

Cognitive Vitality Reports® are reports written by neuroscientists at the Alzheimer's Drug Discovery Foundation (ADDF). These scientific reports include analysis of drugs, drugs-in-development, drug targets, supplements, nutraceuticals, food/drink, non-pharmacologic interventions, and risk factors. Neuroscientists evaluate the potential benefit (or harm) for brain health, as well as for age-related health concerns that can affect brain health (e.g., cardiovascular diseases, cancers, diabetes/metabolic syndrome). In addition, these reports include evaluation of safety data, from clinical trials if available, and from preclinical models.

Transcranial Direct Current Stimulation (tDCS)

Evidence Summary

Most studies show modest benefits with tDCS treatment in healthy elderly and Alzheimer's patients.

Neuroprotective Benefit: tDCS consistently shows small benefits to Alzheimer's patients and elderly, though no large studies have been conducted

Aging and related health concerns: There is some evidence that tDCS may modulate heart rate variability.

Safety: tDCS may be accompanied by mild side effects at the stimulation site, though long-term effects are not known.

Availability: Available to use at home	Dose: Anodal stimulation at 1-2 mA usually for 20-30 minute sessions.	Chemical formula: N/A
Half life: Effects generally last 1-2 hours after stimulation	BBB: N/A	
Clinical trials: 13 ongoing clinical trials in Alzheimer's patients	Observational studies: 0	

What is it?

Transcranial direct current stimulation (tDCS) is the passage of current through the skull to excite the cortical tissue below. In sham experiments (control experiments for tDCS), stimulation is administered with increasing current for around 30 seconds before being ramped down, mimicking what the participants with real stimulation feel. tDCS is used in a number of clinical applications such as drug addiction, stroke, epilepsy, Parkinson's disease, chronic pain, depression, and Alzheimer's disease ([Zhao et al, 2017](#)).

Neuroprotective Benefit: tDCS consistently shows small benefits to Alzheimer's patients and elderly, though no large studies have been conducted.

Types of evidence:

- 1 meta-analysis of rTMS and tDCS based on 24 studies for healthy elderly and Alzheimer's patients
- 2 multiple session studies in healthy elderly
- 9 single session studies in healthy elderly
- 4 single session studies in Alzheimer's/MCI patients
- 6 multiple session studies in Alzheimer's/MCI patients

Human research to suggest prevention of dementia, prevention of decline, or improved cognitive function?

Meta-analyses for both healthy elderly and Alzheimer's/MCI

[Hsu et al \(2015\)](#) conducted a systematic review/meta-analysis of noninvasive brain stimulation (both rTMS and tDCS) in elderly patients in studies that measured cognitive function, had >10 participants, reported outcome measures quantitatively, and were sham controlled. Most of the studies used tDCS. Based on 13 studies (18 outcomes), cognitive function improved with a Cohen's effect size of $d=0.42$ (95%CI 0.09-0.74). Cognitive outcomes in offline studies (not during a cognitive task) significantly improved ($d=0.92$) while cognitive outcomes in online (during a cognitive task) studies did not ($d=0.23$, n.s.). Studies with multiple sessions were better than studies with a single session ($d=0.89$ vs $d=0.44$).

In Alzheimer's trials that measured cognitive function, had >10 participants, reported outcome measures quantitatively, and were sham controlled, about half used rTMS. Based on 11 studies (20 outcomes, 200 patients), cognitive function improved with a Cohen's effect size of $d=1.35$ (95%CI 0.86-1.84). Cognitive outcomes with offline studies significantly improved ($d=1.04$) as did cognitive

outcomes with online studies ($d=1.79$). Studies with multiple sessions were similar to studies with a single session ($d=1.20$ vs $d=1.49$).

Summary of Individual Summaries – many studies have investigated tDCS in healthy elderly or Alzheimer's disease. A summary of the studies follows. At the end of the report are additional detail for the individual studies. Unless stated otherwise, anodal tDCS (positive stimulation) was performed. The studies are group by how many sessions of tDCS were performed and then the brain region stimulated. There are four primary locations stimulation is performed: dorsolateral prefrontal cortex (DLPFC), inferior frontal cortex temporoparietal cortex, and temporal cortex.

