

Force-related BOLD effects during naturalistic and symbolic effort observation

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Synopsis

In this pilot study, we used a 3-condition fMRI squeezeball paradigm to study the non-linear BOLD response to varying grip force (GF) during action execution (AE, subjects performed the task), action observation (AO, subjects watched a video of the task) and AO with visual cue (AOvc). fMRI activity patterns in brain circuits controlling AE, AO and AOvc account for different GF applied to an object or perceived from others' action. AO and AOvc calls different processing depending on the presence or the absence of the visual cue indicating specific regions and BOLD-GF relations for the effort perception.

Introduction

Activation of the action execution-observation network in subjects observing motor tasks is thought to provide a cue for imitation learning, providing the basis for motor training [1, 2]. Crucially, several motor areas activated during the execution of a motor task are activated during observation of the same task when performed by others [3, 4]. The relationship between an applied grip force (GF) and BOLD signals shows characteristic non-linearity in cerebral and cerebellar regions [5]. Using a squeezeball paradigm, we asked whether the non-linear behaviour of the BOLD response to varying GF levels is reproduced when observing, with or without symbolic cues, others performing the task.

Methods

Subjects: 12 subjects (7 females; 26±3.5 years). MRI protocol: 3T MRI (Philips Achieva) with a 32-channel head coil. Sequence parameters: 1)volumetric 3DT1; 2)GE-EPI fMRI: volumes=200, TR=2.5s, TE=35ms, voxel size=3x3x2.7mm³, FOV=192x192mm², slices=46, flip angle=90°, total scan-time 500s. Paradigm: Three event-related randomised fMRI runs (Figure 1): action execution (AE), observation (AO), observation with visual cue (AOvc). During AE and the video recording the subjects followed visual instructions to squeeze a rubber ball applying forces based on their own maximum voluntary contraction (MVC) (Figure 1(A)). Each squeeze lasted 3s, 5GF targets were interleaved with rest for a total of 75 active and 75 rest trials. Before and after MRI, subjects watched the videos (AO and AOvc) scoring the perceived GF. The AOvc video showed the right hand of a female actor performing the squeezeball task (as in AO) but overlaid with a translucent representation of the visual feedback the actor received during the video recording. Behavioural data (SPSS 21.0) The group mean of perceived GF (pGF) was calculated by considering the different forces (20,30,40,50,60 %MVC of the actor's hand) and the 4 sessions (AO and AOvc before and after MRI). We used paired sample T-tests to test for differences between AO and AOvc ratings. Repeated measure ANOVA allowed us to investigate learning effects (p<0.001). fMRI data (SPM12) Pre-processing: Slice timing; realignments, re-slicing; co-registrations; normalizations and smoothing of EPI volumes (8mm Gaussian kernel). Polynomial expansions up to the 4th order in a general linear model were applied. The contrast images of polynomial coefficients were entered into a between subject analysis and tested with one sample t-tests. For AO and AOvc analysis the GF levels corresponded to those recorded from the actor's performance. Significance: p<0.001 (minimum extent=10 voxels).

Results

Group accuracy in pGF (Figure 2) resulted significantly higher in AOvc than AO and in AOvc“after” relative to AOvc“before” MRI. At the end of the experiment, subjects reported that the cue drove their responses in AOvc. In AE, activations (Figure 3) were detected in the following orders: 0th in motor, premotor and sensory cerebral and cerebellar areas; +1st in the motor cortex; +2nd in frontal, parietal and temporal lobes; +4th in sensorimotor and cerebellar areas; -1st in cerebellar lobule IX; -3rd in frontal, parietal and occipital lobes as well as cerebellum. In AO, activations (Figure 4) were seen in: 0th in visual cortices, premotor and parietal cortices; +3rd in parietal lobe and caudate; -1st in postcentral and supramarginal gyri, insula, middle temporal and inferior frontal gyri; -2nd in middle frontal gyrus and bilateral brainstem; -3rd in inferior parietal lobule, middle temporal gyrus, precentral, occipital and fusiform cortices. In AOvc, activations (Figure 5) were found in: 0th in occipital and temporal lobes, cerebellum, frontal and postcentral gyri; +1st in somatosensory cortex; +2nd in occipital lobe, sensorimotor cortex and thalamus; +4th in cingulate cortex, insula, frontal and temporal gyri, and cerebellum; -1st in thalamus, precuneus, frontal, temporal and angular gyri; -3rd in frontal, fusiform and occipital gyri and superior parietal lobule.

