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EVALUATION OF INHIBITION RESPONSE BEHAVIOR USING THE GO/NO-GO PARADIGM IN NORMAL INDIVIDUALS: EFFECTS OF VARIATIONS IN THE TASK DESIGN

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SUMMARY

Background: Inhibitory control is an important executive function and a deficiency in action inhibition has been characterized as core in a number of neuropsychiatric disorders. The Go/No-Go (GNG) paradigm is a well-known method to evaluate an inhibitory response. We developed seven versions of the GNG to evaluate the effect of different psychometric properties on GNG scores in normal healthy subjects.

Material/ Methods: Fifty seven healthy subjects including 38 (66.7%) males, aged 18 to 55 (mean±SD: 33.7± 8.1) participated in this study. Each subject conducted seven variants of GNG tasks in a randomized order after being given instruction to respond to a selected stimulus displayed on a screen by pressing the space bar as quickly as possible (Go stimuli) and withholding responses to other stimuli (No-Go stimuli). To develop seven versions of varying difficulty, we manipulated the task context by making changes in stimulus complexity, stimulus presentation time, inter-stimulus intervals and the probability of target occurrence.

Results: Decreasing the stimulus presentation time and simultaneously using more complex stimuli caused a significant decrease in true *hits* on Go trials, which is a good marker for response initiation, while an increase in the ratio of No-Go/Go trials led to a decrease in *commission errors* in No-Go trials, which is a good marker of response inhibition. Further analysis revealed that reaction time and age did not influence the GNG task scores while education level and gender may affect scores of Go trials but not No-Go trials.

Conclusions: Manipulation in both stimulus complexity and presentation time caused significant changes in response initiation scores, while alteration in the ratio of No-Go/Go trials led to significant changes in motor inhibition scores. Optimization of GNG tasks to measure response inhibition and initiation could be achieved with psychometric manipulation on various features of stimulus presentation for different target populations.

Key words: No-Go/Go, executive functions, inhibitory control, psychophysics

INTRODUCTION

Inhibitory control is an important part of executive functions and refers to the ability to withhold or suppress inappropriate or unwanted actions in a given behavioral context (Barkley, 2001; Simmonds, Pekar, & Mostofsky, 2008). Inhibitory control is an essential regulatory function and the neuropsychological disorder of impulse control has been characterized as a core deficit in several neuropsychiatric diseases, including attention deficit/hyperactivity disorder (ADHD) (Barkley, 1997; Schachar et al., 2007), conduct disorder, antisocial personality disorder (Bradshaw, 2000), obsessive compulsive disorder (Bradshaw, 2000; Penades et al., 2007. Zielinska et al., 2016), and chronic substance abuse (Fillmore & Rush, 2002; Fillmore, Rush, & Hays, 2002; Monterosso, Aron, Cordova, Xu, & London, 2005).

Many clinical, animal and neuro-imaging studies have investigated the neural correlates of response inhibition and suggested that the ventral prefrontal cortex plays an important role in behavioral inhibition (Butters, Butter, Rosen, & Stein, 1973; Casey et al., 1997; Godefroy & Rousseaux, 1996; Konishi et al., 1999; Liddle, Kiehl, & Smith, 2001). In addition, serotonin, dopamine and noradrenaline have been indicated as critical central neurotransmitters in behavioral inhibition (Eagle, Bari, & Robbins, 2008).

The Go/No-go (GNG) paradigm has been frequently used to measure response inhibition under conditions in which other cognitive/behavioral processes are minimized and consisting of short time trials of Go or No-Go stimulus presentation to the subject followed by an inter-trial interval. The participant has to respond to the Go stimulus as quickly as possible by pressing a button, and avoiding responding to the No-Go stimulus; therefore response inhibition is measured by the ability to avoid response to the No-Go stimulus. Typically, trials containing Go stimuli (Go trials) are used much more frequently than No-Go trials in order to build up a tendency to respond, thereby increasing the inhibitory effort needed to successfully withhold responding to No-Go stimuli.

The classic Go/No-go paradigm has been employed in many neuropsychological studies in combination with neuro-imaging (Casey et al., 1997; Durston, Thomas, Worden, Yang, & Casey, 2002; Elliott et al., 2004; Hare et al., 2008; Rubia et al., 2001; Simmonds et al., 2008; Watanabe et al., 2002) and electrophysiological studies (Donkers & van Boxtel, 2004; Jodo & Kayama, 1992) to evaluate the behavioral inhibition; however, there is wide variation in task parameters across these studies in terms of stimulus type, trial time and the probability of Go stimulus presentation.

