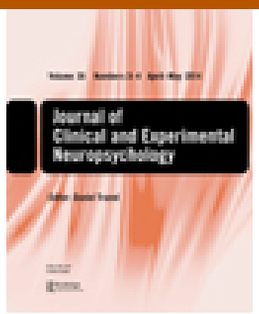

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Improved conceptual generation and selection with transcranial direct current stimulation in older adults

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ABSTRACT

Introduction: Normal aging is associated with deficits in various aspects of spoken language production, including idea generation and selection, and involves activity in frontal brain areas including left inferior frontal cortex (LIFG). These conceptual preparation processes, largely involving executive control, precede formulation and articulation stages and are critical for language production. Noninvasive brain stimulation (e.g., transcranial direct current stimulation, tDCS) has proven beneficial for age-related fluency and naming deficits, but this has not been extended to conceptual preparation mechanisms. **Method**: We investigated whether tDCS could facilitate idea generation and selection in 24 older adults aged 60–80 years. In the first phase, participants completed an idea generation test and a selection test with no stimulation. In the second phase they completed an alternate version of the tests in conjunction with either active or sham stimulation. Active stimulation applied 1-mA anodal tDCS over LIFG for the test duration (10 min). **Results**: Responses were faster following active stimulation than following sham. Furthermore, improvements were specific to test conditions involving novel generation (p = .030) and selection (p = .001) and were not observed in control conditions for which these mechanisms were minimally involved. **Conclusions**: We concluded that tDCS benefits conceptual preparation mechanisms. This preliminary evidence is an important step for addressing age-related decline in propositional language generation, which is integral to conversational speech. This approach could also be extended toward rehabilitation in neurological patients with deficits in these processes.

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Normal aging; conceptual preparation; idea generation; selection; transcranial direct current stimulation

Theoretical models of language production typically propose an initial prelinguistic stage of conceptual preparation, or conceptualizing the basic ideas to be expressed in a message, prior to the linguistic formulation and articulation stages of production (Frederiksen, Bracewell, Breuleux, & Renaud, 1990; Harley, 2014; Levelt, 1999; Sherratt, 2007). While this initial prelinguistic stage has received less focus in aging and language research, deficits in early conceptual preparation processes may contribute to age-related language production impairments (Madden, Sale, & Robinson, 2018). In addition to essential nominal language skills, neuropsychological lesion studies demonstrate that language production also requires higher order conceptual preparation processes including novel idea generation and selection of ideas for language (Crescentini, Lunardelli, Mussoni, Zadini, & Shallice, 2008; Robinson, 2013; Robinson, Blair, & Cipolotti, 1998; Robinson, Shallice, & Cipolotti, 2005). Our recent findings also show that older adults have specific deficits in these conceptual generation and selection processes when compared to younger adults (Madden et al., 2018). It was suggested that these deficits could be linked with age-related neural changes predominantly in frontal brain regions, as well as associated changes in functional language networks, which could be modulated using noninvasive brain stimulation. In this present study we investigated the potential for improving language production in older age by targeting these two conceptual preparation mechanisms using transcranial direct current stimulation (tDCS).

Aging is associated with a decline in several aspects of language production. These have been linked to the linguistic formulation and articulation stages of speech production, including word-finding deficits (Burke & Shafto, 2008; Connor, Spiro, Obler, & Albert, 2004; MacKay, Connor, Albert, & Obler, 2002), increases in dysfluencies (Bortfeld, Leon, Bloom, Schober, &

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Brennan, 2001; Cooper, 1990; Kemper, 1992), and increased frequency of phonological omissions and other speech errors (MacKay & James, 2004). However, some aspects of language decline may involve deficits in earlier, higher order processes that precede formulation and articulation. For instance, older adults produce an even higher rate of dysfluencies than younger adults when discussing a difficult or less familiar topic (Bortfeld et al., 2001). This has been thought to reflect an age-related deficit in constructing language at a conceptual level (Mortensen, Meyer, & Humphreys, 2006), preceding linguistic formulation. Older adults in their mid-70s also show a rapid decline in the rate of connected speech produced on complex picture description tasks (Ardila & Rosselli, 1996; Kemper & Sumner, 2001; Kemper, Thompson, & Marquis, 2001; Soares et al., 2015), with markedly reduced grammatical complexity and propositional density compared to younger adults (Kemper & Sumner, 2001). Likewise, these connected speech deficits are thought to reflect a decline in underlying executive processes that precede later verbal stages in the production process (Cannizzaro & Coelho, 2013). Levelt's model of language production (Levelt, 1989, 1999) suggests that conceptual preparation requires executive control in conceptualizing the preverbal message, but provides little insight into the specific mechanisms involved. A better understanding of these mechanisms has evolved by observing their breakdown in an acquired language disorder known as frontal dynamic aphasia.

Frontal dynamic aphasia is characterized by a severe reduction in spontaneously generated connected speech, despite core language skills such as comprehension, reading, naming, and repetition remaining predominantly intact (Luria, 1970; Luria & Hutton, 1977). As the locus of this production impairment precedes linguistic formulation and articulation stages, the specific deficits observed in frontal dynamic aphasia have provided insight into the mechanisms of conceptual preparation. These deficits include *selection from amongst competing conceptual propositions* (Robinson et al., 1998, 2005), the *generation of novel ideas or thoughts* (Robinson, 2013), and the *fluent sequencing of novel thoughts* (Robinson, Shallice, & Cipolotti, 2006). Each of these three deficits is thought to reflect a mechanism of conceptual preparation. If spoken language is reduced in situations of contextual conflict, for instance, this is thought to indicate a failure in a mechanism for *selecting* and producing a single response from multiple competing ideas (Robinson et al., 1998, 2005). An apparent paucity of ideas to express in spontaneous language is thought to indicate a deficit in a mechanism for *generating* novel conceptual thoughts (Robinson, 2013). An impaired ability to subsequently shift attention from one generated conceptual message to the next is thought to demonstrate an impaired mechanism for *fluent sequencing* of novel thoughts, to allow expression of multiple connected ideas (Robinson et al., 2006). Although these deficits do not all co-occur within each subtype of dynamic aphasia, concurrent deficits in selection, generation, and fluent sequencing have been observed in a case with multiple pathologies (Robinson, 2013). Robinson (2013) concluded that these three mechanisms are all critical for the conceptual preparation of language production, which is a preverbal stage of language that intersects with executive functions.