Discussion and conclusion

AE confirmed previous data [5]. AO and AOvc activate different networks, with some overlaps with AE, indicating that the visual cue introduce a further layer of complexity. Prefrontal activations in AOvc suggest a possible underlying top-down processing of the cue. The behavioural data shows that there is a learning effect during AOvc, where the accuracy in force detection resulted higher than in AO. This indicates that the bar has a facilitator effect and that subjects gain a “hand-bar” correspondence insight as the experiments goes on. The presence of non-linear effects in AO, though, confirms that effort can be appreciated from the pure naturalistic experiment (potentially suggested by the tendon contraction) with processing confined to the parietal lobe, caudate [6], frontal gyrus and brainstem. Further experiments are needed to define the contribution of the cue to different orders and regions.

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References

- [1] Porro, C.A., et al., 2007. Enhancement of force after action observation: behavioural and neurophysiological studies. *Neuropsychologia*. 45, 3114-21.
- [2] Caligiore, D., et al., 2013. The contribution of brain sub-cortical loops in the expression and acquisition of action understanding abilities. *Neurosci Biobehav Rev*. 37, 2504-15.
- [3] Gatti, R., et al., 2016. The effect of action observation/execution on mirror neuron system recruitment: an fMRI study in healthy individuals. *Brain Imaging Behav*.
- [4] Kilner, J.M., Friston, K.J., Frith, C.D., 2007. Predictive coding: an account of the mirror neuron system. *Cogn Process*. 8, 159-66.
- [5] Alahmadi, A.A., et al., 2016. Complex motor task associated with non-linear BOLD responses in cerebro-cortical areas and cerebellum. *Brain Struct Funct*. 221, 2443-58.
- [6] Kurniawan, I.T., et al., 2010. Choosing to make an effort: the role of striatum in signaling physical effort of a chosen action. *Journal of Neurophysiology* 104(1):313-21.

Figures

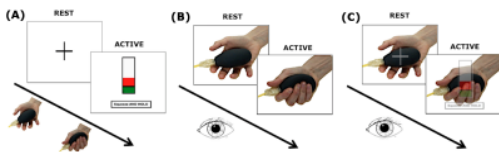


Figure 1| Paradigm. Pictorial representation of the 3 conditions that were used in training and fMRI runs: (A) action execution (AE); (B) action observation (AO); (C) action observation with visual cue (AOvc). The stimuli are shown above the arrows whereas the activity of the subject is shown below the arrow. During fMRI, every run lasted 8:33 min and the trials were administered in a counter-balanced randomised order. Active squeeze ball trials of 3s each were repeated 75 times and were divided equally between the 5 GFs (every trial lasted 3 s). The rest time between active trials lasted 2-12 s.

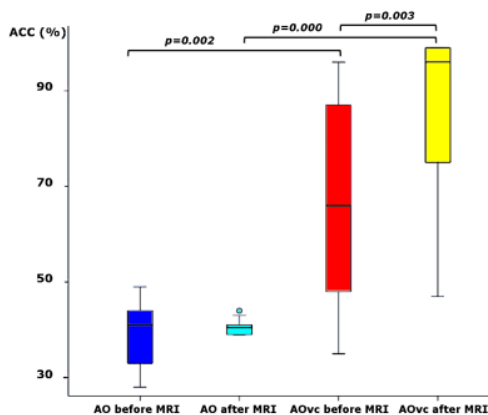


Figure 2| Group performance during AO and AOvc behavioural tasks. The box plot shows the relative accuracy (ACC) of force estimation in different AO and AOvc behavioural sessions (before and after the MRI session). Significant differences between conditions are indicated (paired t-test). The large standard deviation of accuracy reported for the AOvc may be linked to different strategies used while looking at the hand and visual cue together – subjects were not instructed about the association between the 2 stimuli.