Healthy Elderly

Multiple Sessions

- [Park et al \(2014\)](#): parallel design; 40 healthy elderly; 10 sessions with cognitive training bilaterally over prefrontal cortex or sham. **Benefit**: 7 and 28 days later – verbal working memory, digit span. **No Benefit**: visual span test, visual learning test, 6 other computer-assisted neuropsychological tests
- [Jones et al \(2015\)](#): parallel design; 72 healthy elderly; 10 sessions with cognitive training over right prefrontal cortex (PFC), right parietal cortex (PC), alternating right PFC/PC, or sham. **Benefit**: 1 month later – trained and transfer tasks. **No Benefit**: At end of stimulation period (day 10).

Single Session

- [Sandrini et al \(2014\)](#): parallel design; 36 healthy elderly; 10 minutes over left DLPFC with a verbal memory task. **Benefit**: less forgetting in stimulation group.
- [Boggio et al \(2010\)](#): parallel design; 28 healthy elderly; 15 minutes during a gambling task over left or right DLPFC or sham. **Effect**: left stimulation over the DLPFC increased risk taking on gambling task. **No Effect**: right stimulation for gambling task.
- [Harty et al \(2014\)](#): cross-over design; 24 healthy elderly; stimulation during an error awareness task with anodal stimulation over right or left DLPFC. **Benefit**: error awareness with stimulation over anodal left DLPFC. **No Benefit**: accuracy in any group. Error awareness with anodal right DLPFC.
- [Maneti et al \(2013\)](#): cross-over design; 32 healthy elderly; stimulation during the entire retrieval phase of a verbal working memory task over the left or right DLPFC or the left or right PC or sham. **Benefit**: reaction time over left DLPFC and left PC. **No Benefit**: right DLPFC and right PC. No data on accuracy.



- [Berryhill and Jones \(2012\)](#): cross-over design; 25 healthy elderly; 10 minutes during a visual and verbal working memory task over the left, right, and sham prefrontal cortex. **Benefit**: Highly educated participants with both stimulation procedures. **No Benefit**: Pooled results of highly- and less educated participants; less-educated participants on verbal working memory tasks. **Detriment**: less-educated participants on visual working memory task.
- [Holland et al \(2011\)](#): cross-over design; 10 healthy elderly; 20 minutes during naming task over left inferior frontal cortex. **Benefit**: reaction time on naming task. **No Benefit**: accuracy on naming task (possible ceiling effect).
- [Meinzer et al \(2013\)](#): cross-over design; 20 healthy elderly; 20 minutes during a semantic word generation task or sham over the left inferior frontal gyrus. **Benefit**: semantic word generation that reach levels of young controls.
- [Ross et al \(2011\)](#): cross-over design; 14 healthy elderly; 15 minutes during a face and place naming task over left, right, or sham anterior temporal lobes. **Benefit**: left stimulation – face naming; right stimulation – place naming. **No Benefit**: left stimulation – place naming; right stimulation – face naming.
- [Floel et al \(2012\)](#): cross-over design; 20 healthy elderly; 20 minutes during an object location task over temporoparietal cortex or sham and retested 1 week later. **Benefit**: Improvements on delayed recall. **No Benefit**: Immediate recall.

Alzheimer's/MCI patients

Multiple sessions

- [Cotelli et al \(2014\)](#): parallel design; 36 patients with mild-to-moderate Alzheimer's; 25 minutes, 5 days/week for 2 weeks in 3 groups: 1) left DLPFC + computerized memory training, 2) sham + computerized memory training, 3) left DLPFC + computerized *motor* training. Tested 2 weeks, 3 months, and 6 months post-training. **Benefit**: the two memory training groups (sham and stimulation) from baseline on a face-name association task (episodic memory). **No Benefit**: the motor training group on face-name association task. Any group for MMSE, activities of daily living, language tasks, other memory tasks.
- [Khedr et al \(2014\)](#): parallel design; 34 mild-to-moderate Alzheimer's patients; 25 minutes for 10 days over left DLPFC or sham measured at 1- and 2-months post-stimulation. **Benefit**: MMSE by ~2 points after stimulation and ~5-6 points at both 1- and 2-months after stimulation. **No Benefit**: IQ (Wechsler adults intelligence scale) at any time point.
- [Andre et al \(2016\)](#): parallel design; 21 patients with mild vascular dementia; 20 minutes for 4 days over the left DLPFC or sham. **Benefit**: Both groups improved on ADAS-cog by 3-4 points after stimulation period, but there was no difference between groups. Improvement compared