Age-related deficits in conceptual preparation mechanisms may contribute to language decline in older age. The decreased novel propositional content in older adults' connected speech (Kemper & Sumner, 2001; Soares et al., 2015) is consistent with an age-related deficit in idea generation. Older adults also have decreased word fluency (Ardila & Rosselli, 1989; Clark et al., 2009), which has been used in dynamic aphasia as a measure of voluntary verbal generation of multiple concepts from a single cue (Robinson, 2013; Robinson, Spooner, & Harrison, 2015). More specifically, recent findings demonstrate that older adults are impaired compared to younger adults both on a measure of idea generation and on a measure of conceptual selection (Madden et al., 2018). Older adults were shown to have a specific idea generation deficit in a task that required generation of concepts to complete partial sentences. In the selection test, participants were required to select a single component from arrays of colored shape stimuli, each with a varying number of competing response options. Older adults showed increasingly impaired response latencies with increasing selection demands, indicating an age-related deficit in conceptual selection. As these measures have already demonstrated conceptual preparation deficits in older adults, the same two tests were used in the current study to measure idea generation and selection across phases of a noninvasive brain stimulation paradigm.

Conceptual preparation mechanisms are thought to have specialized neurological substrates, as evidenced by neuroimaging studies and localized lesions observed in dynamic aphasia (e.g., Robinson et al., 1998, 2005). Impaired generation of novel ideas, and selection of these ideas, has been linked to left inferior frontal gyrus (LIFG) or frontostriatal damage in dynamic aphasia (Robinson, 2013) and dorsomedial frontal regions in neurological patients with focal frontal lesions (Robinson et al., 2012). Imaging evidence has likewise

implicated the left frontal area in verbal generation. For example, the LIFG specifically has been linked to word fluency tasks (Costafreda et al., 2006; Katzev, Tüscher, Hennig, Weiller, & Kaller, 2013), creative idea generation with increasing LIFG activity thought indicative of greater idea novelty and creativity (Benedek et al., 2014), and conceptual proposition selection (Moss et al., 2005; Zhang, Feng, Fox, Gao, & Tan, 2004). Conceptual preparation deficits in older adults may therefore result from age-related changes involving the same region (Madden et al., 2018).

Various behavioral deficits have been attributed to age-related changes in other language production regions (Marsolais, Perlbarg, Benali, & Joanette, 2014; Motes, Biswal, & Rypma, 2011; Stamatakis, Shafto, Williams, Tam, & Tyler, 2011; Tisserand & Jolles, 2003). For example, word-finding failures in older age are associated with reduced gray matter density in the left insula (Shafto, Burke, Stamatakis, Tam, & Tyler, 2007). Cognitive decline can be linked to various such structural changes in cortical volume, neuronal morphology, and cerebral microvasculature, as well as hormonal and neurochemical variations (Peters, 2006). The greatest reduction in cortical volume is in the frontal cortex after the age of 70 (Peters, 2006; Scahill et al., 2003), which corresponds to a rapid decline in propositional language abilities (Kemper & Sumner, 2001; Soares et al., 2015).

Neurophysiological changes in healthy aging may lead to changes in brain activity within localized regions, such as the LIFG, as well as in functionally connected networks involved in language production processes. While some tasks typically involve lateralized activity in younger brains, such as language production in the left frontal region, this lateralization is reduced in favor of a more distributed pattern of neural activity in older age (Cabeza, 2002; Grady, 2012; Gutchess, 2014). Some changes in activation may represent functional reorganization (Cabeza, 2002; Eyler, Sherzai, Kaup, & Jeste, 2011); however, reduced lateralization and overactivation has been linked to corresponding reductions in behavioral performance (Colcombe, Kramer, Erickson, & Scalf, 2005; Duverne, Motamedinia, & Rugg, 2009; Spreng, Wojtowicz, & Grady, 2010) and is thought to reflect dysfunctional dedifferentiation of neural activity and inefficient over-recruitment of contralateral areas (Li & Lindenberger, 1999; Li, Lindenberger, & Sikstrom, 2001; Rajah & D'Esposito, 2005).

For language production specifically, reduced lateralization of functional connectivity in older adults is associated with reduced behavioral performance. While connections between language areas within the left hemisphere are beneficial and resemble connectivity patterns in younger adults, connections between the left and right hemisphere in the aging brain are thought to impair language production (for a review see Antonenko & Flöel, 2014). This is therefore also likely to be the case for conceptual preparation mechanisms. For example, Meinzer et al. (2009) compared functional magnetic resonance imaging (fMRI) activation patterns in young and old adults in conjunction with behavioral performance in semantic and phonemic fluency tasks. These tasks are thought to tap verbal idea generation (e.g., Robinson et al., 2012) and have been used as a measure of voluntary verbal generation in dynamic aphasia (Robinson, 2013; Robinson et al., 2015) and in healthy older adults (Madden et al., 2018). Meinzer and colleagues (2009) found that both age groups showed similar phonemic fluency, with similar left lateralized frontal activation patterns. By contrast, older adults were impaired on semantic fluency, and only the younger group showed activation lateralized in the left frontal region. Decreased semantic fluency in older adults was characterized by additional right frontal activity. Reduced lateralization of function in older age might therefore also apply to other measures of verbal generation, and extend to other conceptual preparation mechanisms such as conceptual selection. Conceptual preparation in older adults may depend on efficient recruitment of the LIFG, rather than a more bilateral pattern of frontal activity. This would be consistent with the neural correlates of poststroke language recovery. While increased bilateral activation may be partially compensatory during the subacute phase (Saur et al., 2006), optimal long-term recovery is associated with redistribution of activation lateralized toward dominant left language areas in the chronic recovery phase (Saur et al., 2006; Szaflarski, Allendorfer, Banks, Vannest, & Holland, 2013). An increase in lateralized LIFG activity in healthy older adults might be facilitated using noninvasive brain stimulation.

