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Dissociation of reach-related and visual signals in the human superior colliculus

Marc Himmelbach [a,*,1], Walter Linzenbold [a,1], Uwe J. Ilg [b]

[a] Centre for Neurology, Division of Neuropsychology, Hertie-Institute for Clinical Brain Research, Centre for Integrative Neuroscience, Eberhard Karls University, Tübingen, Germany
[b] Hertie-Institute for Clinical Brain Research, Department of Cognitive Neurology, Eberhard Karls University, Tübingen, Germany

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ABSTRACT

Electrophysiological and micro-stimulation studies in non-human animal species indicated that the superior colliculus (SC) plays a role in the control of upper limb movements. In our previous work we found reach-related signals in the deep superior colliculus in humans. Here we show that also signals in more dorsal locations are correlated with the execution of arm movements. We instructed healthy participants to reach for visual targets either presented in the left or in the right visual hemifield during an fMRI measurement. Visual stimulation was dissociated from movement execution using a pro- and anti-reaching task. Thereby, we successfully differentiated between signals at these locations induced by the visual input of target presentations on the one hand and by the execution of arm movements on the other hand. Extending our previous report, the results of this study are in good agreement with the observed anatomical distribution of reach-related neurons in macaques. Obviously, reach-related signals can be found across a considerable depth range also in humans.

Introduction

Although the cortical networks subserving upper limb functions in humans are quite well understood, the contributions of deep brain structures to the control of our arms and hands remained elusive. Our knowledge about the role of brainstem structures in the sensorimotor systems is almost entirely based on animal models. The superior colliculus, located at the dorsal brainstem, is a structure with well-known functions in the context of oculomotor control and visual processing. It contains topographical maps of the visual, auditory and somatosensory world (Cynader and Berman, 1972; Jay and Sparks, 1987; Stein et al., 2002). Additionally, the results of a small number of neurophysiological reports suggested that neurons in the SC and the directly underlying mesencephalic reticular formation are active prior to and during a reaching movement executed with the contralateral arm (Lünenburger et al., 2001; Werner et al., 1997a, 1997b). Just recently, we reported reach-related signals in the human SC, exactly replicating previous findings in animals (Linzenbold and Himmelbach, 2012).

In our previous study (Linzenbold and Himmelbach, 2012) we identified reach-related signals in deep locations of the SC contralateral to the moving arm. We also observed similar signal increases in more dorsal, presumably superficial and intermediate locations of the respective contralateral SC. However, reach-related signals in these dorsal SC locations disappeared in a comparison of reaching with the control task, i.e. execution of reflexive saccades. This finding left us with two possible interpretations. Either, these dorsal reach-related signals were exclusively driven by the visual presentation of targets in both conditions (reaching and saccades) or these signals were, at least partially, driven by the execution of arm movements and the visual stimulation and saccade execution in the control task concealed this signal source. The latter possibility is supported by the anatomical distribution of reach-related neurons throughout the depth range of the primate SC (Werner et al., 1997a, 1997b). Therefore, we dissociated arm movement signals from visual signals in the present study. We separated the visual hemifields of target presentation in individual blocks (left targets vs. right targets) and instructed the participants to execute either direct movements to the presented targets (pro-reaching) or reach to a position opposite to the presented target (anti-reaching).

In agreement with our previous results, we found reliable BOLD signal increases during right arm reaching in dorsal and ventral locations of the left human SC in all conditions (Linzenbold and Himmelbach, 2012). Thus, signals in the left dorsal SC were also clearly above baseline if there was no contralateral visual stimulation. In contrast, in the right SC we found positive BOLD signals in the dorsal location only if there was contralateral visual stimulation.

Materials and methods

Participants

Sixteen subjects (13 females, 3 males, mean age 28 years, range 23–35 years) participated in this experiment. All of them had normal

* Corresponding author. Fax: +49 7071 29 4489.
E-mail address: marc.himmelbach@uni-tuebingen.de (M. Himmelbach).
[1] Both authors contributed equally.

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or corrected-to-normal visual acuity. All participants gave their informed consent to participate in the study that was performed in accordance with the ethical standards established by the 1964 Declaration of Helsinki and approved by the local ethical committee.