Due to a serious lack of published evidence of the effects of GNG task design on the results, this preliminary study aimed to evaluate this effect by manipulating the task properties in a normal population. Seven different versions of the GNG tasks were designed in terms of stimulus complexity, stimulus presentation time (SPT), the inter-stimulus interval (ISI) and the ratio of No-Go to Go stimuli. Likewise, the possible role of underlying demographic factors on GNG measurements was assessed in this study.

METHODS

Participants

Fifty seven healthy subjects including 38 (66.7%) males, aged 18 to 55 (mean± SD: 33.7± 8.1) volunteered for this study through local advertisements or by oral request. They were all healthy, with normal vision and hearing function and at least 5 years of school education (mean±SD: 9.6±3.9 years). None of them had a history of neurological, psychiatric or any other medical problems, and were not on medication for any diseases. All the subjects provided informed oral consent and thereafter they were given seven versions of Go/No-Go tasks.

Procedure

The study was conducted in a condition-controlled room at the neurocognitive laboratory of the Iranian National Center for Addiction Studies (INCAS). At a designated time, each subject came alone to the room and was seated in a comfortable chair in front of a computer with a wide 20-inch monitor and were tested individually. After filling out a demographic form, s/he received verbal instruction to perform seven versions of the GNG task in 7 consecutive runs on a PC computer. Each run contained 80 trials of Go or No-Go targets displayed one by one in the centre of a black screen (a circle with radius of 2.5 cm) and remained briefly visible for a limited duration or until a response occurred by pressing the space bar. The participants were instructed to respond to Go stimuli by pressing the space bar as quickly as possible and withholding response to other stimuli (No-Go stimuli). Each subject conducted the seven variants of GNG tasks in a randomized order, and before each run s/he was given a short break to receive instruction on new target and distracter stimuli.

Measurements

In the neuro-cognitive laboratory of the Iranian National Center for Addiction Studies (INCAS), seven versions of the Go/No-Go task (V1 – V7) are provided, based on the classic Go/No-Go paradigm in which subjects have to respond as quickly as possible to target stimuli and withhold responses to distracter stimuli (Donkers & van Boxtel, 2004). To provide seven versions of the GNG task, we considered version 1 (Target stimulus: blue circle; target probability:20%; Stimulus Presentation Time (SPT): 300 milliseconds; Inter-Stimulus Intervals (ISI): 900 milliseconds) as the basic version and then developed the other six versions by changes in stimulus presentation via variations in stimulus presentation time (V2), inter-stimulus interval (V3), the probability of target occurrence (V4) stimulus type (V5), stimulus spatial presentation (V6) and stimulus complexity (V7). All seven versions of the Go/No-Go tasks were developed using E-Prime V.2 software.

In V1 to V4, the Go stimulus was a blue circle while the No-Go stimulus was a yellow circle, though in V5 the target stimulus was an “O” and the No-Go stimulus was an ‘X’ sign. In version 6 and 7 the target stimulus was a colored circle

at the upper left and / or lower right, and the No-Go stimulus was a colored circle/s at the lower left and/or upper right, respectively. Each version consisted of 80 stimulus presentation trials displayed one by one in a predefined randomized fixed order. The ratio of No-Go to Go stimuli was1:4 (target probability of 20%) in all versions except in version 4 which was 1:1(target probability of 50%). Stimulus Presentation Time (SPT) is defined as the duration of stimuli appearance on the screen which was 300 milliseconds in all versions except V2 with SPT of 1200 milliseconds and the Inter-Stimulus Intervals (ISI) was 900 milliseconds in all versions except V3 with an ISI of 1200 milliseconds. Detailed characteristics of these seven different versions are presented in Table1.

The number of responses to targets (*hits*) and the number of "no" responses to non-targets (s*tops*) are two main measurements which the GNG Task yields. "*Hits"* is the numbers of targets which are correctly detected through Go-trials and "*stops"* are the number of non-targets which are accurately rejected. There are three other scores derived from these "*hit"* and "*stop"* scores: "o*mission errors* (*misses*)" defined as the number of Go stimuli which are mistakenly missed; "*commission errors*" indicate the number of No-Go stimuli which are falsely responded to and could be regarded as the marker of disinhibition. *"Total True Score*" is the sum of "*hits"* and "*stop*s" and shows the total number of true responses to both Go and No-Go stimuli. The number of "*hits*" can be regarded as a measure of behavioral initiation, whereas "*commission errors*" can be considered as measures of inhibitory response.

