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BOLD signal in sensorimotor regions reveals differential encoding of passive forefinger velocity and displacement amplitude

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ABSTRACT

Peripheral encoding of movement kinematics has been well-characterized, but there is little understanding of the relationship between movement kinematics and associated brain activation. We hypothesized that kinematics of passive movement is differentially represented in the sensorimotor network, reflecting the well-studied afferent responses to movement. A robotic forefinger manipulandum was used to induce passive kinematic stimuli and monitor interaction force in 41 healthy participants during whole-brain functional magnetic resonance imaging (fMRI). Levels of forefinger displacement amplitude and velocity were presented in flexion and extension. Increases in velocity were linearly associated with activation in contralateral primary somatosensory cortex (S1), bilateral secondary somatosensory cortex (S2), primary motor cortex, and supplementary motor area. No difference in activation was found for direction of the finger movement. Unexpectedly, S1 and S2 activation decreased nonlinearly with increasing displacement amplitude. We conclude that while straightforward relations were found with velocity, the complex neural representation of displacement amplitude suggests a more nuanced relationship between peripheral responses to kinematic stimuli and sensorimotor network activity. Here we present a novel, systematic characterization of the whole-brain response to passive movement kinematics.

Introduction

The sense of position and movement of our limbs, known as proprioception, plays an important role in motor planning and execution (Johansson and Cole 1992; Sober and Sabes 2003; Sarlegna and Sainburg 2009; Gandevia 2014). For instance, control of precision grip aperture during reaching and grasping requires information on the hand opening velocity and on the position of the arm and finger joints. Such coordination is accomplished through the integration of somatosensory information from muscle spindles, cutaneous mechanoreceptors and joint receptors (Matthews 1981; Stillman 2002; Proske and Gandevia 2009, 2012; Rosker and Sarabon 2010). Muscle spindles provide velocity information thanks to the high sensitivity of their primary afferents to changes in muscle stretch (Matthews 1981; Grill and Hallett 1995; Cordo et al. 2011; Houk and Rymer, 1981), and together with their secondary afferents, they contribute to the sense of position (Proske et al. 2000; Proske and Gandevia 2012). Cutaneous receptors, mainly on the dorsal side of the hand, have also been shown to contribute to the perception of finger movements and position through skin stretch around the joints (Vallbo and Hagbarth 1968; Edin and Abbs 1991; Johnson et al. 2000; Ebied et al. 2004; Collins et al. 2005; Berryman et al. 2006). It is believed that muscle spindles dominate the proprioceptive system, and thus, damaged muscle spindle afferents have been most closely linked to proprioceptive impairments (Van Deursen et al. 1998). Impaired proprioception after brain injury (Smith et al. 1983; Kamper et al. 2003; Semrau et al. 2013) leads to difficulties during reaching (Roby-Brami

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et al. 2003), in bimanual coordination (Torre et al. 2013), and in perceiving limb position (Dukelow et al. 2010).

The cortical and subcortical representation of passive movements, important for isolating afferent contributions to motor control, is incompletely characterized. Early studies in nonhuman primates described the discharge of single neurons during passive movement in the primary somatosensory cortex (S1), primary motor cortex (M1) and cerebellum (CB) (Hore et al. 1976; Rushmer et al. 1976; Rubia and Kolb 1978; Bauswein et al. 1983). Later work using noninvasive neuroimaging techniques in humans mainly addressed the activation differences between active and passive movements. Weiller et al. (1996), using positron emission tomography (PET), were the first to report activation in contralateral sensorimotor cortex, bilateral secondary somatosensory cortex (S2) and supplementary motor area (SMA) during passive elbow movements with a large and constant amplitude induced by a torque motor. In a similar but more controlled study on the middle finger, Mima et al. (1999) showed (nonsignificantly) increased activation in contralateral S1 and S2 during brisk passive finger movement at the metacarpophalangeal (MCP) joint elicited by a servomotor. A third investigation (Radovanovic et al. 2002) focused on differences in neural activation between induced passive movement and illusory movement generated by tendon vibration in the elbow, and reported activation in S1 and S2, as well as M1. Later, the use of functional magnetic resonance imaging (fMRI) assessed activation with greater spatial precision than PET. Several fMRI studies identified activation in the aforementioned brain areas and some additional regions such as the cingulate motor area (CMA), CB and putamen during passive movement of fingers, wrist, hand, leg or ankle induced by an investigator (Thickbroom et al. 2003; Guzzetta et al. 2007; Jaeger et al. 2014). Taken together, these studies suggest that S1, S2, as well as M1, SMA, CMA, CB and occasionally putamen are part of the central network associated with the representation of passive movements. Yet without knowledge of which aspect of the passive movement is being represented, the practical use of these results towards applications such as diagnosis of proprioceptive disorders or brain-machine interfaces is limited.