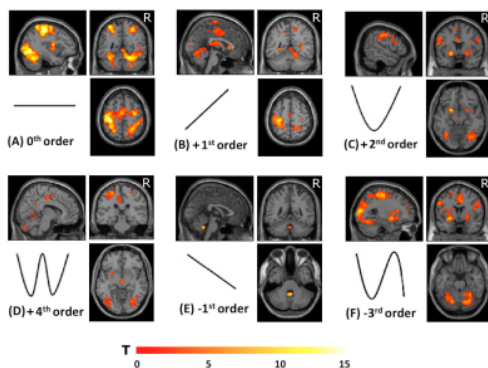


Figure 3| Whole-brain BOLD effects in AE. Brain maps (T values) at the group level corresponding to different orders of the BOLD-GF association in the AE condition. Activation areas for different orders are shown. A threshold $p < 0.001$ ($k=5$) was used for illustration purpose. The shape of the orthogonalized polynomial function that was fitted to signals is shown for (A) 0th, (B) +1st, (C) +2nd, (D) +4th, (E) -1st and (F) -3rd orders below the corresponding image showing significant clusters. In this and all the following figures, right is right and left is left.

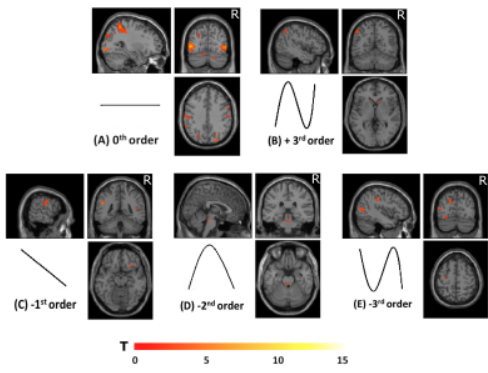


Figure 4| Whole-brain BOLD effects in AO. Brain maps (T values) at the group level corresponding to different orders of the BOLD-GF association in the AO condition. Activation areas at different orders are shown. A threshold $p < 0.001$ ($k=5$) was used for illustration purpose. The shape of the orthogonalized polynomial function that was fitted to signals is shown for (A) 0th, (B) +3rd, (C) -1st, (D) -2nd and (E) -3rd orders below the corresponding image showing significant clusters.

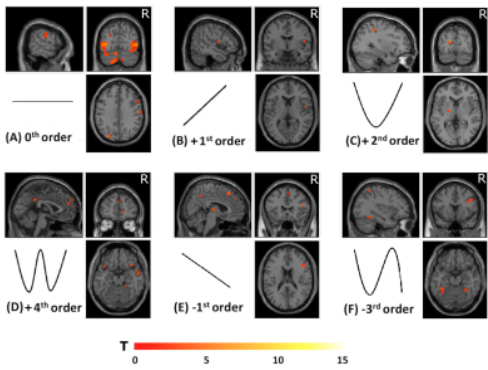


Figure 5| Whole-brain BOLD effects in AOvc. Brain activations (T values) at the group level corresponding to fitting polynomials of different orders to the BOLD signal response. The estimated shape of the fitted orthogonalized polynomial function is shown for (A) 0th, (B) +1st, (C) +2nd, (D) +4th, (E) -1st and (F) -3rd orders in the AOvc condition below the corresponding image displaying significant clusters. A threshold of $p < 0.001$, $k=5$ was used for display purpose; right is right and left is left.