitive rehabilitation on mild cognitive impairment: study protocol for a pilot randomized controlled trial.** Kim JH(1)(2), Han JY(3), Park GC(4), Lee JS(5).

Same as MCI-3

RehaCom-14. J Chiropr Med. 2020 Mar;19(1):1-8. doi: 10.1016/j.jcm.2019.08.002. Epub 2020 Aug 29.

**Influences of Dual-Task Training on Walking and Cognitive Performance of People With Relapsing Remitting Multiple Sclerosis: Randomized Controlled Trial.** Elwishy A(1), Ebraheim AM(2), Ashour AS(2), Mohamed AA(1), Sherbini AEHEE(3).

**OBJECTIVE:** We sought to investigate whether there is any additional effect of coupled cognitive and physical rehabilitation compared to exercise training alone on walking and cognitive performance in individuals with relapsing remitting multiple sclerosis (RRMS). **METHODS:** A randomized controlled trial was conducted from March to November 2015 with 30 individuals with RRMS (aged 20 to 50 years; 21 women, 9 men), who underwent detailed medical and neurologic examination. They were randomly allocated using sealed envelopes to either the study group, who received

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physical and cognitive rehabilitation (dual-task training), or the control group, who received physical rehabilitation alone. Participants (in both groups) were assessed twice (8 weeks apart), before and after rehabilitation. Assessment tools were the Mini-Mental State Examination (MMSE), the Expanded Disability Status Scale (EDSS), neuropsychological evaluation (using RehaCom), and walking tests. RESULTS: After training, the control group significantly improved regarding MMSE, attention/concentration test, and 10-meter walking test, whereas the scores of the study group significantly improved in all studied parameters (Expanded Disability Status Scale, MMSE, logical reasoning, and attention/concentration and walking tests). The differential (delta) scores from before to after rehabilitation were significantly higher in the study group for logical reasoning, attention/concentration, and 2-minute walking distance scores. CONCLUSIONS: Coupled physical and cognitive (dual-task) training showed concurrent improvement in cognitive and walking abilities in individuals with RRMS which exceeded that achieved by physical training alone. © 2020 by National University of Health Sciences. DOI: 10.1016/j.jcm.2019.08.002 PMID: 33192186

RehaCom-15. Medicine (Baltimore). 2020 Jul 17;99(29):e21263. doi: 10.1097/MD.00000000000021263.

**A randomized controlled trial to evaluate the effectiveness and safety of electro acupuncture and transcranial direct current stimulation with computerized cognitive rehabilitation in patients with vascular cognitive impairment.** Park HK(1), Song MK(1), Kim JH(2), Han JY(1).

BACKGROUND: Vascular cognitive impairment (VCI) refers to all cognitive disorders caused by cerebrovascular disorders. For the treatment, many types of pharmacologic and nonpharmacologic treatments are used but their underlying mechanisms and effects are unclear. Regarding nonpharmacologic treatment, electroacupuncture (EA), transcranial direct current stimulation (tDCS), and computerized cognitive rehabilitation treatment (CCRT) are effective. Here, we report the protocol for a randomized controlled trial of the effect and safety of combination therapy of EA or tDCS and CCRT in patients with VCI. METHODS: This study will be a prospective, outcome assessor-blinded, parallel-arm, randomized controlled clinical trial. Participants with cognitive impairment caused by stroke after 3 months of onset (n=45) will be randomly assigned to a CCRT, combination therapy with EA and computerized cognitive rehabilitation treatment, or combination therapy with tDCS and computerized cognitive rehabilitation treatment group. All groups will receive treatment 3 times per week for 8 weeks, giving a total of 24 treatments. The CCRT group will perform a training task like shopping, calculating, and others and involving computerized cognitive assessment and brain training system (RehaCom) for 30 minutes. The combination therapy with EA and computerized cognitive rehabilitation treatment group will receive EA using 8 acupuncture points - baekhoe, sinjeong, both sides of pungji, 4 sites of sishencong - and will be applied using an EA stimulator and receive CCRT for 30 minutes at the same time. The combination therapy with tDCS and computerized cognitive rehabilitation treatment group will receive tDCS treatment and receive CCRT for 30 minutes at the same time. The primary outcome will be evaluated using the Lowenstein occupational therapy cognitive assessment, while other scales assessing walking ability, activities of daily living, and quality of life are considered secondary outcome measures. Outcomes will be evaluated before intervention, at the end of intervention 8 weeks after the first intervention, and 4 weeks after completion of the intervention program. DISCUSSION: This study aims to examine the effect and safety of combination therapy with EA or tDCS and CCRT in patients with VCI. This study can be useful in developing new treatment technologies using collaborative research with combined traditional Korean and conventional medicines. TRIAL REGISTRATION: This trial has been registered with cris.nih.go.kr (registration number, KCT 0003644 Registered 01 April 2019, http://cris.nih.go.kr). DOI: 10.1097/MD.00000000000021263 PMID: 32702911 [Indexed for MEDLINE]

Conflict of interest statement: The authors have no conflicts of interests to disclose.

RehaCom-16. Psychiatry Res. 2019 Sep;279:62-70. doi: 10.1016/j.psychres.2019.06.041. Epub 2019 Jul 1.

**The efficacy of computer-based cognitive training for executive dysfunction in schizophrenia.** Mak M(1), Tyburski E(2), Starkowska A(1), Karabanowicz E(3), Samochowiec A(4), Samochowiec J(5).

The purpose of this study was to assess the effect of computer-based cognitive training on executive dysfunction in patients with schizophrenia. Sixty-five patients with schizophrenia were randomly assigned to a training group (n = 33) or a non-training group (n = 32), and compared in terms of executive performance to a healthy control group (n = 33). Executive function was assessed using the Trail Making Test, the Stroop Color and Word Test, and the Wisconsin Card Sorting Test (computer version). Cognitive training was performed using RehaCom software over a course of 16 individual sessions. Primary outcomes were training (performance at three different timepoints) and neuropsychological components (flexibility and cognitive inhibition, high executive processing, and processing speed). In both clinical groups, all aspects of executive function were found to be deficient. In the patient training group, the use of computer-based training alongside pharmacological treatment was more effective in terms of cognitive improvement than pharmacological treatment alone. However, there was no significant effect of cognitive training on processing speed. Cognitive training in schizophrenia patients was effective at improving several aspects of executive function, but did not improve processing speed. Copyright © 2019 Elsevier B.V. All rights reserved. DOI: 10.1016/j.psychres.2019.06.041 PMID: 31302353 [Indexed for MEDLINE]

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RehaCom-17. Appl Neuropsychol Adult. 2019 Dec 29;1-10. doi: 10.1080/23279095.2019.1692842. Online ahead of print. **Beneficial effect of computer-based multidomain cognitive training in patients with mild cognitive impairment.** Nousia A(1), Martzoukou M(1), Siokas V(2)(3), Aretouli E(4), Aloizou AM(2)(3), Folia V(2)(3), Peristeri E(2)(3), Messinis L(5), Nasios G(1), Dardiotis E(2)(3).

The purpose of the present study was to explore the effects of computer-based multidomain cognitive training program on Greek patients with Mild Cognitive Impairment (MCI). Forty-six patients with MCI were randomly divided into two groups; (a) the training group, which received a computer-based multidomain cognitive training program with the use of the RehaCom software and (b) the control group, which underwent standard-clinical care. The duration of the computer-based training program was 15 weeks, administered twice a week for approximately one hour per session. Analysis of the baseline versus endpoint performance of each group demonstrated that in the control group delayed memory and executive function had deteriorated over the observation period of 15 weeks, while improvement was observed in the training group's performance on delayed memory, word recognition, Boston Naming Test (BNT), Clock Drawing Test (CDT), Semantic Fluency (SF), Trail Making Test-A (TMT-A) and Trail Making Test-B (TMT-B). Comparison between the two groups presented a significant effect of the intervention for most cognitive domains. These findings are promising for the development of training methods designed to delay cognitive decline in patients with MCI, which is considered to be the prodromal stage of Alzheimer's Disease (AD). DOI: 10.1080/23279095.2019.1692842 PMID: 31885287

RehaCom-18. Behav Neurol. 2017;2017:5919841. doi: 10.1155/2017/5919841. Epub 2017 Dec 31.

**Efficacy of a Computer-Assisted Cognitive Rehabilitation Intervention in Relapsing-Remitting Multiple Sclerosis Patients: A Multicenter Randomized Controlled Trial.** Messinis L(1)(2), Nasios G(3), Kosmidis MH(4), Zampakis P(5), Malefaki S(6), Ntoskou K(7), Nousia A(3), Bakirtzis C(8), Grigoriadis N(8), Gourzis P(2), Papathanasopoulos P(9).

