Consciousness and Cognition xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Consciousness and Cognition

journal homepage: www.elsevier.com/locate/concog

The effects of neurochemical balance in the anterior cingulate cortex and dorsolateral prefrontal cortex on volitional control under irrelevant distraction

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A R T I C L E I N F O

Keywords:
Volitional control
Go/No-Go task
Magnetic resonance spectroscopy (MRS)
Anterior cingulate cortex (ACC)
Dorsolateral prefrontal cortex (DLPFC)

A B S T R A C T

Volitional control has been related to the excitatory/inhibitory (E/I) ratio of glutamate-glutamine to γ-aminobutyric acid concentration in the different parts of the frontal cortex. Yet, how the neurochemical balance in each of the brain areas modulates volitional control remains unclear. Here, participants performed an auditory Go/No-Go task with and without task-irrelevant face distractors. Neurochemical balance was measured with magnetic resonance spectroscopy at rest. Participants with higher E/I ratios in the dorsolateral prefrontal cortex (DLPFC) showed less control over No-Go cues under no distraction, whereas participants with higher E/I ratios in the anterior cingulate cortex (ACC) were more prompted to make speeded Go responses under distraction. Therefore, the neurochemical balance in the DLPFC and ACC may be involved in the control over task-relevant and -irrelevant cues respectively.

1. Introduction

Behaviour cannot always be controlled by one's own will (Haggard, 2008). For example, one may experience a delay in starting to drive once a traffic light has changed, or conversely you may pre-emptively start driving upon hearing a car horn before the light has changed. This could be because, besides one's own will, external stimuli could prompt behavioural responses even when the stimuli are not relevant to the task at hand (Wessel & Aron, 2017) or when they reach conscious awareness with various degrees (Dehaene et al., 2003; Koizumi, Maniscalco, & Lau, 2015; van Gaal, de Lange, & Cohen, 2012).

The ability to successfully implement behavioural control varies across individuals, which appears to be, at least partly, driven by the differences of neurochemical balance in the brain (see Duncan, Wiebking, & Northoff, 2014 for a review). Recent progress with magnetic resonance spectroscopy (MRS) enables the estimation of the excitatory/inhibitory (E/I) ratio in particular brain areas (Kondo, Farkas, Denham, Asai, & Winkler, 2017; Shibata et al., 2017; Takeuchi, Yoshimoto, Shimada, Kochiyama, & Kondo, 2017). The E/I ratio is the balance between the predominant excitatory neurotransmitter (glutamate-glutamine; Glx, which reflects the glutamate level as well as other metabolic information and noise) and the predominant inhibitory neurotransmitter (γ-aminobutyric acid, GABA). Thus, the E/I ratio increases when the concentration of Glx increases and/or when the concentration of GABA decreases.

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https://doi.org/10.1016/j.concog.2018.01.001
Received 6 September 2017; Received in revised form 6 January 2018; Accepted 6 January 2018

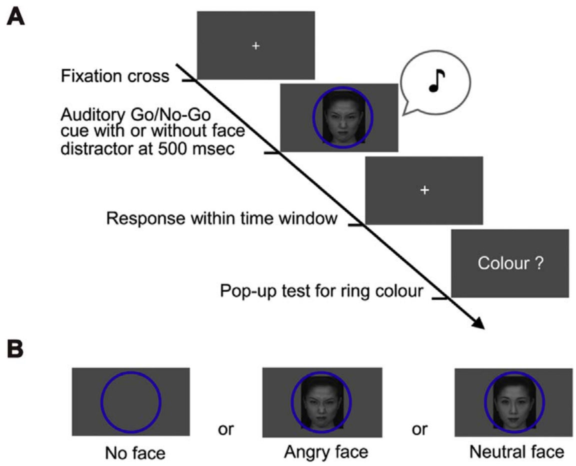

Fig. 1. Schematic representation of task design. (A) Trial sequence of an auditory Go/No-Go task. A high or low tone was used as Go or No-Go cue, which appeared with and without face distractors. Participants made speeded Go responses upon hearing a Go cue in a response time window. They were given an occasional pop-up test for ring colour so as to maintain their attention to the screen. (B) Schematics of face distractors which were presented with a ring coloured in blue or green. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Previous studies suggested that a range of cognitive functions relies on the E/I ratio in the brain areas related to the tasks (Kondo et al., 2017; Shibata et al., 2017). It has been demonstrated that behavioural control may particularly rely on the neurochemical balance in the frontal areas, such as the anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (DLPFC) (Boy et al., 2011; Silveri et al., 2013).

However, it is unclear how the neurochemical balance in each of the frontal areas contributes to behavioural control. One study has demonstrated that adolescents with higher GABA concentration in the ACC are less able to inhibit responses upon seeing No-Go cues (Silveri et al., 2013). Another study has shown that GABA concentration in the supplementary motor area (SMA) is associated with behavioural inhibition elicited with subliminal cues (Boy et al., 2010). This effect was not found in the ACC or DLPFC (Boy et al., 2010), which are widely implicated in behavioural control (Passingham & Wise, 2012). Nevertheless, higher GABA concentration in the DLPFC was related to lower trait urgency scores (Boy et al., 2011). These results suggest that the DLPFC may play a role in inhibitory control at a conscious level that can be introspected.

While behavioural control in general relies on both the DLPFC and ACC in a distributed manner (Nee, Wager, & Jonides, 2007; Swick, Ashley, & Turken, 2011; Wessel & Aron, 2017), the resistance to task-irrelevant distractors may particularly rely on the ACC (Bishop, Duncan, Brett, & Lawrence, 2004; Botvinick, Cohen, & Carter, 2004). This role of the ACC may be especially critical when the irrelevant cues are consciously perceived (Dehaene et al., 2003). Meanwhile, the E/I ratio in the SMA may have little contribution to conscious control of behaviour examined here, because the SMA is more implicated in implicit control (Boy et al., 2010).

To test the effects of E/I ratio in the ACC, DLPFC, and SMA on behavioural control performance, we used an auditory Go/No-Go task, with and without task-irrelevant face distractors (Fig. 1). We assessed the E/I ratio in each of those brain areas and examined its relationships with the participant's ability to implement behavioural control according to task-relevant cues (i.e., Go and No-Go cues), as well as their ability to resist task-irrelevant distractors (i.e., faces).

2. Methods

2.1. Participants

Forty-one participants (27 males, M_{age} = 25.7 years, SD_{age} = 10.5 years, range 21–60) were enrolled in this experiment. All participants were right-handed Japanese with normal or corrected-to-normal vision. None had any history of neurological or psychiatric disorders. The experiments were conducted in accordance with the ethical standards of the 1964 Declaration of Helsinki and approved by the Ethics and Safety Committees of NTT Communication Science Laboratories and ATR-Promotions (protocol numbers: H24-004 and AN14-001). The participants provided written informed consent prior to their participation.

2.2. MRS data acquisition

To minimize confounding factors affecting neurotransmitter concentrations, we conducted the acquisition of MR spectra at a fixed time for all participants, between 1:00 p.m. to 2:30 p.m. (see also Kihara, Kondo, & Kawahara, 2016; Kondo et al., 2017). To reduce noise or bias in measurements, participants were requested to refrain from alcohol for 24 h before the experiment, and from caffeine on the day of the experiment. Data were acquired with a 3 T MRI scanner with a 12-channel receive-only head coil (Magnetom Trio, Siemens). Head motion was minimized with comfortable padding around the participant's head. For assessment of cortical thickness and volume, anatomical images were obtained with a T1-weighted pulse sequence (isotropic voxel size of 1 mm^3).