

Go/NoGo continuous performance task in the psychophysiological research

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Abstract

Introduction: Go/NoGo continuous performance task (CPT) is a neuropsychological test designed for measurement of attention and impulsivity and very often associated with attention deficit hyperactivity disorder (ADHD). The aim of this study was to provide current view of test with its application in future psychophysiological research and clinical practise.

Methods: The studies regarding CPT were collected using scientific databases (PubMed, Medline, SCOPUS). The heart rate variability (HRV) as an index of parasympathetic activity and electrodermal activity (EDA) as a noninvasive index of sympathetic arousal were applied in ADHD and depression during Go/NoGo CPT.

Conclusion: In psychophysiological research, the altered HRV and EDA could represent a noninvasive biomarkers for internalizing/externalizing psychopathology. It seems that Go/NoGo CPT could be used as an important diagnostic tool in mental disorders, however future research is needed.

Key words: Go/NoGo continuous performance task, heart rate variability, ADHD, electrodermal response

Introduction

Stress can be generally defined as a response to demands (usually noxious) on the body (Selye, 1936) or as alterations in psychophysiological homeostatic processes (Burchfield, 1979). The stimulus disrupting homeostasis is called a stressor. Stressors may be divided into several categories: *e.g.* physical (*e.g.* heat, cold), metabolic (*e.g.* hypoxia, hypoglycemia) and mental stressors (*e.g.* public speaking) (Mravec and Zucha, 2006). Stress leads to various changes in nervous system and the complex effect of mental stress depends on cognitive processing by cortical (mainly orbitofrontal and medial prefrontal) areas in cooperation with limbic system (Mravec et al., 2009). Nevertheless, autonomic nervous system (ANS) is very sensitive to mental stressors and its reactivity has been shown associated with physical, behavioral and mental health symptoms (El-Sheikh et al., 2009; Obradovic et al., 2010). Therefore, the ANS reactivity is extremely sensitive to laboratory stressors, such as Stroop and the mental arithmetic tests. Mental stress alters immediately and completely the sympathetic/parasympathetic balance (Martinez-Lavin, 2007), and the effect depends on receptor type

(McCorry, 2007). For example, active stress is linked with higher heart rate, mediated through β -adrenergic activation and passive stress causes changes in blood pressure predominantly through the activation of α -receptors (Chi et al., 1993; Delahanty et al., 1996).

One of the examples of active mental stressor is Go/NoGo continuous performance task (Go/NoGo CPT), which is designed as a neuropsychological test to measure attention and impulsivity. In following proposal, we describe the characteristic of test.

Variants of Go/NoGo CPT

In the traditional Go/NoGo CPT, participants are instructed to respond rapidly, generally with a button-press, to presentation of Go stimuli only, and response inhibition is measured by the ability to appropriately withhold responding to NoGo stimuli. Several variations of Go/NoGo stimuli have been used in various studies, for example the faces with emotions (Yu et al., 2014), coloured circles and geometric shapes (Thomalla et al., 2014), airplanes (as Go stimulus) and bombs (as a NoGo stimulus) (Rubia et al., 2001), numbers (Nelson et al., 1998), as well as the letters or its auditory modalities (Shucard et al., 2008). The example of test using Go/NoGo paradigm with letters stimuli is the Conners' Continuous Performance Test (CCPT). Traditional CCPT requires the subject to press a computer key only after X is presented and the modern version – the CCPT-II requires subject to press the computer key immediately after every letter except the X (Conner, 2000).

The differences in Go/NoGo paradigms are not only in the stimuli but also in the task designs. More traditional is using a simple format of test with a single Go stimulus and single NoGo stimulus. The example of more complex design is a version of the task where X and Y are alternately presented on the screen, and there is a two-letter repeat, which is the NoGo signal: if X is presented, Y will become Go signal and X the NoGo signal, and *vice versa* (Garavan et al., 1999).

The Go/NoGo parameters

Performance efficiency is generally expressed in terms of correct detections, commission and omission errors and reaction time (Table 1.). From the psychological context, the errors of omission are assumed to reflect symptoms of inattention, while errors of commission are supposed to reflect impulsivity (Barkley, 1991; Halperin et al., 1991). Computerized RT measures, as a valuable indicator of cognitive performance have gained renewed attention, because the recognition that reaction time variability (RTV) may convey unique information (Berkson and Baumeister, 1967; Barrett et al., 1986; Jensen, 1992). RTV has been discussed as a potentially important index of the stability/instability of an individual's nervous system (Karalunas et al., 2014). Several studies have used standard deviation (SDRT) to quantify RTV (Geurts et al., 2009; Sinzig et al., 2008). Alternatively, RTV is calculated as a coefficient of variation: SDTR/mean RT or by ex-gaussian decomposition, in which τ reflect both the mean reaction time and standard deviation of the exponential portion of the distribution. However, the ideal metrics of RTV are not yet clear (Karalunas et al., 2014).

