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Modulation of decision-making in a gambling task in older adults with transcranial direct current stimulation

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Abstract

Cognitive performance usually declines in older adults as a result of neurodegenerative processes. One of the cognitive domains usually affected is decision-making. Based on our recent findings suggesting that non-invasive brain stimulation can improve decision-making in young participants, we studied whether bifrontal transcranial direct current stimulation (tDCS) applied over the right and left prefrontal cortex of older adult subjects can change balance of risky and safe responses as it can in younger individuals. Twenty-eight subjects (age range from 50 to 85 years) performed a gambling risk task while receiving either anodal tDCS over the right and cathodal tDCS over the left dorsolateral prefrontal cortex (DLPFC), anodal tDCS over the left with cathodal tDCS over the right DLPFC, or sham stimulation. Our main finding was a significant group effect showing that participants receiving left anodal/right cathodal stimulation chose more often high-risk prospects as compared with participants receiving sham or those receiving right anodal/left cathodal stimulation. This result is contrary to previous findings in young subjects, suggesting that modulation of cortical activity in young and elderly results in opposite behavioral effects; thus supporting fundamental changes in cognitive processing in the elderly.

Introduction

Human beings are constantly exposed to situations requiring a decision. As with other brain processes, decision-making also changes according to the developmental brain level (Denburg *et al.*, 2005; Fein *et al.*, 2007; Lee *et al.*, 2008). In fact, cognitive processing involved in decision-making – such as attention, executive processing, memory, speed of information processing – usually declines in older adults as a result of neurodegenerative processes (Span *et al.*, 2004; Damoiseaux *et al.*, 2008). In addition, past experiences together with emotional processing play an important role in decision-making and seem to be different in older adults as compared with younger adults.

Several studies have shown that the decision-making process is different in older as compared with younger subjects (Fein *et al.*, 2007; Reed *et al.*, 2008). Fein *et al.* (2007) found that subjects older than 55 years had a less favorable performance in the Iowa Gambling Task as compared with subjects younger than 55 years. Other studies correlated physiological measures, such as skin conductance response (SCR) and decision-making performance in the elderly (Denburg *et al.*, 2006). Differential-amplitude anticipatory SCRs preceding choices are usually correlated with losing or gaining outcomes; however, in the older adult groups, as demonstrated by Denburg *et al.* (2006), these correlations are not found because modulation of SCR is not observed as an anticipatory planning to choices.

Given that decision-making performance is different in older subjects and has a social and economic impact in their lives, then it is necessary to study neural processes associated with it. Neural correlates of the decision-making process have been studied via functional magnetic resonance imaging (fMRI; Lee *et al.*, 2008), evoked related potentials (ERPs; Hewig *et al.*, 2007), transcranial magnetic stimulation (TMS; Knoch *et al.*, 2006) and, recently, transcranial direct current stimulation (tDCS; Fecteau *et al.*, 2007). Output from fMRI and ERPs studies are mandatory in cognitive neuroscience as they allow researchers to determine the neural circuitry underlying different related cognitive processes. However, non-invasive brain stimulation is also critical as it can show the behavioral impact of modulation delivered to a given brain area.

To date, TMS and tDCS have been used to investigate decision-making in healthy and young adult volunteers. Knoch *et al.* (2006) demonstrated that TMS applied over the right prefrontal cortex increases risk behavior possibly due to disruption of right prefrontal cortex activity induced by TMS. With anodal tDCS over the right prefrontal cortex, Fecteau *et al.* (2007) observed increased safer

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behavior when compared with sham tDCS. In this case, a modulation (rather than a disruption) might have facilitated information processing due to an enhancement of local brain activity.

We therefore aimed to study whether anodal tDCS applied over the right prefrontal cortex of older adult subjects changed their balance of risky and safe responses. We used the same design we used before in previous studies in younger individuals in order to be able to compare results across studies. The importance of this study is to provide further insights on decision-making-related neural processing associated with ageing.

Materials and methods

Study design

We conducted a single-center, doubled-blinded, randomized and sham-controlled trial to investigate the effect of a single session of tDCS on a decision-making task (Risk Task) in healthy older adults. The experiment was undertaken with the understanding and written consent of each subject, and this study conformed to the ethical standards of the Declaration of Helsinki and was approved by the institutional ethics committee from Mackenzie Presbyterian University, Brazil and also by the National Ethics Committee (SISNEP, Brazil – http://portal2.saude.gov.br/sisnep/).

