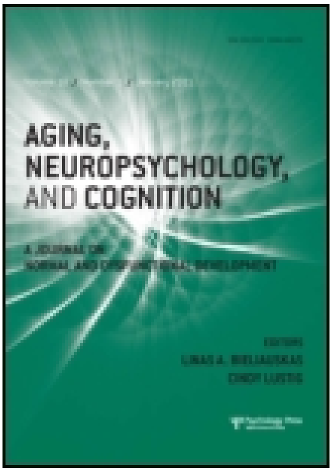

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Neuropsychological and neurophysiological effects of strengthening exercise for early dementia: A pilot study

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ABSTRACT

Research demonstrates a positive effect of aerobic exercise on cognitive functioning in older adults. Unfortunately, aerobic exercise is often contraindicated for older adults due to cardiovascular and functional limitations. Low-intensity strengthening exercise may offer a practical alternative, but the neuropsychological benefits and potential neurophysiological mechanisms are less well understood. The current study evaluated the effects of a 10-week strengthening exercise intervention on cognitive functioning and EEG in a sample of 13 older adults with early dementia, and 9 normative controls. Results revealed beneficial effects of strengthening exercise on verbal memory coupled with frontal beta and delta power asymmetries and N200 amplitude asymmetry. Results point to increased cognitive efficiency following 10 weeks of strengthening exercise. The findings suggest it is feasible to conduct a strengthening intervention with early dementia patients, and to gather neuropsychological and neurophysiological data to evaluate outcomes. Strengthening exercise may serve as a useful alternative to aerobic exercise.

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Alzheimer's disease is the sixth leading cause of death in older adults and it is estimated that by 2050 one in 85 persons will be affected by Alzheimer's disease, raising the number affected to 106 million (Colantuoni, Surplus, Hackman, Arrighi, & Brookmeyer, 2010). Although there is currently no cure for Alzheimer's disease or related dementias, research has shown that behavioral interventions such as exercise, while not a panacea (Mackinnon, Christensen, Hofer, Korten, & Jorm, 2003), do hold promise in the prevention of or delay in the progression of cognitive decline (Chang et al., 2010; Kramer & Erickson, 2007; Larson, 2008; Scarmeas et al., 2009). The literature on the cognitive benefits of exercise is now extensive (Flicker, Liu-Ambrose, & Kramer, 2011; Williamson & Pahor, 2010; Zoeller, 2010), including a number of high quality randomized controlled trials, leading to meta-analyses and a Cochrane review (Angevaren, Aufdemkampe, Verhaar, Aleman, & Vanhees, 2008), which conclude exercise can have a significant impact on cognitive function in normative older adults (Colcombe & Kramer, 2003) as well as those already experiencing cognitive decline as in mild cognitive impairment (MCI; Baker et al., 2010; Geda et al., 2010; Lautenschlager et al., 2008) or dementia (Heyn, Abreau, & Ottenbacker, 2004). Neuropsychological benefits appear primarily in the realm of executive function (Colcombe & Kramer, 2003; Hall, Smith, & Keele, 2001; Hillman, Belopolsky, Snook, Kramer, & McAuley, 2004) and memory (Erickson et al., 2011).

Researchers are now turning to more specific issues, such as clarifying the differential effects of various types of exercise, by contrasting aerobic, strengthening, and combined interventions (Hogan, 2005). Much of the research to date has concentrated on aerobic exercise (Colcombe & Kramer, 2003), but strengthening exercise may be particularly beneficial for many older adults with cardiovascular risk factors or functional limitations for whom aerobic exercise may be problematic. A small increase in physical activity via low-intensity strengthening exercise may be more appealing to older adults who have been sedentary, as they might perceive fewer barriers to starting such a program rather than concluding it is too difficult or too late for them to start exercise (Bunn, Dickinson, Barnett-Page, McInnes, & Horton, 2008). Research suggests that it may never be too late to start, with clear physiological benefits observed of low-intensity strengthening exercise for older adults who have been sedentary (Jette et al., 1999). Some research has found cognitive benefits from strengthening exercise with as little as once or twice a week for community-dwelling older adults (Anderson-Hanley, Nimon, & Westen, 2010; Brown, Liu-Ambrose, Tate, & Lord, 2009; Cassilhas et al., 2007; Liu-Ambrose et al., 2008, 2010), although other research has not found a significant effect (Dorner et al., 2007; Kimura et al., 2010; Miller et al., 2011). One study suggested the intensity of the strengthening exercise moderated outcomes (Lachman, Neupert, Bertrand, & Jette, 2006). A meta-analysis revealed a moderate effect of strengthening exercise on cognition for cognitively impaired older adults (effect size = .7; Heyn et al., 2004). New research also shows long-lasting cognitive and economic benefits of strengthening exercise (Davis et al., 2010).