Cognitive impairment is frequently encountered in multiple sclerosis (MS) affecting between 40-65% of individuals, irrespective of disease duration and severity of physical disability. In the present multicenter randomized controlled trial, fifty-eight clinically stable RRMS patients with mild to moderate cognitive impairment and relatively low disability status were randomized to receive either computer-assisted (RehaCom) functional cognitive training with an emphasis on episodic memory, information processing speed/attention, and executive functions for 10 weeks (IG; n = 32) or standard clinical care (CG; n = 26). Outcome measures included a flexible comprehensive neuropsychological battery of tests sensitive to MS patient deficits and feedback regarding personal benefit gained from the intervention on four verbal questions. Only the IG group showed significant improvements in verbal and visuospatial episodic memory, processing speed/attention, and executive functioning from pre- to postassessment. Moreover, the improvement obtained on attention was retained over 6 months providing evidence on the long-term benefits of this intervention. Group by time interactions revealed significant improvements in composite cognitive domain scores in the IG relative to the demographically and clinically matched CG for verbal episodic memory, processing speed, verbal fluency, and attention. Treated patients rated the intervention positively and were more confident about their cognitive abilities following treatment. DOI: 10.1155/2017/5919841 PMID: 29463950 [Indexed for MEDLINE]

RehaCom-19. J Phys Ther Sci. 2015 Aug;27(8):2487-9. doi: 10.1589/jpts.27.2487. Epub 2015 Aug 21.

**Effect of computerized cognitive rehabilitation program on cognitive function and activities of living in stroke patients.** Yoo C(1), Yong MH(2), Chung J(3), Yang Y(4).

The objective of this study was to examine the effect of cognitive rehabilitation using a computer on cognitive function and activities of daily living in stroke patients presenting impairment of cognitive function. [Subjects] Forty-six stroke patients were divided into two groups (a training group and control group) through random assignment. [Methods] The training group received rehabilitation therapy and an additional computerized cognitive rehabilitation program using The RehaCom software 30 minutes/day, 5 times/week for 5 weeks. The control group received only rehabilitation therapy including physical and occupational therapy. A comparative analysis on all subjects was conducted before and after the experiment using a cognitive test and activities of daily living test. [Results] After 5 weeks of therapy, the training group presented statistically significant improvement in cognitive function assessment items of digit span, visual span, visual learning, auditory continuous performance, visual continuous performance, and others compared with the control group but did not present statistically significant improvement in activities of daily living. [Conclusion] It was revealed through this study that computerized cognitive rehabilitation with the RehaCom program results in improvement in cognitive function and can be used as a treatment tool beneficial to stroke patients presenting cognitive impairment. DOI: 10.1589/jpts.27.2487 PMID: 26355244

RehaCom-20. Psychiatry Res. 2011 Jun 30;192(3):160-6. doi: 10.1016/j.psychres.2010.12.004. Epub 2011 May 2.

**How can cognitive remediation therapy modulate brain activations in schizophrenia? An fMRI study.** Bor J(1), Brunelin J, d'Amato T, Costes N, Suaud-Chagny MF, Saoud M, Poulet E.

Cognitive remediation therapy (CRT) is a non biological treatment that aims to correct cognitive deficits through repeated exercises. Its efficacy in patients with schizophrenia is well recognized, but little is known about its effect on cerebral activity. Our aim was to explore the impact of CRT on cerebral activation using functional magnetic resonance imaging (fMRI) in patients with schizophrenia. Seventeen patients and 15 healthy volunteers were recruited. Patients were divided into two groups: one group received CRT with RehaCom® software (n=8), while a control group of patients (non-CRT group) received no additional treatment (n=9). The three groups underwent two fMRI sessions with

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an interval of 3months: they had to perform a verbal and a spatial n-back task at the same performance level. Patients were additionally clinically and cognitively assessed before and after the study. After CRT, the CRT group exhibited brain over-activations in the left inferior/middle frontal gyrus, cingulate gyrus and inferior parietal lobule for the spatial task. Similar but nonsignificant over-activations were observed in the same brain regions for the verbal task. Moreover, CRT patients significantly improved their behavioural performance in attention and reasoning capacities. We conclude that CRT leads to measurable physiological adaptation associated with improved cognitive ability. Trial name: Cognitive Remediation Therapy and Schizophrenia. <http://clinicaltrials.gov/ct2/show/NCT01078129>. REGISTRATION NUMBER: NCT01078129. Copyright © 2010 Elsevier Ireland Ltd. All rights reserved. DOI: 10.1016/j.psychresns.2010.12.004 PMID: 21543191 [Indexed for MEDLINE]

RehaCom-21. Neural Plast. 2016;2016:4292585. doi: 10.1155/2016/4292585. Epub 2016 Dec 27.

**A Randomised Controlled Trial of Efficacy of Cognitive Rehabilitation in Multiple Sclerosis: A Cognitive, Behavioural, and MRI Study.** Campbell J(1), Langdon D(2), Cercignani M(1), Rashid W(3).

**Aim:** To explore the efficacy of home-based, computerised, cognitive rehabilitation in patients with multiple sclerosis using neuropsychological assessment and advanced structural and functional magnetic resonance imaging (fMRI). **Methods.** 38 patients with MS and cognitive impairment on the Brief International Cognitive Assessment for MS (BICAMS) were enrolled. Patients were randomised to undergo 45 minutes of computerised cognitive rehabilitation using RehaCom software (n = 19) three times weekly for six weeks or to a control condition (n = 19). Neuropsychological and MRI data were obtained at baseline (time 1), following the 6-week intervention (time 2), and after a further twelve weeks (time 3). Cortical activations were explored using fMRI and microstructural changes were explored using quantitative magnetisation transfer (QMT) imaging. **Results.** The treatment group showed a greater improvement in SDMT gain scores between baseline and time 2 compared to the control group (p = 0.005). The treatment group exhibited increased activation in the bilateral prefrontal cortex and right temporoparietal regions relative to control group at time 3 (p < 0.05FWE corrected). No significant changes were observed on QMT. **Conclusion.** This study supports the hypothesis that home-based, computerised, cognitive rehabilitation may be effective in improving cognitive performance in patients with MS. Clinical trials registration is ISRCTN54901925. DOI: 10.1155/2016/4292585 PMCID: PMC5223046 PMID: 28116167 [Indexed for MEDLINE]

**Conflict of interest statement:** Dr. J. Campbell and Professor M. Cercignani have nothing to disclose. Dr W. Rashid has accepted educational grants and travel bursaries from Genzyme, Biogen-Idec, Novartis, and Teva and has also participated in advisory boards with Bayer, Novartis, Biogen-Idec, and Genzyme. Professor D. Langdon (i) has received research grants from Bayer, Novartis, and Biogen and has also participated in advisory board with Bayer, Novartis, and Teva is also in the speaker Bureau for Teva, Roche, Bayer, Novartis, and Biogen.

RehaCom-22. Egypt J Neurol Psychiatr Neurosurg. 2018;54(1):32. doi: 10.1186/s41983-018-0037-8. Epub 2018 Nov 6.


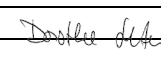
**Effect of transcranial direct current stimulation on cognitive function in stroke patients.** Shaker HA(1), Sawan SAE(1), Fahmy EM(2), Ismail RS(2), Elrahman SAEA(1).

**BACKGROUND:** Cognitive impairment after stroke is common and can cause disability with major impacts on quality of life and independence. Transcranial direct current stimulation may represent a promising tool for reconstitution of cognitive functions in stroke patients. **OBJECTIVES:** This study aimed to investigate the effect of transcranial direct current stimulation on cognitive functions in stroke patients. **PATIENTS AND METHODS:** Forty male stroke patients were included. Patients were divided randomly into two equal groups (A and B). Group A received transcranial direct current stimulation (tDCS) in combination with selected cognitive training program by RehaCom. Group B received sham transcranial direct current stimulation in combination with the same cognitive training program. Cognitive evaluation and functional independence measure (FIM) were done for all patients before and after treatment. **RESULTS:** There was a significant improvement in the scores of attention and concentration, figural memory, logical reasoning, reaction behavior, and FIM post treatment in both groups; the improvement was significantly higher in group A compared to group B. **CONCLUSION:** tDCS is a safe and effective neuro-rehabilitation modality that improves post stroke cognitive dysfunctions. Moreover, tDCS has a positive impact on performance of daily activities. DOI: 10.1186/s41983-018-0037-8 PMCID: PMC6223736 PMID: 30459505 **Conflict of interest statement:** The aim and procedures of the study were explained to every participant, and an informed written consent was obtained from all participants before being enrolled in the study. The study was approved by the ethical committee of Department of Physical Therapy for Neuromuscular Disorders and its Surgery, Faculty of Physical Therapy, Cairo University: No:P.T.REC/012/001071 (4/10/2015).Not applicable. The authors declare that they have no competing interests (financial and non-financial). We declare that the research was conducted in absence of any commercial relationships that could be constructed as a potential conflict of interest. Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

RehaCom-23. Encephale. 2006 Mar-Apr;32(2 Pt 1):189-95. doi: 10.1016/s0013-7006(06)76144-9.

