Enhancing inhibitory control and risky decision-making with brain stimulation: A randomized and sham-controlled study

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Abstract--- *Inhibitory control and risky decision making are critical cognitive functions, particularly to determine more appropriate behaviors that are compatible with achieving goals and preventing unwanted outcomes. Multiple studies have measured the efficacy of brain stimulation to enhance individuals' cognitive abilities. Although some of the results show positive achievements, the generalizability of the results remains open to doubt, particularly in young population contries. Current research examines the effects of cognitive training and brain stimulation to enhancing inhibitory control and risky decision-making in healthy adults in Tehran utilizing computer games training associated with brain stimulation. The experiment involved four groups of 60 healthy volunteers who were residents of Tehran and randomly assigned to groups. A pre-test with post-test analysis, including Go/NoGo and BART tasks used to compare the groups. A single session intervention was applied using 30 minutes of 2 mA tDCS, as well as a computerized game as cognitive training. The control group went under sham-tDCS with a non-cognitive game. Contrary to the various prior studies, the results of the statistical analyses of the data from experimental and control groups showed no meaningful difference. Based on the results of this study, there is no significant effect of rIFG tDCS on the scores of inhibitory control and risky decision-making tasks. This study collected, summarized, and discussed a considerable amount of wide-ranging of relevant investigations. Despite limitations in the number of subjects and stimulation sessions that restricts us to make an exact conclusion, if the same results will appear with the same brain's region, the efficacy of tDCS on enhancing examined functions through rIFG is faced with doubt. It seems that the protocols used in this study require to be repeated in similar studies with more subjects. Furthermore, instead of a single session of intervention, multiple sessions of intervention are suggested.*

Keywords--- *Cognitive Enhancement, Inhibitory Control, Risky Decision-Making, tDCS.*

I. INTRODUCTION AND BACKGROUND

Iran is one of the countries with a young population (Mehrdad, 2009; Vahidi Monfared & Moini, 2018) and, in an unbound relativity, this territory bygone embraced all types of risks (Alcaro et al., 2018; Daniel, 2012; Zamani-Alavijeh et al., 2009), cognitive enhancement might worth considered as an option to improve behavior and decision facing risks. At least for whom at the sensitive or key positions.

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Performance enhancement in human, as an interdisciplinary approach, refers to the act of augmenting the individuals' skills, functions, and capabilities through the use of medicine or technologies which are designed to rehab or increase one's performance competency (Hildt & Franke, 2013). Moreover, developing core mental capabilities via improving the external/internal systems involved in information processing can be represented as the "Cognitive Enhancement" (Bostrom & Sandberg, 2009). Regardless of pros and cons and ethical, philosophical, and legal debates on it, the term cognitive enhancement, in the last two decades, has been growing in importance and attracting researchers' attention. This trend happened due to the convergence of cognitive science and neuroscience, as well as the development of technology of making powerful modern tools (Hildt & Franke, 2013).

A quantitative review of the effectiveness of Cognitive Training (CT) on improving executive functions in 2014 demonstrated significant benefits for healthy adults (Karr et al., 2014). Another systematic review and meta-analysis in the same year indicated the same results (Kelly et al., 2014). Also, studies on computerized CT show effectiveness at enhancing cognitive performance in healthy elderly adults (Lampit et al., 2014). Due to these results, it can be argued that one of the effective methods for cognitive enhancement is CT (Traditional/Computerized).

One of the used methods for cognitive enhancement is Brain Stimulation (BS). Although BS has a long and old story the same as the history of medicine and physics (Schwalb & Hamani, 2008), the first report of the human electrical BS refers to the 1820s by a French physiologist (Morgan, 1982). However, recently, Nitsch and his colleagues reintroduced and developed BS through weak direct currents as a non-invasive method. In fact, transcranial direct current stimulation (tDCS) has appeared as one of the main tools to affect cortical excitability in the human brain (Nitsche & Paulus, 2011). Also, brain polarization in the form of tDCS, which affects various functions such as motor and learning processes, has been recommended by considerable studies as a helpful strategy to enhance the effects of neurorehabilitation training (Gandiga et al., 2006). Furthermore, several meta-analyses on the use of tDCS to enhance the cognitive and motor functions reported significant positive results (Brunoni & Vanderhasselt, 2014; W.-Y. Hsu et al., 2015; Summers et al., 2016).

