Functional localization of working memory: activation likelihood estimation of the n-back task

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Introduction

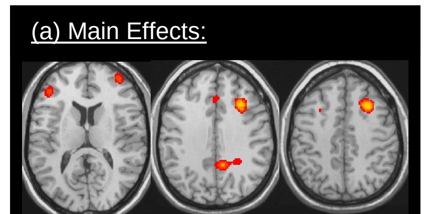
One of the more common paradigms used to study working memory is the n-back task, which requires subjects to determine if target stimuli match those presented n trials previously. There are many variations to this task: stimuli may be presented via different modalities (visual, auditory, olfactory), the task may require the monitoring of either the identity or location of the stimuli, targets are not restricted to a certain type (often they are letters, shapes, faces, or pictures), and varying n can give differing loads to this working memory task. As there is typically some subject variability in higher-order cognitive tasks, quantitative meta-analyses provide a method of accurately determining the degree of concordance across multiple studies. Results of meta-analyses can be useful in forming new hypotheses or interpreting results from neurologically abnormal subjects. A novel method for meta-analysis of functional neuroimaging results has been developed independently by Turkeltaub *et al*. [1] and Chein *et al*. [2], and has been applied here to more completely characterize the activation patterns in the n-back task.

Methods

To find the published corpus of literature dealing with the n-back task in normal subjects, several literature searches were completed using Medline. In addition, references from all relevant papers were examined. From these results, only those papers that reported activations as coordinates in stereotactic space (x,y,z) were considered. Papers merging the effects of reward or calculation with the memory task were omitted. Results from 26 fMRI or PET papers were selected (365 foci). From this list, the studies were divided into 5 groups based on stimulus type and task requirements: main effects (all papers), stimuli composed of letters, stimuli composed of shapes, faces, and pictures, tasks monitoring the identity of the stimuli, and tasks monitoring the location of the stimuli. Coordinates were transformed to MNI305-space using a Brett transform [3]. The activation likelihood estimate (ALE) maps were created for each group of studies by modeling each focus as a three-dimensional Gaussian function with a FWHM of 14 mm [1]. Statistical significance was determined using a permutation test of randomly distributed foci, and the resultant maps were thresholded at $p<0.0001$.

Results

Activation in several structures involved in working memory was noted in the main effects meta-analysis (Figure 1a, Table 1). Based on previous work, the left DLPFC (BA 46) appears to be related to the active maintenance of information over a delay or manipulation of this information. The cingulate gyrus is typically activated during increased effort or task complexity. Insular activity is noted in paradigms involving long-term memory and WM, and therefore could be involved with matching internally stored depictions to externally presented ones. The areas found by the main effects meta-analysis are in good agreement with the individual studies. When viewing the differences in activations obtained by dividing the studies into groups based on stimulus type (Letters vs. Shapes, Faces, and Pictures – Fig. 1b vs. 1c) or by task requirements (Identity vs. Location – Fig. 1d vs. 1e) it is clear that the same regions of activation are involved. However, the lateralization effects of parsing the studies into groups are immediately apparent. Activation patterns for Letters (Fig. 1b) and Identity (Fig. 1d) are lateralized to the left while patterns for Shapes, Faces, and Pictures (Fig. 1c) and Location (Fig. 1e) are lateralized to the right.



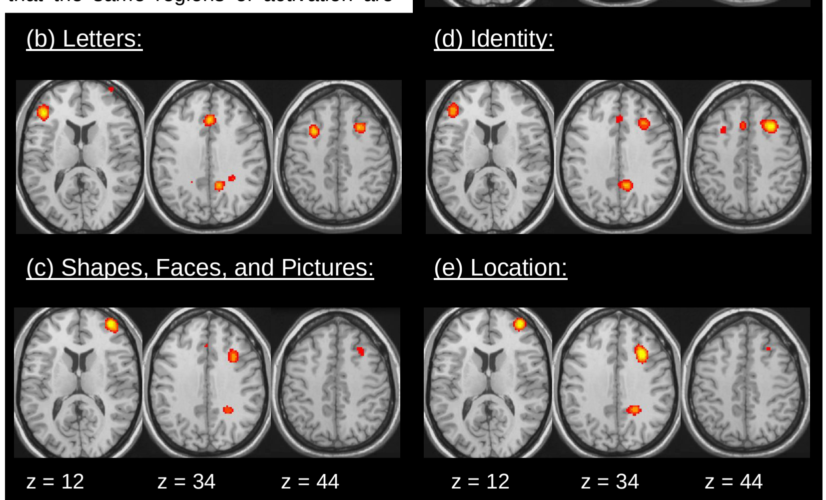


Figure 1. Activation Likelihood Estimation (ALE) maps of 5 meta-analyses of the n-back task divided by stimulus type and task requirements.

x	y	z	Anatomical Label	(mm^3)
28	21	36	R MFG (BA 9)	3992
13	-46	34	R posterior cingulate (BA 31)	1672
38	51	12	R MFG (BA 10)	1504
-44	36	9	L IFG (BA 46)	1024
0	28	28	Anterior cingulate (BA 32)	664
-36	-34	25	L insula (BA 13)	328
-27	16	37	L MFG (BA 9)	280

Table 1. Location and description of clusters determined by the main effects n-back meta-analysis (seen in Fig. 1a). MFG = middle frontal gyrus; IFG = inferior frontal gyrus.

Conclusions

Rather than revealing the hemispheric differences between verbal and non-verbal stimuli or task requirements, the meta-analyses presented here may provide insight to the nature of the processing mechanisms employed in the different variations of the n-back task. Taken together, the left lateralization seen in Letters (Fig. 1b) and Identity (Fig. 1d) and the right lateralization seen in Shapes, Faces, and Pictures (Fig. 1c) and Location (Fig. 1e) suggest differences due to changes between controlled and automatic processing [4]. By pooling all published n-back results together in a quantitative meta-analysis, it is apparent that further progress may be made in understanding the mechanisms of working memory.

References

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