**[Impact of a new cognitive remediation strategy on interpersonal problem solving skills and social autonomy in schizophrenia]. [Article in French]** Cochet A(1), Saoud M, Gabriele S, Broallier V, El Asmar C, Daléry J, D'Amato T.

**INTRODUCTION:** Despite recent developments, the impact of pharmacotherapy on social autonomy and interpersonal problem solving skills in patients with schizophrenia remains limited, with consequences in terms of socio-professional functioning. Indeed, independently of the positive, negative and/or disorganization symptoms, functional deficits in

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patients with schizophrenia rely mainly on various cognitive impairments. OBJECTIVES: To determine the impact of a new Cognitive Remediation Strategy on interpersonal problem solving skills, social autonomy and symptoms in patients with schizophrenia. METHODS: Thirty patients with schizophrenia were enrolled in a program consisting of 14 training sessions of 4 cognitive functions (attention/concentration, topological memory, logical reasoning, executive functions) using the REHACOM software. Measurements of attention (Continuous Performance Test, CPT), memory (Rivermead Behavioural Memory Test, RBMT) and executive functions (Wisconsin Card Sorting Test, WCST) as well as interpersonal problem solving skills (Assessment of Interpersonal Problem-Solving Skills, AIPSS) and social autonomy (Social Autonomy Scale, EAS) and finally schizophrenia symptoms (Positive And Negative Syndrom Scale, PANSS) were undertaken at the beginning and the end of the 14 remediation meetings. RESULTS: Cognitive functions, interpersonal problems solving skills, social autonomy and symptoms were significantly improved by the Cognitive Remediation Strategy. CONCLUSION: Our results confirm the therapeutic impact of a Cognitive Remediation Strategy among 30 schizophrenic patients stabilised on clinical, therapeutic and functional levels. The question of the long-term maintenance of such improvements still requires further investigation. DOI: 10.1016/s0013-7006(06)76144-9 PMID: 16910619 [Indexed for MEDLINE]

RehaCom-24. Behav Sci (Basel). 2017 Dec 30;8(1):4. doi: 10.3390/bs8010004.

**Effectiveness of a Computer-Based Training Program of Attention and Memory in Patients with Acquired Brain Damage.** Fernandez E(1), Bergado Rosado JA(2), Rodriguez Perez D(3), Salazar Santana S(4), Torres Aguilar M(5), Bringas ML(6)(7).

Many training programs have been designed using modern software to restore the impaired cognitive functions in patients with acquired brain damage (ABD). The objective of this study was to evaluate the effectiveness of a computer-based training program of attention and memory in patients with ABD, using a two-armed parallel group design, where the experimental group (n = 50) received cognitive stimulation using RehaCom software, and the control group (n = 30) received the standard cognitive stimulation (non-computerized) for eight weeks. In order to assess the possible cognitive changes after the treatment, a post-pre experimental design was employed using the following neuropsychological tests: Wechsler Memory Scale (WMS) and Trail Making test A and B. The effectiveness of the training procedure was statistically significant (p < 0.05) when it established the comparison between the performance in these scales, before and after the training period, in each patient and between the two groups. The training group had statistically significant (p < 0.001) changes in focused attention (Trail A), two subtests (digit span and logical memory), and the overall score of WMS. Finally, we discuss the advantages of computerized training rehabilitation and further directions of this line of work. DOI: 10.3390/bs8010004 PMID: 29301194 Conflict of interest statement: The authors declare no conflict of interest.

RehaCom-25. Cogn Neuropsychiatry. 2016 Jul;21(4):315-334. doi: 10.1080/13546805.2016.1208610. Epub 2016 Jul 18.

**Preliminary study of a rehabilitation program based on attentional processes to treat auditory hallucinations.** López-Luengo B(1), Muela-Martínez JA(1).

INTRODUCTION: Despite the effectiveness of pharmacological treatment, residual hallucinations do not completely resolve in some medicated patients. The aim of this study was to investigate the efficacy of attention training for reducing hallucinations in individuals with psychosis. METHODS: A randomised controlled trial was performed in which 20 individuals suffering auditory hallucinations received auditory stimulation similar to their internal voices, which was integrated into the RehaCom program of attention training. An equal number of individuals suffering auditory hallucinations did not receive this training. Cognitive and symptomatological variables were evaluated before and after the intervention period in both groups. RESULTS: Only data of 16 subjects were analysed. Auditory hallucinations no longer occurred by the end of the training program in five of eight individuals, whereas their frequency, intensity and negative content and associated anxiety were significantly reduced in the remaining three. No changes in hallucinations were observed in the control group. Attentional processes and executive functions were significantly better in patients who underwent the training than in those who did not at the end of the intervention period. CONCLUSIONS: Attention training can help people with auditory hallucinations develop an ability to ignore them, which can reduce or eliminate them entirely. DOI: 10.1080/13546805.2016.1208610 PMID: 27424464 [Indexed for MEDLINE]

RehaCom-26. Encephale. 2009 Apr;35(2):160-7. doi: 10.1016/j.encep.2008.02.010. Epub 2008 Jun 2.

**[Cognitive remediation and cognitive assistive technologies in schizophrenia]. [Article in French]** Sablier J(1), Stip E, Franck N.

BACKGROUND: Cognitive impairments are a core feature in schizophrenia. They impact several cognitive abilities but most importantly attention, memory and executive functions, consequently leading to great difficulties in everyday life. Most schizophrenia patients need assurance and require assistance and help from care workers, family members and friends. Family members taking care of a patient have additional daily work burden, and suffer psychological anguish and anxiety. Therefore, improving cognitive functions in schizophrenia patients is essential for the well-being of patients and their relatives. Reducing these deficits may decrease the economic burden to the health care system through lower numbers of hospital admissions and shorter hospitalisation periods, for example. Cognitive rehabilitation was developed to address the limited benefits of conventional treatments on cognitive deficits through the use of assistive technology as a means of enhancing memory and executive skills in schizophrenia patients. OBJECTIVE: To provide clinicians with comprehensive knowledge on cognitive trainings, programs of remediation, and cognitive assistive technologies. METHOD: Literature review. A search in the electronic databases (PubMed, EMBASE, Index Medicus) for recent articles

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in the last 10 years related to cognitive remediation published in any language using the words: cognitive and remediation or rehabilitation and schizophrenia, and a search for chapters in psychiatry and rehabilitation textbooks. RESULTS: We found 392 articles and 112 review paper mainly in English. First, we identified cognitive remediation programs that were beneficial to schizophrenia patients. Programs available in French (IPT, RECOS, and RehaCom) and others (CET, NET, CRT, NEAR, APT and CAT) were identified. In addition, since memory and executive function impairments could be present in people without schizophrenia, we reviewed inventories of cognitive assistive technologies proven to enhance cognitive skills in other populations. Finally, we present a review of recent studies testing innovative devices developed to assist schizophrenia patients. DISCUSSION: First, we found several cognitive programs proven to be effective with schizophrenia patients, but only three were validated in French. It could be useful to adapt other programs for French-speaking populations. Unfortunately, we found that very few of the existing cognitive assistive technologies are proposed to be used with schizophrenia patients. In fact, most of the available cognitive orthoses were tested primarily in people with neurological injuries (for example, various memory impairments caused by traumas), and in elderly illnesses (like Alzheimer disease). Devices for patients with mental deficits (e.g., mental retardation) were developed later, and only very recently explored for use in schizophrenia. As a result of an international collaboration between France and Canada, currently a tool called MOBUS is being tested. This technology aims at improving the autonomy of schizophrenia patients, by helping them plan and remember their daily activities. Furthermore, it encourages patient-caregiver communication, and permits monitoring patients' subjective reports of their symptoms. The use of cognitive assistive technologies is not meant to isolate patients by replacing the human element of relatives and caregivers by a machine. On the contrary, they offer a sense of security and they improve interpersonal relationships by permitting enhanced autonomy and greater self-confidence. Finally, a literature review of cognitive remediation in schizophrenia emphasizes the importance of a structured application of the technique in order for it to succeed. First, it is crucial to detect the impairments that will be targeted in each patient presenting a specific pattern of impairments. For this purpose, validated and customised neuropsychological tests are required. Then, cognitive remediation programs must be customised to each patient's needs in order to motivate the patient to participate. Finally, long-term effects must be assessed in order to verify whether reinforcement is needed. Following these steps, most of the studies show an improvement in the well-being of patients with schizophrenia. These recommendations are also suitable for the cognitive remediation programs, as for treatments with cognitive assistive devices. An important hurdle facing the advance of cognitive assistive technology programs is that different research groups work individually without a coordinated effort to improve and validate the existing programs. CONCLUSION: Schizophrenia treatments must take into account not only patients' symptoms, but also the associated cognitive deficits which constitute an important factor in their social problems. It has been shown that several cognitive remediation programs are efficient in schizophrenia. New technologies complement the benefits of such programs, and support pharmacological treatments and psychotherapies. DOI: 10.1016/j.encep.2008.02.010 PMID: 19393385 [Indexed for MEDLINE]