Table 1. Standard evaluating parameters in Go/NoGo CPT

Correct detection	indicate the number of times the client responded to the target stimulus
Ommision errors	indicate the number of times the target was presented, but the client did not respond/click the button
Commision errors	indicate the number of times the client responded but no target was presented
Reaction times (RT)	this measure the amount of time between the presentation of the stimulus and the client's response

CPT seems to be helpful in differential diagnosis of mental disorders, in which the ability to suppress inappropriate and unwanted actions is impaired. The most notable is attention deficit/hyperactivity disorder (ADHD) (Barkley, 1997). Karalunas et al. (2014) in their meta-analyse of several studies found increased RTV among individuals with ADHD compared with typically-developing controls. Moreover, this parameter has correlated with measures of behavioral inattention (Nigg, 1999; Wahlstedt, 2009; Wahlstedt et al. 2009), and it has to correlate with hyperactivity-impulsivity in other study (Gomez-Guerrero et al., 2011). However, the application of CPT, in particular RTV as a specific diagnostic tool remains questionable and without general acceptance as a „gold standard“ in externalizing psychopathology (McGee, 2000; Gualtieri et Johnson; 2005). For example, higher RTV has been observed in other mental disorders such as autism (Verte et al., 2005), schizophrenia (Kaiser et al., 2008) and bipolar disorder with psychotic symptoms (Bora et al., 2006).

Physiological responses to Go/NoGo test

Brain activation

The Go/NoGo tasks are focused on executive functions, that refer to the ability to plan and execute behaviour (Simmonds et al., 2008). The ability to suppress irrelevant stimuli or impulses is essential for normal thinking processes and ultimately for successful living. Inhibitory control of behaviour, composing of motor, emotional, cognitive, and social abilities, is phylogenetically one of the highest developed human self-control functions (Williams et al., 1999). The beginning of inhibitory abilities also marks an important milestone in cognitive development, and is considered as a characteristic of frontal lobe maturation (Diamond, 1990). Previous studies have investigated the neural correlates of response inhibition. For example, the human lesion studies

demonstrated the involvement of the frontal cortex (Drewe, 1975; Godefroy and Rousseaux, 1996), with more specific localization of the superior medial (Drewe, 1975; Floden and Stuss, 2006; Picton et al., 2006) and right inferior prefrontal cortical areas (Aron et al., 2003; Chambers et al., 2006). Recent studies using an objective neuroimaging methods found frontal lobe activation during Go/NoGo CPT (Garavan et al. 1999; Rubia et al. 2001). However, localization within the frontal cortex varies across studies depending on the task specificity (Mostofsky et al., 2003). It seems that the simple format of Go/NoGo task is examination of response inhibition under conditions in which other cognitive/behavioral processes are minimized, while more complex designs of Go/NoGo task demand also short term/working memory. The studies using simple format of Go/NoGo task demonstrated activation in the presupplementary motor area (pre-SMA) bilateral occipital regions and the precuneus, and the studies using the complex format of CPT found activation in the pre-SMA, right middle/inferior frontal gyrus, bilateral inferior parietal regions, bilateral putamen, bilateral insula, right middle temporal gyrus, left fusiform gyrus and the left middle gyrus. Moreover, both simple and complex Go/NoGo tasks evoked the activity of the pre-SMA suggesting that recruitment of the pre-SMA is critical to response inhibition irrespective of the task demands (Simmonds et al., 2008).

Autonomic nervous system

As mentioned in the beginning, Go/NoGo CPT as a mental stressor leads to the ANS response and alters the sympathetic/parasympathetic balance. Moreover, the complex analysis of ANS during CPT are rare.