to sham in visual short-term memory task at end of stimulation period and 2 weeks after stimulation. Improvement compared to sham in verbal working memory and executive function reaction time. Improvement in both groups compared to baseline in executive function, but not between groups.

- [Boggio et al \(2012\)](#): cross-over design; 15 patients with mild-to-moderate Alzheimer's; 30 minutes for 5 days over the temporal cortex or sham. Cognition measured after treatment, 1 week later, and 1 month later. **Benefit**: visual recognition memory that persisted for 1 month. **No Benefit**: MMSE, ADAS-cog, visual attention.
- [Bystand et al \(2016\)](#): parallel design; 25 patients with mild Alzheimer's disease; 30 minutes for 6 days over the left temporal cortex or sham. **No Benefit**: No change in California Verbal Learning Test, MMSE, clock drawing test, trail making test A or B, an IQ test.
- [Bystand et al \(2017\)](#): case study; 1 patient with early-onset (not familial) Alzheimer's disease: 4 years after diagnosis, began tDCS 30 minutes per day over the left temporal lobe with cognitive tests 8 months later. **Benefit**: immediate recall, delayed recall, vocabulary. **No benefit**: verbal function, MMSE, attention. **Detriment**: visuospatial function
- [Roncero et al \(2017\)](#): cross-over design; 10 patients with anomic aphasia (difficulty in word finding) Alzheimer's disease or frontotemporal dementia; 30 minutes for 10 sessions over the left inferior parieto-temporal cortex or sham while training on a picture naming task. **Benefit**: After stimulation, patients performed better than sham on the picture naming task, an effect that lasted 2 weeks. Two weeks after stimulation, patients also performed better on an untrained digit span task.

Single sessions

- [Meinzer et al \(2015\)](#): cross-over trial; 18 patients with MCI; 20 minutes over left inferior frontal cortex during a semantic word task. **Benefit**: fewer errors in semantic word test and performed as well as healthy age-matched controls.
- [Ferrucci et al \(2008\)](#): cross-over; 10 patients with probable mild Alzheimer's disease; 15 minutes of anodal, cathodal, or sham bilaterally over the temporal cortex, tested with a word recognition and visual attention tests. **Benefit**: anodal tDCS word recognition accuracy. **No Benefit**: visual attention. **Detriment**: cathodal tDCS for word recognition accuracy.
- [Boggio et al \(2009\)](#): cross-over; 10 patients with mild-to-moderate Alzheimer's disease; 30 minutes over left DLPFC, left temporal cortex, or sham while undergoing several cognitive tests. **Benefit**: visual recognition memory with both stimulation conditions. **No Benefit**: Stroop test or digit span test



Mechanisms of action for neuroprotection identified from laboratory and clinical research:

The mechanisms underlying tDCS are not completely known. On theory is that anodal stimulation pushes neuronal membranes toward depolarization, thus allowing them to fire easier. Another theory, however, is that tDCS can induce synaptic changes by adjusting synaptic strength similar to long-term potentiation. Evidence for this is that the effects are reduced by injection of a B-adrenergic receptor antagonist and that BDNF is important for the after-effects of cortical stimulation.

Conclusion

As seen above, there are many varied outcomes with tDCS procedures with some outcomes showing clinical benefit while some showing no effect (although using anodal tDCS $\leq$ 2mA is not detrimental).