In addition to clarifying benefits of different forms of exercise, recent research has also focused in on uncovering the mechanisms linking exercise to cognitive benefit, especially the impact on neuroplasticity. The benefits of aerobic exercise has been well documented and linked to increases in cerebral perfusion, whereby nutrient supply to capillaries is enhanced and neuronal death is decreased (Dierks et al., 2000). More recently, aerobic exercise has been linked to improvements in biomarkers such as brain-derived neurotrophic growth factor (BDNF; Erickson et al., 2011), and even neurogenesis of the hippocampus, which is thought to be critical in memory formation and implicated in cognitive aging (Colcombe et al., 2006; Erickson et al., 2009, 2011; Pereira et al., 2007). However, less is known about the mechanisms that link strengthening exercise to cognitive benefit. One study found an increase in insulin-related growth factor (IGF-1) accompanied cognitive improvement with strengthening exercise in older adults (Cassilhas et al., 2007), while another study found some effects on whole brain volume (Lui-Ambrose, Nagamatsu, Graf, Beattie, Ashe, & Handy, 2010).

An additional research strategy that may help to clarify mechanisms linking strengthening exercise to cognitive benefit is to measure neurophysiological outcomes associated with exercise interventions using resting electroencephalography (EEG) and event-related potentials (ERPs). In cognitive decline to dementia, the earliest spectral changes at rest are an increase in theta activity and a decrease in beta and alpha activity (Luckhaus et al., 2008), while reduced alpha coherence (Hogan, Swanwick, Kaiser, Rowan, & Lawlor, 2003) and increased variability in P300 amplitude were also linked to decline (Hogan et al., 2006). A single bout of aerobic exercise in older adults has been linked to increased frontal asymmetry (greater alpha on the right; Vogt, Schneider, Brümmer, & Strüder, 2010). Deslandes et al. (2010) reported that, after 1 year of aerobic exercise, older adults were less depressed and maintained an asymmetrical cortical activation (increased frontal and parietal alpha on the right), compared with depressed controls. A meta-analysis conducted by Crabbe and Dishman (2004) found that beta, theta, and delta increased post-exercise. However, we know of no prior prospective research investigating the neurophysiological effects (via spectral power measured with EEG) of strengthening exercise in older adults.

With regard to ERP outcomes, increased latency and decreased amplitude, and a decrease of the area under the curve of P300 (a characteristic wave elicited by task-specific stimuli) have also been associated with a decline in cognitive state (Lardon & Polich, 1996), and with lesser physical activity in older adults (McDowell, Kerick, Santa Maria, & Hatfield, 2003). This suggests that among physically non-active older adults there is a decline in neural resources that appears to mirror the brain state associated with cognitive decline. Similarly, greater physical activity or fitness appear related to increased amplitude or decreased latency of P300 in older adults (Hillman et al., 2004), although the complexity of the task may moderate this effect (Pontifex, Hillman, & Polich, 2009). Additionally, physical exercise interventions may reverse the pattern of physiological and cognitive decline seen in ERP measures. For example, one study found that the amplitude of P300 during an oddball task was significantly greater in active when compared with non-active older adults (Hatta et al., 2005); however, this was a cross-sectional, non-intervention study and EEG was only collected at the midline. Another study did not find any significant differences in P300 amplitude or latency between traditional rehabilitation and a Tai Chi intervention for 34 older adults with cerebral vascular disease, although the latter produced better behavioral outcomes (Wang et al., 2010). Kamijo (2009) notes the need for additional research on the neurophysiological effects of exercise in older adults and the relationship to cognition, especially using ERP to evaluate the latency and amplitude of peaks in wave forms in response to stimuli (P300 and N200).

In light of the gaps in the literature, this pilot study examines the feasibility and preliminary neuropsychological and neurophysiological effects of low-intensity strengthening exercise for older adults, with and without cognitive impairment. Given previous research on the cognitive benefits of exercise we focused on executive function and memory as the key neuropsychological outcomes measures. Consistent with recent reports on neurophysiological effects with aerobic exercise, we also explored potential shifts in frontal asymmetry resulting from strengthening exercise by examining resting EEG and activity-related ERP latency and amplitude.

METHODS

Participants

Early stage dementia participants were drawn from the Adult Day Care Program (ADCP) at a Veterans Affairs Medical Center (VAMC) in the northeast United States, and were selected by the head nurse and the geriatric physician based on the following criteria. Inclusion criteria were: (i) attending ADCP at least twice a week; (ii) able to complete cognitive tasks (no significant verbal, visual, or motor impairments); (iii) no significant psychiatric or substance abuse history; (iv) absence of Parkinson's or other motor-related dementia; and (v) interest in the study. Normative older adult participants were either employees or volunteers at the same facility recruited by fliers;

an exclusion criterion was a known history of neurologic condition. The mean age of the 13 enrolled early dementia participants was 79.3 years (*SD* = 11.0; range = 60–95) and the mean age of the 9 normative older adult participants was 62.8 (*SD* = 7.2; range = 55–78). The mean level of educational attainment of each group, respectively, was 11.5 years (*SD* = 2.6; range = 6–16) and 11.6 years (*SD* = 2.1; range = 8–13). All early dementia participants were male veterans, and one normative participant was female.

The study was approved by the IRB at the Stratton VAMC and written informed consent or assent was obtained from all participants. All early dementia patients were evaluated with the Impaired Decision Making Capacity tool, to evaluate competence to consent to research participation. If a patient was unable to give their own consent ($n = 4$), a surrogate consent was used.

