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Original contribution

Targeted brain activation using an MR-compatible wrist torque measurement device and isometric motor tasks during functional magnetic resonance imaging

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ABSTRACT

Dedicated pairs of isometric wrist flexion tasks, with and without visual feedback of the exerted torque, were designed to target activation of the CBL and BG in healthy subjects during functional magnetic resonance imaging (fMRI). Selective activation of the cerebellum (CBL) and basal ganglia (BG), often implicated in movement disorders such as tremor and dystonia, may help identify pathological changes and expedite diagnosis. A prototyped MR-compatible wrist torque measurement device, free of magnetic and conductive materials, allowed safe execution of tasks during fMRI without causing artifacts. A significant increase of activity in CBL and BG was found in healthy volunteers during a constant torque task with visual feedback compared to a constant torque task without visual feedback. This study shows that specific pairs of motor tasks using MR-compatible equipment at the wrist allow for targeted activation of CBL and BG, paving a new way for research into the pathophysiology of movement disorders.

1. Introduction

The healthy human body is able to perform fast, accurate and efficient motor actions and is able to correct for perturbations while performing these actions. The central nervous system is responsible for the execution of voluntary as well as involuntary actions like reflexes using a network of multiple interconnected control loops. This network includes the cerebellum (CBL) and basal ganglia (BG) [1]. Part of the role of the CBL is to integrate sensory information and it concerns the unconscious neuromuscular control of a joint [2], which includes correcting for errors [3]. BG is a collective term for a group of brain regions including the caudate nucleus, putamen and globus pallidus. The role of the BG in motor control is less apparent. The BG are supposedly involved in the control of complex patterns of motor activity [1,4].

Movement disorders impair the ability to produce and control bodily movements [5], resulting in immobility and social inconvenience [6]. Over 28% of the population over 50 years old suffers from movement disorders [7]. Many of these disorders have unknown pathophysiology [8–10]. Although specific brain regions, including the CBL and BG, have been implicated in specific movement disorders, still most are being diagnosed by symptoms. Unfortunately, diagnosis of movement disorders can be hindered by the similarity of their symptoms [11]. An incorrect diagnosis could not only lead to ineffective treatment, but also to adverse consequences [12]. Developing tools to aid physicians diagnose patients with movement disorders may facilitate effective treatment by early detection and improved accuracy of the diagnosis.

Functional magnetic resonance imaging (fMRI) is a non-invasive technique for visualizing neural activity, which enables imaging of deep brain structures like the BG. fMRI recordings suffer from image distortions due to movement of the subject's head [16] and to the use of magnetic or conductive materials [17]. Using fMRI to study blood oxygenation level dependent (BOLD) activations in the CBL and BG during the execution of motor tasks and comparing results between

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healthy subjects, and patients with certain movement disorders, may help identify pathological changes associated with those movement disorders. The number of studies that investigate brain activation in the CBL and BG during motor tasks with feedback is limited, especially studies that incorporate feedback to enable corrective actions and facilitate the activation of the CBL and BG. Hidler et al. [13] did not find activity in the CBL or BG in an isometric wrist torque task where the subject at 1 Hz interchanged between exerting a certain torque with visual feedback and relaxing compared to a rest task. This finding suggests that a fast switching task is executed using feedforward control. On the other hand, Vaillancourt et al. [14] did find activity in the CBL and BG in healthy subjects when comparing a grip force task with visual feedback to the same task without visual feedback. Visual feedback appears to facilitate adaptation of the subject's motor commands during the task. Klarhöfer et al. [15] found activity in the CBL in healthy subjects when comparing a gripping task with visual feedback to the same task with force perturbations, generated using a haptic manipulator. Hence, increased activation in both CBL and BG, only CBL, and in neither CBL nor BG has been demonstrated using motor tasks during fMRI. However, these activation combinations have been achieved on different joints, areas of focus and experimental setups. This study aims to show these activations on one single joint using an isometric setup.

Creating a paradigm using a pair of subtly different motor tasks and contrasting the recorded fMRI data enable visualization of differences in brain activation between these tasks. Therefore, using fMRI to achieve a better understanding of movement disorders, requires an MR-compatible measurement setup that enables safe execution of motor tasks without causing image artifacts and a measurement paradigm to consistently activate the CBL and BG. Since the wrist is often affected in movement disorders and since it is relatively easily accessible when a subject is in the MR scanner, we aimed for motor tasks using flexion torque of the wrist.

The goal of this research was to selectively evoke brain activity in the CBL or BG using isometric motor tasks during fMRI in healthy subjects. Measurements were performed in an MR scanner using an MR-compatible wrist torque measurement device which was developed specifically for this study.