[Liu et al \(2017\)](#) reviewed 12 different tDCS publications in MCI or Alzheimer's patients (most of which were reviewed above) and discussed several reasons for the different outcomes:

- Single session vs. multiple sessions of tDCS – tDCS alters cortical excitability. In single sessions, these effects seem to diminish in about 1-2 hours. However, multiple sessions can product cumulative excitatory and long-term effects.
- Electrode size – electrode sizes ranged from 25-35 cm² in the previous studies. The relationship between electrode size and underlying current density is complex and not completely understood.
- Current intensity – 2mA is the max current intensity deemed to be safe. At or below 2mA, anodal tDCS causes an increased cortical excitability. At 2mA, cathodal tDCS can increase cortical excitability, but at lower intensities decreases cortical excitability.
- Electrode placement – electrode placement varied between studies (e.g. temporal lobe, DLPFC, etc.) which could affect the outcome.
- Reference electrode – generally the anodal electrode is place on the region of interest in the cathode on the deltoid muscle. However, some studies reported placing the cathode on the contralateral side which could affect the results.
- Different cognitive batteries – different outcomes on different cognitive batteries could be due to different electrode placements or stage/type of dementia.
- Brain and cortical anatomy – brain sulci depth, CSF thickness, cortical thickness, skull thickness, and bone density could all affect the outcomes of the studies.
- Baseline cognition – some studies suggest that baseline cognition could affect the outcome of the results.



- Genetic differences – Brain derived neurotrophic factor (BDNF) promotes neuronal growth, synaptic plasticity and long-term potentiation and has been reported to be affected by tDCS. Genetic differences are reported to affect BDNF expression which could be another source of variance.

Conclusions

Although some studies suggest cognitive benefits using tDCS in elderly individuals or patients with Alzheimer's, there is little consistency in stimulation procedure between studies. Larger controlled studies are needed.

APOE4 interactions: None reported

Aging and related health concerns: There is some evidence that tDCS may modulate heart rate variability.

Types of evidence:

- 1 meta-analysis for heart rate, blood pressure, and heart rate variability outcomes

In a meta-analysis of non-invasive brain stimulation (NIBS) studies looking at the response of heart rate, blood pressure, and heart rate variability, [Makovac et al \(2017\)](#) reported that heart rate and HRV significantly improved, while blood pressure did not (Hedge's $g=0.17$, 0.3 , and 0.21 not significant., respectively). However, when only comparing studies that used a sham stimulation, heart rate no longer significantly decreased. There was significant heterogeneity in all the studies in the meta-analysis.

Safety: tDCS may be accompanied by mild side effects at the stimulation site, though long-term effects are not known.

Types of evidence:

- 1 review of safety

The most common mild adverse effects with tDCS include mild tingling, mild pain, and transient redness. A review of 102 subjects receiving 567 tDCS sessions (1mA) reported side effects including mild tingling (70%), moderate fatigue (35%), light itching sensation (30%), headache (11%), nausea (3%), insomnia (1%) – though these side effects were mild, tolerated, and transient ([Zhao et al, 2017](#)). Skin



lesions are possible due to temperature increase and chemical reactions in the interface with the skin and electrodes. These are more common with higher stimulation intensity, skin impedance, duration of stimulation, accumulation of electrochemically produced toxins, and dissolution products of the sponge ([Zhao et al, 2017](#)).

Drug interactions:

Theoretically, the same drugs that interact with rTMS might also interact with tDCS, though the likelihood of seizure with tDCS is lower.

The most potentially hazardous drug interaction with rTMS includes drugs that may lower the threshold for seizure including: imipramine, amitriptyline, doxepine, nortriptyline, maprotiline, chlorpromazine, clozapine, foscarnet, ganciclovir, ritonavir, amphetamines, cocaine, ecstasy, phencyclidine, ketamine, GHB, alcohol, and theophylline ([Rossi et al, 2009](#)).

Drugs that are less hazardous, but should still be used with caution include: mianserin, fluoxetine, fluvoxamine, paroxetine, sertraline, citalopram, reboxetine, venlafaxine, duloxetine, bupropion, mirtazapine, fluphenazine, pimozide, haloperidol, olanzapine, quetiapine, aripiprazole, ziprasidone, risperidone, chloroquine, mefloquine, imipenem, penicillin, ampicillin, cephalosporins, metronidazole, isoniazid, levofloxacin, cyclosporin, chlorambucil, vincristine, methotrexate, cytosine arabinoside, BCNU, lithium, anticholinergics, antihistamines, sympathomimetics ([Rossi et al, 2009](#)).