RehaCom-27. Z Exp Psychol. 1996;43(1):1-21.

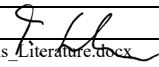
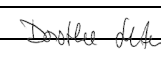
**[Training in cognitive functions in neurologic rehabilitation of craniocerebral trauma]. [Article in German]**  
 Friedl-Francesconi H(1), Binder H.

This study evaluates a new cognitive rehabilitation therapy for patients after severe head injury. In addition to the standard neurological rehabilitation therapy, one group was trained by the Wiener Determinationsgerät (WDT), a second group was treated by the new program REHACOM, while a third group received only conventional neurological rehabilitation therapy. The three groups each consisted of 12 patients; two groups received 20 sessions of training, each lasting 40 minutes. At the beginning as well as after the therapy a psychological test battery was applied, consisting of HAWIE, TULUC, ACHENER APHASIETEST, and BENTON-Test. They were also tested by a specific neuropsychological battery regarding hemispheric specialization. REHACOM showed significantly higher values on the HAWIE as well as on BENTON-Test than the other two groups. REHACOM also improved in right-hemispheric dimensions while WDT group did not improve in attention. Right-hemispheric training was more effective than attentional stimulation. PMID: 8705811 [Indexed for MEDLINE]

RehaCom-28. Schizophr Res. 2011 Feb;125(2-3):284-90. doi: 10.1016/j.schres.2010.10.023. Epub 2010 Nov 19.

**A randomized, controlled trial of computer-assisted cognitive remediation for schizophrenia.** d'Amato T(1), Bation R, Cochet A, Jalenques I, Galland F, Giraud-Baro E, Pacaud-Troncin M, Augier-Astolfi F, Llorca PM, Saoud M, Brunelin J.

OBJECTIVE: There is considerable interest in cognitive remediation for schizophrenia. Our study aimed to evaluate, in a large sample of patients with schizophrenia, the interest of a computer-assisted cognitive remediation program on cognitive performances of patients as well as in clinical and functional outcome. METHOD: Seventy-seven patients with remitted schizophrenia were randomly assigned to 14 2-hours individual sessions of computer-assisted cognitive remediation (n=39) or a control condition (n=38). Remediation was performed using RehaCom ® software. Four procedures were chosen to train four cognitive functions involved in different stages of the information processing: attention/concentration, working memory, logic, and executive functions. Primary outcomes were remediation exercise metrics, neuropsychological composites (episodic memory, working memory, attention, executive functioning, and processing speed), clinical and community functioning measures. RESULTS: Cognitive performances concerning Attention/vigilance, verbal working memory and verbal learning memory and reasoning/problem solving improved significantly in the remediation condition when no difference was reported in the control condition between the 2 assessments. However, there were no significant benefits of cognitive remediation on non-verbal working memory and learning and speed of processing or functional outcome measures. CONCLUSIONS: Cognitive remediation for people with

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schizophrenia was effective in improving performance, but the benefits of training did not generalize to functional outcome measures. Long term follow-up studies are needed to confirm the maintenance of such improvements. Copyright © 2010 Elsevier B.V. All rights reserved. DOI: 10.1016/j.schres.2010.10.023 PMID: 21094025 [Indexed for MEDLINE]

RehaCom-29. Iran J Psychiatry. 2014 Oct;9(4):209-15.

**The effectiveness of computerized cognitive rehabilitation training program in improving cognitive abilities of schizophrenia clients.** Mohammadi MR(1), Keshavarzi Z(2), Talepasand S(3).

OBJECTIVE: The aim of this study was to evaluate the efficacy of a computer - based training program of attention, memory and executive functions in enhancing neuropsychological performances as well as functional outcome in clients with schizophrenia. METHOD: A total of 15 clinically stable out patients with Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR) criteria for schizophrenia, diagnosed with different types of schizophrenia: paranoid, disorganized, residual, based on DSM- IV-TR were selected to participate in this study. All patients were randomly selected using a conventional sampling method and assigned to 60 hours individual sessions of computer - assisted cognitive remediation (CACR). This was a pre- experimental study with pretest and posttest in a single group. Cognitive functions were checked with Continuous Performance Test (CPT), Wechsler Adult Intelligence Scale (Wds) and Prospective and Retrospective Memory Questionnaire (PRMQ). The symptoms of patients were measured with the Positive and Negative Syndrome Scale (PANSS). Remediation was performed utilizing the RehaCome® software. Patients received the cognitive remediation program including attention, concentration and working memory. All participants were followed up after an interval of one month and three months. Data were analyzed using repeated measures analysis. RESULT: After 3 months, the findings showed that patients' scores improved in the time factor. Also, a significant improvement favoring cognitive remediation was found in several cognitive measures including Reaction Time (F = 4015p<.05, Eta = 0.242), Wds (F = 11.806, p<.05, Eta = .48) PRMQ1(F = 3.314, p<.05, Eta = 0.20) PRMQ7(F = 2.85, p<.05, Eta = 0.18). CONCLUSION: Computer-assisted cognitive remediation training program was effective in improving the performance of schizophrenic patients. CACR did not have any effects on the positive and negative symptoms. Long- term follow-up studies are needed to confirm the maintenance of such improvements. PMID: 25802533

### 3. Search in PubMed, search term "NEUROvitalis" (4 results)

NEUROvitalis-1. Parkinsonism Relat Disord. 2014 Nov;20(11):1196-202. doi: 10.1016/j.parkreldis.2014.08.023. Epub 2014 Sep 16.

**Effects of cognitive training in Parkinson's disease: a randomized controlled trial.** Petrelli A(1), Kaesberg S(2), Barbe MT(3), Timmermann L(4), Fink GR(3), Kessler J(4), Kalbe E(5).

BACKGROUND: In Parkinson's Disease (PD), cognitive dysfunctions which can reduce patients' quality of life occur frequently. Data on non-pharmacological intervention effects on cognitive functions in patients with PD are rare. The aim of this study was to examine the effects of different cognitive group trainings (structured vs. unstructured) on cognition, depression, and quality of life in non-demented PD patients. METHODS: In this randomized controlled trial, 65 non-demented patients with PD according to UK Brain Bank criteria (Hoehn & Yahr I-III) were allocated to one of two cognitive multi-component treatments ("NEUROvitalis", a structured training, or the unstructured training "Mentally fit" with randomly assembled cognitive tasks, each including 12 group-sessions à 90 min over 6 weeks) or a waiting list control group (CG). A neuropsychological test battery was performed before and after the training. RESULTS: Compared to the CG, patients from the "NEUROvitalis" group improved in short-term memory (word list learning "Memo": p < .01) and working memory (digit span reverse from "DemTect": p < .05), whereas depression scores were reduced in the "Mentally fit" group (Beck Depression Inventory-II: p < .05). The "NEUROvitalis" group improved significantly more in working memory than the "Mentally fit" group (DemTect: p < .05). DISCUSSION: Cognitive and affective functions can be improved by cognitive trainings in PD patients. Specific effects (e.g. on memory and working memory versus depression) seem to be dependent on the type of training. Further research is needed to define long-term effects and the efficacy in PD patients with different extent of cognitive and neuropsychiatric symptoms. Copyright © 2014 Elsevier Ltd. All rights reserved. DOI: 10.1016/j.parkreldis.2014.08.023 PMID: 25242806 [Indexed for MEDLINE]

NEUROvitalis-2. Eur J Neurol. 2015 Apr;22(4):640-7. doi: 10.1111/ene.12621. Epub 2014 Dec 22.