Noninvasive brain stimulation has shown promise in improving a variety of cognitive and motor skills in older adults (Tatti, Rossi, Innocenti, Rossi, & Santarnecchi, 2016). tDCS involves the application of a weak electrical current (0.5–2 mA) via a pair of electrodes (anode and cathode) positioned on the scalp to modulate cortical excitability (Schlaug, Renga, & Nair, 2008). Anodal tDCS (a-tDCS) and cathodal tDCS have been associated with increases and decreases in cortical excitability, respectively. Stimulation typically increases cortical excitability under the anode through depolarization of resting membrane potentials, and decreases excitability

through hyperpolarization of membranes under the cathode. Longer lasting changes in cortical excitability following stimulation are thought to involve postsynaptic processes similar to long-term potentiation and depression (Stagg & Nitsche, 2011).

tDCS can be applied to improve behavioral performance in the language domain, including acute benefits for word fluency (Cattaneo, Pisoni, & Papagno, 2011; Iyer et al., 2005) and naming (Fertonani, Rosini, Cotelli, Rossini, & Miniussi, 2010; Sparing, Dafotakis, Meister, Thirugnanasambandam, & Fink, 2008) in young adults, as well as picture naming (Fertonani, Brambilla, Cotelli, & Miniussi, 2014; Holland et al., 2011), face naming (Ross, McCoy, Coslett, Olson, & Wolk, 2011), and semantic word generation (Meinzer, Lindenberg, Antonenko, Flaisch, & Flöel, 2013) in healthy older adults. Meinzer et al. (2013) presented converging behavioral and functional-imaging-based evidence indicating that a single session of a-tDCS to the LIFG can temporarily improve cognition and functional connectivity in elderly adults in relation to a semantic word generation task. tDCS improved behavioral performance to the level of young control participants and reduced task-related bilateral frontal hyperactivity that was associated with decreased performance in older adults. Task-absent resting-state fMRI also showed that a-tDCS partially reversed frontotemporal hyperconnectivity and posterior network hypoconnectivity in older adults, thus restoring a pattern of functional network connectivity observed in young controls. A single stimulation session can therefore temporarily reverse age-related changes in neural activity and connectivity to produce behavioral performance benefits in the language domain. As reduced lateralization and increased bilateral hyperactivity are also likely to underlie conceptual preparation deficits in older age, a similar stimulation protocol was used in the current study to investigate whether tDCS can produce immediate behavioral benefits for idea generation and selection in healthy older adults.

Meinzer et al. (2013) used task-concurrent stimulation in their tDCS protocol. For motor tasks, stimulation is typically more effective when administered during the task (online) rather than before (offline), for both healthy young adults (e.g., Stagg et al., 2011) and healthy older adults (e.g., Cabral et al., 2015; see Summers, Kang, & Cauraugh, 2016, for a review). However, this effect of stimulation timing appears to differ across task types in older adults. In a recent meta-analysis of noninvasive brain stimulation effects in healthy aging, Hsu, Ku, Zanto, and Gazzaley (2015) found that across a range of cognitive tasks, there was a larger effect size when stimulation was administered before rather than during the task. However, this analysis pooled participants from studies using both tDCS and transcranial magnetic stimulation (TMS), which may operate differently in older adults (Heise et al., 2014). The majority of the studies in the meta-analysis also focused on memory and other cognitive skills outside the language domain. Within language, stimulation during the performance task has been a successful approach in older adults (e.g., Meinzer et al., 2013). For example, Fertonani et al. (2014) found that while both online and offline stimulation were beneficial for picture naming response times in young adults, older adults only benefited from stimulation when it was administered during the task execution. There is evidence for context-dependent modulation of neural networks with tDCS across various domains. Specificity and effectiveness can be improved by combining stimulation with task-relevant cortical activity to preferentially activate the targeted networks and improve behavioral outcomes (see Sale, Mattingley, Zalesky, & Cocchi, 2015, for a review). Stimulation was therefore applied during the generation and selection tests in the current tDCS protocol. As the left inferior frontal region has been implicated in these mechanisms (Benedek et al., 2014; Moss et al., 2005; Robinson, 2013; Robinson et al., 1998, 2005; Zhang et al., 2004), the LIFG was targeted under the anode.

The current study investigated effects of tDCS applied concurrently with idea generation and selection tests in older adults. Participants completed an idea generation test and a selection test (Madden et al., 2018) with no stimulation in the first phase. In the second phase, participants completed an alternate version of the tests in conjunction with either active stimulation or a sham protocol (Gandiga, Hummel, & Cohen, 2006). It was expected that response latencies would be reduced with active stimulation compared to sham, for test conditions that require novel generation and selection abilities. Hypotheses were based on impairments previously demonstrated in older adults compared to younger adults on these tasks (Madden et al., 2018). In the selection test, older adults were significantly impaired compared to younger adults in the high selection condition (Madden et al., 2018). Older adults were also slower than young adults in the low selection condition, but the effect size was smaller. There was no age difference in the no selection control condition. It was therefore predicted in the current study that active stimulation would significantly improve response times compared to sham stimulation in the high selection condition. As older adults only show a mild impairment when a low level of selection is required, only a small benefit of active

stimulation was predicted compared to sham stimulation for the low selection condition. No benefit of active stimulation was expected over sham stimulation in the control condition. This would demonstrate that tDCS in older adults can produce specific benefits for conceptual selection.

In the generation test, older adults were slower than younger adults when novel generation was required, but not when minimal novel generation was required in the control condition (Madden et al., 2018). It was therefore predicted in the current study that active stimulation would significantly reduce response latencies compared to sham stimulation for the single and multiple generation conditions, but not in the control condition. This would demonstrate a specific benefit of active stimulation for idea generation.

Method

Participants

A total of 24 healthy participants aged 60–80 years were randomly assigned to either an active or a sham stimulation group. Each stimulation group consisted of six males and five females. The active group had a mean age of 70.73 years (*SD* = 7.00), and the sham group had a mean age of 70.09 years (*SD* = 6.17). All participants reported English as their first language and the only language they spoke on a regular basis.

Procedure

Each experiment consisted of two testing phases (Phase 1 and Phase 2). In Phase 1, all participants completed the generation test and the selection test with *no stimulation*. Each participant then completed an alternate version of the tests in Phase 2 in conjunction with either sham or active stimulation, depending on their assigned condition. The stimulation paradigm applied a 1-mA current between the anode and the cathode (in accordance with Meinzer et al., 2013), both of which were 5 × 7 cm^2 in size. The anode was placed over the LIFG, between FT7 and FC5 positions of the 10–10 electroencephalography (EEG) system. The reference electrode was located over the right supraorbital region. The current was ramped up over 10 s, constant for a period of either 15 s (sham group) or 15 min (active group), then ramped down over 10 s. The stimulation period in the active group briefly outlasted the task duration. The order of alternate test versions was counterbalanced across test phases in each stimulation condition, and the change in test performance within participants was compared across sham and active stimulation groups for each test condition.