Withdrawal from the following drugs are potentially hazardous due to increased seizure potential: alcohol, barbiturates, benzodiazepines, meprobamate, and chloral hydrate ([Rossi et al, 2009](#)).

Sources and dosing:

There are a number of consumer tDCS devices available. However, none have been validated in a clinical setting. Generally, sessions are 20-30 minute with anodal stimulation at 1-2mA.

Research underway:

There are [13 ongoing studies](#) looking at tDCS in Alzheimer's patients. The largest is the "Prevention of Alzheimer's Disease with CR Plus tDCS in Mild Cognitive Impairment and Depressions (PACt-MD)". PACt-MD is a five year study that will enroll 375 patients with MCI or depression. Patient will receive tDCS and cognitive remediation over 24-60 months. tDCS will be administered 5 days/week for 8 weeks then 5 days every 6 months for 30 minutes. The primary outcome is change in cognition with a secondary outcome of developing dementia ([NCT02386670](#)).

Search terms:

PubMed:

Transcranial direct current stimulation + alzheimer's, aging, elderly cognition

Google:

Transcranial direct current stimulation Alzheimer's

Details of Individual Studies**Healthy Elderly***Multiple session – offline stimulation*

In a parallel designed trial, [Park et al \(2014\)](#) conducted anodal tDCS in 40 healthy elderly bilaterally over the prefrontal cortex for 10 sessions during computer-assisted cognitive training. Each session was 30 minutes at 2mA. Participants underwent working memory tests and computerized neuropsychological tests before the sessions, and 0, 7, and 28 days after the sessions. Verbal working memory improved in the stimulation group compared to the sham at days 0, 7, and 28 (% correct in stimulation went from 48% to 57% at day 28). A digit span test improved at day 7 in the stimulation group compared to the sham, but not at days 0 or 28. There were no changes in a visual span test, visual learning test, or any of 6 computer-assisted neuropsychological tests.

In a parallel designed trial, [Jones et al \(2015\)](#) conducted anodal tDCS in 72 right-handed healthy elderly over the right prefrontal cortex, right parietal cortex, alternating right prefrontal and parietal cortex, or sham over 10 days while participants were undergoing a visuospatial working memory task. Each session was 10 minutes long with 1.5mA stimulation. At day 1, 10, and 1-month follow-up, participants were tested on visuospatial working memory tasks (trained tasks) and transfer tasks (near transfer – similar to visuospatial working memory tasks, and far transfer). At the end of the 10 sessions, all groups performed similarly, which was expected due to the cognitive training. However, one month later, all stimulated groups showed improvements on cumulative trained and transfer tasks. In a post-hoc analysis, these improvements were driven by recall tasks (for trained tasks) and more challenging, near transfer tasks (transfer tasks).

Single session – offline stimulation

In a parallel designed trial, [Sandrini et al \(2014\)](#) taught 36 healthy elderly a list of 20 words. On day 2, the elderly received either anodal tDCS for 10 minutes over the left DLPFC at 1.5mA plus a reminder of the words, stimulation without a reminder, or a sham stimulation plus a reminder. On day 3 and 30,



participants were asked to remember the words. There was less forgetting in both stimulation groups than the sham stimulation group at both time points.

Single session – online stimulation

In a cross-over trial, [Ross et al \(2011\)](#) performed left, right, or sham anodal tDCS over the anterior temporal lobes in 14 right-handed healthy elderly at 1.5mA for 15 minutes during a face and place naming task. For responses with longer recall (suggesting that the participant must think more to recall): for face naming, participants with left anodal stimulation improved more than sham (29%-40% correct) while for places right anodal stimulation improved more than sham (21%-33% correct).

In a parallel designed trial, [Boggio et al \(2010\)](#) performed anodal tDCS over the left DLPFC (cathode over right), anodal tDCS over the right DLPFC (cathode over the left), or sham stimulation for 15 minutes at 2mA during a gambling task in 28, mostly right-handed, healthy elderly. Participants receiving anodal tDCS over the left DLPFC made more risky decisions than the other groups.