As an executive cognitive function, inhibitory control allows us to inhibit our impulses and inherent, habitual, and deep-rooted responses to stimuli supposing to select a more useful reaction which is compatible with wanted outcomes (Diamond, 2013; Ilieva et al., 2015). While the defect in this function may cause an inefficient response to stimuli, suppressing actions, thoughts/emotions occur times and times in the daily life of a healthy person. Furthermore, the prefrontal cortex (PFC) has surveyed as a source of the inhibitory control widely (Munakata et al., 2011). By searching and studying relevant researches conducted from 2008 to 2017, as shown in Table 1, it is clear that various studies have utilized tDCS to improve inhibitory control. A brief review of the protocols and results of nine (well-founded) studies have summarized in Table 1. Based on summarized data, the number of stimulation on rIFG, with positive results, was more than other regions, which ultimately convinced us this region is a better target for the stimulation.

Table 1- Studies on the effect of tDCS on inhibitory control (IC)

Author and year	tDCS type	tDCS parameters	Stimulated region	Task	Main result
Beeli, 2008	Cathod vs anod	1.5 mA for 5.5 min	rDLPFC	Go/NoGo	Positive
Hsu, 2011	Anod vs Cathod	1.5 mA for 10 min	preSMA	Stop Signal	Positive
Jacobson, 2012	Anod	1.5 mA for 15 min	rIFG	Resting	Positive
Kwon, 2013	Anod	1 mA for 10 min	PreSMA, M1	Stop Signal	Positive
Cunillera, 2016	Anod vs Cathod	1.5 mA for 20 min	l-rIFG	GNG/SS	Positive
Hogeveen, 2016	Anod HD vs conv.	1 mA for 20 min	rIFG vs control	Stop Signal	Positive when High-Definition tDCS used
Cai, 2016	Anod	1.5 mA for 15 min	rIFG, rIPL, Visual Cortex (VC)	Stop Signal	Positive for rIFG > IPL/VC

Castro-M, 2016	Anod	1.5 mA for 15 min	rPFC	Stop Signal	Positive Reactive IC
Campanella, 2017	Anod	2 mA for 20 min	rIFG	Go/NoGo	Positive

The decision-making process is modelable through a cognitive functions network (Boy, 2005). Also, decision making requires a choice among alternatives, and in a "cold" decision, the choice may be made after estimating benefits and risks, mostly by using emotional responses and intuition about options, or a mix of these ways (Buelow & Blaine, 2015). Risk defined as the potential in which decisions may lead to a loss or facing unwanted outcomes. While most of the human decisions are accompanied by some risks, some choices are much riskier than others (Lu J., Jain L.C., 2012). A neurocognitive perspective published by Bechara (2005), in the Nature Neuroscience, argued on areas of the brain related to inhibition and decision, indicates that risky decision making and inhibitory control are functions with overlaps, and the rIFG region is one of the engaged active areas in both.

Ditye et al., (2012) findings showed tDCS-combined CT was an effective method to enhance the ability to suppress responses through stimulating rIFG. And in the present study, we examined the effects of both CT and BS to enhance inhibitory control and improve risky decision-making in healthy adults in Tehran. The experiment designed to test the possibility of the effectiveness of a computerized (cognitive) game training combined with tDCS on rIFG. The study's central hypothesis was that the enhancement of inhibitory control and risky decision-making through both CT and tDCS is applicable but different priorities of these two, lead to different results.