**Cognitive training in Parkinson's disease reduces cognitive decline in the long term.** Petrelli A(1), Kaesberg S, Barbe MT, Timmermann L, Rosen JB, Fink GR, Kessler J, Kalbe E.

BACKGROUND AND PURPOSE: Patients with Parkinson's disease (PD) are at high risk for cognitive dysfunction. Non-pharmacological interventions have attracted increasing interest for enhancing PD patients' cognitive functions. METHODS: One-year follow-up data (T2 ) of a randomized controlled trial evaluating two 6-week cognitive trainings - a structured (NEUROvitalis, NV) and an unstructured (mentally fit, MF) program - compared with a waiting list control group (CG) in non-demented PD patients (Hoehn and Yahr I-III) are presented. Forty-seven PD patients were examined at T2 . Effects on overall cognitive functions (Mini-Mental State Examination and DemTect) were compared between all groups with repeated measurement analyses of variance. A combined score of the percentage change value from baseline (T0 ) to T2 was calculated to identify patients who retained or improved their cognitive state (responders). The

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risk of developing mild cognitive impairment (MCI) was analyzed. RESULTS: Significant time × treatment effects on overall cognitive functions were found for both training groups, each compared separately to the CG (DemTect,  $P < 0.05$ ). Nine patients (56.3%) of the NV group, seven (41.2%) of the MF group and three (21.4%) of the CG were responders. Comparing NV to CG the odds ratio was 4.7 [95% confidence interval (0.8; 33.3)], and comparing MF to CG it was 2.6 [95% confidence interval (0.4; 17.4)]. MCI risk for patients without prior MCI was 40.0% in CG, 18.2% in MF and 18.2% in NV. The odds ratio was 3 comparing NV to CG, MF to CG. DISCUSSION: This study gives evidence that cognitive training may be effective to prevent cognitive decline and onset of MCI in PD patients. © 2014 EAN. DOI: 10.1111/ene.12621 PMID: 25534579 [Indexed for MEDLINE]

NEUROvitalis-3. Diagn Progn Res. 2020 May 21;4:7. doi: 10.1186/s41512-020-0071-8. eCollection 2020.


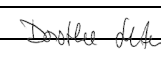
**Prognostic factors for change in memory test performance after memory training in healthy older adults: a systematic review and outline of statistical challenges.** oheger M(1), Folkerts AK(1), Krohm F(1), Skoetz N(2), Kalbe E(1).

BACKGROUND: The goal is to investigate prognostic factors for change in memory test performance in healthy older adults and to report and discuss the different statistical procedures used for investigating this topic in the literature. METHODS: Prognostic factors were here understood as any measures that were investigated to estimate change in memory test performance. MEDLINE, Web of Science Core Collection, CENTRAL, and PsycInfo were searched up to November 2019. Prognostic factor and prognostic factor finding studies investigating prognostic factors on verbal and non-verbal short- and long-term memory after conducting memory training in healthy older adults were included. Risk of bias was assessed using the QUIPS tool. RESULTS: Our search yielded 12,974 results. We included 29 studies that address prognostic factors of change in memory test performance, including sociodemographic, (neuro-)psychological, genetic, and biological parameters. Studies showed high variation and methodological shortcomings with regard to the assessment, statistical evaluation, and reporting of the investigated prognostic factors. Included studies used different types of dependent variables (change scores vs. post-test scores) when defining change in memory test performance leading to contradictory results. Age was the only variable investigated throughout most of the studies, showing that older adults benefit more from training when using the change score as the dependent variable. CONCLUSION: Overall, there is a need for adequate reporting in studies of prognostic factors for change in memory test performance. Because of inconsistencies and methodological shortcomings in the literature, conclusions regarding prognostic factors remain uncertain. As a tentative conclusion, one may say that the higher the age of the participant, the more profound the improvement in memory test performance will be after memory training. TRIAL REGISTRATION: CRD42019127479. © The Author(s) 2020. DOI: 10.1186/s41512-020-0071-8 PMCID: PMC7240921 PMID: 32478173 Conflict of interest statement: Competing interests EK has received grants from the German Ministry of Education and Research, ParkinsonFonds Deutschland GmbH, the German Parkinson Society; honoraria from: Oticon GmbH, Hamburg, Germany; Lilly Pharma GmbH, Bad Homburg, Germany; Bernafon AG, Bern, Switzerland; Desitin GmbH, Hamburg, Germany. EK is author of the cognitive training program NEUROvitalis but receives no corresponding honoraria. AKF has received a grant from the German Parkinson Society, and honoraria from ProLog Wissen GmbH, Cologne, Germany and pro auditio Switzerland, Zürich, Switzerland. AFK is author of the cognitive training program NEUROvitalis but receives no corresponding honoraria. MR has received a grant from the Brandau-Laibach Stiftung, and a grant from the German Ministry of Education and Research. FK and NS do not declare any conflict of interests.

NEUROvitalis-4. Parkinsons Dis. 2020 Nov 30;2020:4068706. doi: 10.1155/2020/4068706. eCollection 2020.

**Enhancement of Executive Functions but Not Memory by Multidomain Group Cognitive Training in Patients with Parkinson's Disease and Mild Cognitive Impairment: A Multicenter Randomized Controlled Trial.** Kalbe E(1), Folkerts AK(1), Ophéy A(1), Eggers C(2)(3), Elben S(4), Dimenshteyn K(4), Sulzer P(5), Schulte C(5), Schmidt N(6), Schlenstedt C(6), Berg D(6), Witt K(6)(7), Wojtecki L(4)(8), Liepelt-Scarfone I(5).

BACKGROUND: Meta-analyses have demonstrated cognitive training (CT) benefits in Parkinson's disease (PD) patients. However, the patients' cognitive status has only rarely been based on established criteria. Also, prediction analyses of CT success have only sparsely been conducted. OBJECTIVE: To determine CT effects in PD patients with mild cognitive impairment (PD-MCI) on cognitive and noncognitive outcomes compared to an active control group (CG) and to analyze CT success predictors. METHODS: Sixty-four PD-MCI patients (age:  $67.61 \pm 7.70$ ; UPDRS-III:  $26.58 \pm 13.54$ ; MoCA:  $24.47 \pm 2.78$ ) were randomized to either a CT group or a low-intensity physical activity CG for six weeks (twice weekly, 90 minutes). Outcomes were assessed before and after training. MANOVAs with follow-up ANOVAs and multiple regression analyses were computed. RESULTS: Both interventions were highly feasible (participation, motivation, and evaluation); the overall dropout rate was 4.7%. Time × group interaction effects favoring CT were observed for phonemic fluency as a specific executive test ( $p=0.018$ ,  $\eta^2 p^2=0.092$ ) and a statistical trend for overall executive functions ( $p=0.095$ ,  $\eta^2 p^2=0.132$ ). A statistical trend for a time × group interaction effect favoring CG was shown for the digit span backward as a working memory test ( $p=0.098$ ,  $\eta^2 p^2=0.043$ ). Regression analyses revealed cognitive baseline levels, education, levodopa equivalent daily dose, motor scores, and ApoE status as significant predictors for CT success. CONCLUSIONS: CT is a safe and feasible therapy option in PD-MCI, yielding executive functions improvement. Data indicate that vulnerable individuals may show the largest cognitive gains. Longitudinal studies are required to determine whether CT may also attenuate cognitive decline in the long term. This trial is registered with DRKS00010186. Copyright © 2020 Elke Kalbe et al. DOI: 10.1155/2020/4068706 PMCID: PMC7721510 PMID: 33312495 Conflict of interest statement: EK has received grants from the German Ministry of Education and Research, Parkinson Fonds Deutschland gGmbH, and the German Parkinson Society and honoraria from Oticon GmbH, Hamburg, Germany; Lilly Pharma GmbH, Bad Homburg, Germany; Bernafon AG, Bern, Switzerland; and Desitin GmbH, Hamburg, Germany. AKF has received a

