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Strategic Memory Alzheimer's Rehabilitation Training (SMART): Cognitive Intervention for Amnesic-type Mild Cognitive Impairment (MCI)

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ABSTRACT

Dementia is a growing world-wide phenomenon, impacting more than six million people in the United States. Despite its high projected prevalence, it is a significantly under-represented phenomena, with estimates ranging from 15-25% of the general population. The effect of the aging of the population and significant increase in life expectancy has combined to catapult dementia into the range of one of most alarming healthcare problems. The SMART Memory Program is a cognitive intervention designed to help promote the reduction of mild cognitive impairment (MCI) and early-stage dementia. Although it has been found useful in all forms of dementia, it is particularly useful in amnesic-type MCI. A longitudinal study examined 356 clients (220 females, all amnesic-type MCI) across an approximate two-year span. Results revealed an improvement of approximately 3 MoCA points at the conclusion of a program session. Particular improvements were noted in delayed recall. These results were found to be particularly beneficial secondary to the advent of the Kirtan Kriya methodology.

Keywords: SMART, mild cognitive impairment, dementia, Alzheimer's disease, cognitive prevention, cognitive intervention.

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INTRODUCTION

The increasing prevalence of dementia has become a major topic in both neuropsychology and society alike. With an elderly person diagnosed with dementia every minute, there is an increasing personal and economic (in addition to professional) interest in this disease. Despite its increased prevalence and a dawning increase in awareness and education, dementia is still a significantly under-represented phenomena, with underestimate ranges from 15-25% of the general population (National Institute of Health, 2016). The combined effect of the aging population (caused primarily by baby boomers aging into the range of dementia) and significant increase in life expectancy has combined to project dementia into the playing field of one of our world's largest healthcare problems (National Geographic, 2013). Despite this fact, patients and practitioners alike are relatively ignorant of the subversive and deleterious impact of this disease.

Worldwide, there is an estimated 47.5 million people with confirmed dementia diagnoses (World Health Organization, 2015). By the year 2030, the number of adults over the over the age of 65 is expected to increase to approximately 86 million, with this generation representing 20-25% of the US population (Alzheimer's Association, 2016). Currently, there are about 87.7 million people that have received recent dementia diagnoses (National Institute of Health, 2016). In the State of Arizona, there is a projected 44-72% increase in dementia. (State of Arizona Department of Health, 2015).

Although researchers have begun to identify the significant and increasing prevalence of dementia in the general population, researchers have begun the early prevention and intervention of this disease. This is highlighted by statements that "interventions that can prevent, slow, or even reverse the underlying pathology of these progressive neurodegenerative illnesses are desperately needed" (Ringman & Cummings, p. 334, 2006). The current failure of science to adequately address this issue is significantly juxtaposed by this dramatic (sub)population increase of this disease.

The SMART program is a cognitive prevention and intervention program designed to assist in the reduction of MCI and early-stage dementia. Although the program has been found to be useful in mitigating cognitive and functional decline in all forms of dementia, it is particularly targeted to individuals with MCI. There are two forms of this program which correspond to the clinical continuum of dementia: a computerized program which incorporates digital exercises specifically designed for older adults (ages 55-75) primarily interested in dementia prevention (SMART Brain University®), while a paper-and-pencil version of this program was designed for geriatric adults interested in dementia intervention

(SMART Memory Program®). The Memory Program employs a caregiver/coach, who helps the participant by motivating them and structuring the exercises appropriately.

This paper will focus almost exclusively on research concerning the SMART Memory Program, highlighting the current research study examining it's efficacy.

Brief Literature Review

For purposes of parsimony, this paper will not provide a comprehensive review of past and present literature. Rather, only select major research studies will be reviewed.

Although research in the area of cognitive prevention/intervention has certainly been lacking, there has been a burgeoning and significant literature base. The most prominent studies will be reviewed here.

Valenzuela and Sachdev (2009), in a literature review of 22 studies involving approximately almost 30,000 individuals, found an overall risk reduction of 46% in individuals that were found to engage in a high level of regular cognitive activity. Perhaps more importantly, they found a dose-dependent relationship between cognitive exercise and reduction of dementia, which had not been found prior to publication of the study. Secondary to concerns about lack of established causality, the researchers performed a meta-analysis of cognitive intervention models (7 studies, about 3200 healthy participants). The main findings, published in the *American Review of Geriatric Psychiatry*, found that a dose of 2-3 months of cognitive intervention (in the form of new and novel learning) may have long-lasting and persistent protective effects on cognitive aptitude over a number of years. The researchers found that combining cognitive intervention with physical exercise was of maximal benefit. Interestingly and importantly, they found that the cognitive intervention protocols used in the study appeared to generalize to cognitive and functional domains beyond those specifically designed for the intervention.