Heart rate variability-index of parasympathetic activity

Cardiac function is extremely sensitive to autonomic influences. The heart rate variability (HRV), *i.e.*, the amount of the heart rate fluctuations around the mean heart rate, provides insight into the autonomic control of the heart and gives important information about cardiac sympathetic and parasympathetic interaction (Stein and Kleiger, 1999; Van Ravenswaaij-Arts et al., 1993). The mental arousal which follows a laboratory mental stress test produces a centrally induced shift of ANS balance towards the sympathetic activation associated with vagal withdrawal. Therefore, it can be used as an ideal model to study the magnitude and complex dynamics of heart rate autonomic regulatory inputs (Visnovcova, et al. 2014). HRV is traditionally quantified by linear methods- time and frequency (spectral) domain analysis- providing the information about the heart rate variability magnitude and frequencies (Task Force, 1996). Spectral analysis of HRV allows to isolate the faster high frequency respiratory-coupled oscillations as an index of cardiac vagal function (Bertson et al., 1997; Martinmäki et al., 2006). Recently, nonlinear methods measuring qualitative characteristic of the cardiac time series, *i.e.* complexity, and other system dynamic features have been shown to be more suitable for a detailed description of heart rate autonomic control (Javorka et al., 2009; Porta et al., 2009). Moreover, series of neuroimaging studies have provided evidence that HRV has been related to the activity of the prefrontal cortex (Lane et al., 2009). Therefore, it is proposed that HRV is related to cognitive performance (Thayer et al., 2009), which was supported by findings that subject with high HRV had a significantly higher number of correct responses compared to subject with low HRV during Go/NoGo task (Hansen et al., 2003; Eisenberg and Richman, 2011).

In our study, we assessed HRV during Go/NoGo CPT in ADHD as an externalizing disorder, depressive patient as an internalizing disorder and control subject. Our protocol type sent two stimuli types, a target -green circle and non-target -red coloured letter. In control subject, HRV was decreased during test indicating a shift of ANS dynamic balance to vagal withdrawal and sympathetic arousal (Fig. 1). It indicates physiological response of autonomic flexibility and adaptability. On the other hand, we found different heart rate reactivity in mental disorders compared to controls indicating a potential alteration in cardiac autonomic flexibility in ADHD and

depression (Figures 2 and 3). It seems that HRV could represent an important predictive marker in psychophysiological research, however, this hypothesis is needed to validate in future longitudinal studies.

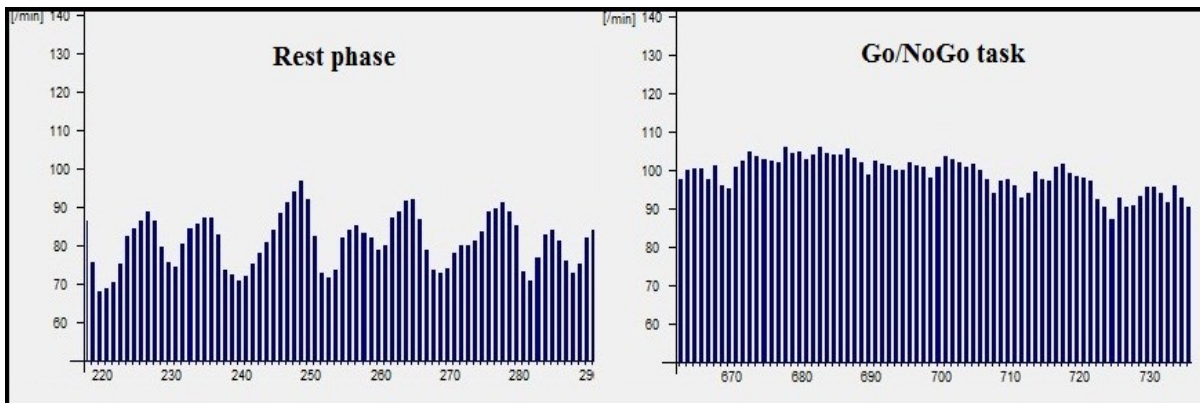


Fig. 1 HRV in rest phase and during CPT in healthy subject indicates a physiological response of ANS

