Neuropsychologia 69 (2015) 130–139

Contents lists available at ScienceDirect

Neuropsychologia

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

Double dissociation of error inhibition and correction deficits after basal ganglia or dorsomedial frontal damage in humans

Eldad Yitzhak Hochman [a,*], Seqian Wang [a], Theodor E. Milner [b], Lesley K. Fellows [a]

[a] Montreal Neurological Institute, Department of Neurology & Neurosurgery, McGill University, 3801 University Street, Montreal, Canada QC H3A 2B4
[b] Department of Kinesiology & Physical Education, McGill University, 3801 University Street, Montreal, Canada QC H3A 2B4

ARTICLE INFO

Article history:
Received 6 August 2014
Received in revised form
14 January 2015
Accepted 16 January 2015
Available online 17 January 2015

Keywords:
Error inhibition
Error correction
Performance monitoring
Action selection
Basal ganglia
Prefrontal cortex

ABSTRACT

Effective self-control relies on the rapid adjustment of inappropriate responses. Understanding the brain basis of these processes has the potential to inform neurobiological models of the many neuropsychiatric disorders that are marked by maladaptive responding. Research on error processing in particular has implicated the dorsomedial frontal lobe (DMF) and basal ganglia (BG) in error detection, inhibition and correction. However there is controversy regarding the specific contributions of these regions to each of these component processes. Here we examined the effects of lesions affecting DMF or BG on these error-related processes. A flanker task was used to induce errors that in turn led to spontaneous, online corrections, while response kinematics were measured with high spatiotemporal resolution. The acceleration of errors was initially greater than that of correct responses. Errors then showed slower acceleration compared to correct responses, consistent with engagement of inhibition shortly after error response onset. BG damage disproportionately disrupted this early inhibitory phenomenon, above and beyond effects on baseline motor performance, but did not affect the kinematics of the corrective response. DMF damage showed the opposite pattern, with relatively delayed onset and weaker initial acceleration of the corrective response, but error suppression kinematics similar to that of the control group. This work clarifies the component processes and neural substrates of online post-error control, providing evidence for dissociable contributions of BG to error inhibition, but not correction, and DMF to rapid error correction, but not error suppression.

1. Introduction

As any veteran of highway driving knows, rapidly recognizing and correcting errors can be a matter of life and death. The brain basis of error processing has been the subject of intense study. In the speeded choice paradigms widely used to study performance monitoring, errors emerge in a stream of action selection events: mechanisms must exist to detect that an on-going response is wrong, to interrupt it, and to replace it with a correct response. Regions within the dorsomedial frontal lobes (DMF), and the basal ganglia (BG) are thought to be key nodes in error processing (Ullsperger et al., 2014a, 2014b), but the critical contributions of these two regions to the various components of error processing remain unclear.

Regions within DMF have been implicated in error detection, inhibition, and correction. Both the anterior cingulate (ACC) and the pre-supplementary motor (pre-SMA) divisions of the DMF have been implicated in detection of overt errors, and in detection of response conflict more generally, primarily based on electrophysiological and fMRI evidence (ACC, (Charles et al., 2013; Dehaene et al., 1994; Gehring et al., 2012; Nee et al., 2011; Orr and Hester, 2012; Yeung et al., 2004); pre-SMA, (Garavan et al., 2003; Herrmann et al., 2004; Hochman et al., 2009; Nee et al., 2011)). However, whether damage to DMF interferes with error detection (Modirrousta and Fellows, 2008a) or conflict monitoring (di Pellegrino et al., 2007; Fellows and Farah, 2005) is still controversial. In addition, this region has been implicated in the inhibition of unwanted responses: There is human lesion evidence that intact pre-SMA is necessary for rapid inhibition of pre-potent, unwanted responses (Nachev et al., 2007), but whether this mechanism is engaged in error inhibition has not been established. Indeed, even the existence of error inhibition is under debate (Gehring et al., 2012).

Electrophysiological, fMRI and TMS studies in healthy subjects also support a role for DMF in error correction (Agam et al., 2011; Hochman et al., 2009, 2012, 2014; Wessel et al., 2014) and closely related action selection processes (Nee et al., 2011; Neubert et al.,

* Corresponding author.
E-mail address: eldadho@gmail.com (E.Y. Hochman).

http://dx.doi.org/10.1016/j.neuropsychologia.2015.01.023
0028-3932/

2010). Existing lesion studies provide some support for this claim, showing that DMF is necessary for rapid error correction (Modirrousta and Fellows, 2008a; Swick and Turken, 2002). However, the paradigms used in these studies do not fully disambiguate error detection and inhibition from error correction.

Other work has focused on the role of the BG in these three putative components of error processing (Holroyd and Coles, 2002). Studies of patients with BG dysfunction, and neuroimaging studies in healthy subjects, implicate the BG in error detection (Donamayor et al., 2012; Ruiz et al., 2014; Siegert et al., 2014; Smith et al., 2000) but not in error correction (Ullsperger and von Cramon, 2006). The BG appear to participate in response inhibition triggered by external cues (Schmidt et al., 2013). However, direct evidence that this region is required for error inhibition is lacking, although such a role has been proposed in a recent model (Wiecki and Frank, 2013).

