Spatial memory activation patterns classify females but not males

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Introduction

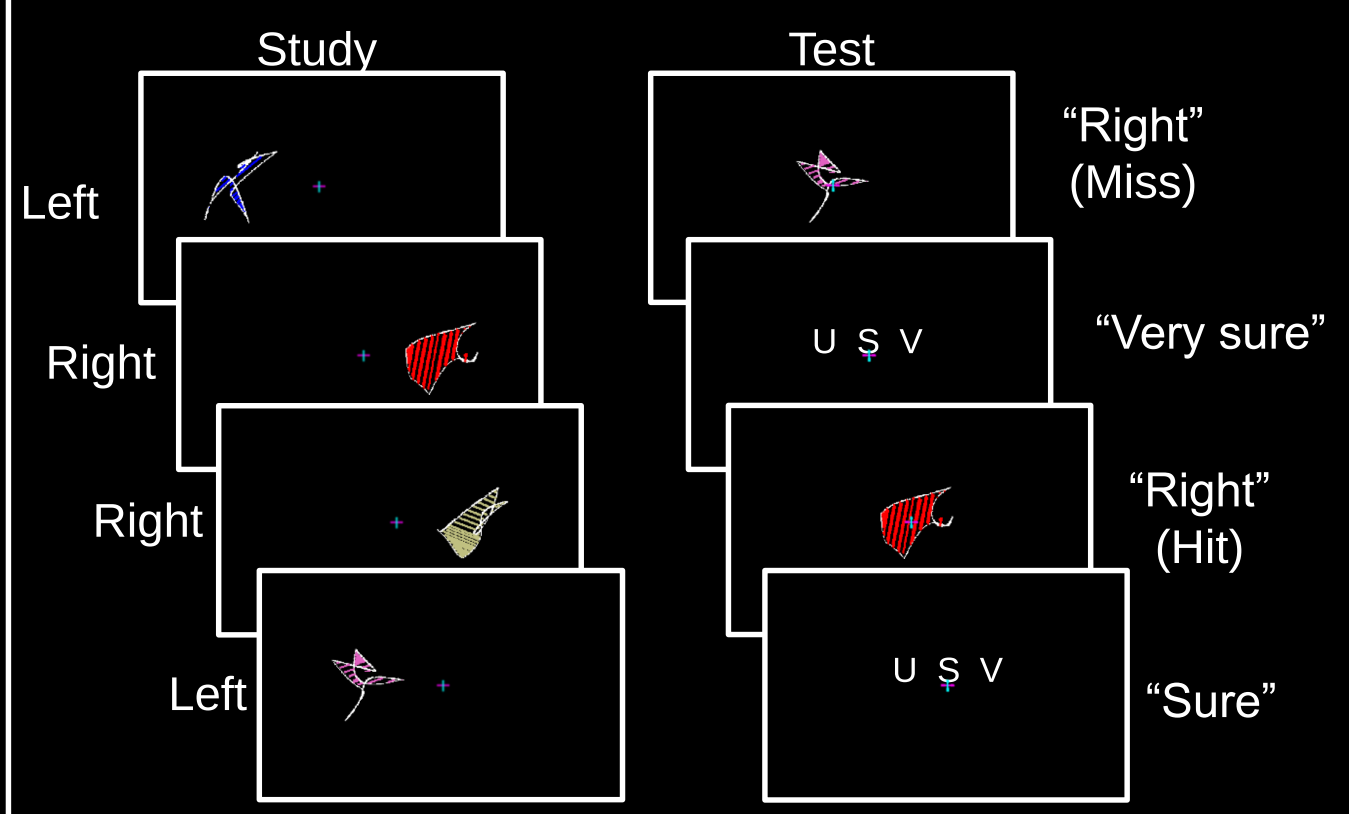
- We reanalyzed functional magnetic resonance imaging (fMRI) data from four spatial long-term memory experiments and found that during spatial long-term memory, females and males produce different patterns of activity [1]
- However, it is currently debated whether differences in brain activity can be used to classify sex [2]

Present Aim

- We ran a multi-voxel pattern analysis (MVPA) on independently defined functional regions-of-interest (ROIs) to determine if patterns of activity during spatial long-term memory could classify sex