Materials

Selection test

The selection test has been used previously to investigate age-related differences in conceptual selection (Madden et al., 2018). Participants were presented with 36 arrays of colored shape stimuli on a screen and were asked to verbally identify a component of each array as quickly as possible (i.e., the *color*, *shape*, or *number* of shapes depicted). The level of selection required was varied across conditions by varying the number of competing response options as shown in Figure 1.

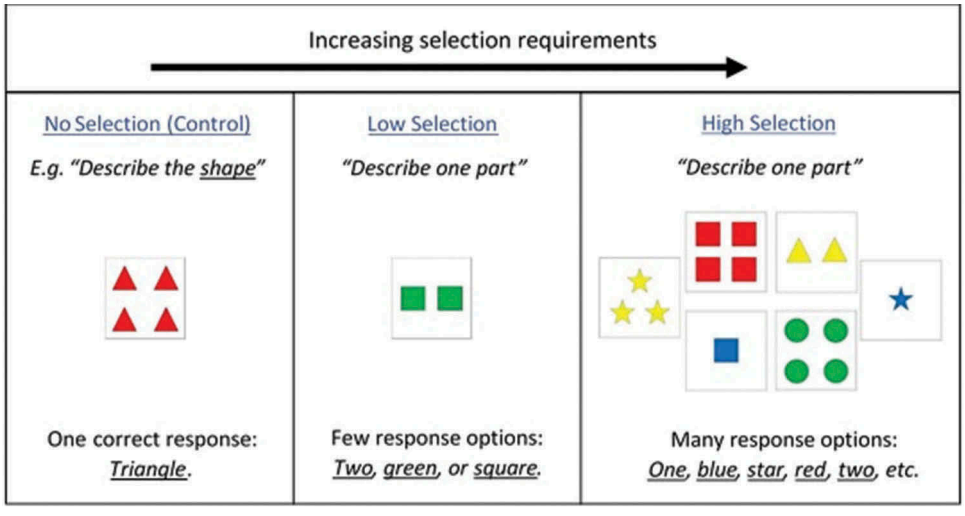

Figure 1. Selection test: example stimuli, instructions, and responses for selection conditions. To view a color version of this figure, please see the online issue of the Journal.

The high selection condition required participants to select any one aspect from a vast array of competing response options. By contrast, the low selection condition presented only a limited number of response options. The control condition required no selection, as participants were told which component to name. These test conditions were presented in a pseudorandom order, and response latency was used as the performance measure. An audio recording was used to calculate response latency from the onset of stimulus presentation until the end of the response was produced. The percentage of correct responses was also compared across conditions to ensure that there was no speed–accuracy trade-off that could undermine interpretation of the results. Incorrect responses and items not answered within 10 seconds were counted as errors in the error analysis.

Generation test

The generation test has been used previously to investigate age-related differences in idea generation (Madden et al., 2018). This test presented a series of 24 sentences with various words missing. Participants were required to read each sentence aloud, generating a single concept to fill each gap as quickly as possible as they read, in order to complete the sentence. The degree of novel generation required was varied across three conditions, as shown in Figure 2.

The multiple generation condition included sentences with several gaps throughout, for example, *The ___ threw the ___*. Participants were therefore required to generate multiple novel concepts to create a meaningful sentence. The single generation condition presented sentences with only a single word missing at the end—for example, *They went to see the famous ____*. As with multiple generation, in the single generation condition there was minimal restriction on the concepts that could be generated to meaningfully complete the sentence. Participants were therefore required to generate a novel, relevant idea that would determine the message expressed by the sentence. By contrast, meaningful completion of sentences in the control condition was limited to one or two dominant responses that were somewhat predictable and constrained based on the provided portion of the sentence—for example, *Father carved the turkey with a ____*. This meant that the sentence was a cue for semantic retrieval of the correct ending, and minimal novel idea generation was required. Response latency was used as the performance measure. Incorrect responses and items not answered within 10 seconds were scored as errors and were included in the error analysis. The percentage of correct responses was compared over test conditions and across stimulation groups to ensure that there was no speed–accuracy trade-off in the active stimulation condition that could undermine interpretation of the response latency analyses.

Statistical analyses

Response time data were screened against analysis of variance (ANOVA) assumptions, and a ±2.5-standard-deviation threshold was used to identify extreme scores from studentized residuals. There were no significant outliers in the selection test data, the Shapiro–Wilks test revealed no significant deviation from normality ($p > .05$), and Levene's test demonstrated homogeneity of variances across conditions ($p > .05$). A three-way ANOVA was conducted. One participant from each group was excluded from the analysis because there were data missing for these tests, due to an error with the audio recording. Though Mauchly's test showed no significant sphericity violation ($p > .05$), Greenhouse–Geisser epsilon adjustments were used, and actual degrees of freedom were reported.

Selection test error data violated a number of ANOVA assumptions. A reciprocal transformation improved normality, homogeneity of variances, and sphericity, but the results of the analysis did not change as a result of the transformation. The three-way mixed

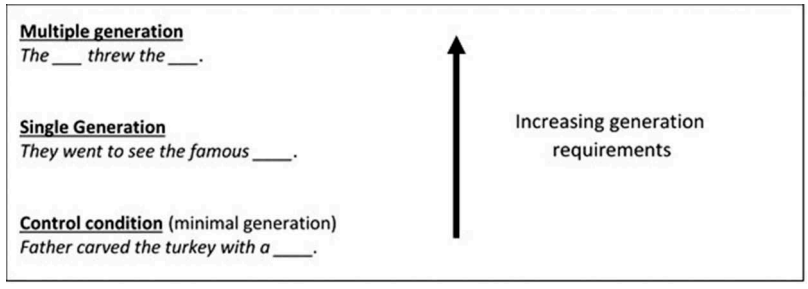

Figure 2. Generation test: example items for each generation condition.