Procedures

The exercise intervention lasted 10 weeks and both early dementia and normative older adult participants were instructed to ease into the strengthening program aiming for three to five times per week. Participants followed a low-intensity strengthening exercise routine designed by Tufts University for seniors for prevention of osteoporosis (Seguin, Epping, Buchner, Bloch, & Nelson, 2002), which primarily consisted of chair and standing exercises, involving small free weights. The exercise was aimed at strengthening muscles and improving balance, and have known applicability for seniors with some impairments, even those in a wheel chair (for sample exercises and adaptations see: www.nia.nih.gov/HealthInformation/Publications/ExerciseGuide). Early dementia participants were guided by adult day care staff while watching a video recording of an instructor leading older adults through the exercises. The exercise routine lasted 45 minutes and participants were encouraged to adjust weights and repetitions to match their ability. To guard against injury, participants were instructed to make adjustments to weights and repetitions gradually. Exercise frequency of early dementia participants was recorded by ADCP staff. Normative participants were provided with a copy of the video recording of the exercise program for practice at home, and tracked their own exercise sessions in a personal log.

Measures

Neuropsychological Measures

Pre- and post-exercise cognitive function was measured with a brief battery to maximize compliance in the early dementia sample. Given prior research the focus was on executive function and memory as measured with the following tests.

Executive Function

Three tests were administered that measure aspects of executive function including: measures selective attention and cognitive flexibility. Stroop C (45-item version adapted by van der Elst, van Boxtel, van Breukelen, & Jolles, 2006) followed administration of Stroop A and B. Three sets of stimuli were presented for timed verbal naming: (A) colored blocks, (B) black words, and (C) mismatched colored words (in which participants were asked to ignore the written word and name the color of the ink). Color Trails 2 (D'Elia, Satz, Uchiyama, & White, 1996) was administered after Color Trails 1. Participants were first asked to connect numbered circles in ascending order. In Color Trails 2, participants were asked to connect numbered circles in ascending order, while also alternating the color of the circle (pink or yellow). Alternate forms were used for pre- and post-tests. Digit Span Backwards (Strauss, Sherman, & Spreen, 2006) was administered following Digit Span Forwards. First, strings of numbers of increasing length were read, and the participant was asked to repeat each string of numbers. In digit span backwards, participants were to repeat the string in reverse order. Scores can range from 0 to 14 with one point for each string correctly reversed.

Verbal Memory

The Fuld Object Memory Evaluation (Fuld, 1981) employs multisensory encoding to evaluate memory in older adults, including touch, sight, and verbal presentation of 10 common objects concealed in a bag. In this study, we utilized the shortened version of the test in which only one immediate recall and reminder session is employed (LaRue, Romero, Ortiz, Liang, & Lindeman, 1999). In this task, a bag with 10 common objects is presented to a participant. The participant is asked to reach into the bag and feel for an object, but not pull it out. The participant is asked to identify the object by touch, without looking. Next, the participant is asked to pull the item out and identify the object visually. When all 10 objects have been identified, a brief distractor task ensues (verbal fluency for names of their sex within 60 seconds). Then, the participant is asked to recall the object. Objects that are omitted are dictated at a rate of one object every 5 seconds. The participant is then asked to recall the objects 15 minutes later. Alternate forms (different objects) were administered at pre- and post-test.

Visuospatial Skill and Memory

Participants were presented with a complex figure to copy and subsequently recall after a 30-minute delay. Two alternate figures were utilized for pre- and post-tests: the Rey–Osterrieth (Osterrieth, 1944) and the Taylor (Taylor, 1969). Each complex figure was scored by two different raters according to published scoring criteria (Lezak, Howieson, Loring, Hannay,

& Fischer, 2004) and prorated and averaged, so that scores could range from 0 to 36.

Neurophysiological Measures

For each of the EEG recording components, participants were seated comfortably in a slightly reclined position (approximately 45° angle) with lights dimmed. EEG data was recorded using a commercially available cap (Quik-Cap from Compumedics, Inc.). The cap consisted of 38 Ag/AgCl electrodes in the 10–20 system (Jasper, 1958) referenced to A1/A2 on the mastoid bones. The cap was fixed in place with a chin strap in order to minimize shifting. Each electrode was filled with Electro-Gel (Neuromedical Supplies, Inc.) in order to reduce impedance. Impedance was lowered below 10 kΩ for all electrodes included in the analysis. Signal was amplified using a commercially available amplifier (NuAmps from Compumedics, Inc.) and sampled at a rate of 250 Hz.

Resting Electroencephalography (EEG)

For resting EEG, participants were asked to lie comfortably in a reclining chair with their eyes closed for 5 minutes, then open their eyes upon request and lie comfortably with their eyes open for 5 minutes during the EEG recording. Participants were asked to make sure to not fall asleep, to move as little as possible and to not cross their arms or legs.