"Reaction time of hits" and "*reaction time of commission errors*" show the time interval in millisecond (ms.) between the appearances of a Go or No-Go stimulus,

Table 1. Psychophysics characteristics of seven versions (V1 to V7) of GNG task regarding stimulus presentation

Variants	Go Stimulus	No-Go Stimulus	SPT (ms)	ISI (ms)	No-Go/Go Ratio	Number of Trials	Stimulus Position
V1	●	●	300	900	1/4	80	Center
V2	●	●	1200	0	1/4	80	Center
V3	●	●	300	1200	1/4	80	Center
V4	●	●	300	900	1/1	80	Center
V5	**O**	**X**	300	900	1/4	80	Center
V6	● and ●	● and ●	300	900	1/4	80	Center
V7	● or ●	● or ●	300	900	1/4	80	As illustrated

SPT: Stimulus presentation time; ISI: Inter-stimulus interval

Table 2. Go/No-Go task scores definition and range of variability

Variable	Definition	Range
Total true score	True hits on Go and No-Go trials	0-80
Hit	True hits on Go trials	0-64 (All), 0-40 (V4)
Stop	True inhibitions on No-Go trials	0-16 (All), 0-40 (V4)
Omission error (Miss)	Missed Go trials	Similar to Hit
Commission error	False hits on No-Go trials (Disinhibition)	Similar to Stop
Reaction Time of hits	Reaction time of true Go trials in milliseconds	100 - 1000
Reaction Time of commission errors	Reaction time of false No-Go trials in ms	100 - 1000

and pressing the space bar. The GNG task measurements and their range of variability are summarized in Table 2.

Statistics

The results are presented as mean ± SD (standard deviation) for the quantitative variables and are summarized by frequency (percentage) for the categorical variables. With respect to the normal distribution of the scores, a one-way analysis of variance (ANOVA*)* was used to compare Go/No-Go task measurements in various versions. Pairwise comparisons were conducted via the Post Hoc Tukey Test. A difference of $p<0.01$ was considered statistically significant between groups. To assess the consistency of results across the main scores within various versions of the GNG task, the internal consistency reliability was assessed by calculating Cronbach's Alpha. To evaluate the effect of reaction time, age, education and gender on the main GNG task scores, we pooled all the data from the seven versions, after which Pearson's correlation coefficients(r) were used for quantitative variables, and independent-sample t-tests were used for the nominal variable of gender. Pearson's correlation coefficient (r) was also used to identify the underlying factors which may have affected the reaction time scores. For the statistical analysis, the statistical software SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL) was used.

RESULT

All the scores are presented as percentiles in Table 3 to facilitate understanding. To assess the consistency of the main scores within these various versions, the internal consistency reliability index was calculated, which showed a good consistency reliability across the *hits* with Cronbach's Alpha=0.929 and the *stops* with Cronbach's Alpha=0.748. Figure 1, shows that none of the versions were significantly different from the basic version of V1 in terms of the Go trial measurements. As can be seen from Table 1, subsequent pairwise comparison between versions showed that V2 and V3 are significantly different from V5, V6 and V7 in terms of Go-trials scores while significantly higher "*hits"* and lower "*omission errors"* resulted from using V2 and V3 in comparison to the equal scores yielded via V5, V6 and V7 (all P-values<0.01).

With regard to No-Go trials, V4 was the only version which significantly differed from V1 with higher *"stops"* and lower *"commission errors"* . Significantly higher *"stops"* and lower *"commission errors"* are yielded in V4 in comparison to all the other five versions (V4 versus V1, V2 and V7: p-value<0.001; V4 versus V5: p-value<0.01; V4 versus V6: p-value<0.05).

In Figure 1 and Figure 2, the mean of Go scores and No-Go scores of manipulated versions are compared with the basic version1. As it can be seen, there is no significant difference between versions in terms of *hits* and *omission errors* as scores of Go the trial (Fig1a,b). However, version 4 differed significantly from the basic version 1 (P-value<0.001) with regard to *stops* and *commission errors* as scores of the No-Go trials (Fig2a,b)

