Evaluating Sex Differences in the Brain for Language Processing

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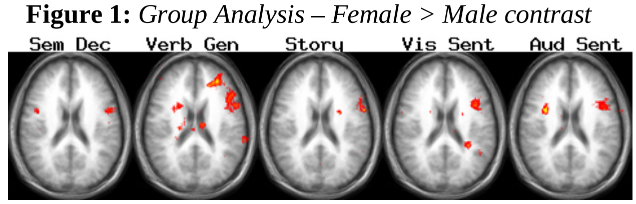
Introduction: Several research groups have investigated sex differences in cortical language representation using various neuroimaging techniques, but the results have been inconsistent. Possible reasons for the discrepancies between studies are differences in tasks (test conditions), baseline conditions, and the methods used to measure the differences. If differences do exist, gender effects will need to be carefully considered when evaluating any language task used for neuroimaging. We evaluated possible fMRI gender differences for 6 different tasks using individual subject measures (laterality indices (LI), extent of activation) and group analysis.

Methods: 38 right handed volunteers (20 female) performed 6 different fMRI language tasks. The tasks examined were: confrontation naming (line drawings), verb generation (audio noun presentation), auditory and visual sentence comprehension, semantic decision-making (visual noun presentation), and story listening. All tasks were block design paradigms consisting of 192 image volumes with variable active and baseline durations (12-30 seconds). Baseline conditions for the audio tasks consisted of the same audio stimuli played in reverse while baseline conditions for visual tasks consisted of simple line designs to match low level visual processing. For the functional images, twenty-one contiguous 5 mm axial slices were obtained with a gradient echo, echo-planar imaging sequence (TR = 2 s, TE = 50 ms, flip angle = 90°, FOV = 22 cm, 64 x 64 matrix) using a 1.5T GE Signa MRI system. A co-planar 3D T1-weighted volume was obtained using a fast SGPR sequence was acquired for anatomical reference.

Statistical maps were generated using a multiple regression algorithm using a boxcar (6 second lag) reference waveform with linear trends were included as covariates (AFNI). Activation maps were determined by a p-value and cluster size threshold ($\alpha < .05$). Regions of interest (ROI) of the inferior frontal (BA 44-47) and temporoparietal (BA 22,39) regions were hand drawn according to Talairach coordinates utilizing the Talairach Atlas. Extent of activation (# active voxels) and LIs were calculated for each ROI. LI calculation was based on the sum of the F-statistics within each ROI above a given threshold [(left-right)/(left+right)] and the final LI for each ROI was the average over a range of thresholds. For the group analysis the statistical maps (regression coefficients) were smoothed with a 6 mm FWHM Gaussian kernel and group maps for each task were performed by calculating the mean for each voxel (threshold p<.01).

Results: There were no significant gender differences in LI values for any of the tasks (Table 1). The biggest difference was for confrontation naming (p=.08) in which females were less lateralized than males. Regarding extent of activation, there was significantly more activation for females within the RH inferior frontal ROI with the confrontation naming (p=.02) and auditory sentence tasks (p=.05) and for males within the RH temporoparietal ROI with the semantic decision task (p=.05). The group analysis (Females vs. Males) revealed areas of increased activation for females in the left inferior frontal ROI for all tasks except confrontation naming (Figure 1). There was greater female activation in the RH insular region for all tasks except sentence and story listening. There was also greater female activation in the LH temporoparietal region for sentence listening and greater male activation in the RH temporoparietal region for semantic decision.

Figure 1: *Group Analysis – Female > Male contrast*



Discussion: The method for determining hemispheric differences of FMRI activation between male and females influenced the results and should be considered when comparing studies. Laterality calculations did not reveal significant differences, although there was a large gender difference for confrontation naming. The laterality indices are not heavily dependent on individual thresholds and are a relative value that is normalized within each individual. Comparing extent of activation within each ROI did reveal some significant gender differences, most notably for confrontation naming. The individual analysis is based on large ROIs while the group comparisons are based on a voxel-wise basis. The group comparison revealed specific areas in the inferior frontal regions in which the activation correlation was stronger for females compared to males. While confrontation naming revealed gender differences within the inferior frontal ROI with the individual analysis, the other five tasks revealed inferior frontal gender differences in the group analysis.

	Semantic Decision			Verb Generation			Confrontation Name			Visual Sentences			Audio Sentences			Story Listening		
Gender	Ave	p-val	>.6	Ave	p-val	>.6	Ave	p-val	>.6	Ave	p-val	>.6	Ave	p-val	>.6	Ave	p-val	>.6
Female	0.77	0.34	85.0	0.81	0.12	84.2	0.43	**0.08**	45.0	0.58	0.65	55.0	0.53	0.38	61.1	0.73	0.24	80.0
Male	0.68		61.1	0.88		94.4	0.66		83.3	0.62		66.7	0.64		61.1	0.61		64.7
Female	0.56	0.53	65.0	0.79	0.75	78.9	0.46	0.29	55.0	0.74	0.69	75.0	0.72	0.75	80.0	0.57	0.60	60.0
Male	0.53		61.1	0.79		88.9	0.55		66.7	0.73		83.3	0.75		72.2	0.55		52.9

Table 1: top = inferior frontal ROI, shaded = temporoparietal ROI. >.6 = % subjects with LI > .6. p-value is for gender t-test.