Participants

Twenty-eight healthy elderly persons (three men; aged 50–85 years; one left-handed) were recruited from Mackenzie Presbyterian University to participate in this study. Written advertisements were posted around campus and interested subjects contacted the study coordinator to enroll; the study coordinator explained the risk/benefits of the study and screened interested individuals for eligibility. Subjects were regarded as suitable to participate in this study if they fulfilled the following criteria: (i) age between 50 and 85 years; (ii) no clinically significant or unstable medical, or neuropsychiatric disorder; (iii) no history of substance abuse or dependence; (iv) no use of CNS-effective medication; (v) no history of brain surgery, tumor or intracranial metal implantation; (vi) Mini Mental State Examination adjusted to the level of education to exclude possible dementia [we used the cut-off of 20 for participants with no former (or < 4 years) education and 24 for participants with more than 4 years of formal education as suggested for our population; Almeida, 1998]. We also administered a visual analog scale (VAS) with 14 items evaluating mood. The demographic characteristics of the volunteers are summarized in Table 1. All subjects were naive to tDCS and the Risk Task. All study participants provided written, informed consent. In addition we compared these results with our previous study using the same methodology, however, in younger subjects (mean age: 20.3 ± 1.7 years).

tDCS

tDCS is based on the application of a weak direct current to the scalp via two saline-soaked surface sponge electrodes (35 cm^2) and delivered by a battery-driven, constant current stimulator. We used a device developed by our group that is particularly reliable for double-blind studies as a switch can be activated to interrupt the electrical current while maintaining the ON display (showing the stimulation parameters throughout the procedure to the experimenter and participant). Although there is significant shunting of current in the scalp, sufficient current penetrates the brain to modify the transmembrane neuronal potential (Miranda *et al.*, 2006; Wagner *et al.*, 2007), thus influencing the level of excitability and modulating the firing rate of individual neurons. The effects on cortical excitability depend on current orientation, such that anodal stimulation generally increases cortical excitability, while cathodal stimulation decreases it (Nitsche & Paulus, 2000).

TABLE 1. Demographic characteristics of the volunteers

	Right tDCS (n = 10)	Left tDCS (n = 9)	Sham tDCS (n = 9)	*P*-value*
Gender [females (%)]	9 (90)	7 (78)	9 (100)	0.3
Laterality [right-handed (%)]	10 (100)	9 (100)	8 (89)	0.3
Marital status (%)	–	–	–	0.4†
Married	4 (40)	5 (56)	3 (33)	
Divorced	1 (10)	1 (11)	0 (0)	
Widow	5 (50)	3 (33)	4 (44)	
Single	0 (0)	0 (0)	2 (22)	
Age (years)	69.4 ± 8.9	68.9 ± 12.6	67.0 ± 9.0	0.9
Education (years)	9.2 ± 5.2	7.0 ± 5.2	5.2 ± 4.5	0.2
MMSE	27.4 ± 2.0	26.7 ± 3.0	26.2 ± 3.3	0.7
VAS				
Alert/drowsy	2.9 ± 1.7	3.6 ± 3.2	3.3 ± 2.0	0.8
Calm/restless	4.5 ± 3.4	5.7 ± 3.7	4.6 ± 2.1	0.7
Strong/weak	3.8 ± 2.7	4.9 ± 3.1	4.2 ± 2.2	0.7
Confused/lucid	8.8 ± 1.7	6.9 ± 2.2	7.6 ± 1.9	0.1
Sharp/blunt	3.2 ± 1.7	3.2 ± 2.0	2.7 ± 1.9	0.8
Apathetic/dynamic	8.5 ± 1.7	7.9 ± 1.6	7.8 ± 2.6	0.7
Satisfied/unfulfilled	4.2 ± 3.6	3.4 ± 3.0	2.8 ± 2.3	0.6
Worried/unconcerned	6.2 ± 3.5	6.2 ± 3.4	6.0 ± 3.0	1.0
Fast mind/slow mind	8.4 ± 1.7	6.6 ± 2.4	6.9 ± 2.3	0.2
Tense/relaxed	6.3 ± 2.8	6.7 ± 3.0	6.8 ± 2.2	0.9
Attentive/neglectful	2.4 ± 1.8	3.3 ± 2.5	3.9 ± 1.5	0.3
Inept/competent	8.4 ± 2.0	8.1 ± 2.0	8.6 ± 1.6	0.9
Happy/sad	2.8 ± 2.9	3.1 ± 2.9	3.1 ± 1.7	1.0
Hostile/friendly	7.9 ± 3.1	8.7 ± 2.0	8.4 ± 2.1	0.8