Methods

Memory Paradigm



- Encoding: in Experiments 1, 2, and 3, abstract shapes were presented in the left or right visual field. In Experiment 4, abstract shapes were presented in each quadrant of the visual field (upper-left, upper-right, lower-left, and lower-right)
- Retrieval: in all experiments, shapes were presented at fixation. In Experiments 1 and 2, participants classified old and new shapes as "old-left", "old-right", or "new". In Experiments 3 and 4, participants classified old shapes as previously in the "left" or "right" for Experiment 1 and "upper-left", "lower-left", "upper-right", or "lower-right" for Experiment 2 followed by "unsure", "sure", or "very sure" judgments

GLM Analysis

- General linear model analysis (Male N=18, Female N=18 selected from 40 females across four experiments to match spatial memory accuracy for males)
- Individual voxel threshold $p < .001$, corrected for multiple comparisons to $p < .05$ by requiring a cluster extent threshold of 10 resampled voxels
- Spatial memory was isolated and contrasting spatial memory hits and spatial memory misses

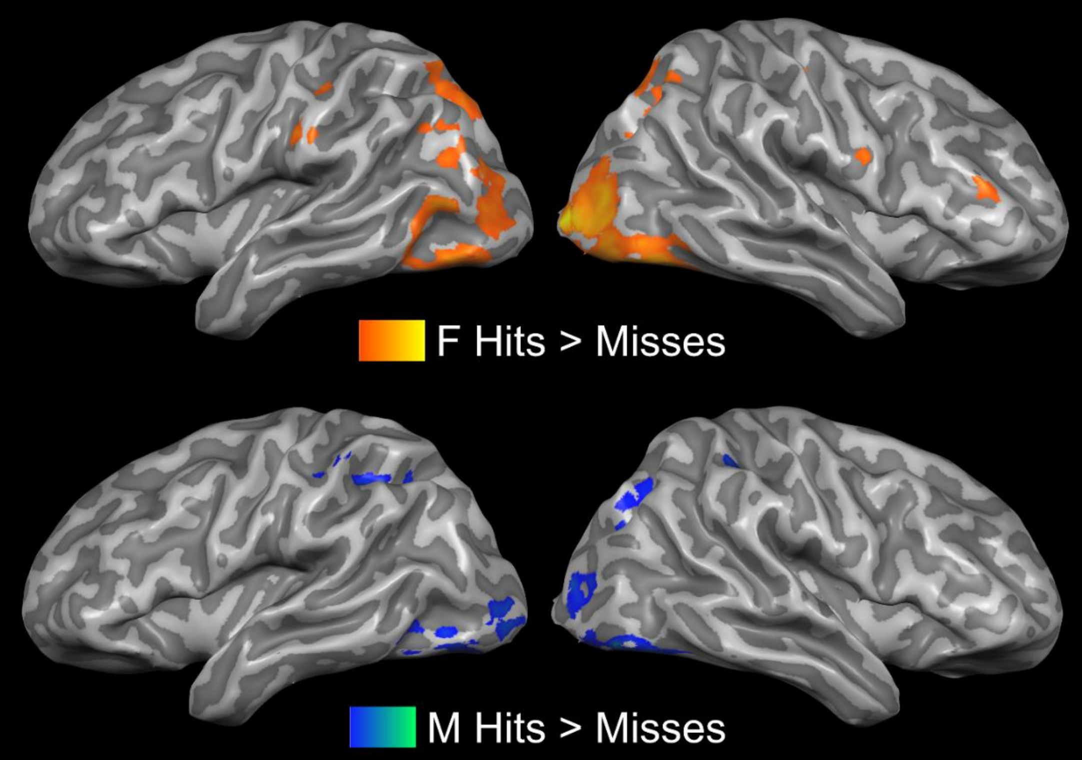
Multi-voxel Correlation Analysis

- For each pair of left-out participants (1 female, 1 male), an independent functional ROI was defined from the remaining participants as the union of activity produced from the contrasts of female spatial hits versus misses and male spatial hits versus misses (each ROI was thresholded such that each contrast produced the same number of activated voxels)
- A female template and male template were created from the remaining participants by averaging the response magnitude for each sex within the functional ROI
- The sex of each left-out participant was classified depending on whether their activation pattern was more highly correlated with the female template or male template