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grant from the German Parkinson Society and honoraria from ProLog Wissen GmbH, Cologne, Germany, and pro audito Switzerland, Zürich, Switzerland. AFK and EK are the authors of the cognitive training program NEUROvitalis but received no corresponding honoraria. AO, SE, KD, PS, and CS declare that there are no conflicts of interest. CE has received grants from the German Research Foundation (KFO219, TP 10) and the Medical Faculty of the Philipps University Marburg, Germany, and the German Ministry of Education and Research and honoraria from AbbVie, Wiesbaden, Germany; UCB, Monheim, Germany; Daiichi Sankyo, Munich, Germany; Medtronic, Meerbusch, Germany; Bayer Vital, Leverkusen, Germany; and Bial, Mörfelden-Walldorf, Germany. NS has received grants from the German Federal Ministry of Education and Research. CS received funding from the Copenrath-Foundation, the Parkinson Fonds Germany and honoraria from AbbVie, Wiesbaden, Germany. DB has received grants from Janssen Pharmaceutica N.V., German Parkinson's Disease Association (dPV), BMWi, BMBF, Parkinson Fonds Germany gGmbH, UCB Pharma GmbH, TEVA Pharma GmbH, EU, Novartis Pharma GmbH, Lundbeck, and Damp foundation. She received honoraria for talks or consultant work from AbbVie, Biogen, BIAL, Lundbeck, and Desitin. KW has received grants for the German Research Foundation and the German Federal Ministry of Education and Research. He received speaker honoraria from BIAL, BAYER, Medtronic, Boston Scientific, Novartis, Desitin, and the German Society of Neurology. LW has received honoraria from Meda, Boehringer, Cephalon Pharma, TEVA, Desitin, AbbVie St. Jude Medical/Abbott, and Medtronic and grants from HHU Düsseldorf, DFG Forschergruppe (FOR 1328), ERANET-Neuron/BMBF (TYMON 01EW141), German Parkinson's Disease Association (dPV), Parkinson Fonds Germany, and Hilde Ulrichs Stiftung für Parkinsonforschung. ILS reports grants from the Parkinson Fonds Deutschland gGmbH, Janssen Pharmaceutical Companies of Johnson & Johnson, European Commission, H2020-TWINN-2015, and the Michael J Fox Foundation.

Beurteilung Qualität / Validität hoch / mittel / gering	Beurteilung Relevanz relevant / nicht relevant	Beurteilung Gewichtung hoch / mittel / gering
hoch	relevant	hoch, Metaanalyse

#### 4. NEUROvitalis studies (not listed in PubMed) (18 results)

NEUROvitalis-5. Parkinson's Disease,

**Cognitive Stimulation for Individuals with Parkinson's Disease Dementia Living in Long-Term Care:**

**Preliminary Data from a Randomized Crossover Pilot Study** Folkerts AK, Dorn M, Roheger M, Maassen M, Koerts J, Tucha O, Altgassen M, Sack AT, Smit D, Haarmann L, Kalbe E (2018).

Background. While the efficacy of cognitive stimulation (CS) has been demonstrated in patients with dementia, no study has included patients with Parkinson's disease dementia (PDD). Objective. For the first time, this randomized crossover pilot study examined the feasibility and potential effects of CS in PDD. Methods. All residents of a PDD-specific long-term care unit in the Netherlands that were eligible for the study (n 12) were randomly allocated to group A (n 6) receiving CS (eight weeks, twice weekly for 60 minutes) or group B (n 6) receiving usual care (control group, CG). The CG participated in CS afterwards, resulting in an experimental group (EG), consisting of n 12. Pre- and postassessments and a six-week follow-up (FU) were conducted for cognition, neuropsychiatric symptoms, quality of life (QoL), and activities of daily living (ADL) outcomes. Results. Between-group analysis with difference scores from pre- to posttest revealed a group difference for global cognition (CERAD total score) favoring the EG, with a moderate effect size and a p value just failing to reach statistical significance (p 0.067; r 0.43). A further statistical trend was observed for neuropsychiatric symptoms, again with a moderate effect size (p 0.075; r 0.42). Within-group analyses indicated improvement only in the EG with large effects also just failing to reach significance for global cognition (short term, p 0.060; r 0.70) as well as for depression (long term, p 0.072; r 0.61). ADL deteriorated significantly at FU in the EG (p 0.014; r 0.71). Conclusions. Although our data are preliminary due to the small sample size, this study shows that CS is feasible and potentially effective for cognitive and noncognitive outcomes in PDD patients. Randomized controlled trials with larger sample sizes are needed to confirm these promising results.

NEUROvitalis-6. Frontiers in Aging Neuroscience, 10:407. doi: 10.3389/fnagi.2018.00407, Clinical Trial, published 18 Dec 2018

**Effects of a Cognitive Training With and Without Additional Physical Activity in Healthy Older Adults: A Follow-Up 1 Year After a Randomized Controlled Trial.**

Kalbe E, Roheger M, Paluszak K, Meyer J, Becker J, Fink GR, Kukolja J, Rahn A, Szabados F, Wirth B, Kessler J (2018).


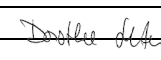
Background: Combining cognitive training (CT) with physical activity (CPT) has been suggested to be most effective in maintaining cognition in healthy older adults, but data are scarce and inconsistent regarding long-term effects (follow-up; FU) and predictors of success.

Objective: To investigate the 1-year FU effects of CPT versus CT and CPT plus counseling (CPT+C), and to identify predictors for CPT success at FU.

Setting and Participants: We included 55 healthy older participants in the data analyses; 18 participants (CPT group) were used for the predictor analysis.

Interventions: In a randomized controlled trial, participants conducted a CT, CPT, or CPT+C for 7 weeks.

Outcome Measures: Overall cognition, verbal, figural, and working memory, verbal fluency, attention, planning, and visuo-construction.

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Results: While within-group comparisons showed cognitive improvements for all types of training, only one significant interaction Group × Time favoring CPT in comparison to CPT+C was found for overall cognition and verbal long-term memory. The most consistent predictor for CPT success (in verbal short-term memory, verbal fluency, attention) was an initial low baseline performance. Lower education predicted working memory gains. Higher levels of insulin-like growth factor 1 (IGF-1) and lower levels of brain-derived neurotrophic factor at baseline (BDNF) predicted alternating letter verbal fluency gains.

Discussion: Within-group comparisons indicate that all used training types are helpful to maintain cognition. The fact that cognitive and sociodemographic data as well as nerve growth factors predict long-term benefits of CPT contributes to the understanding of the mechanisms underlying training success and may ultimately help to adapt training to individual profiles.

Clinical Trial Registration: WHO ICTRP (<http://apps.who.int/trialsearch/>), identifier DRKS00005194.

NEUROvitalis-7. *Frontiers in Human Neuroscience*. *Cogn Behav Neurol* 2019;32:76–86

**Structured Cognitive Training Yields Best Results in Healthy Older Adults, and Their ApoE4 State and Baseline Cognitive Level Predict Training Benefits** Roheger M, Kessler J, Kalbe E (2019).

Background: Cognitive training has been shown to improve cognitive functions in healthy older adults. However, little is known about which specific variables are responsible for the improvement.

Objective: Our aim was to evaluate whether healthy older adults benefit more from a structured cognitive training program than an unstructured brain jogging program and to identify possible predictors for training success, including apolipoprotein E4 (apoE4).

Methods: In a randomized controlled trial, participants completed either a 6-week structured cognitive training program (n = 35) or a 6-week unstructured brain jogging program (n = 35). A control group received no training and was not part of the randomization procedure (n = 35). Overall, 105 participants were included in the training data analyses, focusing on verbal memory, attention, and executive functions. Data from an additional 45 previously trained, healthy older adults were used for the predictor analysis.

Results: A significant Time × Training interaction in favor of the structured cognitive training program was found in verbal memory. Low baseline performance on neuropsychological tests was a significant predictor for benefits in verbal memory, attention, and executive functions. A subgroup analysis (n = 35) revealed that only noncarriers of the apoE4 allele showed significant gains in long-term verbal memory and attention.

Conclusions: Our results support the greater effectiveness of structured cognitive training on verbal memory compared with brain jogging and no training. The success of this type of training program may be predicted by sociodemographic, cognitive, and genetic variables.

NEUROvitalis-8. *Journal of Alzheimer’s disease*, 54 (1016), 253-268.

**Cognitive Stimulation for People with Dementia in Long-term Care Facilities: Baseline cognitive level predicts cognitive gains, moderated by depression. Evidence from a Randomized Controlled Trial.**

Middelstädt J, Folkerts AK, Blawath S, Kalbe E (2016).

Background: Increasing evidence demonstrates the efficacy of cognitive stimulation (CS, NEUROvitalis) in individuals with dementia. However, conducting studies in nursing homes engenders specific challenges that have limited the data gathered on this topic so far.