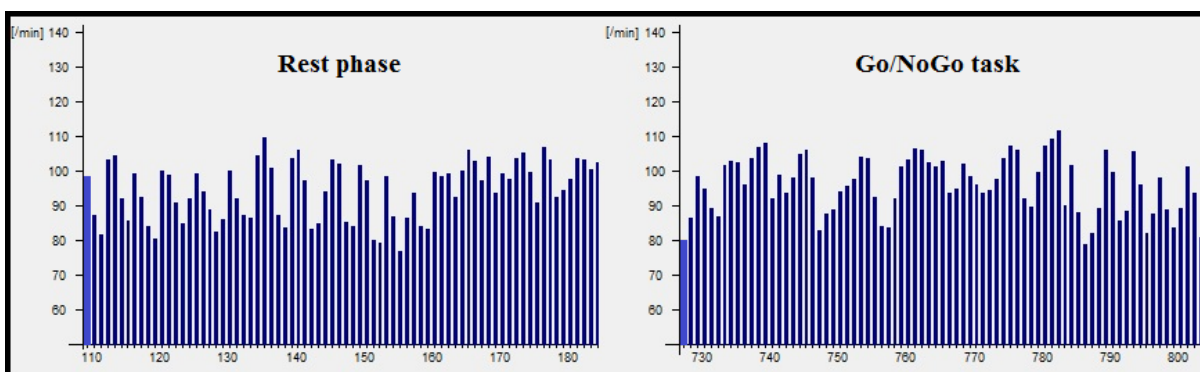


Fig. 2 Altered HRV in rest phase and during CPT in ADHD patient

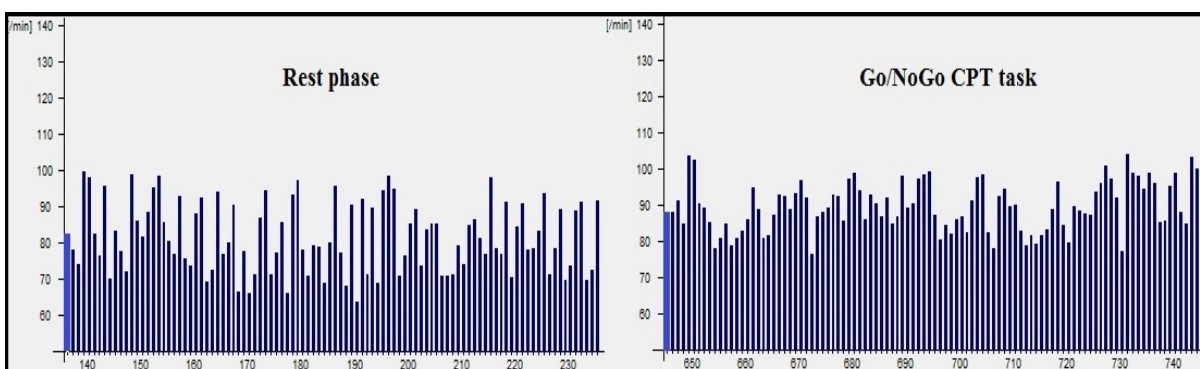


Fig. 3 Altered HRV in rest phase and during CPT in depressive patient

Electrodermal activity - index of sympathetic activity

Electrodermal activity (EDA) is accepted as a noninvasive marker of sympathetic arousal in response to stress in psychophysiological research (Ionescu-Tirgoviste and Pruna, 1993; Jacobs et al., 1994). Value of skin conductance depends of amount of sweat produced by ecrine sweat glands regulation by sympathetic nervous system. When the sweat duct is filled with sweat, more conductive area originates on the nonconductive corneum (Dawson et al., 2007). In our study, we assessed EDA in response to CPT in the same patient mentioned above (Figures 4,5,6). EDA amplitude (μS) was evaluated in a percentage value from resting phase (5 min.) and the CPT response (5 min.). Our individual pilot results found the lowest EDA reactivity in ADHD patient (23,73%) compared to depression (58,06%) and healthy subject (65,49%) indicating a potential sympathetic underarousal typical for externalizing psychopathology. Therefore, we suggest that electrodermal response to CPT could represent a biomarker for externalizing/internalizing psychopathology differences.