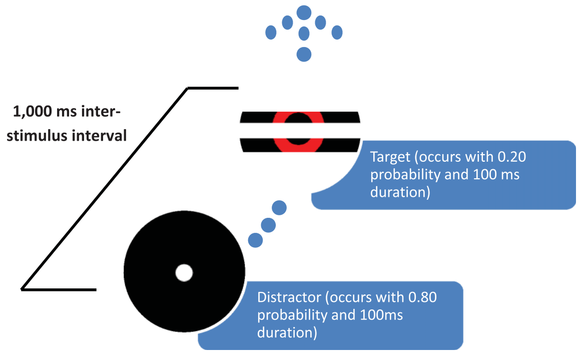
Event-related Potentials (ERP)

For ERP recordings participants were presented with stimuli on a computer screen about 0.50 m away from the participant. An oddball paradigm was recreated following an existing protocol (Pontifex et al., 2009), in which a target (5.5 cm diameter black circle with red outline on black background) and a distractor (3 cm white circle on black background) were presented for 100 ms duration with 1000 ms inter-stimulus interval for two counterbalanced blocks of 200 trials (Figure 1). The target was randomly presented on 20% of the trials. Participants were asked to respond as quickly and as accurately as possible to the target only by pressing a mouse button. One block of 300 trials of the oddball task was administered. The same random seed was used for each participant.

Data Analysis

For each of the neuropsychological tests described above and neurophysiological outcomes below, average raw scores were converted to standardized *Z*-scores by subtracting pre- (T1) from post- (T2) scores and dividing by the mean. This conversion allowed for comparison and combining of intra-individual relative change scores, across groups.

FIGURE 1. Schematic of the oddball paradigm.



Electrophysiological data were recorded in AC mode with a gain of 500 and a band pass of 0.5–30 Hz. The A/D conversion rate was decimated to 250 Hz for all trials. EEG activity was recorded via a Quik-cap worn by each participant and connected for the duration of the tasks to the Neuroscan Synamps (Scan 4.3) ERP recording system (Compumedics, Inc.). Scalp potentials were obtained using a 32-channel array with linked mastoid (ground) reference electrodes and an anterior scalp ground (Afz). Vertical eye movements were recorded with two electrodes placed above and below the left eye. Silver/silver-chloride (Ag/AgCl) electrodes were used at all sites. Recording commenced when electrical impedance had been reduced to less than 10 kΩ by light abrasion of the scalp and addition of commercially available EEG electrolyte gel. Bad channels caused by faulty connections were deleted manually from the continuous EEG recordings. All sweeps in the ERP component of the study were baseline corrected using the pre-stimulus interval as the baseline interval and epoched into single sweep recordings, from –100 ms pre-stimulus to 924 ms post-stimulus. Incorrect responses and nonresponses were manually selected from these EEG sweeps and were excluded from the subsequent analysis. All sweeps in the resting EEG component of the study were epoched into 512-ms segments and baseline corrected using the entire sweep. For both ERP and resting EEG components, sweeps in which amplitudes exceeded ±100 μV at any scalp electrode were automatically rejected. The remaining epochs were combined to produce grand average waveforms. Waveform component structure was defined in an *a priori* manner without any knowledge of effects that may be in the data. For each electrode, an overall grand average waveform for the entirety of each task was generated by collapsing across conditions for each group. In this way, the latency of the components of interest (in this case the N200 and P300) could be identified through visual inspection. The N200 was defined to be the most negative peak within a latency window of 100–350 ms post-stimulus; the latency window for the P300 in this task was 300–700 ms.

Given the limited sample size and to minimize escalating error rates, hypotheses were focused based on prior research regarding regions of interest, and thus only data from frontal lobe leads (FP1, FP2, F7, F8) were analyzed. Additionally, an index of hemispheric asymmetry was calculated that controls for overall power differentials in individuals and yields an index of change that can be more readily interpreted for all participants (right – left)/(right + left); Vogt et al., 2010). This asymmetry index was applied to all four spectral power bands, as well as to the latency and amplitude of P300 and N300.

All statistical tests were conducted with SPSS v.17 for Windows (IBM, Inc.). Repeated measures ANOVA were used to examine Group (dementia vs. normative) × Time (pre/post) interactions in neuropsychological and neurophysiological evaluations. Paired *t*-tests were used to examine change in neuropsychological and neurophysiological variables from pre- to post-exercise. Pearson correlations were computed to evaluate the relationship between change in neuropsychological outcomes and neurophysiological measures.

RESULTS

Attrition

Two of 9 normative participants, had to be dropped from analyses due to limited participation in the exercise program (less than once per week on average; health problems and snowy weather were the main limiting factors) and one dementia exerciser was dropped because he did not complete any of the outcome measures. Overall participation was 81% and is on par with prior exercise intervention research (Lautenschlager et al., 2008). No adverse events were reported.