II. Materials and Methods

- **Design and participants**

The research method was a single-blind sham-controlled and randomized study (i.e., subjects had not any information about the protocol of tDCS they received). The participants of this study were all healthy adults between the ages of 25 and 40 who lived in Tehran in 2018. Sampling was done among 60 participants who gained a score of less than 22 at a general health test. A normalized 28-item version called the General Health Questionnaire (GHQ28) was used to assess the mental health situation of participants (Malakouti et al., 2007; Noorbala et al., 2004). Participants were randomly assigned in groups to receive a single session of 30-min active anodal tDCS and CT or 30-min sham tDCS with a non-cognitive training as below:

- Group One: 15 subjects with 30-min of active anodal tDCS on rIFG in addition to 30-min CT at the same time.
- Group Two: 15 subjects with 30-min of active anodal tDCS on rIFG and after that 30-min CT was not at the same time with the stimulation but exactly after it.
- Group Three: 15 subjects with 30-min of CT and then 30-min of active anodal tDCS on rIFG not at the same time with the CT but exactly after it. (The difference between group two and three was in prioritization of tDCS and the computerized game as CT)
- Group Four (Control Group): 15 subjects with 30-min of sham tDCS on rIFG in addition to 30-min of non-cognitive training at the same time.

Also after the intervention to determine possible side effects, we asked about the general physical and mental status of the subjects using a self-report (no side effects reported).

Participants were invited to participate in the study via a local notification in social media (participants were promised to receive a free cinema ticket). Secondly, consents form were provided to inform the subjects about the purpose and possible side effects that they should sign it.

Entry criteria for participants

- Willingness to participate
- Age between 25 and 40 years
- The maximum score of 21 in GHQ28
- Being right-handed
- No drug addiction and alcohol consumption
- Having no mental or other personality disorders (via a clinical interview)
- Having no chronic physical illnesses
- Not co-participation in other experiments or a treatment program

Printed informing approval was collected from all participants before study entry. For the next stage, subjects were randomly assigned to four groups. At the very beginning, the Go/No-Go and BART tasks were performed on 60 participants before the intervention.

In the next stage, the interventions were carried out. For each person, the electrodes were placed on the specified region (the anode electrode on rIFG and the cathode on left OFC). The stimulation process by tDCS was performed in a relaxed state in the mornings (between 9 and 11 AM). The tDCS set on 2 mA for 30 minutes at one session. In addition, CT has been performed using the "Fruit Ninja" game (a commercial game, Halfbrick Studios, Brisbane, Australia). It is worth mentioning that SHAM tDCS has been used for the control group and instead of playing the Fruit Ninja, the game "Angry Birds" (a video game created by Finnish company Rovio Entertainment). After performing all interventions, BART and Go/NoGo tests were performed again as a posttest on 60 participants, and all scores were gathered and filed.

- **Tools**

In this study we used Go/No-Go and BART tasks from PEBL battery (S. T. Mueller, 2018; Shane T Mueller & Piper, 2014), the Nerurostim device tDCS (Brain Stimulation Device</i>, 2018), two computerized game, one "Fruit Ninja" as cognitive Go/No-Go game (Liu et al., 2015) and another "Angry Birds" as non-cognitive game which is similar in difficulty to the Fruit Ninja but not specified to target inhibitory control. And as mentioned before a 28-item questionnaire (GHQ28) to discover the general mental health of participants. All software ran through a portable personal computer (ASUS laptop, model: U30S, Processor: Intel Core i5 2520M/2410M, Graphics: Integrated Intel GMA HD and NVIDIA GT 520M with 1GB DDR3 VRAM, Display: 13.3" 16:9 HD (1366x768) Color-Shine). As instruction, a tutorial was recorded for all tasks previously, so that the same information was available for all participants.

✓ **Go/No-Go test**

In this study, a Go/No-Go test, which is well known as an assessment tool for inhibitory control (Simmonds et al., 2008) was used. The primary variable which was used to compare groups was an average of the "Go" reaction time.

As Ouellet et al. (2015) described, the test included the provision of two stimuli, letters "R" and "P", to the subject by the PEBL software. In the first stage, 160 stimuli (of P and R) are rendered randomly and the subject only needs to click on the "P". The second stage is the same as the trigger, but he/she should click if only the letter "R" is presented. Before each stage, a warm-up containing 10 trials runs.