Procedures

All measurements were conducted in complete darkness. We used a black, opaque film to cover all windows and panels until no light sources could be detected even after an adaptation time of ~30 min. The participants lay supine in the scanner with their heads tilted approx. 30°. They looked directly at a vertical perspex plate positioned at the level of the abdomen and used their right arm for reaching. The position of the plate was adjusted individually to ensure a comfortable movement to the targets with the index finger of the right arm. To minimise body and head movements, the right upper arm was restrained to the scanner bed. All visual stimuli were generated by LEDs located outside the scanner room and connected to optical fibres that were running to the perspex plate. Targets were positioned at 7.5°, 5°, and 2.5° to the right and to the left of the fixation position that was located at body midline. During the whole session a dimmed white central fixation light was presented. Multiple target positions were chosen to avoid the execution of automatic movements by the participants to an overlearned target location. We chose positions relatively close to the fixation because of general spatial limitations in the MR scanner and the need for a comfortable movement execution to targets in the right and left hemifield. Because of the use of a block design (see below) it was not possible to analyse the effect of target position. The fixation light was set to a level that was just sufficient to detect its position but insufficient to illuminate the workspace. The participants were instructed to maintain fixation throughout each experimental fMRI run. Reaching blocks of 17.2 s duration alternated with fixation baseline periods of the same duration. Immediately after each fixation baseline, a dimmed light next to the fixation position appeared for 2.5 s cueing the upcoming task (red for anti-reaching blocks; green for pro-reaching blocks). In the case of pro-reaching, the participants reached to the position of the flashed target, shortly touched the target with their index finger, moved back and placed their finger on a fixed home position at the sternum. In the case of anti-reaching movements, the participants executed a reaching movement to a virtual position that was exactly opposite to the actually presented targets with respect to the fixation position. These variations resulted in a 2 (target hemifield) × 2 (spatial congruency) within-subject design with the following conditions: target in the left visual field and movement to the target (LVF-PRO), target in the right visual field and movement to the target (RVF-PRO), target in the left visual field and movement opposite to the target (LVF-ANTI), and target in the right visual field and movement opposite to the target (RVF-ANTI). After each experimental block the fixation light was turned off for 500 ms indicating the end of the block. Each block consisted of 6 trials. The sequence of all reaching blocks was pseudo-randomised resulting in ITIs of max. 149 s. Each condition was repeated 4 times in one experimental run. Each participant underwent six experimental runs resulting in 144 movements per condition.

Eye and arm movement recordings

Eye movements were recorded throughout the whole fMRI measurements in both experiments with a long-range video system (SMI SensoMotoric Instruments). Video recordings of the right or left eye position, depending on eye dominance as measured by the Porta test, were sampled at 25 Hz. The synchronisation of the eye movement videos with fMRI data acquisition was ensured by the use of a TTL pulse for the start of video recording. The occurrence of occasional saccades was determined manually in a frame-by-frame analysis of the video recordings. Due to the tilted head position and the shallow viewing angle the control of eye position by eye tracking algorithms is less reliable than thorough manual inspections. The eye movement videos were analysed by an assistant who was blind to the individual sequence of experimental conditions. Two MR compatible infrared cameras positioned outside the scanner recorded the arm movements. The videos of the arm movements were sampled at 30 Hz. Onsets and offsets of the arm movements were detected and verified manually. The synchronisation of fMRI data acquisition with the hand movement videos was ensured offline by the detection of target presentations in the videos. These target presentations were controlled by a custom MatLab programme which in turn was continuously synchronised with repeated TTL pulses from the scanner.

MRI data acquisition

All experiments were conducted using a 3 T MRI scanner (Siemens Magnetom Trio, Erlangen, Germany) with a standard 12-channel head coil system. Each run consisted of 219 T2*-weighted EPI volumes (slice thickness = 2 mm, ascending acquisition of 20 slices, TR = 2.87 s including a gap of 1.5 s, TE = 33 ms, flip angle = 80°, FOV = 192 mm × 192 mm, 96 × 96 matrix) acquired in oblique coronal orientation for BOLD based imaging. Target presentations were synchronised with image acquisition and started 200 ms before the gap. The participants were instructed to execute the whole arm movement during the gap. We oriented the slices individually in parallel to the brainstem at the height of the pons. Additionally, we acquired a single whole brain EPI image from each subject with the same parameters. These images were used to facilitate the co-registration of EPI and structural datasets. Additionally, high-resolution T1-weighted anatomical volumes were acquired for each subject using an MP-RAGE sequence (TR = 1.3 s, TE = 3.22 ms, flip angle: 15, FOV = 256 mm × 256 mm, 256 × 256 matrix, 176 sagittal slices, slice thickness 1 mm).

fMRI data analysis

Image analysis was carried out using SPM8 (Wellcome Department of Imaging Neuroscience, London, UK) implemented in MATLAB 7.5 (MathWorks Inc.). The first five images of each measurement were discarded to allow the MRI signal to reach a steady state. The remaining images of each participant were realigned to the first image to correct for head movements during the experiment. The individual whole brain EPI volume was co-registered to the mean of the series of partial functional EPI images of a subject. The anatomical T1 volume was then co-registered to the whole brain EPI image. For both co-registrations we used rigid-body transformations (3 rotations, 3 translations) that were estimated based on the normalised mutual information between the respective two images, average distances between sampled points of 4 and 2 mm for repeated co-registrations with increasing precision, corresponding tolerance values of 0.02, 0.02, 0.02, 0.001, 0.001, 0.001, 0.01, 0.01, 0.01, 0.001, 0.001, and 0.001 for translations and rotations, and Gaussian smoothing of the joint histogram with 7 × 7 bins. This procedure resulted in an accurate co-registration between the functional and structural scans of our subject group (Fig. 1). Subsequently, the T1 scan was normalised to match the T1 MNI template distributed with SPM8 using the unified segmentation–normalisation approach. The calculated transformations were applied to all functional images for spatial normalisation, resampling images at a resolution of 2 × 2 × 2 mm^3. Images were smoothed with an isotropic 3 mm full-width half maximum Gaussian kernel. The fixed-effects first-level analysis included the removal of low-frequency drifts in the signal using a high pass filter with a cut-off period of 300 s and a correction for temporal autocorrelation in the data was applied using an autoregressive AR(1) process as implemented in SPM8. Predictors for each experimental condition were constructed by a convolution of arm movement onsets with the canonical haemodynamic response function. We modified the canonical haemodynamic response