Treatment Effects

Neuropsychological Effects

The raw cognitive scores before and after strengthening exercise for early dementia and normative exercise participants were compared using repeated measures ANOVAs (see p values for Group × Time interactions in Table 1). Only performance on Digit Span Backwards was significantly different between the two groups ($p = .01$) suggesting that the pattern of impact of exercise on this test may differ for normative versus dementia participants (normative participants experienced a greater increase in digit span backwards). However, the lack of significant Group × Time differences across the rest of the neuropsychological battery suggests that the pattern of effect of exercise (or lack thereof) may generally be similar in both groups even though the pre-exercise performance is different between groups. That is, the relative change within the groups may be similar (e.g., both may increase in a similar fashion relative to their own pre-exercise performance). Given the limited differences in patterns of change between the two groups, our desire to maximize power to detect effects of exercise in this small pilot, and the fact that intra-individual relative change was most salient, we combined the two exercise groups for the following analyses.

Paired *t*-tests of the combined groups allowed analysis of the relative intra-individual change despite differences in pre-test scores across groups. In order to clarify any impact due to variability in exercise consistency and handedness, *t*-tests were repeated with two sets of restrictions on the sample: (1) inclusive ($n = 19$): all exercisers (normative and with dementia) who completed an average of one session per week allowing for two missed weeks due to illness or weather and (2) restrictive ($n = 10$): only right-handed, more regular exercisers who completed an average of 1.5 sessions per week allowing for two missed weeks due to illness or weather; $n = 16$). The inclusive sample exercised on average 21.7 times over the 10 weeks ($SD = 8.6$); restrictive sample exercised on average 21.9 times over the 10 weeks ($SD = 8.5$). Table 1 reveals that across both sets of criteria (inclusive and restrictive), immediate verbal and delayed visuospatial memory were significantly improved for the combined exercise groups. Additionally, with the more restrictive criteria, delayed verbal memory and visuospatial skill were also significantly improved for the combined exercise groups.

Neurophysiological Impacts

Given that the above neuropsychological effects were significant for the least restrictive criteria (e.g., at least weekly exercise participation), EEG and ERP analyses were conducted with this inclusive sample to maximize power (Tables 2 and 3, respectively). Resting EEG and ERP results for the frontal lobe can be seen in Figures 2 and 3, respectively. Significant frontal asymmetry shifts were found in beta (right > left; $t = –4.53$, df = 11, $p = .005$), delta (left > right; $t = 1.85$, df = 11, $p = .04$), and N200 amplitude (right > left; $t = –2.60$, df = 12, $p = .02$).

Relationship Between Neuropsychological and Neurophysiological Impacts

Change in significant EEG and ERP outcomes (post–pre) noted above were correlated with change on neuropsychological outcomes (post–pre). Pearson correlations revealed that improvement in verbal memory correlated significantly with a decrease in N200A asymmetry (Fuld immediate recall: $r^2 = –.67$, $p = .05$; Fuld delayed recall: $r^2 = –.77$, $p = .02$), and an increase in delta asymmetry (Fuld delayed recall: $r^2 = .60$, $p = .05$).

TABLE 1. Neuropsychological change: Between and within group comparisons

							Inclusive ($n = 19$)				Restrictive ($n = 16$)
	Normative			Dementia			Group × Time			*t*-Tests	*t*-Tests
	Mean	*SD*	*n*	Mean	*SD*	*n*	*F*	df	*p*	*p*	*p*
Stroop C											
Pre	56.17	(10.34)	6	139.67	(102.30)	6	0.30	10	.60	.55	.52
Post	55.13	(11.08)	6	116.51	(64.44)	6					
Digit Span Backwards											
Pre	5.50	(2.59)	6	4.10	(1.73)	10	8.27	14	**.01**	.25	.53
Post	6.83	(2.71)	6	3.90	(1.10)	10					
Trails 2											
Pre	124.00	(67.97)	5	250.00	(186.45)	5	1.64	8	.24	.54	.87
Post	96.11	(19.97)	5	259.01	(197.63)	5					
Fuld Semantic Recall											
Pre	18.80	(8.76)	5	10.60	(3.66)	10	0.01	13	.93	.95	.68
Post	18.60	(5.86)	5	10.60	(4.27)	10					
Figure Copy											
Pre	28.67	(3.99)	3	16.44	(6.96)	9	0.47	10	.51	.08	**.05**
Post	30.33	(3.62)	3	22.06	(9.96)	9					
Figure Delayed Recall											
Pre	14.50	(7.86)	3	3.28	(4.41)	9	0.05	10	.84	**.02**	**.02**
Post	18.25	(3.25)	3	7.81	(4.52)	9					
Fuld Immediate Recall											
Pre	6.60	(1.34)	5	2.90	(2.38)	10	0.22	13	.64	**.02**	**.05**
Post	7.60	(1.52)	5	4.40	(1.65)	10					
Fuld Delayed Recall											
Pre	8.40	(1.14)	5	2.60	(2.41)	10	3.10	13	.10	.07	**.05**
Post	8.20	(0.45)	5	4.50	(2.72)	10					

Note: Inclusive, Exercise at least 1×/week; Restrictive, 1.5×/week, right-handed only.