ANOVA with the untransformed data is therefore reported.

The generation test response time data showed two outliers only just above the adopted threshold, with the most extreme at 2.57 standard deviations. There were only minor deviations from normality, but Levene's test indicated a slight inequality of error variances (p = .042). Following a square-root transformation, Levene's test demonstrated homogeneity of variances across conditions (p > .05). There were no longer significant outliers in the dataset; the Shapiro–Wilks test demonstrated normality in all conditions (p > .05). However, as there were no material changes to the results of the analysis with the transformation, a three-way mixed ANOVA with the untransformed data was reported. Although Mauchly's test showed no significant sphericity violation (p > .05), Greenhouse–Geisser epsilon adjustments were used, and actual degrees of freedom were reported.

A reciprocal transformation was conducted on the generation test error data to improve normality and homogeneity of variances, but Levene's test was still significant for many of the conditions (p < .05). Greenhouse–Geisser epsilon adjustments were used to account for the sphericity violation, and actual degrees of freedom were reported. A three-way ANOVA was conducted using transformed data, and scores are reported in reciprocal units.

An independent groups t test was used to compare the number of years of education for active and sham stimulation groups. Bivariate correlations were then calculated for each stimulation group to assess the association between the number of years of education and response times on each test. Correlations were also calculated for each group between education and the change in test performance across test phases, quantified as the difference in response times from Phase 1 to Phase 2.

Results

Selection test

Response time analysis

Response latencies were reduced by active stimulation compared to sham, and this was only the case when selection demands were high. This was evident from the differential effects of stimulation in the different selection conditions, $F(2, 40) = 8.05$, p = .001, η_p^2 = .29, ε = .97. In the control condition, there was no benefit of active stimulation. There was no change overall from Phase 1 to Phase 2, $F(1, 20) = 0.19$, p = .667, η_p^2 = .01, and this lack of effect was the same for both the active and sham groups, $F(1, 20) = 0.28$, p = .601, η_p^2 = .01.

In the easy selection condition, there was an apparent benefit of active stimulation, but this was no better than the reduction in response times seen with sham. There was an overall decrease in response latencies from Phase 1 (M = 1.49, SD = 0.20) to Phase 2 (M = 1.35, SD = 0.21), $F(1, 20) = 19.36$, p < .001, η_p^2 = .49, but a similar decrease was observed for both active and sham stimulation, $F(1, 20) = 0.80$, p = .382, η_p^2 = .04.

In the hard selection condition, there was a significant benefit of active stimulation over sham. There was a decrease in response latencies from Phase 1 to Phase 2 for both active (Phase 1: M = 1.83, SD = 0.39; Phase 2: M = 1.35, SD = 0.22), $F(1, 10) = 43.17$, p < .001, and sham stimulation (Phase 1: M = 1.85, SD = 0.25; Phase 2: M = 1.68, SD = 0.26), $F(1, 10) = 9.98$, p = .010, but the decrease in response latencies from Phase 1 to Phase 2 was significantly greater for active stimulation than for sham, $F(1, 20) = 11.74$, p = .003, η_p^2 = .37. These effects are depicted with cell means in Figure 3. For ease of visual comparison, the comparative effects of sham and active stimulation are then depicted as percentage change from Phase 1 in Figure 4.

Error analysis

There was no benefit or detriment of active stimulation compared to sham in terms of response accuracy. There was a similar percentage of correct responses in the active group (97%) and the sham group (90%), $F(1, 19) = 4.40$, p = .050, η_p^2 = .19, and this was the case across both test phases, $F(1, 19) = 2.10$, p = .164, η_p^2 = .10.

Response accuracy did not improve overall from Phase 1 to the Phase 2 phase, $F(1, 19) = 3.79$, p = .066, η_p^2 = .17, indicating that there was no overall practice or placebo effect. The percentage of correct responses varied with selection demands, $F(2, 38) = 5.27$, p = .010, η_p^2 = .22. While there was no significant difference between the control condition (97%) and easy selection (94%; p = .079), or between easy and hard selection (90%; p = .052), there were more errors in hard selection than in the control condition (p = .021). This indicates that there were more errors overall in the hard selection condition; however, this was equally the case for both active and sham groups, $F(2, 38) = 2.48$, p = .097, η_p^2 = .12. Errors were also similarly higher in the hard selection condition even before stimulation was applied, $F(2, 38) = 0.42$, p = .663, η_p^2 = .02, and this was true for both stimulation groups, $F(2, 38) = 1.24$, p = .302, η_p^2 = .06, ε = .70.

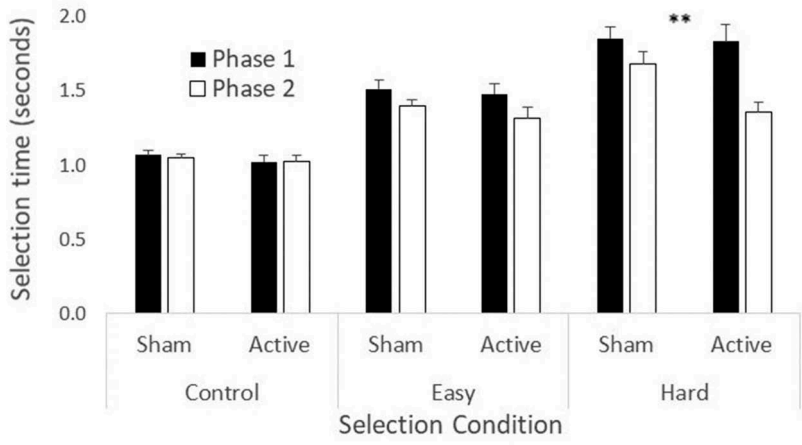

Figure 3. Selection test: Phase 1 and Phase 2 response latencies for each selection condition for the sham group and the active stimulation group (error bars represent standard error of the mean).