*One-way ANOVA for the comparison of continuous variables and Pearson chi-square test for the comparison of categorical variables (results showed no differences across groups). Values of age, education, Mini Mental State Examination (MMSE) and visual analog scale (VAS) are presented as mean ± SD. †From Pearson chi-square test.

The electrodes montage was the same as used in a previous study (Fecteau *et al.*, 2007) where healthy young volunteers performed the Risk Task during prefrontal tDCS. This strategy was adopted to make possible a comparison between both studies. As in the prior study, participants were randomly assigned to receive left anodal/right cathodal tDCS (n = 9), right anodal/left cathodal tDCS (n = 10) or sham stimulation (n = 9). For left anodal/right cathodal tDCS, the anode electrode was placed over the left F3 (international EEG 10/20 system) and the cathode electrode was placed over the right F4. For right anodal/left cathodal stimulation, the polarity was reversed: the anode electrode was placed over F4 and the cathode electrode was placed over F3. For both studies, the rationale of choosing a bifrontal electrode montage was an attempt to induce a simultaneous activity enhancement/diminishment effect on the right and left dorsolateral prefrontal cortex (DLPFC). For active stimulation, subjects received a constant current of 2 mA intensity with 10 s of ramp up and down. tDCS started 5 min before the task began and was delivered during the entire course of the risk task, which lasted 10 min. The same procedure was used for sham stimulation, but current was applied just for the first 30 s. This procedure is reliable to blind subjects for the respective stimulation condition (Gandiga *et al.*, 2006).

Risk task

The Risk Task (Rogers *et al.*, 1999) is a decision-making task used in several previous studies that involve gambling. This task has interesting characteristics as it measures decision-making under risk; however, involves very little strategy and working memory. There are 100 trials and, in each one of them, participants are presented with six horizontally arranged boxes colored as pink or blue. The ratio of pink and blue boxes varies from trial to trial, being, therefore, 5 : 1, 4 : 2 or 3 : 3.

Participants have to choose the color of the box they believe has the 'winning token'. They are told that the token has equal probability of being hidden in any of the boxes. Therefore, for each trial, the ratio of pink to blue boxes (referred as 'level of risk') effectively determines the probability of finding the winning token – for instance, if the ratio is 5 : 1 (blue : pink), the participant has a probability of 5/6 to be correct if her answer is blue, and only 1/6 if her answer is pink. Therefore, color choice determines the level of risk of the choice.

Participants are rewarded with points when they guess the color of the box that is hiding the winning token correctly, but are also punished (they loose points) when they pick the incorrect color. The amount of reward (or penalty) points associated with any scenario (e.g. five blue and one pink box) varies (90 : 10, 80 : 20, 70 : 30, 60 : 40; referred to as 'balance of reward') and is clearly indicated on the screen. Importantly, there is an inherent conflict in risk taking as the largest reward is always associated with the least likely of the two outcomes (i.e. the most risky option). For example, in a trial with five blue boxes and one pink box, the winning token is more likely to be one of the blue boxes (five in six probability); however, the blue, in this case, would be associated with a smaller number of points awarded. However, if the participant picks the wrong color, he also looses the same amount of points. The participants' aim is to earn as many points as possible.

Statistical analysis

We performed an analysis similar to our previous study (Fecteau *et al.*, 2007). The outcome measures in the present study were as follows. (i) the choice of low risk (i.e. safe prospect) vs. high risk in each trial – binary variable. This measure is the percentage of instances in which participants choose the high-probability option [i.e. the choice of low risk; the color corresponding to more boxes and therefore less rewards (in terms of points)]. (ii) The decision time (i.e. how long it took the participants to decide the color of the box, measured in ms) – treated as a continuous variable.