✓ **BART**

Balloon Analogue Risk Task (BART), is a famous computer-based test for assessment of risky decision-making (Lejuez et al., 2002). Lejuez et al. in two different studies (Lejuez et al., 2002, 2003) have found that, for young people between 18 and 25, riskiness results of the task is associated with the self-reported risky behavior in the real-world, for instance, substance use like smoking, crimes such stealing, and in safety domain like does not care to wear a seatbelt. (For further details, see Lejuez et al., experiment on smokers and nonsmokers, 2003)

The compared output that used in this test was the average number of pumps (Ouellet et al., 2015).

- ✓ **Questioner**

The subject's demographic information included age, gender, marital status, and educational level was gathered by a demographic information questionnaire in addition to an evaluating with the 28-item version of the General Health Questionnaire (GHQ28).

- ✓ **tDCS**

In this study, as the tDCS tool, the NEURO STIM device, a product of the Iranian Sina Cognitive Science Institute, was used. The source of this device is a 7-volt battery, with a maximum current of 4 mA and a maximum voltage of 82 V DC. For any trial, electrodes of conductive-rubber were placed in sponges which were wetted and saturated with saline then by a flexible cap fixed over rIFG and left OFC regions (Based on 10-20 EEG system, respectively, between F6-FC6 and FP1) (Herwig et al., 2003; Sallard et al., 2018).

Data Analysis

In order to analyze the data, the mean and standard deviations of the research variables were investigated using the Kolmogorov-Smirnov test for testing the normal distribution of data. Based on the results, probability values indicate that the distribution of all variables is normal. Therefore, we should use a parametric test to analyze the data. In order to compare the experimental and control groups after the intervention, a multivariate analysis of covariance (MANCOVA) was used to test the hypothesis. Data analysis of this study was accomplished based on the pre-test and post-test scores of all groups for gathered particular variables. In this study, descriptive statistics such as mean and standard deviation were used to provide descriptive information about groups and covariance analysis was performed for comparing groups. Also, the collected data from each sample are presented in two sections: Descriptive and Inferential statistics.

- **Describe the data**

Table 2- Frequency (Experimental and Control Groups)

Groups	Frequency	Valid Percent	Age Mean	Standard Deviation	Female Percent	Male Percent	Edu. (Years)	GHQ28 Mean
1	15	25.0	30.67	3.75	53.3	46.7	16.67	18.93
2	15	25.0	29.80	4.39	53.3	46.7	15.87	19.47
3	15	25.0	30.33	3.63	46.7	53.3	16.67	19.53
4	15	25.0	29.60	3.83	53.3	46.7	16.13	19.07
Total	60	100.0	30.1	3.83	51.7	48.3	16.33	19.25

As shown in Table 2, 45 participants (75%) were in the experimental groups and 15 (25%) in the control group. Approximately, both genders are equally involved, and the percentage of each gender for groups are nearly the same. The mean age was 30.10 ± 8 years, and totally 51.7% of participants were females. Furthermore, the average duration of subjects' education was 16.33 ± 1.56 years, also mean scores on the questionnaire of general health (GHQ28) was 19.25±1.71. Overall, no notable differences between the four groups in terms of gender, age, education, and GHQ28 ($p > 0.10$ for all) were saw.

III. RESULTS

Standard deviation and the mean of the research variables have listed in Table 3. The normal distribution of continuous variables in the research have investigated using the Kolmogorov-Smirnov test and its results have presented in the Table. As shown, the probability of values indicates that the distribution of all research variables is normal. Therefore, parametric tests should analyze the data.

Table 3: Pre-test, post-test scores (Mean, standard deviation, Kolmogorov-Smirnov test and P Value)

Group	Variable	Pretest				Posttest			
		Mean	Std. Dev.	KS-Z	P	Mean	Std. Dev.	KS-Z	P
1	IC*	987.00	13.35	0.530	0.942	970.47	15.70	0.858	0.453
	RDM	300.27	167.39	0.677	0.750	317.93	187.93	0.731	0.660
2	IC*	988.67	23.95	0.493	0.968	973.20	18.26	0.612	0.849
	RDM	289.40	169.63	0.602	0.861	294.00	171.99	0.595	0.871
3	IC*	983.60	18.78	0.808	0.531	968.40	23.62	0.553	0.920
	RDM	289.47	165.15	0.602	0.862	295.60	170.52	0.563	0.908
4	IC*	985.60	19.935	0.453	0.987	967.13	22.08	0.602	0.862
	RDM	291.00	170.60	0.602	0.862	291.67	166.05	0.593	0.873

