The functional selectivity for lexical search guided by letter, semantic category and sentential cues: An fMRI Investigation

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Introduction: Lexical-semantic knowledge undergoes prolonged developmental changes throughout childhood and provides an ideal case for developmental research. Both neuropsychological and fMRI investigations of verbal fluency have been widely used to evaluate language and executive control processes in the human cortex. However, the majority of verbal fluency investigations have been limited to single-word or word-pair tasks without paying much attention to sentence level comprehension. It has been shown that verbal fluency relies on coordinated activities of a number of brain areas, particularly in the frontal and temporal lobes of the left hemisphere. Damage to the left frontal lobe (e.g. left inferior frontal cortex [LIFC]) has consistently been shown to impair verbal fluency[1]. In this study, we investigated verbal fluency to lexical-semantic search guided by letter, semantic category and sentential cues in order to evaluate differential involvement of specific neural correlates of functional selectivity in human cortex during free recall, word generation and filling-the-blank in sentences.

Methods:

<u>Subject</u>: Ten, right-handed, native English speaking healthy adults with no history of neurologic or psychiatric conditions and no reading/vocabulary difficulties participated in the study (5 male; age range 21–45 years). All participants gave informed written consent approved by the IRB of Penn State College of Medicine.

<u>Paradigms</u>:

Verbal fluency task: Participants were presented with three letters (one at a time) and were instructed to silently think of as many words beginning with the letter on the screen as they can (Example: <u>S</u> →“sauce”, “shoe”, “sundae”, etc).

Semantic category task: Participants were presented with three semantic categories (one at a time) and instructed to silently think of as many words associated with that category as they can (Example: <u>Fruit</u> →“apple”, “banana”, “watermelon”, etc).

Sentence-embedding task: Participants were presented with a string of 8 nonsense sentences (baseline block), and instructed to just look at each sentence (Example: Rdse sdkln _____ lewo iskd). During the experimental block consisting of 8 simple sentences, the participants were instructed to silently fill in the bank in each sentence (Example: A young cat is called a ____).

Each letter or semantic-category task was performed in a block design with 30s intervals of stimulus presentation interleaved with 20s rest intervals. For the Sentence-embedding task, both active and control blocks lasted for 28s each. Within each condition each stimulus lasted 3s, separated by a 0.5s crosshair.

<u>fMRI Protocol</u>: Images were acquired on a 3T (Siemens Trio) with echo-planar imaging (EPI). Imaging parameters were: TR/TE/FA= 2000ms/30ms/90^0; FOV = 230×230×120mm^3; matrix 80×80; 30 axial slices; slice thickness 4mm. Number of repetitions for verbal fluency paradigm was 162 and for sentence paradigm was 175. T1-wighted axial structural image with resolution $2 \times 2 \times 2$ mm^3 was also collected from each subject.

<u>Data Processing and Analysis</u>: All fMRI images were processed with SPM5 and normalized to the Montreal Neurological Institute brain template and filtered with a Gaussian kernel of $8 \times 8 \times 8$ mm^3 (FWHM). Activation maps for each paradigm were constructed at the individual level using the general linear model (GLM). Activation maps of letter, semantic category and sentence-embedding tasks were then compared based on a paired t-test.

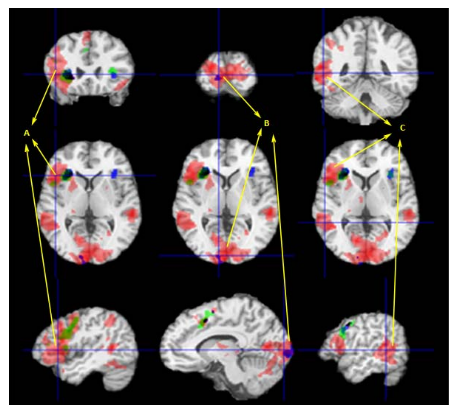

Fig.1. Significant and differently clusters of activation effects for the letter vs. semantic-category vs. sentence-embedded within the:
A. The sentence-embeddedtask yielded greater activity cluster in left temporal lobe.
B. The sentence-embedded/semantic-category tasks yielded activity cluster in the occipital (visual) cortex.
C. The letter, semantic-category and sentence-embedded tasks all yielded activity in the left frontal lobe.

Results: The letter task yielded activity concentrated in the left middle/superior frontal gyrus, with less activation in the inferior frontal gyrus. The semantic category task yielded activity mainly concentrated in the left occipital (visual) cortex and the inferior/middle frontal gyrus. However, the sentence-embedding task yielded greater activity clusters than letter and semantic-category tasks: with more activation in left temporal, inferior/middle frontal gyrus, supramarginal gyrus, hippocampus, angular gyrus and in bilateral occipital (visual) cortex, and fusiform gyrus. Additionally, significant activation was also detected in the right hemisphere including a large cluster centered in the right superior/middle temporal gyrus that extended to the right temporal pole. Significant activation was also observed in the left thalamus and in the bilateral cerebellum. The semantic category task and the sentence-embedding task also showed significant activation in the left insula. Finally, all three tasks showed similar activity in the bilateral supplementary motor area, and the bilateral pre- and post central gyrus.

Discussion: The results reveal remarkable anatomical differences in brain activity among all three tasks in healthy adults. The three tasks differentially recruit the frontal, temporal and occipital (visual) lobes. A similarly differential recruitment was also observed in supramarginal gyrus, hippocampus gyrus, angular gyrus, fusiform gyrus, left thalamus and in bilateral cerebellum. We hypothesize that the observed differences may relate to word form processing demands when word retrieval is guided by letter, semantic category or sentential cues. These findings provide converging evidence that letter, semantic category and sentence-level performance is dependent on distinctive and yet overlapping neural circuits. Our findings show that both the location and amount of cortical activity can be modulated by varying task demands of the verbal fluency task. In particular, the sentential task clearly showed that brain activity related to language processing during reading comprehension and production demands more neural resources. Our results is highly relevant clinically because they can provide measures of the efficiency of selecting and retrieving phonological /orthographic and semantic category information that requires efficient task initiation, planning, organization, and flexibility [3]. The GLM results can also be combined with functional and effective connectivity analysis to investigate brain connectivity networks subserving each task. The results demonstrate the advantage of investigating the language circuitry using verbal fluency tasks, and provide motivation to examine the underlying networks using powerful data-driven techniques such as Independent Component Analysis (ICA) [4].

References: [1] Li, P., Cognitive Science, 33 (2009) 629–664. [2] Erin Nicole Moore-Parks, Brain & Language. 2010. [3] Rasmus M. Birn., NeuroImage. 2010. [4] Karunanayaka PK et al., *Neuroimage,* 34 :349–60, 2007. [5] Karunanayaka et al., NeuroImage 2010; 51:472-87.