

## Investigation of microscopic functional specificity using multi-echo-train EPI

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**Purpose** A functional area of a human brain is usually activated by multiple stimuli, and category-selective areas (i.e. fusiform face area (FFA) & parahippocampal place area (PPA)) are also activated by a non-preferred stimulus as well as the preferred stimulus [1,2]. With using conventional fMRI method, it is difficult to know whether all of the neurons in activated areas respond to both the preferred and non-preferred stimuli or whether a part of neuronal population is separately activated by each stimulus. In the present study, we measured fMRI responses using multi-echo-train echo-planar-imaging (MET-EPI) to discriminate the neuronal populations in a functional area.

**Methods (Pulse sequence)** MET-EPI sequence was modified to have two additional echo trains from a typical single-shot gradient-recalled EPI of Siemens, which produced three images with different echo times in a single RF excitation.

**(Derivation of images)** The simple decaying curve of MRI signal follows the equation of  $S(t) = S_0 \exp(-R2^* \cdot t)$ , where  $S_0$  is the signal at  $TE = 0$  and  $R2^*$  is the transverse relaxivity ( $= 1/T2^*$ ) [3]. Through the equation, two  $R2^*$  values, i.e.,  $R2^*_{1}$  and  $R2^*_{2}$ , were derived from the TE1 and TE2 images and from the TE2 and TE3 images, respectively. As well, the magnetic susceptibility feature after activation was estimated on the basis of the ratio of  $\%R2^*_{2}$  relative to  $\%R2^*_{1}$ .

**(Imaging protocol)** All MRI experiments were performed using a Verio system (Siemens, Germany) with a standard, 12-channel head matrix coil operating at 3 Tesla. For functional imaging, MET-EPI sequence was used with TR of 2 sec., three TEs of 13, 38 and 63 msec., 90 degree flip angle, 220 mm field of view,  $64 \times 64$  mm matrix size, and 3.4 mm slice thickness with 0.5 mm gaps. Twenty slices parallel to the AC-PC were acquired for each volume.

**(Functional experiment protocol)** An MRI scan for function lasting 240 seconds consisted of a total of eight blocks. Out of the eight blocks, each four blocks of face and building stimulation were interspersed in a control state with 12 seconds duration and a post-stimulus duration of 16 seconds. During the control state, a picture with a gray crosshair at the center of a black background was presented. Each event block consisted of 8 different pictures. Each picture was presented at the center of the visual field for 1 second with an interpicture interval of 0.5 seconds.

**(Data analysis)** The image data obtained from fMRI were processed using Brain Voyager QX (Brain Innovation B.V., Postbus, The Netherlands) software. All image data from the functional session for each subject were preprocessed with Brain Voyager QX and motion correction, scan time correction, and high-pass filtering with a cut-off frequency of 0.005 Hz.

MRI data acquired at TE2 ( $TE = 38$  msec.) was used to localize regions of interest (ROIs) of the primary visual cortex (V1), FFA and PPA. V1 was defined as obtained by contrasting the stimulation condition to the control. FFA and PPA were identified by a conjunction analysis (face > building and building > rest) and (building > face and building > rest).

Percent signal changes for  $R2^*_{1}$  and  $R2^*_{2}$  were calculated at the ROIs by the event-related-averaging option implemented in Brain Voyager. Ratios of the percent signal changes of  $R2^*_{2}$  to that of  $R2^*_{1}$ , i.e.,  $\%R2^*_{2}$  and  $\%R2^*_{1}$ , were derived at each condition and each area.

**Results** The original images acquired using MET-EPI are shown in the upper row of Figure 1. The image contrast was stronger with a longer TE. The images of  $R2^*_{1}$  and  $R2^*_{2}$  calculated from the original images are shown in the lower row of Figure 1.  $\%R2^*_{1}$  and  $\%R2^*_{2}$  were derived from the response signals for TE1, TE2, and TE3 in each area for each participant (Fig. 2), and they were used to calculate the ratio  $r (= \%R2^*_{2} / \%R2^*_{1})$ , i.e.,  $r_f$  for the face images and  $r_b$  for the building images (Fig. 3). In Figure 3, the V1 ratios did not differ significantly between the face and building. In contrast, there were significant differences in the ratios for FFA and PPA.