Performance on all 100 trials of the task (excluding the neutral conditions, i.e. equal number of blue and pink boxes) was analysed. We then calculated the choice in each trial and the decision time during the three stimulation conditions (left anodal/right cathodal, right anodal/left cathodal and sham stimulation). Analyses were performed using STATA (College Station, TX, USA). We used a mixed linear regression model (using an unstructured covariance structure) to analyse the decision time difference across the groups. We modeled decision time change using the covariates of group (left anodal/right cathodal stimulation, right anodal/left cathodal stimulation, sham stimulation), balance of reward (90 : 10, 80 : 20, 70 : 30, 60 : 40), level of risk (low risk, high risk), and interaction terms group × balance of reward × level of risk. For the outcome considering the choice of low risk vs. high risk (binary outcome), we performed a logistic regression model in which the dependent variable was the choice (low risk, high risk) and the independent variables were group (left anodal/right cathodal stimulation, right anodal/left cathodal stimulation, sham stimulation), balance of reward (90 : 10, 80 : 20, 70 : 30, 60 : 40) and interaction group × balance of reward. As we used multiple tests, we used Bonferroni adjustments for multiple comparisons.

Results

None of the volunteers experienced adverse effects during or after tDCS. Some of the participants perceived a slight itching sensation under the electrodes during approximately the first 30 s of stimulation.

We initially tested our main *a priori* hypothesis based on our previous findings (Fecteau *et al.*, 2007), which hypothesizes that participants receiving anodal tDCS to the right DLPFC coupled with cathodal tDCS to the left DLPFC would display risk-averse behavior on the risk task. To do so, we used a specific logistic regression model using choice [risky choice (less likely to find the token but associated with more rewards and losses) and the safer choice (more likely to find the token but less gains and losses)] as the dependent variable. Results revealed a main effect of group (logistic regression, $z = 7.69$, $P < 0.0001$). Interestingly, results were opposed to the findings in young subjects as participants receiving left anodal/right cathodal stimulation chose more often high-risk prospects as compared with participants receiving sham stimulation (OR = 1.53, 95% CI = 1.37–1.71) and those receiving right anodal/left cathodal stimulation (OR = 1.82, 95% CI = 1.48–2.25). Finally, there was a small difference between groups receiving right anodal/left cathodal and sham stimulation (OR = 1.28, 95% CI = 1.03–1.6), however, also showing that right anodal/left cathodal was associated with an increase in risk prospect (Fig. 1). Although we only had a few male subjects, there was no significant difference between women and men in their choices – the term gender and education in the model was not significant (logistic regression, gender: $z = -1.14$, $P = 0.25$; education: $z = 0.34$, $P = 0.733$). In fact, excluding men from the analysis, the results would not change. However, it should be noted that this analysis is likely underpowered due to the small sample size.

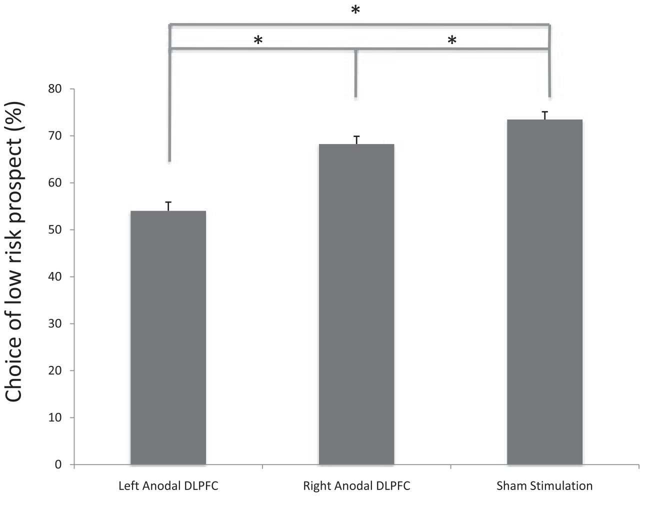

FIG. 1. Choice between low-risk and high-risk prospect (in percentages). Choice of low-risk prospect was significantly different across groups. Participants receiving left anodal/right cathodal stimulation chose more often high-risk prospects as compared with participants receiving sham stimulation and those receiving right anodal/left cathodal stimulation. Also, right anodal/left cathodal stimulation was associated with an increase in risk prospect. *$P < 0.05$. DLPFC, dorsolateral prefrontal cortex.

