Use of independent component analysis to define regions of interest for fMRI studies

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Introduction
Regions of interest (ROIs) are frequently used in fMRI studies in order to limit an analysis to an anatomically or functionally defined area, or to investigate interactions between groups of voxels. Whether functional ROIs are defined on the basis of independent data, or non-independently based on contrasting a subset of conditions within the experiment, investigators face a number of arbitrary choices concerning the statistical threshold to employ and the method for delineating ROI boundaries. (Poldrack, 2006). We propose a method for defining ROIs using independent component analysis (ICA). This method avoids many of the shortcomings of general linear model (GLM) based ROI definition, and is robust and easy to implement using FSL (http://www.fmrib.ox.ac.uk/fsl). As a demonstration, we apply this method to define ROIs in the cortex and cerebellum that respond selectively to aurally paced movements of the lips, hands, and feet.

Methods
Seventeen healthy adults were recruited as controls for a study of sensorimotor representations in amputees. Magnetic resonance imaging was performed in a Siemens Allegra 3T head-only scanner. The imaging protocol included a high-resolution T1 structural scan, a field map, and a fourteen-minute BOLD epi scan (TR = 2 sec, FOV = 200 x 200 mm, resolution 64 x 64, slice thickness = 4 mm) during which the subject performed paced movements. The epi scans utilized prospective motion correction via Siemens' PACE option. Subjects were asked to move the toes on each foot, open and close each hand, and purse their lips. All movements were cued in pseudorandom order by audio instructions and paced by a 1 Hz tone. Each body part was moved for 16 seconds, followed by a 12 second rest. Because a subset of participants' data were left-right flipped for comparison with matched amputees, we refer to the cerebral and cerebellar hemispheres as "contralateral" or "ipsilateral" to the moving hand or foot rather than to "left" or "right." Both the GLM and ICA analyses were carried out using FSL (Smith, 2004).

GLM based ROI definition
GLM analysis was performed at the individual subject level and statistical maps were obtained corresponding to movements of lips, each hand, each foot, and the response to the audio cues. A second-level mixed effects analysis was applied to these results. The statistical maps for the mean response of all control subjects during each type of movement were used to define ROIs for further investigation. The maps were thresholded using a z cutoff of 2.3 and a clusterwise correction of $p< .05$. For hand and foot movements, clusters in the contralateral primary sensorimotor cortex and ipsilateral cerebellum were identified. For lip movements, clusters in bilateral primary sensorimotor motor cortex were identified, but no clusters in the cerebellum survived thresholding. The location of the peak voxel in each cluster was used to center spheres (radius = 20 mm in the cortex, 10 mm in the cerebellum); these spheres were intersected with the thresholded z-stats in order to define ROI masks.

ICA based ROI definition
Tensor ICA (Beckman, 2005) was performed on the data. The time course of each component was compared with the time courses of each movement type after convolution with the hemodynamic response function in a post-hoc regression in order to identify components corresponding to lip, hand, and foot movement. The component maps were thresholded using a mixture model fit and a probability for being in the "active" class of 0.5. The largest contiguous sets of thresholded voxels in the cortex and in the cerebellum were used to define ROIs.

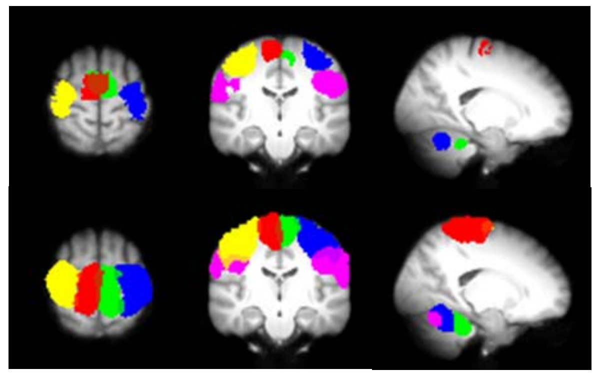

Figure 1 ROIs defined by GLM analysis (top) and by ICA results (bottom). Red & green = foot, yellow & blue = hand, violet = lips

Discussion
The ROIs defined using each method are shown in figure 1. In general, the ROIs are in good agreement with each other and with known somatotopy of sensorimotor cortex (Penfield, 1937) and cerebellum (Grodd, 2001), but there are also some striking differences. In the GLM analysis, nearly every voxel within the cerebellar spheres was above threshold. In this case the boundary of the ROI is not functionally defined, illustrating one of the problems with the intersection approach. A more serious problem is illustrated by the foot ROIs, which have a high degree of overlap in the GLM results (despite sitting on opposing banks of the longitudinal fissure) and are more anterior than expected. A closer look at the GLM results (figure 2) reveals that the foot regions are part of a single cluster that also includes the supplementary motor area (SMA). The fact that the peak voxel within this large cluster sits in the SMA could compromise the validity of the GLM-based ROI definition. Subtractively contrasting foot with another movement condition (e.g., hand) might eliminate the SMA, but would risk losing voxels showing mixed responses due to partially overlapping somatotopic representations. By contrast, the tensor ICA results nicely separate increases in activity related to movements of specific effectors from increases that are common across all movement conditions.

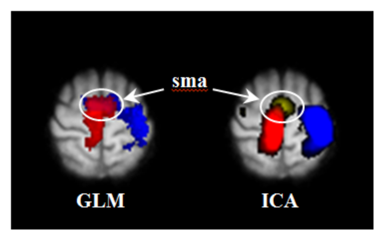

Figure 2 Thresholded activations corresponding to movement of one hand (blue) and the contralateral foot (red). Note that SMA is present in the GLM maps, but is in a separate component (shown in yellow) in the ICA results.

Conclusion
Independent component analysis provides a useful means of defining functional ROIs. The ability of ICA to segregate activity into multiple components is particularly helpful in identifying the boundaries of functional regions. At the group level, tensor ICA is appropriate for studies with consistent timing, such as this one, but concatenated ICA could have been used as well, and could be used for ROI definition based on resting state data. This approach could also readily be modified to give subject-specific ROIs by using each individual's ICA results.

References
C.F. Beckmann and S.M. Smith, Tensorial extensions of independent component analysis for multisubject FMRI analysis. NeuroImage, 25(1):294-311, 2005.
W. Grodd et al, Sensorimotor mapping of the human cerebellum: fMRI evidence of somatotopic organization. Hum Brain Map 13 (2): 55-73, 2001.
W. Penfield and E. Boldrey, Somatic motor and sensory representation in the cerebral cortex of man as studied by electrical stimulation. Brain, 60: 389-443, 1937.
R. Poldrack, Region of interest analysis for fMRI. Social Cognitive and Affective Neuroscience, 2(1): 67-70, 2006.
S.M. Smith et al, Advances in functional and structural MR image analysis and implementation as FSL. NeuroImage, 23(S1):208-219, 2004.

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