**$p < .01$.

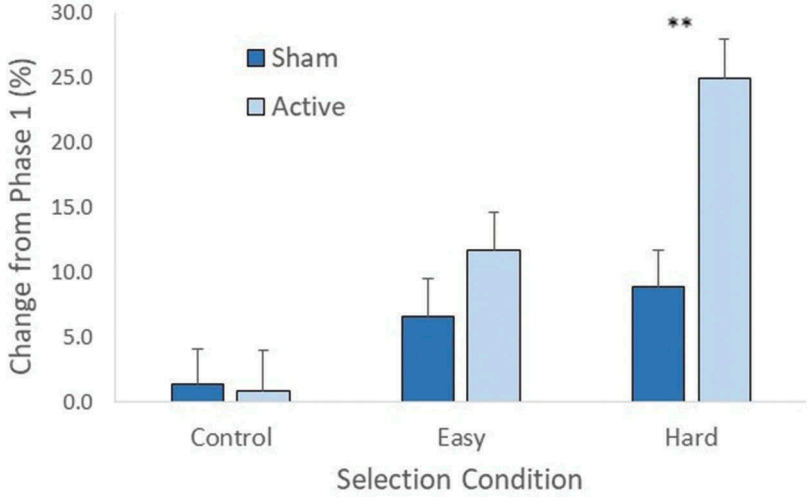

Figure 4. Selection test: change in response latencies from Phase 1 to Phase 2, expressed as a percentage of Phase 1 scores for each stimulation group and each selection condition (error bars represent standard error of the mean).

**$p < .01$.

Generation test

Response time analysis

There was a significant reduction in response latencies with active stimulation compared to sham, but only when generation demands were high. This was apparent from the differential effects of stimulation in the different generation conditions, $F(3, 57) = 3.87$, $p = .030$, $\eta_p^2 = .17$, $\varepsilon = .88$. In the control condition, there was no benefit of active stimulation. There was no effect of test phase when averaging over stimulation groups, $F(1, 19) = 2.30$, $p = .146$, $\eta_p^2 = .11$, and this did not differ across active and sham groups, $F(1, 19) = 0.13$, $p = .720$, $\eta_p^2 = .01$.

There was also no significant benefit of active stimulation in the single generation condition. There was no overall effect of test phase when averaging over stimulation groups, $F(1, 19) < 0.01$, $p = .995$, $\eta_p^2 < .01$. Response latencies from Phase 1 to Phase 2 trended in opposite directions for active (Phase 1: $M = 4.07$, $SD = 0.76$; Phase 2: $M = 3.79$, $SD = 0.74$) and sham groups (Phase 1: $M = 4.64$, $SD = 0.59$; Phase 2: $M = 4.91$, $SD = 1.07$), but these effects did not significantly differ, $F(1, 19) = 2.55$, $p = .127$, $\eta_p^2 = .12$.

There was a significant benefit of active stimulation over sham in the multiple generation condition. This was evident from the differential effect of test phase across stimulation groups, $F(1, 19) = 7.84$, $p = .011$,

η_p^2 = .29. There was a decrease in response latencies with active stimulation (Phase 1: M = 6.19, SD = 0.73; Phase 2: M = 5.36, SD = 0.91), $F(1, 10)$ = 12.05, p = .006, η_p^2 = .55, but not with sham, $F(1, 9)$ = 1.55, p = .245, η_p^2 = .15. These effects are depicted with cell means in Figure 5. For ease of visual comparison, the comparative effects of sham and active stimulation are then depicted as percentage change from Phase 1 in Figure 6.

Error analysis

There was no improvement or decline in response accuracy for active stimulation compared to sham. There was no difference in error rate overall across stimulation groups, $F(1, 19)$ = 0.50, p = .489, η_p^2 = .03. Participants made fewer errors in the Phase 2 (.011) than in the Phase 1 (.014), $F(1, 19)$ = 4.81, p = .041, η_p^2 = .20, but this was equally true for both active and sham groups, $F(1, 19)$ = 0.76, p = .395, η_p^2 = .04, and similar across generation conditions, $F(2, 38)$ = 0.20, p = .147, η_p^2 = .10, indicating a general practice effect.

The error rate varied across generation conditions, $F(2, 38)$ = 4.20, p = .023, η_p^2 = .18. There was no significant difference between the control condition (.010) and single generation (.012; p = .152), or between single and multiple generation (.014; p = .376), but there were more errors in multiple generation than in the control condition (p < .001). While there were more errors overall in the multiple generation condition, this was equally true for

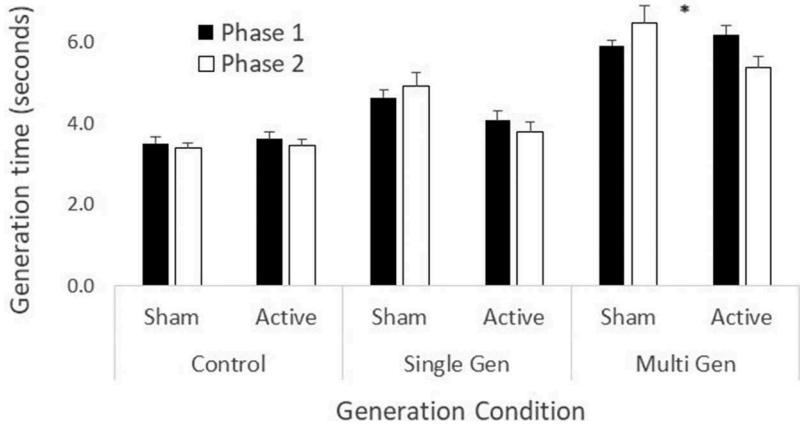

Figure 5. Generation test: Phase 1 and Phase 2 response latencies for each generation condition for the sham group and the active stimulation group (error bars represent standard error of the mean).

*p < .05.

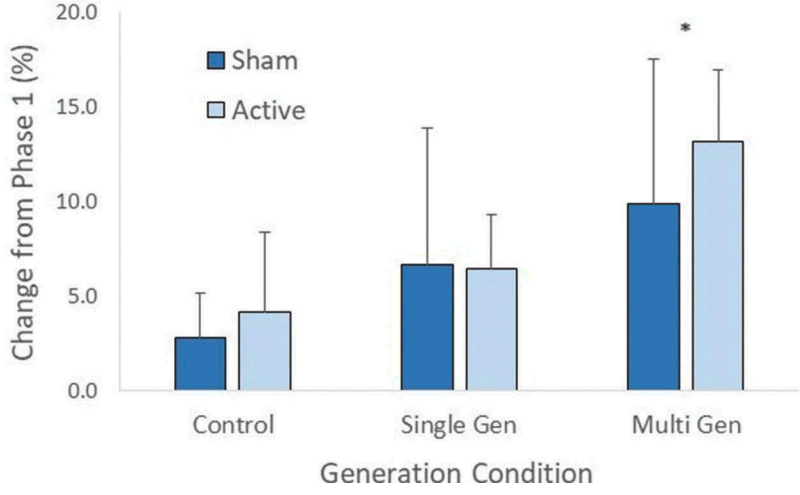

Figure 6. Generation test: change in response latencies from Phase 1 to Phase 2, expressed as a percentage of Phase 1 scores for each stimulation group and each generation condition (error bars represent standard error of the mean).