A large meta-analysis was conducted by Olazaran et al. (2010). In this study, 13 studies that were considered high quality were examined. Of these studies, seven demonstrated positive results in favor of cognitive intervention for MCI intervention. The combined effects of cognitive intervention and family support were found to result in delaying cognitive decline and reducing the possibility of institutionalization and death of persons receiving care. Interestingly, the use of cognitive intervention was significantly improved when compared to psychopharmacological agents. There was no significant difference for other outcomes measures (including activities of daily living (ADL's), performance, and mood) when cognitive intervention was compared to pharmacological treatment.

Additional research has found that cognitive stimulation has had increased beneficial effects on early-stage dementia when compared to medication. Specifically, Aguirre, Woods,

Spector, and Orrell (2013) found that, in a review of 15 studies, participants who were grouped in cognitive intervention groups demonstrated significant improvement when compared to control groups across cognitive and quality of life measures. This was shown as significantly beneficial when compared to anti-cholinergic medication (e.g., Aricept). The results have translated to improved neurocognitive performance.

Literature has also focused on participants without confirmed diagnoses of dementia. Wilson et al. (2002), in a prospective study involving more than 700 non-demented participants, found that a person at the 90th percentile in cognitive activity, when compared to those at the 10th percentile, were 47 percent less likely to develop Alzheimer's-related dementia. Importantly, this effect was found independent of education or age.

In addition to the literature reviewed above, research has also focused on the benefits of cognitive strategies on psychosocial outcomes. Specifically, Sitzler, Twamley, and Jeste (2006) examined the effects of two categories of cognition: compensatory and restorative strategies. Compensatory strategies were defined as developing new ways of performing cognitive tasks by working around their existing deficits, while restorative strategies involve more direct intervention in areas of impairment (e.g., memory, speed of processing). The researchers found that, overall, there were not significant differences between restorative and compensatory strategies; they concluded that although effect sizes were small, cognitive interventions can improve cognitive and functional outcomes with individuals with dementia of the Alzheimer's type. Interestingly, the researchers emphasized the importance of family members in providing assistance with cognitive stimulation activities.

An additional study was conducted by Werd, Bolen, Rikkert, and Kessels (2013). In this particular study, researchers utilized an errorless learning protocol among individuals with dementia. Also utilizing functional tasks (e.g., teaching participants to use common devices), the researchers found that of 25 studies reviewed, 17 demonstrated significant improvement of participant performance when compared to control groups; these results were observed over time.

Improvement on Standardized Tests

Additional research has demonstrated significant efficacy in improving standardized score performance. Yu et al (2009) found an average improvement of 1.5 points on the Mini Mental Status Examination (MMSE). This is in comparison to an average decline across 3 points. Ultimately, this resulted in a 4.5 point difference in participants, which was both clinically and statistically significant. Similar methodology was utilized in the present study. Jean, Bergerson, Thivierge, and Simarad (2010) conducted a meta-analysis of 15 cognitive rehabilitation studies with MCI of the amnesic type, finding gains on 44% of standard

neuropsychological assessment measures. Although many other studies (e.g., Gates, Sachdev, Fiatarone Singh, & Valenzuela, 2011) have noted challenges in preventing memory reduction associated with dementia, the researchers found significant memory findings by utilizing techniques like mind mapping, visual imagery, face-name association, and other heuristics.

In an excellent meta-analysis, Willis et al. (2006) examined over 3000 individuals. Participants were randomly assigned to one of three cognitive training intervention groups: memory, reasoning, and speed of processing. Main findings revealed significant and pervasive improvements, with cognitive and functional gains observed over a period of 5 years.

Martin et al. (2011) conducted another study examining cognitive interventions with MCI. In looking at a cognitive intervention methodology across 24 studies, significant improvements were noted for 2,299 participants. For both the healthy and MCI groups, the study showed significant effects for both the healthy and MCI groups. It should be noted that significant effects were only found for both immediate and delayed recall (amnestic MCI).

When examining cognitive change over time, researchers often employ reliable change index (RCI). These scores are often utilized to assess whether an individual's change over time (often after an intervention) is significant (Heaton et al., 2001). This is calculated for each test and, if applicable, should take into account the practice effects of the measure in question (Parsons, 2009). This is often partnered with change scores, which are designed to measure the specific effect of this change over time. Whereas alpha levels are often designed to assess statistical significance, kappa coefficients are often utilized to further define clinical significance (Lakens, 2013). The above methodological and statistical structure is, fortunately, recognized by major and diverse bodies, including the Federal Trade Commission (most notably portrayed in their most recent Lumosity ruling – Federal Trade Commission, 1/5/16). As such, this type of statistical analysis is highly applicable for the current study.