Thus, while physiologists have examined detailed peripheral responses to kinematic passive movement parameters, neuroimaging research has only looked at brain representation of passive movements without consideration of kinematics parameters. In this work, we asked whether the commonly studied kinematic parameters of movement, velocity, displacement amplitude and direction, have a differential representation in the brain, reflective of the peripheral response of these parameters. We expected to find a stronger increase of activation in somatosensory areas for velocity than for displacement amplitude due to the primacy of muscle spindle receptors in proprioception (Proske and Gandevia 2012; Gandevia 2014). Additionally, since flexion and extension arise from different receptors, we expected a differential representation of direction. We designed two separate experiments using parametric factorial designs. In the first experiment, we explored how the BOLD (blood oxygen level-dependent) signal changes with forefinger velocity, displacement amplitude and movement direction in a fast event-related design. In the second experiment, we validated our initial findings by using a slow event-related design. In this study, we report the neural effects of changes in passively induced forefinger kinematics along with their respective linearity and sensitivity.

Methods

Participants

A total of forty-eight neurologically intact right-handed subjects participated in this study: twenty-one subjects (7 males, aged 29 ± 8.8 (mean $\pm$ SD) years), participated in Experiment 1 and twenty-seven subjects (13 males, aged 25 ± 2.7 (mean $\pm$ SD) years), participated in Experiment 2. Seven subjects were excluded from the study due to excessive head movement (>one voxel size), leaving a total of 19 (6 males) and 22 (12 males) subjects, in Experiments 1 and 2, respectively. Each subject participated in the experiment in a single session. A summary of subject characteristics is shown in Table S1. The study was conducted according to the requirements of the Cantonal Ethics Committee, Department of Health of the Canton of Zurich, Switzerland (KEK 2010-0190). All participants provided written informed consent statements in accordance with the Declaration of Helsinki and were financially compensated for their participation.

Experimental setup

Subjects lay in a supine position in an MRI scanner with their right arm and wrist in the anatomically neutral position. Passive forefinger movement was imposed with an MRI-compatible robot fixed to the scanner bed, adjusted to fit the forefinger and thumb of the right hand, and ensuring movement of the forefinger solely in the flexion-extension direction. The thumb was kept static (Fig. 1a). This setup was tested and used during our previous pilot experiment (Sulzer et al. 2013). The interaction force during passive movement was measured with an MRI-compatible fiber optic-based force sensor, and the position of the actuator was monitored via an integrated electro-optical encoder.

Prior to the fMRI data acquisition, subjects' maximum aperture between thumb and forefinger was measured outside the MRI room using a scale on a flat surface, with distal phalanges oriented perpendicularly to the surface. Subjects were then exposed to all conditions outside the bore to familiarize themselves with the task. While lying in the MR scanner, subjects' hand and arm muscles were inspected manually to ensure a relaxed state when positioned in the robotic manipulandum. Since the present study was intended to investigate the whole brain activation with forefinger proprioception, participants were asked to ignore the induced movements and keep their eyes closed, but also to stay awake and relaxed during the whole acquisition, thus reducing secondary effects related to awareness of forefinger movement (Burton et al. 1999; Desmurget and Sirigu 2009).

Experimental protocol

In Experiment 1, passive displacement of the right forefinger was modulated in a $3 \times 3 \times 2$ parametric factorial design, with 3 displacement amplitudes, 3 velocities and 2 movement directions (flexion and extension), resulting in a total of 18 conditions. A single condition is thus composed of a given displacement amplitude, velocity and movement direction. The displacement amplitudes were 10, 20 and 40% of individual maximum aperture (A_{10}, A_{20}, and A_{40}), and velocities at 20, 40 and 80% of maximum aperture/sec (V_{20}, V_{40}, and V_{80}) following a minimum-jerk trajectory. As illustrated in Fig. 1b), all conditions were pseudo-randomly ordered. All passive displacements were interspersed with a hold period of 4 ± 2 s between movements.

Experiment 2 consisted of a simplified parametric factorial design ($2 \times 2 \times 2$), with displacement amplitudes of 10 and 40% of maximum aperture (A_{10} and A_{40}), velocities at 5 and 20% of maximum aperture/sec (V_5 and V_{20}) and in both flexion and extension directions. Altogether, this resulted in a total of 8 conditions. In contrast to Experiment 1, and illustrated in Fig. 1c), passive extension was always followed by passive flexion, and vice versa. All passive displacements were interposed with a hold period of 12 ± 2 s between movements, thus ensuring the return of the BOLD response to baseline (DeYoe et al. 1994; Glover 1999).

During the fMRI sessions, the protocol for Experiment 1 consisted of 4 runs with 8 repetitions of each condition per run, resulting in 32 repetitions per condition. In Experiment 2, the protocol consisted of 4 runs with 5 repetitions of each condition per run, resulting in 20 repetitions per condition. In Experiment 1, each finger trajectory had a roving baseline (starting position) which was based on the previous trajectory (Fig. 1b). In contrast, Experiment 2 used the same constant baseline for all repetitions (Fig. 1c). For both experiments, we ensured that finger extension never exceeded 50% of the maximum aperture, avoiding both