Slowing Cognitive Decline and Supporting Resilience in Patients with Dementia

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RESEARCH SUMMIT ON DEMENTIA CARE
Building Evidence for Services and Supports

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Cognitive Training in Dementia

- Neuronal plasticity: adaptation in CNS
- Regular activation of brain networks by cognitive and physical stimulation can improve cognition
- ? Increase in cognitive reserve
- Cognitive stimulation, training, rehabilitation
- Compensatory and restorative (global, specific) strategies
- Type of intervention is variable across studies
- Strategy training may be effective
- Post-training: process switching in neural networks

- Buschert et al, Nat Rev Neurol 6:508-517, 2010

Cognitive Stimulation	Cognitive Training	Cognitive Rehab
Range of activities mostly administered in groups; the goal of stimulation is to enhance cognitive and social functioning in a general, nonspecific manner	Sets of artificial, guided tasks which aim to improve cognition function in areas like attention, memory, and problem solving. Skills learned in these tasks are meant to transfer to everyday life and accomplish independent living amongst patients.	Emphasis on treatment is placed on improving everyday life and preventing further deterioration. This approach is more individualized for each patient and family's strengths, weaknesses, and goals.
Troyer et al. (2007): Improved memory-strategy knowledge and use; no improvement in memory beliefs or objective memory performance	**Cipriani et al. (2006):** improvement in tasks concerning working memory and psychomotor function; improvement in behavioral memory.	**Kinsella et al. (2009):** Improvements in performance on prospective memory tasks and knowledge and use of memory strategies

Cognitive Training in Patients with Dementia

- **Huntley et al 2015**
  - 33 studies reviewed
  - Cognitive training not effective. Cognitive stimulation may be more effective, improving ADAS-Cog and MMSE (g= .26 and .35 respectively)
  - Cognitive Stimulation
    - Reality orientation, social activities, sensorimotor, often in groups; general non-specific approach for engagement

- **Bahar-Fuchs et al 2013**
- Similar conclusions to Huntley
  - Cognitive training: 11 RCTs
  - Cognitive rehabilitation: 1 RCT, n=69, single-blind, 3 groups: CR, relaxation, no treatment. Multiple outcomes, several goals met

Huntley et al BMJ Open; 2015; 5, e5247

Bahar-Fuchs et al Cochrane Database Syst Rev; 2013;6;C3260

Clare L et al. Am J Geriatric Psychiatry 18:928-939, 2010

Cognitive Training in MCI and Dementia

Gates NJ et al, BMC Geriatrics 11:55, 2011

- Only 3 RCT at the time of review
- Inconsistent outcome measures across studies
- Cognitive training and memory exercises often confounded by addition of occupational therapy, behavioral training, life-style education, computer-assisted attention training, executive exercises
- Regimens involving repetitive exercises did well, learning strategies less so

Hill NT et al, Am J Psychiatry 174:329-340, 2017

- Meta-analysis of computerized cognitive training (CCT) in MCI (Hedges g=.35 for global cog; g=.42 for memory; significant also for attention and working memory with g>.50). RCTs=17
- Small, non significant effect on IADLs
- CCT is unlikely to be effective in dementia, but three Nintendo Wii studies showed improved overall cognition and visuospatial skills in dementia
- Immersive, engaging stimulation might be more appropriate than CCT in dementia

Conclusions from the Literature

- Cognitive training has limited efficacy in dementia
- Cognitive stimulation and cognitive rehabilitation have small effect sizes but may be more effective in dementia
- Cognitive training is efficacious in MCI in impacting a variety of cognitive constructs, including memory and attention, as well as global measures of cognition
- Impact on IADLs is small in MCI
- Other approaches, including combination treatments, have not been studied systematically
- Mavros et al, JAGS 65:550-559, 2017. Progressive physical resistance training in patients with MCI improved ADAS-Cog

Gaps in the Field

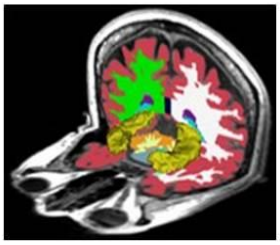
- No discussion of instrument development for outcome measures
- Training in which domains (memory, executive, divided attention, speed) leads to the largest near and far transfer improvements
- Comparative efficacy of CCT, cognitive stimulation and rehabilitation is unclear
- Subjects cannot be blinded; how large are expectancy effects?
- Impact of diet, exercise, education, and other factors on cognitive training or stimulation or rehabilitation needs further research
- Little work on the impact of cognitive training or stimulation or rehabilitation on neuropsychiatric symptoms (apathy, agitation, depression, anxiety)
- What is the best time to intervene (preclinical, prodromal, genetic high risk) and with what degree of intensity remains unclear
- How large and enduring are improvements and at what stage of disease progression are they attenuated requires further work

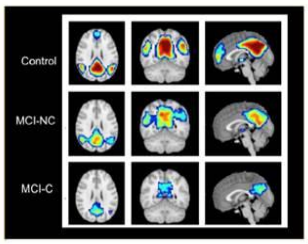
Outstanding Research Questions

- What is the active therapeutic ingredient in cognitive training?
- When is the best time to intervene and with what frequency and intensity?
- Given the lack of blindness, how best to manage expectancy effects?
- How large and enduring are cognitive improvements and at what stage of disease progression are they attenuated? Is there a dose-response curve?
- Which is more effective: cognitive training, stimulation, rehabilitation, and in which populations?
- What are the mechanisms, e.g., cognitive reserve, neuroplasticity, that underlie improvement?
- What has prevented demonstrations of far transfer? Does training in specific cognitive domains, e.g., executive function, lead to functional improvement? Are direct interventions to improve function necessary?

Computerized Cognitive Training and Neuroplasticity in MCI

- Randomized trial with an active group (Lumosity computerized exercises/games) and a control group (crossword puzzles):
- 4-30 minute sessions of computerized training each week for 12 weeks
- 4 in-clinic booster sessions to 78 weeks (endpoint of study)
- ADAS-Cog11 and UPSA Performance-based functional competency (primary)
- Neuropsychological Composite Score (secondary)
- Functional Activity Questionnaire (exploratory)
- Progression from MCI to AD after 18 months
- Hippocampal volume
- Default Mode network in rsBOLD





Recommendations

- Instrument development to better capture changes in cognitive function
- Use of big data from commercial brain training companies
- Identify the mechanisms by which cognitive training "works"
  - Cognitive reserve? Residual plasticity in affected circuitry? Plasticity in preserved circuitry?
- Distinguish between cognitive exercises and memory strategy training; consistent operational definitions are needed
- RCTs with better active control conditions (sham training) are needed
- Assess generalization by testing cognitive, behavioral, quality of life, functional, mood, and psychological well-being outcomes
- Study training frequency and duration; dose-response relationships
- Combination studies with diet, physical exercise, other measures