2. Methods

2.1. Subjects

Ten subjects (5 men), all right-handed with a laterality index greater than 75 according to Edinburgh Handedness Inventory [18] and aged between 25 and 30, were included and provided written informed consent prior to participation in this study, which was approved by the medical ethics committee of the Academic Medical Center Amsterdam (#2011_161). Exclusion criteria were: metal inside the body, claustrophobia, reluctance to be informed about observed abnormalities in MR images, pregnancy, known psychiatric history, known neurological conditions, use of centrally active medication, substantial daily use of alcohol (>2 U per day) or drugs, and use of alcohol or drugs within 24 h before participation in the research.

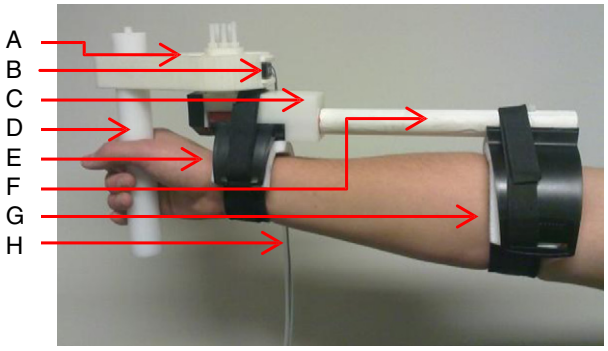

Fig. 1. Isometric wrist torque measurement device with arm support. The device consisted of a polyamide 12 deformable structure [A], light emitter and sensor [B], polyoxymethylene mounting block [C], polyoxymethylene handle [D], plastic armrests [E&G] with moldable foam and Velcro straps, fiberglass rod [F] and 10 m optical fiber [H].

2.2. Equipment

An MR-compatible wrist torque measurement device without magnetic and conductive materials was developed to ensure safety and minimize artifacts (see Fig. 1). Torque was measured (range: ± 1.5 Nm) from deformation of a deformable structure using light intensity measurements (see Fig. 2) (FS-N11MN, Keyence, Osaka, Japan) inside the MR scanner room while all electronics were located in the MR control room. The deformable structure of the wrist torque measurement device was selective laser sintered out of polyamide 12 and was designed to be compliant in one direction with low cross-sensitivity by using a hub-spoke topology. The sensor head (FU-38, Keyence, Osaka, Japan) was made entirely from polymers and was equipped with one emitting and one receiving optical fiber. Torque data were processed in real-time using MATLAB (MathWorks, Natick, MA, USA). The deformable structure was mounted on a lower arm support, which was attached to the right forearm of a subject. The advantages of attaching the wrist torque measurement device to the subject's lower arm instead of to the MR scanner bed were twofold. Firstly, the device could be attached to the subject's arm outside of the MR scanner room thereby saving costly time occupying the MR scanner room. Secondly, subjects did not exert forces on the MR scanner when producing wrist torque, reducing head motion. The right forearm of the subject with attached torque sensor was placed on a sandbag alongside the body without the right forearm touching the hip. A sliding handle and moldable foam allowed for accommodation of a wide range of hand and arm sizes. The 3 T MR scanner (Philips Intera, Best, The Netherlands) was equipped with an eight channel head coil, and a visual information system using a mirror, a projection screen and a beamer, which presented the subject in the MR scanner with task-related information (see Fig. 3). An anatomical scan was acquired using a resolution of 0.875 × 0.875 mm and a slice thickness of 1.2 mm. The functional scans were acquired using: T2* weighted echo planar imaging with an echo time of 30 ms, a repetition time of 2500 ms, a flip angle of 80 , resolution of 2.29 × 2.29 mm and a slice thickness of 3 mm. Each of the 40 slices in a functional scan had a field of view of 220 mm and all 356 functional scans were acquired consecutively. Settings were optimized for fast-paced functional scans of the majority of the brain; however a part of the orbitofrontal cortex was not scanned.

2.3. Hypotheses, contrasts and tasks

Based on the literature the following hypotheses were formulated and pairs of tasks were devised to test these hypotheses.

Hypothesis 1: Comparing a fast switching torque/rest task (1 Hz) with visual feedback to the same task without visual feedback will result in no increased activity in the CBL and the BG since both tasks involve fast movements which entail less error correction. Hypothesis 1 will be evaluated by testing contrast 1: the increase of brain activity during task 1 compared to task 2.

Task 1: Fast switching torque task where the subject was instructed to alternate between relaxing and exerting the amount of torque as indicated by the target on the projection. The exerted torque was also presented on the screen (visual feedback). The target switched from 0 to 0.75 Nm and back at 1 Hz.