*p < .05.

both active and sham groups, $F(2, 38) = 1.45$, $p = .248$, $\eta_p^2 = .07$, and this did not change from Phase 1 to Phase 2, $F(2, 38) = 0.77$, $p = .468$, $\eta_p^2 = .04$.

Education

The number of years of education was matched across sham ($M = 14.86$, $SD = 3.86$) and active ($M = 14.90$, $SD = 3.00$) stimulation groups, $t(19) = -0.02$, $p = .981$. Education was not correlated with response times on any task condition ($p > .05$). However, education was positively correlated with difference scores on the single generation task for both sham ($r = .73$, $p = .017$) and active ($r = .67$, $p = .033$) groups. This meant that in both sham and active stimulation conditions, participants with more education showed greater improvement from Phase 1 to Phase 2 in the single generation task. Education was not correlated with difference scores in any other condition ($p > .05$).

Discussion

Older adults have specific deficits compared to younger adults in idea generation and selection (Madden et al., 2018), both of which are considered to be crucial mechanisms of conceptual preparation for language production (Robinson, 2013; Robinson et al., 2015). We investigated whether tDCS could improve idea generation and selection in older adults, given that tDCS has previously proven beneficial for other aspects of language such as fluency (Cattaneo et al., 2011; Iyer et al., 2005) and naming (Fertonani et al., 2010; Sparing et al., 2008). The current study demonstrated a reduction in response latencies with active tDCS compared to sham stimulation, specifically in test conditions requiring novel generation and selection. This shows that a-tDCS over the LIFG produces online benefits for these conceptual preparation mechanisms in elderly adults.

The use of a sham stimulation control group excluded any potential placebo effects of tDCS, as well as any practice effects that could have resulted from the pre–post design. Analyses of test errors also excluded the possibility of a trade-off in speed and accuracy as an explanation for the reduction in response latencies resulting from active stimulation. The current findings can therefore be interpreted as direct evidence for the benefits of active stimulation.

The selection test showed that in accordance with predictions, there was no reduction in response latencies in the control condition for either stimulation group. No benefit of stimulation was expected in the control condition given that no selection was required, and older adults were not impaired in this control condition in our recent study (Madden et al., 2018). In the low selection condition, there was a reduction in response latencies from Phase 1 to Phase 2. Contrary to expectations, this reduction was similar across active and sham groups. As this condition involved a minimal degree of selection, only a small reduction in response latencies was expected. A reduction was in fact observed with active stimulation; however, a similar reduction was also observed with sham. This indicates that participants improved from Phase 1 to Phase 2 due to some other factor such as a placebo or practice effect. In either case, improvement in the sham condition would limit the potential for a comparatively greater reduction to be seen in the active stimulation condition if there was a floor effect. A floor effect is likely in this low selection condition, given that older adults only show a mild impairment compared to younger adults to begin with (Madden et al., 2018). By contrast, there was more potential for improvement in the high selection condition. It was expected that active stimulation would significantly reduce response latencies compared to sham stimulation in the high selection condition, as this is the condition in which older adults have shown the greatest impairment (Madden et al., 2018). As predicted, high selection response latencies were decreased significantly with active stimulation compared to sham. These findings suggest that tDCS produces online benefits to response latencies when a higher degree of selection is required.

The error analysis indicated that the effect of active stimulation on response latencies could not be accounted for by a trade-off in speed for accuracy. A trade-off in this case would be indicated by a reduction in accuracy coinciding with the reduction in response latencies in the hard selection condition for active compared to sham stimulation. While the error rate was higher for the hard selection condition than in the control condition, unlike with response latencies, this effect did not vary across stimulation groups. This shows that the benefit of tDCS for response latencies is not countered by an associated increase in error rate.

Results of the generation test showed that, as predicted, there was no reduction in response latencies in the control condition for either stimulation group. This was expected given that minimal novel generation is required in the control condition, and older adults are not impaired in this condition to begin with (Madden et al., 2018). Contrary to predictions, however, the benefit of active stimulation was not significant in the single generation condition. As this condition had a low generation requirement, a small reduction in response latencies was expected. Response latencies

did show a numerical decrease from Phase 1 to Phase 2 with active stimulation, but the effect did not reach significance. This may be due to a floor effect in this condition, since it only required generation of a single concept. As such, there may have been a restricted capacity for improvement compared to the multiple generation condition. This would have limited the potential effect size and therefore the statistical power to detect an effect of active stimulation in single generation with the small sample size used in the current study. It is also possible that this nonsignificant finding indicates ineffectiveness of active stimulation for idea generation. However, this seems unlikely given the results for the multiple generation condition. It was expected that active stimulation would significantly reduce response latencies compared to sham stimulation in the multiple generation condition, as older adults are known to be significantly impaired on multiple generation compared to younger adults (Madden et al., 2018). In accordance with predictions, multiple generation response latencies significantly decreased for the active stimulation group but not for the sham group. These results suggest that tDCS produces online benefits to response latencies when there is a high level of novel idea generation required.

The analysis of errors in the generation test showed that the reduction in response latencies with active stimulation could not be accounted for by a decrease in response accuracy. In fact, there was a decrease in errors from Phase 1 to Phase 2 for both stimulation groups. Though there were more errors in multiple generation than in the control condition, the decrease from Phase 1 to Phase 2 was similar across all generation conditions. These results show that the reduction in response latencies with active stimulation was not linked to an increase in errors in the generation test.