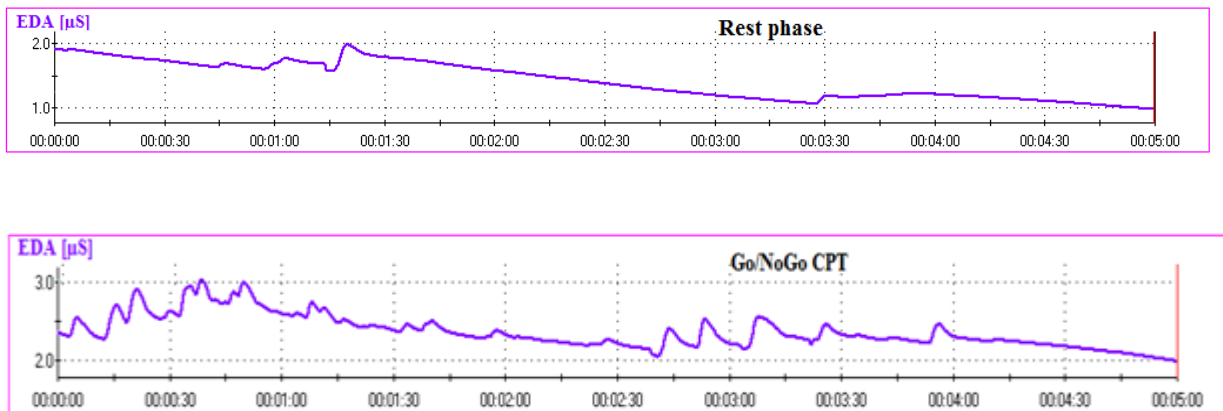


Fig. 4 Increased EDA in control subject indicating sympathetic arousal in response to stress

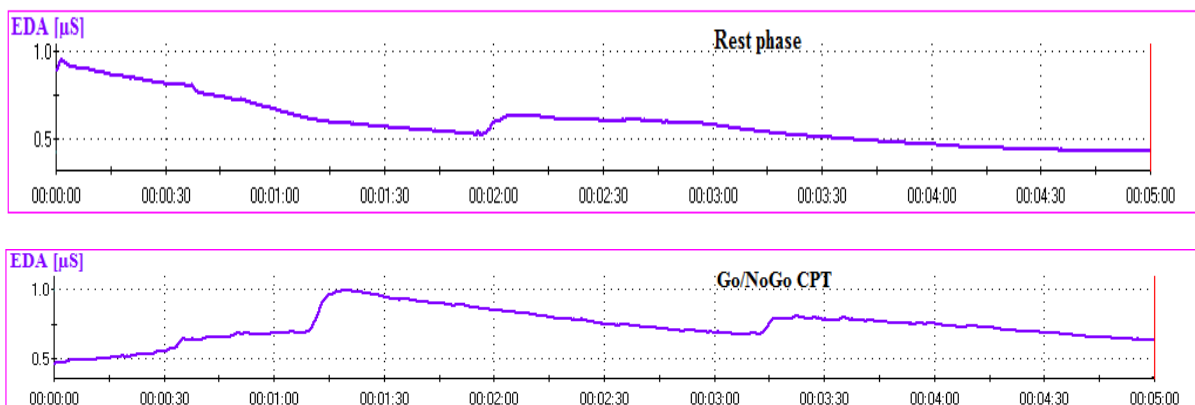


Fig. 5 EDA in ADHD patient indicating a potential sympathetic hypoarousal

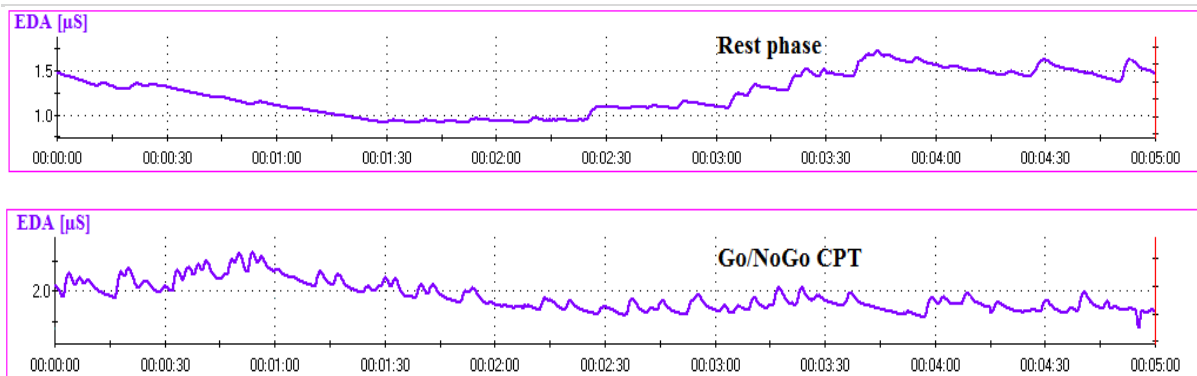


Fig. 6 EDA in depression patient indicating sympathetic arousal in response to stress

Conclusion

Go/NoGo CPT represents a neuropsychological test of vigilance and sustained attention, but it is not standard diagnostic tool in mental disorders. We suggest that diminished HRV and electrodermal activity in response to CPT could indicate abnormal autonomic regulation associated with higher risk of adverse health outcomes. It seems that complex psychophysiological approach may be useful in clinical application for differential diagnosis of mental disorders. Future research is needed.

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