In sum, there is evidence that both DMF and BG are involved in error processing, but controversy as to their specific contributions. Part of the difficulty with this literature is that there are several closely related processes playing out over time as errors are detected, inhibited and corrected, even in the course of a single trial, and in the simplest, two choice tasks (Ullsperger et al., 2014b). Are both regions critical for all of these processes, acting as a tight network, or do they make unique contributions? Lesion studies can test the dissociability of putative component processes, and can establish whether specific regions are necessary for those processes. Here, we combine this method with sensitive kinematic measurements of large amplitude responses to probe the effects of focal brain damage on putative components of error processing at a fine time resolution.

We tested patients with chronic focal damage to the BG or DMF, and demographically matched healthy subjects. Participants performed an arrowhead version of the flanker task known to induce corrected errors (Gehring et al., 2012). We focused on overt errors, aiming to trace the dynamic evolution of both the error and the correct response. Based on existing evidence, we hypothesized that processes related to the error (detection and inhibition) could be dissociated from the processes allowing the corrective response to be produced, with BG critical only for the former, and DMF only for the latter.

2. Methods

2.1. Participants

All patients were identified through the McGill Cognitive Neuroscience research registry; healthy participants were recruited through advertisement in the community. Lesions resulted from ischemic stroke or tumor resection, and occurred at least 6 months prior to testing (range, 9 months–6 years). Participants were included if their lesion affected one of the two regions of interest, based on review of the most recent clinical imaging. Five patients with damage to the BG, 5 patients with damage to the DMF, and 10 healthy, age- and education-matched (age, $F(2,17)=0.73$, $p=0.5$; education, $F(2,17)=0.89$, $p=0.43$) controls participated in the study (Table 1).

In keeping with standard methods (Kimberg et al., 2007; Fellows, 2012), a neurologist experienced in lesion analysis and blind to experimental performance manually registered each individual lesion from the patient's most recent magnetic resonance or computed tomography brain imaging to the Montreal Neurological Institute standard brain template to allow lesion overlap images to be generated in a common space, using MRIcro software (Rorden and Brett, 2000) (Fig. 1). All 5 BG lesions and three DMF lesions were unilateral. BG lesions affected the right hemisphere in 1 patient, the left hemisphere in 4. Unilateral DMF lesions all affected the left hemisphere. BG damage was due to ischemic stroke in all cases, and primarily affected the caudate-putamen, with varying impact on the closely associated fibers of the internal capsule. DMF damage was due to low grade tumor resection in 4 cases, and ischemic stroke in once case. Damage variably affected pre-SMA/SMA ($N=2$), dACC ($N=1$), or both ($N=2$), along with underlying white matter to varying degree. One DMF lesion extended caudally into medial premotor and motor regions. Fig. 1 shows the location of the individual lesions and the lesion overlap in each group; images are oriented by radiological convention (left is left).

Table 1 summarizes the demographic information in all groups. Screening tests showed no evidence of hemispatial neglect in any of the patients. Two BG patients had mild difficulty with language comprehension, one of those was also mildly impaired on confrontation naming. Performance on basic attention and executive function screening tests is shown in Table 1. Controls had no history of psychiatric or neurological disorders, substance abuse or closed head injury. All participants provided written informed consent and received monetary compensation for their time and inconvenience. The local Research Ethics Board approved the study.

2.2. Apparatus

The experiment was performed using a wrist manipulandum connected to a torque motor (PMI U16M4) under computer control (Fig. 2). The position and velocity of the motor response were measured by a potentiometer and tachometer, respectively, while torque was measured by a linear strain gauge mounted on a cylinder, coupling the motor shaft to the manipulandum. The signals were sampled and digitized at 2 kHz. The subject was seated comfortably in a chair with the forearm resting on a padded support. The forearm was oriented midway between pronation and supination and immobilized to allow only flexion and extension of the wrist. The subject moved the manipulandum by applying force to two curved pads, which were securely clamped against the palmar and dorsal surface of the hand; the subject did not grip the manipulandum. These pads were positioned to align the axis of rotation of the wrist over the axis of the torque motor. The manipulandum position (i.e. the angular position of the wrist) controlled a cursor appearing on a computer screen. All patients with unilateral lesions responded with the contralesional hand; in all but one patient (in the BG group) this was the dominant hand. Controls and patients with bilateral lesions responded with the dominant hand.

2.3. Kinematic analysis

In keeping with other kinematic work (Milner, 2002), position data were low pass filtered to remove high frequency noise, here using a FIR low-pass digital filter (http://www.mathworks.com/help/signal/ref/fir1.html) with a Hamming window with 128 points and a low-pass cut off frequency of 200 Hz. Movement acceleration was calculated as the derivative of the velocity:

$$A(t) = \frac{V(t+\tau) - V(t-\tau)}{2\tau}$$

where τ is the sampling interval, A is the acceleration, V is the velocity and t (ms) is current time.

2.4. Flanker task

Participants performed an arrowhead version of the Eriksen flanker task (Eriksen and Eriksen, 1974) (Fig. 2). At the start of each