TABLE 2. EEG spectral power change: Between and within group comparisons

							Inclusive ($n = 19$)				Restrictive ($n = 16$)
	Normative			Dementia			Group × Time			*t*-Tests	*t*-Tests
	Mean	*SD*	*n*	Mean	*SD*	*n*	*F*	df	*p*	*p*	*p*
alpha-L											
Pre	7.03	(5.20)	5	2.25	(1.14)	9	3.50	12	.09	.19	.28
Post	4.08	(2.56)	5	2.17	(1.13)	9					
alpha-R											
Pre	6.26	(4.23)	5	2.26	(1.27)	9	4.01	12	.07	.25	.48
Post	4.14	(2.80)	5	2.35	(1.12)	9					
alpha-asymmetry											
Pre	−0.02	(0.09)	5	−0.01	(0.06)	9	0.37	12	.56	.15	.17
Post	0.00	(0.08)	5	0.05	(0.10)	9					
beta-L											
Pre	3.44	(3.74)	5	1.36	(0.53)	9	1.66	12	.22	.19	.16
Post	1.41	(1.20)	5	1.06	(0.93)	9					
beta-R											
Pre	2.83	(2.79)	5	1.33	(0.78)	9	2.12	12	.17	.34	.85
Post	1.39	(1.08)	5	1.35	(1.03)	9					
beta-asymmetry											
Pre	−0.03	(0.10)	5	−0.05	(0.13)	9	1.10	12	.31	**.005**	**.001**
Post	0.06	(0.18)	5	0.12	(0.18)	9					
delta-L											
Pre	14.78	(11.55)	5	18.77	(10.52)	9	0.02	12	.88	.52	.25
Post	17.20	(3.87)	5	20.28	(14.62)	9					
delta-R											
Pre	14.43	(8.72)	5	21.45	(10.14)	9	0.02	12	.88	.87	.60
Post	15.37	(4.84)	5	21.59	(14.55)	9					

(*Continued*)

TABLE 2. (Continued)

							Inclusive ($n = 19$)				Restrictive ($n = 16$)
	Normative			Dementia			Group × Time			*t*-Tests	*t*-Tests
	Mean	*SD*	*n*	Mean	*SD*	*n*	*F*	df	*p*	*p*	*p*
delta-asymmetry											
Pre	0.02	(0.12)	5	0.07	(0.10)	9	0.85	12	.37	**.04**	.09
Post	−0.07	(0.08)	5	0.04	(0.14)	9					
theta-L											
Pre	4.93	(4.25)	5	4.36	(3.28)	9	0.77	12	.40	.27	.34
Post	2.90	(1.10)	5	3.93	(2.48)	9					
theta-R											
Pre	4.49	(3.16)	5	4.48	(3.42)	9	0.82	12	.38	.25	.34
Post	2.85	(0.80)	5	4.11	(2.60)	9					
theta-asymmetry											
Pre	0.01	(0.10)	5	0.00	(0.05)	9	0.12	12	.73	.64	.72
Post	0.01	(0.07)	5	0.02	(0.06)	9					

Note: Inclusive, Exercise at least 1×/week; Restrictive, 1.5×/week, right-handed only.

TABLE 3. ERP change: Between and within group comparisons

							Inclusive ($n = 19$)				Restrictive ($n = 16$)
	Normative			Dementia			Group × Time			*t*-Tests	*t*-Tests
	Mean	*SD*	*n*	Mean	*SD*	*n*	*F*	df	*p*	*p*	*p*
P300L-L											
Pre	437.60	(83.69)	5	502.33	(115.79)	8	.27	11	.61	.45	.58
Post	376.53	(18.42)	5	487.67	(156.83)	8					
P300L-R											
Pre	430.93	(82.35)	5	501.17	(101.68)	8	.10	11	.76	.12	.08
Post	391.20	(35.96)	5	440.92	(151.41)	8					
P300L-asymmetry											
Pre	−0.01	(0.04)	5	0.00	(0.08)	8	3.05	11	.11	.31	.09
Post	0.02	(0.03)	5	−0.06	(0.05)	8					
P300A-L											
Pre	2.50	(1.67)	5	1.89	(1.09)	8	2.16	11	.17	.90	.99
Post	3.17	(2.61)	5	1.55	(0.64)	8					
P300A-R											
Pre	2.88	(1.97)	5	1.53	(1.34)	8	.29	11	.60	.41	.99
Post	2.42	(1.92)	5	1.40	(0.71)	8					
P300A-asymmetry											
Pre	0.08	(0.16)	5	−0.21	(0.35)	8	4.44	11	.06	.95	.53
Post	−0.16	(0.17)	5	−0.05	(0.16)	8					
N200L-L											
Pre	164.00	(81.91)	5	212.50	(117.41)	8	.02	11	.90	.46	.79