Neuroplasticity and Aging

Pharmaceutical Interventions for Aging and Dementia (AD)

Despite recent progressions in the science, and significant personal and business amounts of money spent, there is reported “scant evidence” for the Food and Drug Administration (FDA)-approved treatments for Alzheimer's disease significantly prevent and/or reduce the cognitive and/or psychological effects of dementia. This is hardly a knock on the researchers at work on this endeavor, as the neuropathological complexity of this disease state has only recently begun to be unraveled.

The majority, if not all, drugs for dementia target enhancement of cholinergic activity by attempting to enhance the activity of this agent by providing precursors for acetylcholine, reducing the breakdown of this chemical via AchE inhibition. At present, there are 5 FDA-approved medications for the treatment of this treatment: donepezil (Aricept), Namenda, and Exelon (among others).

Glutamate. According to Ringman and Cummings (2006), the neurotransmitter glutamate has been found to play a potentially important role. As the major excitatory neurotransmitter in input pathways to the hippocampus (via the entorhinal cortex) and in cortico-cortical pathways, this neurotransmitter was found to be a major role in memory and dementia (particularly Alzheimer's type) since the beginning of research. As stated by a variety of researchers (e.g., Hyman et al., 1996), the pathways noted above have been demonstrated to be dramatically affected in AD. Research in the area of neurotransmitter systems and dementia has been less consistent, with most pathways ultimately affected later in the disease (Ringman & Cummings, 2006).

Although the use of cognitive intervention techniques for MCI and/or early stage dementia has not been a topic that has been addressed in a comprehensive manner, there has been select notable research on this topic at present. This includes foundational work by Wilson and Kapur (2008). In their chapter, the authors note a few key points (selected from a list taken on page 522 of their text): structured teaching is often required to help memory-impaired individuals utilize memory aids, in addition to memory problems, many individuals will have other cognitive and emotional problems that need to be addressed and that these issues should be treated together, internal strategies (e.g., mnemonics and rehearsal techniques) can be effective and aging adults with dementia can/will use these with appropriate coaching. Additionally, the authors point out that new technology may be of significant assistance, including the use of the Internet (see below). The technique of errorless learning, adapted from work with individuals with learning disorders, has also been found to be effective in helping older adults with memory problems. Beginning with the work of Baddeley and Wilson (1994), a strong line of research has shown that amnesic patients with MCI have been shown to receive significant benefits in terms of memory. Findings have revealed that this type of learning is far superior to trial-and-error type learning (Squires et al., 1996; Wilson & Evans, 1996). The above research, as well as others, form the basis on which the SMART Memory Program was created.

Lowenstein and Acevedo (2008) also provide a fairly comprehensive list detailing a multitude of interventions in the area of mild cognitive impairment (MCI). In cognitively normal adults, training often results in significant improvement (e.g., Backman, 1996).

Although select research has found a lack of research efficacy in individuals with Alzheimer's Disease, the lack of research efficacy may be due in part to the reliance of episodic memory (Loewenstein & Acedvedo, 2008), as episodic memory (secondary to hippocampal degeneration), is compromised early in the AD stage process.

Method

Participants and Measures

This study was approved by an Institutional Review Board and in conductance with all policies for Human Research.

Participants were 356 clients (203 females, mean age 85). Patients displayed an average MoCA baseline score of approximately 20. Importantly, these patients were determined to have amnesic type MCI, as displayed by an average MoCA Delayed Memory score of approximately 2/5.

The Mayo Norms were utilized as a control group. This age and education-matched group was also matched on MoCA scores, when appropriate data was present.

Participants were included in the study that achieved MoCA baseline scores of 19-24; no scores under 18 or over 24 were included. Additionally, MoCA Delayed Recall inclusion score range was 0-3. Scores from participants over 3 on Delayed Recall were not included.

Participants with the following medical conditions were excluded from participation: history of traumatic brain injury with loss of consciousness (15), cerebrovascular accident (CVA) (14), seizure (2), and/other neurological disorders (e.g., multiple sclerosis; 2).

Participants were defined as amnesic secondary to recall scores on the MoCA – Delayed Recall portion, as defined above.

The study also employed a quality of life measure (the WHO-QOL) and a measure of depression, the Geriatric Depression Scale (Brief Form). The results of these measures were positive; they will not be reviewed here.

In addition the above, the SMART program also employed the Kirtan Kriya (KK) methodology. The KK methodology is a meditation program developed by the second author and offered by the Alzheimer's Research Prevention Foundation. More information can be found on the <http://www.alzheimersprevention.org/>.

As previously mentioned, a longitudinal study with Reliable Change Indices (RCI) was employed. Results are presented below. It was hypothesized that participants with amnesic MCI would demonstrated standardized score curves that more closely resembled dementia as opposed to normal aging.

RESULTS AND DISCUSSION

Clinical significance was conducted utilizing the Jacobson-Truax method ($RCI = (\text{posttest} - \text{pretest}) / SE_{\text{meas}}$) (Jacobsen & Traux, 1991). The overwhelming majority of the participants (92%) were classified as “improved” following the conclusion of the intervention, and approximately the same percentage were noted as “deteriorated” during the approximate 4-week break following the post test.