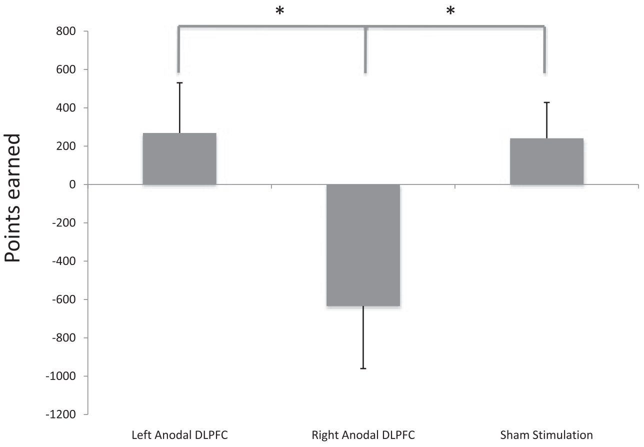

FIG. 2. Total points earned. Participants receiving right anodal/left cathodal stimulation earned significantly less points as compared with those receiving left anodal/right cathodal and sham stimulation. $*P < 0.05$.

An important covariate is the balance of reward, i.e. whether decision-making (in this case choosing the low vs. high risky prospect) depends on monetary gain. Results revealed a significant main effect of balance of reward (logistic regression, $z = 3.44$, $P = 0.001$); interestingly, participants tended to be more conservative when its associated reward was diminished (e.g. during the conditions 40 : 60 and 30 : 70) – similar findings to our young subjects study. We then investigated whether the difference in regards to the balance of reward was similar across groups, and although participants in the left anode/right cathode seem to have opposite behavior (i.e. take more risk when the reward is less) as compared with the other active and the sham condition – the interaction term group × balance of reward was not significant (logistic regression, $z = -1.23$, $P = 0.21$).

As participants gained or lost points according to their decision, we then tested the total points earned (see Fig. 2), the ANOVA showed a main effect of group of stimulation ($F_{2,25} = 3.7$, $P = 0.039$). Interestingly, participants receiving right anodal/left cathodal stimulation earned significantly less points as compared with those receiving left anodal/right cathodal ($t = 2.07$, $P = 0.036$) and sham stimulation ($t = 3.41$, $P = 0.0046$). There was no difference between the total points earned between participants with left anodal/right cathodal stimulation as compared with sham stimulation ($t = 0.08$, $P = 0.93$), showing that the riskier profiled associated with left anodal/right cathodal stimulation did not result in less earned points.

We then tested whether changes in risk taking were due to changes in execution time. Our analysis showed that the main effect of group was not significant (linear regression, $t = -0.37$, $P = 0.71$), therefore suggesting that reaction time was similar across groups of stimulation. We then tested whether the decision times were longer when participants were confronted with a 4 : 2 vs. 5 : 1 scenario, as found in Rogers *et al.* (1999), Knoch *et al.* (2006) and Fecteau *et al.* (2007). There was a main effect of level of risk (linear regression, $t = -2.47$, $P = 0.014$). Participants decided slower when confronted with the safer scenario (4 : 2 choice) as compared with the higher-risk scenario (5 : 1 choice). There was no interaction group × level of risk (linear regression, $t = 0.52$, $P = 0.61$).

Discussion

Our main finding was a significant effect of group, showing that participants receiving left anodal/right cathodal stimulation chose more often high-risk prospects as compared with participants receiving sham stimulation or those receiving right anodal/right cathodal stimulation. This effect is opposed to the findings previously reported in young subjects (Fecteau *et al.*, 2007). In addition, we found a small difference between groups receiving right anodal/left cathodal and sham stimulation, but also showing the opposite direction as in young subjects: right anodal/left cathodal stimulation was associated with an increase in risk prospect.

In this study, we used exactly the same methodology used in our study in healthy young subjects, and here we showed that stimulation of the same areas has an opposite effect in older subjects: it increases rather than decreases risk behavior. Several hypotheses can be speculated to explain differences in risk taking between younger and older subjects. In this context, we have to consider some previous findings with respect to normal aging and its impact on brain hemispheric asymmetry. Two different models of hemispheric asymmetry and aging have been proposed. One of them is the so-called Hemispheric Asymmetry Reduction in Old Adults model(HAROLD). The idea of this model is that frontal activity has a tendency to be less lateralized in older than in younger adults during cognitive demands. This model is extensively supported by fMRI data (Cabeza, 2002; Li *et al.*, 2009). The second model is the right hemi-aging model that proposes that right hemisphere cognitive functions are prominently more affected by aging as compared with the left hemisphere cognitive functions. This model is usually based on behavioral studies showing inferior performance on right hemisphere-related tasks in comparison with left ones in older adults (Gerhardstein *et al.*, 1998; Dolcos *et al.*, 2002; Cherry *et al.*, 2005; Prodan *et al.*, 2007). These models are seen as related to functional dedifferentiation or compensation (Dolcos *et al.*, 2002). In our study, despite giving the impression of being incompatible, both concepts, taken together, fit well with our results.