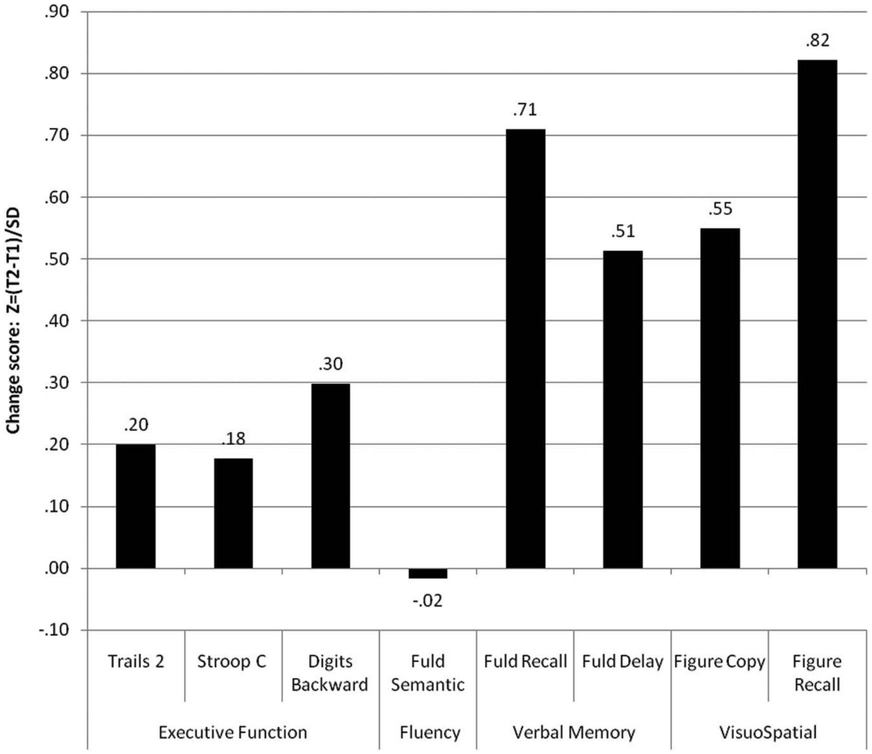
(*Continued*)

Table 3. (Continued)

	Normative			Dementia			Inclusive ($n = 19$)				Restrictive ($n = 16$)
							Group × Time			*t*-Tests	*t*-Tests
	Mean	*SD*	*n*	Mean	*SD*	*n*	*F*	df	*p*	*p*	*p*
Post	193.60	(100.69)	5	233.00	(55.87)	8					
N200L-R											
Pre	223.73	(64.04)	5	213.00	(81.43)	8	1.62	11	.23	.30	.54
Post	213.33	(42.85)	5	257.00	(81.60)	8					
N200L-asymmetry											
Pre	0.18	(0.23)	5	0.14	(0.48)	8	.02	11	.89	.58	.65
Post	0.12	(0.34)	5	0.03	(0.21)	8					
N200A-L											
Pre	−2.28	(0.91)	5	−2.20	(1.17)	8	.65	11	.44	.80	.39
Post	−1.65	(0.85)	5	−2.39	(2.12)	8					
N200A-R											
Pre	−2.40	(0.77)	5	−2.38	(1.17)	8	.18	11	.68	.42	.73
Post	−2.50	(1.02)	5	−2.83	(1.83)	8					
N200A-asymmetry											
Pre	0.04	(0.14)	5	0.05	(0.12)	8	.81	11	.39	**.02**	**.02**
Post	0.23	(0.15)	5	0.14	(0.17)	8					

Note: Inclusive, Exercise at least 1×/week; Restrictive, 1.5×/week, right-handed only.

FIGURE 2. Neuropsychological change after 10 weeks of strengthening exercise.
Note: Inclusive sample data is displayed. Timed tasks were multiplied by a factor of –1 to reveal relative change in the same direction for ease of visual interpretation. From pre- to post-exercise, immediate and delayed verbal memory were significantly improved.

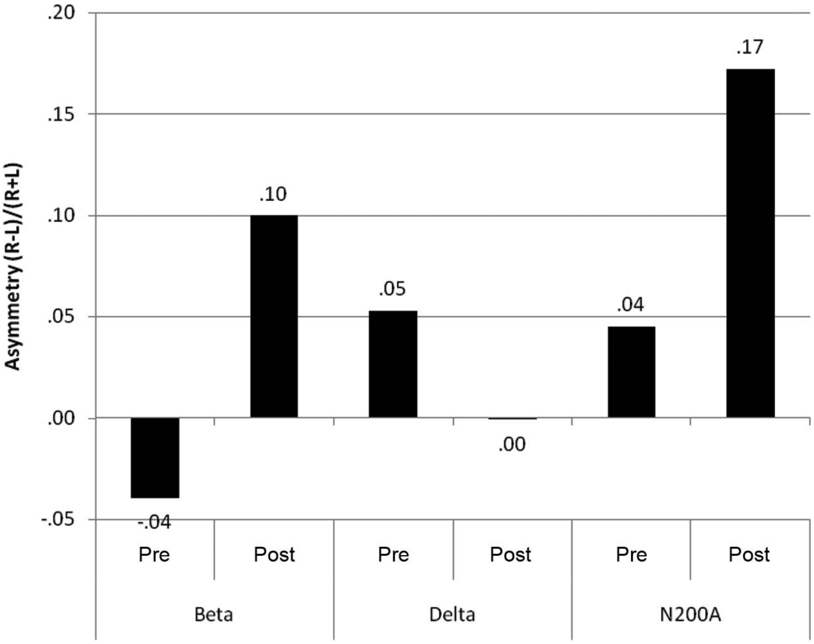


DISCUSSION

This study aimed to conduct an exploratory pilot to replicate and extend prior work on the cognitive benefits of strengthening exercise for both early dementia and normative older adults. This is the first known study to also examine potential change in neurophysiological markers (EEG/ERP) resulting from a strengthening exercise intervention for older adults. Thirteen early dementia patients and nine normative older adults enrolled in the study ($n = 22$) and completed some aspects of evaluation or of the 10-week low-intensity exercise. Neuropsychological outcomes (executive function and memory) and electrophysiological data (at rest and during cognitive activity) were analyzed from 19 participants who met a minimum threshold of compliance with prescribed exercise and evaluations.