Objective: The aim of this randomized controlled trial was to investigate the effects of CS on cognition, quality of life (QoL), behavioral symptoms, and activities of daily life in persons with dementia living in nursing homes. We further aimed to identify predictors of the intervention’s benefits.

Methods: Seventy-one persons with mild to moderate dementia were randomly allocated to the experimental group (EG; n = 36) that visited a CS program twice weekly for eight weeks or to the control group (CG; n = 35) that was receiving usual care. Neuropsychological tests were conducted before and after the intervention period and at six-week follow-up.

Results: There were no significant interaction effects Time Group for the outcome measures. However, regression analysis revealed that a low cognitive baseline level predicted cognitive improvements. Furthermore, a low baseline level of QoL predicted a QoL benefit. For both findings, depression was a significant moderator, meaning that persons with fewer depressive symptoms had a higher probability of showing improvements.

Conclusion: This study provides data on profiles of patients who are most likely to profit from CS intervention in nursing-home settings and demonstrates that treatment of depression is of the utmost relevance for a positive outcome of CS. Living conditions will have to be considered more thoroughly in future research.

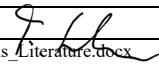
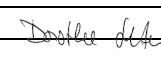
NEUROvitalis-9. *European Journal of Neurology*, 22, 640-647.

**One-year follow-up of cognitive training in Parkinson’s disease.** Petrelli A, Kaesberg S, Barbe MT, Timmermann L, Rosen J, Fink GR, Kessler J, Kalbe E (2015).

The abstract is available at the University of Cologne.

NEUROvitalis-10. *Frontiers in Aging Neuroscience*, 7, 187.

**Cognitive training with and without additional physical activity in healthy older adults: cognitive effects, neurobiological mechanisms, and prediction of training success.** Rahe J, Becker J, Fink GR, Kessler J, Kukulja J, Rahn A, Rosen JB, Szabados F, Wirth B, Kalbe E (2015).

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Data is inconsistent concerning the question whether cognitive-physical training (CPT) yields stronger cognitive gains than cognitive training (CT). Effects of additional counseling, neurobiological mechanisms, and predictors have scarcely been studied. Healthy older adults were trained with CT (n = 20), CPT (n = 25), or CPT with counseling (CPT+C; n = 23). Cognition, physical fitness, BDNF, IGF-1, and VEGF were assessed at pre- and post-test. No interaction effects were found except for one effect showing that CPT+C led to stronger gains in verbal fluency than CPT (p = 0.03). However, this superiority could not be assigned to additional physical training gains. Low baseline cognitive performance and BDNF, not carrying apoE4, gains in physical fitness and the moderation of gains in physical fitness × gains in BDNF predicted training success. Although all types of interventions seem successful to enhance cognition, our data do not support the hypotheses that CPT shows superior CT gains compared to CT or that CPT+C adds merit to CPT. However, as CPT leads to additional gains in physical fitness which in turn is known to have positive impact on cognition in the long-term, CPT seems more beneficial. Training success can partly be predicted by neuropsychological, neurobiological, and genetic parameters. Unique Identifier: WHO ICTRP (<http://www.who.int/ictrp>); ID: DRKS00005194.

NEUROvitalis-11. Aging, Neuropsychology, and Cognition, 22, 620-638.

**Sex differences in cognitive training effects of patients with amnesic mild cognitive impairment.** Rahe J, Liesk J, Rosen JB, Petrelli A, Kaesberg S, Onur OA, Kessler J, Fink GR, Kalbe E (2015).

Cognitive training has been shown to be effective in improving cognitive functions in patients with Mild Cognitive Impairment (MCI). However, data on factors that may influence training gains including sociodemographic variables such as sex or age is rare. In this study, the impact of sex on cognitive training effects was examined in N = 32 age- and education-matched female (n = 16) and male (n = 16) amnesic MCI patients (total sample: age M = 74.97, SD = 5.21; education M = 13.50, SD = 3.11). Patients participated in a six-week multidomain cognitive training program including 12 sessions each 90 min twice weekly in mixed groups with both women and men. Various cognitive domains were assessed before and after the intervention. Despite comparable baseline performance in women and men, we found significant interaction effects Time × Sex in immediate (p = .04) and delayed verbal episodic memory (p = .045) as well as in working memory (p = .042) favoring the female MCI patients. In contrast, the overall analyses with the total sample did not reveal any significant within-subject effects Time. In conclusion, our results give preliminary evidence for stronger cognitive training improvements of female compared to male MCI patients. More generally, they emphasize the importance of sex-sensitive evaluations of cognitive training effects. Possible underlying mechanisms of the found sex differences are discussed and directions for future research are given.

NEUROvitalis-12. Clinical Interventions in Aging, 19, 297-310.

**Effects of cognitive training with additional physical activity compared to pure cognitive training in healthy older adults.** Rahe J, Petrelli A, Kaesberg S, Fink GR, Kessler J, Kalbe E (2015).

Introduction: Cognitive training (CT) has been reported to improve cognition in older adults. Its combination with protective factors such as physical activity (CPT) has rarely been studied, but it has been suggested that CPT might show stronger effects than pure CT.

Materials and methods: Healthy older adults (aged 50–85 years) were trained with CPT (n=15) or CT (n=15). Interventions were conducted in 90-minute sessions twice weekly for 6.5 weeks. Cognitive functions were assessed before and immediately after the interventions, and at 1-year follow-up.

Results: The main finding was an interaction effect on attention, with comparable gains from CPT and CT from pre- to post-test, but stronger effects of CPT to follow-up (P=0.02). Significant effects were found in subjects in terms of cognitive state (P=0.02), letter verbal fluency (P=0.00), and immediate (P=0.00) and delayed (P=0.01) verbal memory. Post hoc analyses indicated that these latter domains were affected differentially by CPT and CT. No significant between-subject effects were found.

Conclusion: Our results suggest that CPT might lead to stronger long-term effects on attention. However, as the difference between CT and CPT was only evident at follow-up, these effects cannot be interpreted as a direct consequence of CPT; they may have been related to sustained physical activity after the training. Other domains were improved by both interventions, but no typical pattern could be identified. Possible underlying mechanisms are discussed, and directions for future research are suggested.


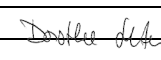
NEUROvitalis-13. Zeitschrift für Gerontologie und Geriatrie, 48, 275-281.

**Kognitive Stimulation und Musikintervention bei stationär versorgten Menschen mit Demenz. Eine Pilotstudie, Probleme & Perspektiven.** Liesk J, Hartogh T, Kalbe E (2014).

Methode: Über einen Zeitraum von 6 Wochen besuchten randomisiert 24 Personen mit einer leichten bis mittelschweren Demenz 2-Mal wöchentlich für je 90 Minuten ein kognitives Stimulationsprogramm (NEUROvitalis) oder ein Musikprogramm. Vor und nach der Intervention wurden die Teilnehmer Neuropsychologisch getestet.

Ergebnisse: Auf Gruppenebene zeigten sich keine signifikanten Verbesserungen in den untersuchten Funktionsbereichen, sondern sogar Verschlechterungen. Auf der Einzelfallebene wurden in beiden Gruppen sehr heterogene Ergebnisse beobachtet. Einzelnen Teilnehmer verbesserten sich deutlich.

Diskussion: Die Ergebnisse deuten zumindest in der Einzelfallebene auf das Potential der verwendeten Intervention hin. Künftige randomisierte, kontrollierte Studien in Pflegeeinrichtungen sollten die logistische Besonderheit bedenken, hohe Drop-out-Raten bei der Stickprobenplanung einbeziehen, Ein- und Ausschlusskriterien adäquat formulieren sowie passende Testinstrumente auswählen.

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NEUROvitalis-14. Parkinsonism & Related Disorders, 20, 1196-1202.

**Effects of cognitive training in patients with Parkinson´s disease: a randomized controlled trial.** Petrelli A, Kaesberg S, Kessler J, Barbe MT, Fink GR, Timmermann L, Kalbe E (2014).

Background: In Parkinson's Disease (PD), cognitive dysfunctions which can reduce patients' quality of life occur frequently. Data on non-pharmacological intervention effects on cognitive functions in patients with PD are rare. The aim of this study was to examine the effects of different cognitive group trainings (structured vs. unstructured) on cognition, depression, and quality of life in non-demented PD patients.

Methods: In this randomized controlled trial, 65 non-demented patients with PD according to UK Brain Bank criteria (Hoehn & Yahr I-III) were allocated to one of two cognitive multi-component treatments ("NEUROvitalis", a structured training, or the unstructured training "Mentally fit" with randomly assembled cognitive tasks, each including 12 group-sessions à 90 min over 6 weeks) or a waiting list control group (CG). A neuropsychological test battery was performed before and after the training.