Madden et al. (2018) suggested that education may act as a protective factor against the effects of normal aging for generation and selection. In line with this in the current study, participants with more education showed greater improvement across test phases for single generation. While education was not associated with performance in any other test condition in the current study, this may be partly due to the limited sample size of each stimulation group, as well as the limited variation in the education of this generally highly educated sample. Other associations with prior education could emerge in a larger sample with a more diverse educational background, though this is not the focus of the current investigation. Most importantly, these findings demonstrate that prior education was not problematic for the interpretation of the experimental results. The number of years of education was balanced across stimulation groups, and the benefits of more education across phases in the single generation condition were observed under both sham and active stimulation conditions.

Previous studies have demonstrated that tDCS produces behavioral improvements for various tasks in the language domain, including word fluency (Cattaneo et al., 2011; Iyer et al., 2005) and naming (Fertonani et al., 2010; Sparing et al., 2008) in young adults, as well as picture naming (Fertonani et al., 2014; Holland et al., 2011), face naming (Ross et al., 2011), and semantic word generation (Meinzer et al., 2013) in healthy older adults. The current results support and extend these previous findings to include behavioral performance benefits for conceptual preparation in older adults. However, investigating the mechanisms underlying these behavioral improvements was not within the scope of the current study. Meinzer et al. (2013) demonstrated that behavioral improvements in semantic word generation were associated with changes in underlying task-related activity and resting-state functional connectivity during stimulation. They found that tDCS reduced task-related bilateral frontal hyperactivity that was associated with decreased performance in older adults, and reversed age-related network-level changes to restore a more youth-like pattern of functional connectivity. We speculate that the observed behavioral improvements for conceptual preparation in the current study were associated with similar underlying changes during tDCS.

As the left inferior frontal region has been implicated in idea generation and selection (Benedek et al., 2014; Moss et al., 2005; Robinson, 2013; Robinson et al., 1998, 2005; Zhang et al., 2004), behavioral deficits in conceptual preparation mechanisms may be associated with age-related changes in the LIFG and resulting changes in functional language networks. Though tasks in domains such as language are typically characterized by lateralized neural activity in younger adults, this lateralization of function is gradually replaced with a more distributed pattern of neural activity in older age (Cabeza, 2002; Grady, 2012; Gutchess, 2014). This is thought to reflect dysfunctional dedifferentiation of neural activity and inefficient over-recruitment of contralateral areas (Li & Lindenberger, 1999; Li et al., 2001; Rajah & D'Esposito, 2005). For language production, connections between language areas within the left hemisphere resemble those in young adults and are thought to beneficial, whereas connections between the left and right hemisphere are detrimental for behavioral performance (for a review see Antonenko & Flöel, 2014). For example, Meinzer et al. (2009) showed

that decreased semantic fluency performance in older adults was associated with additional right frontal activity, in contrast to the strongly lateralized pattern of left frontal activity in young adults. Given that semantic fluency has been used as a measure of voluntary verbal generation in dynamic aphasia (Robinson, 2013; Robinson et al., 2015) and in healthy older adults (Madden et al., 2018), reduced lateralization and increased bilateral hyperactivity may account for conceptual preparation deficits in older adults. Idea generation and selection would therefore improve with efficient, youth-like recruitment of the LIFG, which may have been facilitated by the current tDCS protocol to produce the observed improvements in behavioral performance. A paradigm similar to that used by Meinzer et al. (2013), with concurrent tDCS and functional imaging, could be used to confirm whether such underlying mechanisms can account for the current behavioral findings.

Generation and selection deficits in neurological populations (e.g., Crescentini, 2008; Robinson, 2013; Robinson et al., 1998, 2005) may involve similar underlying changes in functional language networks. For instance, reduced lateralization of language following stroke is thought to reflect an inefficient (Heiss, Kessler, Thiel, Ghaemi, & Karbe, 1999; Winhuisen et al., 2007) and even maladaptive attempt at functional adaptation to left hemisphere damage (Belin et al., 1996; Rosen et al., 2000). Optimal outcomes for language recovery are achieved through recruitment of left-hemisphere perilesional areas (Heiss & Thiel, 2006; Shah, Szaflarski, Allendorfer, & Hamilton, 2013). tDCS may therefore facilitate this process by directly increasing excitability over perilesional areas (see Prehn & Flöel, 2015) to facilitate the modulation of a distributed neural network for language (Fregni & Pascual-Leone, 2007; Martin, Naeser, & Theoret, 2004; Winhuisen et al., 2005), as was the proposed underlying mechanism of improvement for older adults in the current study. It is unclear whether this may extend to producing behavioral benefits for neurological patients with deficits in conceptual preparation mechanisms. The current findings should therefore be extended in future studies to investigate whether tDCS can similarly improve generation and selection in these neurological populations. This would add to the numerous documented benefits of tDCS for language in aphasia following stroke and in the context of neurodegeneration (for a review see Antonenko & Flöel, 2016; Monti et al., 2013).

The use of concurrent stimulation in the current study meant that the duration of stimulation benefits was not investigated. It is not clear for how long, if at all, the benefits outlast the stimulation protocol itself. Future studies could administer follow-up tests to investigate the duration of behavioral benefits. Evidence from healthy young adults also suggests that the duration of behavioral effects can be extended through the use of multiple spaced sessions (Reis et al., 2009; Stagg & Nitsche, 2011). Future studies could therefore utilize multiple sessions and investigate the resulting effect size and duration of performance benefits for generation and selection in older adults. It can then be investigated whether improvements in task performance extend to generation and selection ability in natural language contexts. Benefits for conceptual preparation mechanisms may also be evident from improvements in aspects of propositional language such as speech rate, grammatical complexity, and propositional density (Kemper & Sumner, 2001).

Conclusions

The current study provides preliminary evidence that tDCS over the LIFG applied concurrently with idea generation and selection tests produces benefits for these conceptual preparation mechanisms. Response latencies were reduced for test conditions with high requirements for idea generation and selection, which corresponds to the pattern of deficits previously observed in older adults (Madden et al., 2018). Placebo and practice effects were excluded in both tasks with a sham stimulation group, and analyses of test errors showed that the benefits of active stimulation for response latencies were not marred by any associated decrease in response accuracy. As these conceptual preparation mechanisms are crucial for language production, this is an important step toward addressing propositional language impairment in older age and in neurological patients. The next step should be to replicate these preliminary findings with a larger sample. Future studies can then determine the potential for using tDCS to produce lasting benefits for conceptual preparation and language production in older adults and in neurological populations with deficits in these generation and selection mechanisms.

Disclosure statement

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