**Discussion** The aim of the present study was to determine whether a neuronal population activated by one category stimulus was different from that activated by another category stimulus. As assumed that a functional area recruited the same neuronal population to process the face and building image stimuli, only the magnitudes of changes of  $R2^*_{2}$  &  $R2^*_{1}$  could be influenced and the ratio of them should be the same for both stimuli. The data of V1 was parallel with this assumption. However, the data in the FFA and PPA showed significant difference of the ratios, which seem to reflect that the FFA and PPA have different magnetic susceptibility features depending on whether the stimulus was preferred or not. (V1 area is considered to have little priority to visual stimuli.) Thus, it supports that the neuronal population activated in FFA or PPA differed according to different category stimuli. Especially, the difference of the neuronal population activated in the FFA is consistent with the predictions of previous conventional fMRI studies [4,5].

**Conclusion** The present study suggests that the microscopic functional characteristics of a functional site could be examined using the proposed method.

**References** [1] Choi U-S et al., Neuroreport 2013; 24: 53-7. [2] Grill-Spector K. Curr Opin Neurobiol 2003; 13: 1-8. [3] Ogawa S et al., Biophys J 1993; 64: 803-12. [4] Andrews TJ et al., Neuroimage 2004; 23: 905-31. [5] Sung Y et al., Brain Res 2011; 1366: 54-9.

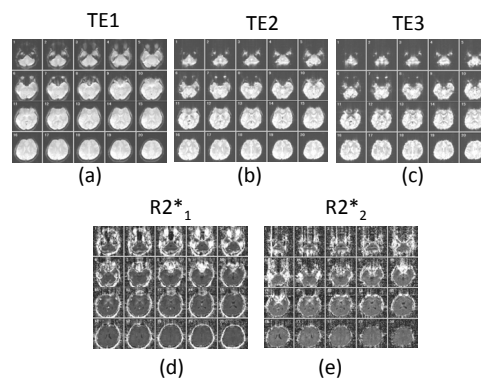


Fig. 1. MRI images (a) at TE1=13 ms, (b) at TE2=38 ms, and (c) at TE3=64 ms.  $R2^*$  images. (d)  $R2^*_{1}$  was estimated from TE1 and TE2, whereas (e)  $R2^*_{2}$  from TE2 and TE3.

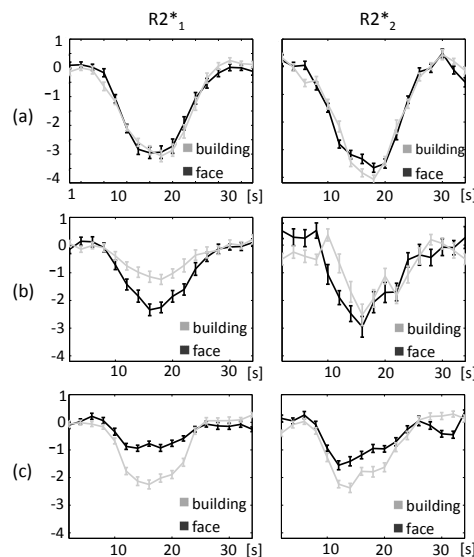


Fig. 2. Changes in the response after stimulation based on the  $R2^*$  values of (a) V1, (b) FFA, and (c) PPA. The error bars represent the S.E.M. of eight participants.

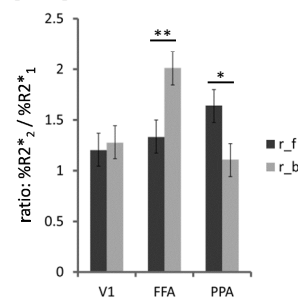


Fig. 3. Ratios of  $\%R2^*_{2}$  relative to  $\%R2^*_{1}$  for the V1, FFA, and PPA. The ratios of eight participants were averaged for each area.  $r_f$  is the ratio for face images and  $r_b$  is the ratio for building images. \*  $p < 0.03$ ; \*\*  $p < 0.01$