In a cross-over trial, [Holland et al \(2011\)](#) performed anodal tDCS over the left inferior frontal cortex in 10 healthy elderly for 20 minutes at 2mA during a naming task. Stimulation slightly improved reaction time (~25ms) with no change in accuracy (because of a ceiling effect). This was accompanied by decreased fMRI activity in Broca's area (suggesting less brain power needed to answer).

In a cross-over trial, [Berryhill and Jones \(2012\)](#) performed anodal tDCS over the left, right, and sham prefrontal cortex over 10 minutes during a visual and verbal working memory task at 1.5mA in 25 healthy elderly who were right handed. There was no effect on working memory. However, when they separated out participants with high and low education (16.9 vs. 13.5 years of education), surprisingly there were benefits with both stimulation procedures in highly educated participants with both stimulus locations on both tasks. Participants with less education performed worse with right prefrontal cortex stimulation on a visual working memory task.

In a cross-over trial, [Floel et al \(2012\)](#) performed anodal tDCS in 20 healthy elderly over the right temporoparietal cortex for 20 minutes during an object location task at 1mA and then retested 1 week later. There was no improvement in immediate recall. However, the number of correct objects remember 1 week later improved from 10%-30% with stimulation.

In a cross-over trial, [Maneti et al \(2013\)](#) performed anodal tDCS in 32 healthy elderly over the left or right DLPFC (16 subjects) or the left or right parietal cortex (PARC, 16 subjects). Thus, there were six

experiments, L/R DLPFC, L/R PARC, and sham for each. The task was a verbal memory task, and stimulation (at 1.5mA) occurred during the retrieval phase. Reaction time was improved (~150ms) when anodal tDCS was applied over the left DLPFC or left PARC. There was no data on accuracy.

In a cross-over trial, [Meinzer et al \(2013\)](#) performed anodal tDCS in 20 healthy elderly over the left inferior frontal gyrus for 20 minutes during a semantic word generation task at 1mA. Young participants using a sham stimulation were also used as controls. Stimulation improved performance in elderly over sham to a level seen in young participants. During the sham stimulation, a task-related fMRI study suggested enhanced bilateral prefrontal activity that was associated with reduced performance, suggesting that stimulation reduced prefrontal hyperactivity.

In a cross-over trial, [Harty et al \(2014\)](#) performed tDCS in the following paradigms: anodal over right DLPFC, anodal over left DLPFC, cathodal over right DLPFC, and a repeat of anodal over right DLPFC. There were 24 healthy elderly in each experiment and a sham experiment served as the control. The task was an error awareness task, and the stimulation was applied during the task at 1mA. There were no changes in accuracy for any group. However, those in the anodal left DLPFC group were more aware of mistakes that they made during the stimulation procedure. (50% vs. 60%).

Alzheimer's patients

Individual studies

Single Sessions

In a cross-over trial, [Ferrucci et al \(2008\)](#) performed 15 minutes of 1.5mA tDCS (anodal, cathodal, or sham) bilaterally over the temporal cortex in 10 patients with probable mild Alzheimer's disease and tested them for word recognition accuracy and visual attention 30 minutes later. Anodal tDCS improved word recognition accuracy (15/24 words compared to 18/24 words) while cathodal tDCS worsened it (16/24 words vs 13/24 words – interaction between groups significant). There was no difference in sham tDCS. There were no changes in a visual attention task. A follow-up analysis found that anodal tDCS increased high-frequency and low-frequency EEG coherence (indicative of better EEG signals) suggesting a possible mechanism for the beneficial effect of anodal tDCS on memory in Alzheimer's patients ([Marceglia et al, 2016](#)).

In a cross-over trial, [Boggio et al \(2009\)](#) performed 30 minutes of 2mA anodal tDCS over the left DLPFC, left temporal cortex, or sham in 10 patients with mild to moderate Alzheimer's disease and simultaneously conducted several cognitive tests (Stroop, digit span, and visual recognition memory). Patients had ~15% improvement in both tDCS conditions compared to sham on the visual recognition

memory test. There was no significant improvement in either other test and no difference based on Alzheimer's severity.