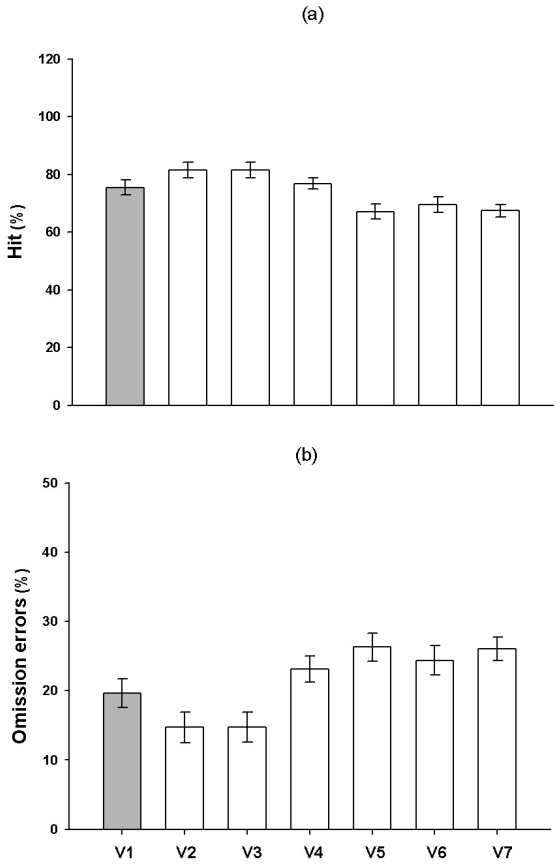

Fig. 1. Comparison between the basic and six different versions of the GNG task in terms of Go trial measurements. a: Hits; b: Omission errors

According to Table 3, there is a significant difference in terms of the *"reaction time of hits"* but not in the "*reaction time of commission errors"* among these seven versions. To evaluate the influence of reaction time and also other demographic variables such as age, education, and gender on the GNG task main scores, we pooled the data of all these seven versions and computed the associations between these variables. As can be seen in Table 4, reaction time scores do not correlate with either *"hits"* or *"stops"*(p-value>0.05) and thus did not affect the GNG task scores. However, a significant -- albeit weak -- association was found between *"hits"* and education (r:0.314; p-value<0.01). Likewise, there was a significant association between gender and *"hits"* (p-value<0.01). Thus, it appears that females and highly-educated participants tended to achieve more "*hits*" when compared to corresponding groups.

"Reaction time of hits" widely varied between some versions of the GNG tasks. Further analysis revealed that the *"reaction time of hits"* significantly associated with "*stimulus presentation time (SPT)"* (r= 0.477;p-value<0.001), age (r= 0.449; p-value<0.001) and education (r= -0.172**;** p-value<0.01), indicating

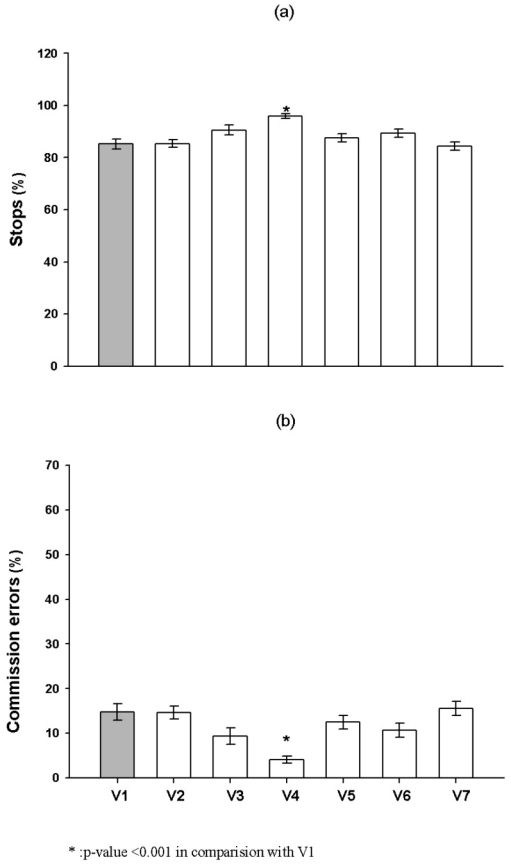

Fig. 2. Comparison between the basic and six different versions of GNG task in terms of No-Go trial measurements. a: Stops; b: Commission errors

Table 3. Go/No-Go task performance measures of normal subjects using seven versions (V1 to V7)

	Overall Score	**Go trials scores**			**No-Go trials scores**		
		Hit (%)	Omission error (%)	Reaction time (ms)	Stop (%)	Commission error (%)	Reaction time (ms)
V 1	77.4±15.4	75.5±19.4	19.6±15.5	378±63	85.2±14.1	14.8±14.1	322±134
V 2	82.9±16.6	82.3±20.2	14.1±16.1	480±101[1]	85.3±10.9	14.7±10.9	284±132
V 3	83.3±15.7	81.5±20.5	14.8±16.4	401±85[2]	90.6±13.8	9.4±13.8	314±168
V 4	86.3±6.9	76.8±14.1	23.2±14.1	366±50[2]	**95.9±6.2**[1,2,5,7]	**4.1±6.2**[1,2,5,7]	324±160
V 5	**71.2±14.6**[2,3,4]	**67.2±18.9**[2,3]	**26.3±15.0**[2,3]	351±52[2,3,7]	87.5±11.6	12.5±11.6	274±69
V 6	**73.5±15.2**[2,3,4]	**69.5±20.0**[2,3]	**24.4±16.0**[2,3]	345±56[2,3,7]	89.2±11.8	10.7±11.8	313±97
V 7	**70.8±12.7**[2,3,4]	**67.5±15.9**[2,3]	**26.0±12.7**[2,3]	394±58[2,6]	84.4±11.9	15.6±11.9	345±110