Results: Compared to the CG, patients from the "NEUROvitalis" group improved in short-term memory (word list learning "Memo":  $p < .01$ ) and working memory (digit span reverse from "DemTect":  $p < .05$ ), whereas depression scores were reduced in the "Mentally fit" group (Beck Depression Inventory-II:  $p < .05$ ). The "NEUROvitalis" group improved significantly more in working memory than the "Mentally fit" group (DemTect:  $p < .05$ ).

Discussion: Cognitive and affective functions can be improved by cognitive trainings in PD patients. Specific effects (e.g. on memory and working memory versus depression) seem to be dependent on the type of training. Further research is needed to define long-term effects and the efficacy in PD patients with different extent of cognitive and neuropsychiatric symptoms.

NEUROvitalis-15. Neurologie & Rehabilitation, 18, 187.

**Kognitive Trainingseffekte des neuropsychologischen Programms NEUROvitalis in Kombination mit physischer Aktivität.** Rahe J, Petrelli A, Kaesberg S, Baller G, Kessler J, Kalbe E (2012).

The abstract is available at the University of Cologne.

NEUROvitalis-16. Zeitschrift für Neuropsychologie, 22, 194.

**Strukturiertes Training NEUROvitalis versus Hirnjogging bei Patienten mit leichten kognitiven Störungen und gesunden Älteren: eine randomisierte, kontrollierte Studie.** Kalbe E, Kaesberg S, Petrelli A, Baller G, Fink GR & Kessler J (2011).

The abstract is available at the University of Cologne.

NEUROvitalis-17. Zeitschrift für Neuropsychologie, 22, 228.

**Non-pharmakologische Intervention bei Patienten mit Multipler Sklerose – Effekte des neuropsychologischen Trainings NEUROvitalis.** Müller K, Kaesberg S, Petrelli A, Kalbe E, Baller G, Sack AT, Kessler J (2011).

The abstract is available at the University of Cologne.

NEUROvitalis-18. Zeitschrift für Neuropsychologie, 22, 230.

**Kognitives Basisniveau und Antrieb als Prädiktoren für den Trainingserfolg von Patienten mit idiopathischem Parkinson-Syndrom im neuropsychologischen Gruppentraining NEUROvitalis.** Petrelli A, Kaesberg S, Barbe MT, Timmermann L, Kessler J, Baller G, Fink GR, Kalbe E (2011).

The abstract is available at the University of Cologne.

NEUROvitalis-19. Zeitschrift für Neuropsychologie, 21, 221.

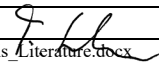
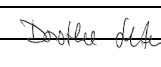
**NEUROvitalis®: Effekte eines neuen neuropsychologischen Trainings bei gesunden Älteren sowie bei Patienten mit Mild Cognitive Impairment und beginnender Alzheimer Demenz.** Kaesberg S, Mayer A, Schlegel M, Baller G, Fink G, Kessler J, Kalbe E (2010).

The abstract is available at the University of Cologne.

NEUROvitalis-20. Alzheimer's and Dementia, 5, 332.

**NEUROvitalis®: effects of a new neuropsychological training in healthy elderly individuals as well as patients suffering from Mild Cognitive Impairment and early-stage Alzheimer's Disease.** Kaesberg S, Kalbe E, Mayer A, Baller G, Sack A, Kessler J (2009).

The abstract is available at the University of Cologne.

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NEUROvitalis-21. Aktuelle Neurologie, 36, 149.

**NeuroVitalis®: Effekte eines neuen neuropsychologischen Trainings bei Patienten mit leichten kognitiven Störungen und Patienten mit Alzheimer Demenz.** Kalbe E, Kaesberg S, Mayer A, Schlegel M, Baller G, Fink GR, Kessler J (2009).

Fragestellung: Bislang wird bei Patienten mit leichten kognitiven Störungen (Mild Cognitive Impairment, MCI) und Alzheimer Demenz (AD) selten neuropsychologisches Training eingesetzt. In dieser Studie wurden MCI- und AD-Patienten und gesunde ältere Menschen mit dem kognitiven Gruppentraining NeuroVitalis® trainiert und Leistungsänderungen überprüft.


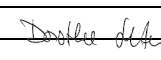
Methoden: NeuroVitalis® ist ein 6-wöchiges Trainingsprogramm mit zwölf 90-minütigen Einheiten plus Hausaufgaben. Es fokussiert Gedächtnis- und Aufmerksamkeitsleistungen und exekutive Funktionen. Es wurde bei 18 MCI-Patienten (12Männer, Alter=71,8J., SD=5,6, Bildung=14,6J., SD=2,9, DemTect=11,8, SD:1,6), 12 AD-Patienten (6Männer, Alter=72,0J., SD=8,9, Bildung=12,4J., SD=4,8, DemTect=7,8, SD=2,0) und einer Kontrollgruppe 17 gesunder Personen (3Männer, Alter=70,4, SD=6,7; Bildung=12,2J., SD=2,9J., DemTect=17,2, SD=0,8) durchgeführt. Vor und nach dem Training wurde eine ausführliche neuropsychologische Testbatterie durchgeführt. Prä- Posttestvergleiche wurden mit t-Tests für abhängige Stichproben ( $\alpha$ -Niveau: 0,01) berechnet und mit den Daten von 8 nicht trainierten Gesunden (2Männer, Alter=70,0, SD=7,0; Bildung=12,9J., SD=3,6J., DemTect=16,0, SD=1,9) verglichen.

Ergebnisse: NeuroVitalis® wurde von allen Teilnehmern sehr gut akzeptiert. Während sich bei der nicht trainierten Kontrollgruppe keine signifikanten Leistungsänderungen zeigten, ergaben sich bei allen trainierten Gruppen Leistungsverbesserungen: bei der MCI-Gruppe beim verbalen und nonverbalen Gedächtnis (unmittelbare [ $p=0,007$ ] und verzögerte Abfrage [ $p=0,001$ ] des Memo-Tests, verzögerte Abfrage des DemTects [ $p=0,008$ ], verzögerte Abfrage der Rey-Osterrieth-Figur [ $p<0,001$ ]) und im kognitiven Gesamtniveau (MMST:  $p=0,008$ , DemTect:  $p=0,005$ ), bei der AD-Gruppe im kognitiven Gesamtniveau (DemTect:  $p=0,009$ ) und bei den Gesunden beim verbalen Gedächtnis (verzögerte Abfrage des Memo-Tests [ $p=0,008$ ] und des DemTects [ $p=0,001$ ]) sowie beim Wortgenerieren (FAS-Test:  $p=0,001$ ). Schlussfolgerung: Mit NeuroVitalis® ist bei MCI- und auch leichten AD-Patienten eine Verbesserung des kognitiven Gesamtniveaus zu erreichen. Bei MCI-Patienten und gesunden älteren Menschen verbessern sich die Gedächtnisleistungen deutlich, bei gesunden Älteren zusätzlich exekutive Leistungen. Das Programm eignet sich daher als therapeutische Intervention zur kognitiven Leistungssteigerung bei den genannten Patientengruppen und ist auch bei älteren Menschen ohne kognitive Beeinträchtigungen effektiv.

NEUROvitalis-22. Health. 2018, 10, 20 - 55

**Computerized Cognitive Training in Healthy Older Adults: Baseline Cognitive Level and Subjective Cognitive Concerns Predict Training Outcome.** Elke Kalbe, Christophe Bintener, Anja Ophey, Christian Reuter, Stefan Göbel, Silvie Klöters, Gisela Baller, Josef Kessler

Abstract: Computerized cognitive training (CCT) can improve cognition in older adults. However, specific programs for this target group have rarely been developed, and predictors of training success are largely unclear. In a randomized controlled pilot trial, we examined effects of a six-week CCT, tailored to the cognitive profile of healthy older adults (EG,  $n = 21$ ) as compared to a nonspecific CCT (CG,  $n = 18$ ) matched in frequency and intensity. No interaction effects Group \* Time were found. However, within-group analysis showed significant gains in verbal and non-verbal memory, executive and visuospatial functions and subjective cognitive concerns (SCC) in the EG, while the CG only benefitted in non-verbal memory and set-shifting. Low cognitive performance and lower SCC at baseline were the most consistent predictors of cognitive gains in the EG. Thus, CCTs specifically tailored to older adults seem advantageous compared to non-specific CCT. Further, we conclude that SCC may be related to reduced cognitive plasticity.

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