1. Our findings showing a tendency to a risk-taking behavior can be related to a reduction of prefrontal right hemisphere activity (right hemi-aging model) as activity in this area is usually related to conservative behavior.
2. The non-specific effect of tDCS in the elderly (i.e. in both hemispheres tDCS tends to induce risk-taking behavior) can be supported by the HAROLD model – the lower the functional asymmetry, the lower the probability of specific effects related to the stimulated hemisphere.

Therefore, the different findings we observed in older as compared with younger subjects in the decision-making task can be explained by some of the aging-related changes in cortical activity.

One interesting point is that we showed, similar to our study with younger subjects (Fecteau *et al.*, 2007), that older adults tend to be more conservative when its associated reward was diminished (e.g. during the conditions 40 : 60 and 30 : 70). This was also observed in Rogers *et al.* (1999) and Knoch *et al.* (2006) studies. These results are interesting as they reinforce our hypothesis showing that although the strategy when performing this task is similar in the older and younger subjects, different neural networks are activated. One important issue here is that the differential effects between young and old subjects might not be explained by a differential response to tDCS, as a recent study has shown that response of tDCS in older subjects seems similar to young subjects (Quartarone *et al.*, 2007). In addition, it shows that increase in risk behavior was not a consequence of subjects not understanding the task.

Another potential alternative explanation to account for the differences between young vs. elderly subjects is the difference in education level. Because the young subjects had a higher formal educational level (on average 12.3 ± 0.5 years) as compared with elderly subjects (on average 7.21 ± 5.1 years), it is possible that potential differences in the effects of tDCS on decision-making are due to this formal educational difference rather than the age difference. In fact, school education level might be associated with the strategic approach during the decision-making task (in other words, subjects with fewer years of education might have a more simplistic strategy) and therefore be associated with a differential neural network activation. Although this is possible, the task used in this study is rather a simple task that can be understood even by subjects with few years of education. In addition, the situation addressed in the task is a situation that is commonly seen in daily life (e.g. bank investments). Finally, we were not able to address whether years of education was an important factor to differentiate the results from the two groups as the group of younger subjects had a very homogenous educational level (subjects were from the same class of an undergraduate psychology course). Therefore, the variable education could not be detangled from the variable age in our analysis. Future studies should enroll patients with different educational levels so as to address this important issue.

In addition to our results showing that older adults maintain the same rationale of being attracted to safe prospects when the reward was smaller, it is worthy of note that there was no difference across groups regarding the balance of reward and choice of risk, suggesting that the effects of stimulation do not change the overall strategy of subjects to maximize gains.

Finally, participants earned similar amounts of points, except for participants receiving right anodal/left cathodal stimulation who earned significantly less points as compared with those receiving left anodal/right cathodal and sham stimulation. Although this result might seem paradoxical at first glance, it may give additional support to our finding showing a differential effect in the older compared with younger subjects. In addition, younger subjects earned more points than the older ones in all conditions, the reason underlying this difference is that risk-taking behavior is more prominent in the older adults group in comparison to the younger ones. The final important issue is that reaction time was similar across groups of stimulation. In other words, the change in risk-taking behavior after active stimulation was not due to faster or slower responses.

In conclusion, our findings provide important information about the impact of tDCS applied in the elderly. The opposite behavioral effect observed in this population compared with that observed in the younger group can be regarded as further evidence of the effects of aging on brain asymmetry. In particular, the effects observed indicate a possible reduction of a lateralized functioning and also a decline that is more evident in the right hemisphere.

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Abbreviations

DLPFC, dorsolateral prefrontal cortex; ERP, evoked related potential; fMRI, functional magnetic resonance imaging; SCR, skin conductance response; tDCS, transcranial direct current stimulation; TMS, transcranial magnetic stimulation; VAS, visual analog scale.

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