Data are presented as mean±SD ;[1,2,..7]:The versions which are significantly different from the superscripted version in equal score (p-value<0.01)

Table 4. Pearson's correlation (r) between demographic characteristics, reaction time and GNG task main scores

	Hit	Stop
Reaction time of Hits	0.089	0.059
Reaction time of commission errors	0.021	-0.028
Hit	1	**-0.155****
Stop	**-0.155****	1
Age	0.040	-0.017
Education	**0.314****	0.058

**: p-value<0.01

that while performing the same version, older and less-educated people respond to the stimulus more slowly than younger and more highly-educated people.

DISCUSSION

The present study evaluates the effect of the manipulation of GNG task parameters on the task measurements within a normal population. With all manipulations, increase in the ratio of No-Go/Go trials led to a decrease in commission errors in the No-Go trials, which is a good marker of inhibitory control, while no other changes of the time trial, stimulus type, stimulus spatial presentation and stimulus complexity affected the GNG scores. Simultaneous manipulations of the time trial and stimulus may affect Go trial scores, i.e. decrease in the trial time and using more complex stimuli additively caused a significant decrease in truly detected stimuli on Go trials, which might be considered as a marker of executive function and working memory.

Increasing the "*stimulus presentation time(SPT)"* from 300 ms (V1) to 1200 ms (V2), decreased -- albeit insignificantly -- "*omission errors"* in Go trials, while using more complex stimuli in V5 to V6 rather than the simple blue and yellow circles in V1 similarly raised the *"omission error"* rate in the Go trials and resulted in a trend for lower *"hits"* in these more complex versions. The additive effect of these changes, significantly decreased "*hits*" in V5 throughV7 compared to V2 and -- as was expected -- a reverse pattern was seen in terms of the derived score of *"omission errors".* As for the No-Go scores, none of these changes including trial time or stimulus complexity affect the results. Since the score of the Go trials could be considered as a measure of behavioral initiation and executive function (Simmonds et al., 2008), the lower score of "*hits"* and thus the higher score of "*omission errors"* in Go trials in versions with more complex target and a shorter presentation time indicated the higher demands of the working memory function in these trials. Consistent with these findings, Simmonds et al. in a meta-analysis including 10 event-related studies based on fMRI, showed that complex stimuli demands increased working memory in comparison to simple No-Go stimulus (Simmonds et al., 2008).

According to the probability of stimulus presentation across trials*,* V4 was the only version which showed a significantly different pattern from all these seven versions in which the probability of the Go trials presentation decreased from

75% to 50% and thereby led to a decrease in the habitual response and a tendency to make false responses to No-Go stimuli. On V4, *"stops"* and *"commission errors"* were significantly higher and lower respectively compared to V1 and all other five versions. Thus this version could be considered less sensitive but more specific than the other versions for the evaluation of the inhibition response indicating that less inhibitory effort is needed to successfully withhold responding to No-Go stimuli in the GNG task version with a lower probability of Go stimulus. In line with our results, Donker et al. recorded a larger amplitude of event-related potentials and thus a higher level of inhibitory control demand when the GNG task is presented in a context of frequent GO signals (80% vs. 50%) (Donkers & van Boxtel, 2004). Likewise, Durston et al in a fMRI study on the evaluation of task context on inhibitory process, showed an increased function in premotor cortex when the No-Go response preceded by 5 Go stimulus but not after 1 or 3 (Durston et al., 2002).

Amongst the demographic variables, age did not influence the GNG task scores. Education and gender affect Go trials scores. However, No-Go trial scores seem to be independent of these variables. Since, the Go-trial score could provide a fairly good estimation of working memory, females and highly educated persons seemed to be better in the executive function compared to corresponding groups. In this regard, Speck et al., examined working memory function and gender differences in a fMRI study during the working memory task and found that female subjects performed the task more accurately than the males (Speck et al., 2000). Thus, considerations on the interaction between the Go trial score and these two variables (gender and education) may lead to a better interpretation of GNG results in future neuropsychological studies and a manipulation of GNG task features may help future investigators to optimize the task to measure response inhibition and initiation for different target populations.

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