The main hypothesis was confirmed, in that the majority of participants were deemed “unchanged” at the conclusion of the research study.

The RCI Index set was .87 around the standard error of measurement.

Minimally clinically significant important difference (MID) analysis was also conducted. This revealed that the study met criteria for MID when pre and post-test scores were compared.

Kappa analysis was also conducted. Cohen’s *d* was utilized. Large effect sizes were obtained, with effect size estimates ranging from .3 to almost .6.

DISCUSSION

As hypothesized, the SMART Memory program produced positive cognitive changes at the conclusion of each training session. Unfortunately, at the conclusion of each training session the patient’s standardized scores reverted to near-baseline levels. This is similar to other research in this area, which displayed notable yet temporary improvement post cognitive intervention.

One of the most notable results from the current study is that this SMART Program was found to significantly mitigate expected declines in delayed memory. This is significant, in that Delayed memory has been shown to be the primary hallmark in dementia progression.

Based upon research that has found that neuropsychological tests have great utility in predicting performance (Farias et al., 2003, McCue et al., 1990), neuropsychologists are increasingly being called upon to offer intervention efforts based upon their initial assessment, similar to psychotherapy. Specifically, serial neuropsychological assessment has been emphasized to test treatment efficacy (Teri, Logsdon, Uomoto, & McCurry, 1997). The use of the SMART program may be reflective of neuropsychologists increasingly entering the arena of cognitive prevention and intervention for early stage dementia.

This effort of prevention and intervention of early stage dementia will ultimately require an interdisciplinary approach. This team includes (but is not limited to) general practitioners (who are on the forefront of dementia), geriatricians, and geriatric psychiatrists, as well as neuropsychologists, speech-language therapists, and occupational therapists.

Like any emerging subfield, there are several new areas of growth. This paper will highlight select possibilities. One such potential area is in the current trend towards “Memory Clinics s.” Unfortunately, these clinics are not so much based in dementia prevention and intervention, but are rather based solely in dementia assessment (usually after the dementia has progressed to mid-to-late stage), without any intervention efforts. With the help of a growing research trend, it is hoped that the growing need of dementia prevention/intervention. This may be particularly helpful and/or pertinent for patients at VA Healthcare Centers, where dementia (in particular, vascular dementia) is found in disproportionate numbers.

There are several drawbacks to the current study. These include, but are not limited to, modest sample size, lack of a diversity of standardized measures, and, perhaps most notably, lack of a proper control group. Although this study is certainly limited in the nature described above, it is perhaps important to note that no studies have, at present, incorporate a control group (see Lumosity ruling).

As noted in the above reviewed research, future research may bring an increased focus in the area of activities of daily living (ADL). This may also incorporate specific partner report. Additional measures, as well as subjective report, may be further utilized to address day-to-day improvement in functioning. Future research may also incorporate functional neuroimaging as well. Although this may include 3T (and perhaps eventually 5T-weighted images, they may also include fMRI and/or SPECT neuroimaging. Both of these areas may serve to offer concurrent validity to standard neuropsychological assessment measures.

Dementia prevention mechanisms may also incorporate valuable (and perhaps pertinent) on-line technology. The brain-game industry is certainly a large market, as delineated by the reported approximate 75 million users of Lumosity. Although this market has become increasingly competitive, at present there are no medically-driven, empirically-supported models. This market has tremendous potential for ethical and transparent research from legitimate academicians.

As delineated by Robertson and Fitzpatrick (2008), cognitive neuroscience may have an increasing role in the future of cognitive neurorehabilitation. The author’s main point here is that future cognitive neuro-intervention studies should be able to not only empirically (with a control group) but also to verify the effect of the program on the life of the individual, but to show these effects in the brain, potentially via neuroimaging.

As Medicare does successfully reimburse for cognitive intervention for speech and language services (under multiple CPT and diagnosis codes), the SMART program (or other programs like it) may be reimbursable under the Medicare system. At present, the SMART Memory

Program has approximately 10 clinics in the Phoenix Valley area, with the practitioners having reimbursed for multiple visits on the Memory Program under both primary Medicare, Medicare-advantage, as well as commercial plans. Future immediate plans are to enter into the Medicare insurance arena.

As previously mentioned, the results were found to be particularly beneficial secondary to the use of the Kirtan Kriya methodology. This innovative technique was found to be significantly beneficial when used in combination with the SMART methodology. This is not surprising, given the existing research support on the KK methodology. Although a modest (yet successful) start, the findings do have significant implications for driving the field and society forward. As the “silver tsunami” invades our world culture and effects practitioners at every level, we will continue to need multiple avenues of dementia prevention and intervention.

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