*Abbreviation: IC = Inhibitory Control, RDM = Risky Decision Making,
Std. Dev. = Standard Deviation, KS = Kolmogorov–Smirnov

Findings

To examine the hypothesis, we used Multivariate Covariance Analysis (MANCOVA). Before performing the analysis, several fundamental assumptions are necessary:

Normality of pre-test and post-test scores

As can be seen (Table 3), the results of the Kolmogorov–Smirnov test indicate that all distributions are normal.

Equality of variances of the compared groups

According to Table 4, results for Levene's test in inhibitory control and risky decision-making variables respectively are f=0.510, 1.682, and freedom degrees 1 and 56 at the significant level, p>0.05 indicated the equality of variances.

Table 4- The results of the analysis of equality of variance (Levene's test)

Variable	F	df1	df2	Sig
Inhibitory Control	1.682	3	56	0.181
Risky Decision Making	0.510	3	56	0.677

Equality of slope regression line

As shown in Table 5, the equality assumption of the slope of the regression line with the value of F(3, 56)=0.410 for the total error is not significant.

According to the above findings, covariance analysis used to investigate the hypothesis, the results of which have presented in Table 5.

Table 5- The results of the hypothesis of equality of the slope of the regression line

Source	Sum of Squares	Df	Mean Square	F	Sig
Group	0.708	3	0.708	0.410	0.52
Pretest	700315	3	700315	405949	0.001

Group*Pretest	1330	3	1330	0.771	0.385
Error	72456	56	1725		

In order to compare the experimental and control groups after the intervention, the MANCOVA was used to compare the scores. To answer the research hypothesis, we have used Lambda-Wilkes test statistics, and results have reported in Table 5, which seems that statistics are not meaningful. Also, the value of F(0.396) is not at a significant level (0.05). There is no significant difference between the scores of the experimental and control groups in inhibitory control and risky decision-making scores (Tables 5 and 6).

Table 6- The results of multivariate analysis for all groups' comparison

Variable index	Test	Value	F	Sig
Group	Lambda-Wilkes	0.965	0.316	0.927

Table 7- The results of multivariate analysis for all groups' comparison

The dependent variables		Sum of Squares	Df	Mean Square	F	Sig
Group	Inhibitory Control	367.157	3	121.719	0.291	0.83
	Risky Decision-Making	127.292	3	42.643	0.345	0.79
Error	Inhibitory Control	22608.68	54	418.67		
	Risky Decision-Making	6682.438	54	123.74		
Total	Inhibitory Control	44758.81	60			
	Risky Decision-Making	5645380	60			

IV. Discussion

The fact that the current study had notable limitations is not deniable. Moreover, a considerable range of the previously cited studies reported the contrary results. Probably the number of participants of study groups was below the threshold in which the scores of the utilized tasks be capable of detecting the differences. Moreover, a single session intervention may is not powerful enough to able to give a significant contrast.

Despite the limitations, the present study does not show a significant impact on enhancing inhibitory control and risky decision-making using transcranial Direct Current Stimulation (tDCS) and cognitive training. Moreover, the same results have reported in several previous projects, including a study by Dambacher et al. (2015). They have shown no effects for bilateral tDCS on IFG over inhibitory control and aggression. Furthermore, another assessment of the effects of tDCS on inhibitory control tasks by targeting rIFG showed a weak improvement (Stramaccia et al., 2015).

We suggest using more participants for each group as well as additional intervention sessions for the same studies. Besides, using quantitative electroencephalography (QEEG) is highly recommended for tracing changes that might not be easily detectable through the test scores. In order to enhance inhibitory control and risky decision-making using tDCS in practice, we suggest applying more evidence-based protocols with targeting other regions.

Conflict of Interest: The authors declare that they have no conflict of interest.

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