The results are consistent with a number of prior studies which have found memory benefits of strengthening exercise for both cognitively

FIGURE 3. Change in frontal asymmetries after 10 weeks of exercise.
Note: Inclusive sample data is displayed. Significant frontal asymmetry changes were found in beta, delta, and N200 amplitude.



impaired and normative older adults (Heyn et al., 2004); however it is unclear why executive function was unaffected in this study which contrasts with some prior research (Anderson-Hanley et al., 2010; Brown et al., 2009; Cassilhas et al., 2007; Liu-Ambrose et al., 2008, 2010). A dissociation between neuropsychological and neurophysiological outcomes was reported by Kamijo et al. (2007), who examined the cognitive effects of a 12-week walking program for older adults. Specifically, they found P300 latency and amplitude were affected by the walking program, while behavioral measures (reaction time and error rate) were not. Their finding suggests that ERP measures may be more sensitive to physical activity than behavioral measures. Generalizing this finding to our results, it appears that neurophysiological measures were also more sensitive to exercise effects than neuropsychological measures of executive function.

Increased frontal asymmetry results herein also resonate with recently published pilot EEG and ERP data on the effects of a single bout of aerobic exercise for older adults, which showed an increase in frontal alpha asymmetry (Vogt et al., 2010). Similarly, longer-term exercise for depressed older adults was also found to maintain frontal alpha asymmetry (Deslandes et al., 2010). While our results do not show the same asymmetry effect in the alpha band, our data does show similar shift to right-sided dominance and overall decrease in beta, with a shift to a more balanced delta, perhaps suggesting that the power shift to the right may be a more generalized phenomena. This could be viewed as a more evenly distributed left–right hemisphere activation pattern that may indicate a reduction in cognitive effort, perhaps reflecting increased efficiency of the brain post-exercise. Also, the fact that a similar shift in asymmetry is also observed in an early ERP component (N200 amplitude) suggest that the increased cognitive efficiency, if this is what we wish to call it, is occurring predominantly at an early stage of attentional processing. The fact that an improvement in verbal memory correlated significantly with two of the three significant neurophysiological outcomes supports this assertion.

Strengths of this pilot study include a prospective design with both early dementia participants and normative older adults enabling some controlled comparison. Feasibility was shown of implementing a low-intensity strengthening exercise program in an adult day program and in-home for normative community dwelling participants. Video recordings of exercises assisted staff with implementation and facilitated at-home practice, with good compliance reaching 80%. The feasibility of gathering neuropsychological and neurophysiological data in a cognitively compromised sample was demonstrated. The use of alternate forms of neuropsychological tests in pre- and post-intervention test batteries limits potential practice effects of serial testing. The asymmetry index calculated in this study and applied to ERP measures of P300 and N200 is, to our knowledge, a novel and promising approach. Additional electrophysiological research is needed to evaluate the reliability and validity of this measure in the context of exercise intervention studies, and its relationship to neuropsychological and functional outcomes.

Future research should also evaluate the replicability of the preliminary neuropsychological finding of improved memory with low-intensity strengthening exercise in a larger older adult sample. A larger sample would add statistical power for detecting other possible effects that may have not been found herein due to low power and could address comorbid conditions which was not feasible in the small sample herein. With a larger sample, the potential role of comorbid conditions could be examined, either through statistical control or subgroup analyses, presuming a large enough sample could be obtained (e.g., diabetes which is known to affect cognition; Colberg, Somma, & Sechrist, 2008). Ideally a high quality randomized clinical trial would also clarify the intensity and dose of exercise, as well as the functional benefits implied by the neuropsychological outcomes herein. Random assignment to a non-exercise condition would be useful in ruling out alternate explanations for observed change, such as probable effects from practice or staff attention.

Additionally, because N200 is implicated in mismatch and novelty in cognitive challenges (partially controlled in this experimental protocol by keeping the oddball stimuli shape consistent), it would be interesting to evaluate the N200 in the context of a three-stimulus task.

The current pilot study demonstrates the feasibility of implementing a low-intensity strengthening program for older adults, and adds to the growing evidence of cognitive benefits, specifically in memory, of strengthening exercise for both normative and early dementia participants. This is the first known report of neurophysiological markers of the effects of strengthening exercise using EEG and ERP. Preliminary findings are intriguing, suggesting frontal asymmetry shifts in beta, delta, and N200 amplitude. Additional research is needed to evaluate the replicability, generalizability, and functional significance of these effects.

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