In a cross-over trial, [Meinzer et al \(2015\)](#) performed 20 minutes of 1mA anodal tDCS over the left inferior frontal cortex during a semantic word task. When stimulated, MCI patients (n=18) made fewer errors than when unstimulated (8/60 vs. 11/60) and performed as well as healthy age-matched controls. fMRI studies showed that stimulation reduced task-related prefrontal hyperactivity.

Multiple tDCS Sessions and Long-Term Measures

In a cross-over trial, [Boggio et al \(2012\)](#) performed 30 minutes of 2mA anodal tDCS bilaterally over the temporal cortex over 5 days in 15 patients with mild to moderate Alzheimer's disease. Participants underwent a battery of cognitive tasks (MMSE, ADAS-co, visual recognition memory (VRT), visual attention task (VAT)) after the last stimulation, 1 week later, and 1 month later (not clear how much of a washout time between active treatment and sham). There was a significant improvement in VRT compared to sham (by 9%) that persisted for 1 month (11% improvement). No changes on other cognitive measures.

In a parallel designed trial, [Cotelli et al \(2014\)](#) split 36 patients with mild to moderate Alzheimer's disease into three groups 1) anodal tDCS over the left DLPFC + computerized memory training, 2) sham stimulation + computerized memory training, or 3) anodal tDCS over the left DLPFC + computerized *motor* training. The procedure was 5 days/week for 2 weeks for 25 minutes at 2mA. Participants were tested with a battery of cognitive tasks at 2 weeks post-treatment, 3 months post-treatment, and 6 months post-treatment. The two memory training groups (sham and stimulation) improved in a face-name association task (episodic memory) compared to motor training at 2 weeks and 3 months, but not 6 months (questioning the benefits of the stimulation itself). There were no changes in a battery of other tasks including MMSE, activities of daily living, language tasks, and other memory tasks.

In a parallel designed trial, [Khedr et al \(2014\)](#) performed anodal tDCS, cathodal tDCS, or sham over the left DLPFC for 25 minutes at 2mA for 10 days in 34 mild to moderate Alzheimer's patients. They were given the MMSE and an IQ test (Wechsler adult intelligence scale). MMSE scores for both tDCS groups improved over sham groups by ~2 points after the stimulation period and ~5-6 points both 1- and 2-months post-stimulation. No significant improvement for total IQ scores.

In a cross-over trial, [Roncero et al \(2017\)](#) performed anodal tDCS or sham for 30 minutes over the left inferior parieto-temporal regions at 2mA over 10 sessions while training on a picture naming task in 10

patients with anomic aphasia (difficulty in word finding) Alzheimer's disease or frontotemporal dementia. After stimulation, patients performed better than sham on the picture naming task (40% vs. 19%), an effect that lasted 2 weeks. Two weeks after stimulation, patients also performed better on an untrained digit span task.

In a parallel designed trial, [Bystand et al \(2016\)](#) performed anodal tDCS or sham over the left temporal cortex at 2mA for 30 minutes over 6 days. The reported no differences in the California Verbal Learning Test, MMSE, clock drawing test, trail making tests A and B, or an IQ test.

In a parallel designed trial, [Andre et al \(2016\)](#) performed anodal tDCS or sham over the left DLPFC in four 20-minute sessions at 2mA in patients with mild vascular dementia. Both groups showed 3-4-point improvements in ADAS-cog scores (but no difference between groups). The tDCS group improved compared to sham in a visual short-term memory task. In a task of verbal working memory, there was no improvement in performance in either group, but the stimulation group improved in reaction time compared to baseline. In an executive function task, both groups improved compared to baseline, but only the stimulation group improved in reaction time.

Long-term treatment

One case study ([Bystand et al, 2017](#)) reported treatment of a patient who developed early-onset (not familial) Alzheimer's disease at 56. At 60 he began 2mA tDCS over the left temporal lobe daily for 30 minutes over 8 months using a consumer device, "The Brain Stimulator tDCS device." He had reported improvements in immediate recall, delayed recall, and others.

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