Results

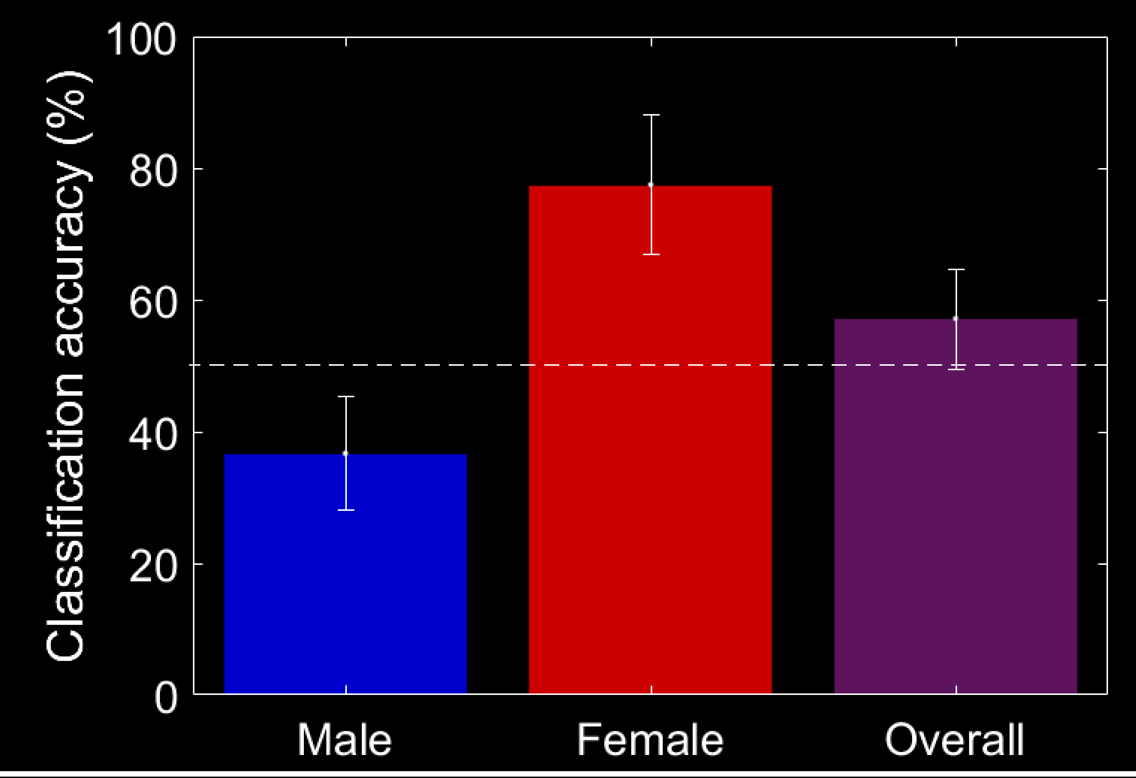
GLM Analysis

- Our initial analysis (with all participants) revealed that females and males produced different patterns of activity during spatial long-term memory. Areas of differential activity included inferior frontal sulcus, precentral gyrus, central sulcus, superior parietal lobule, angular gyrus, supramarginal gyrus, calcarine sulcus, precuneus, and thalamus for females and medial prefrontal cortex, collateral sulcus, inferior temporal sulcus, putamen, and cerebellum for males
- An ROI analysis (with the cluster extent removed) revealed significant activity for females in Wernicke's area and significant activity for males in left hippocampus



Multi-voxel Pattern Analysis

- Correlation within sex for females ($t(17) = 4.57$, $p < .001$) was significantly higher than the correlation between sex ($t(17) = 2.05$, $p > .05$; $t(17) = 2.71$, $p < .05$). This relationship was not found for male participants
- The classification accuracy for females was significantly above chance (77.47%; $t(17) = 3.19$, $p < .001$)
- The classification accuracy for males was not significantly above chance (36.73%; $t(17) = -1.25$, $p > .05$)
- The overall classification accuracy was 57.10%, which was not significantly above chance ($t(35) = 0.94$, $p > .05$; chance = 50%)



Discussion

- To investigate whether or not differences in patterns of activity during spatial long-term memory could classify sex, we ran MVPA on a previously published dataset using independent functional ROIs [1]
- The current results show an above average classification accuracy for females, but not males, suggesting that intrasubject variability in patterns of activity is greater among males than females during spatial long-term memory
- The below chance classification accuracy for males may be due to the large number of folds in the analysis [3]
- These results argue against the hypothesis that sexual dimorphisms in the brain do not exit and that sex differences in the brain are not distinct enough to classify sex [2]
- The current results, alongside reports of functional, anatomic, and molecular sexual dimorphisms, argue against the widespread practice of collapsing across sex in cognitive neuroscience [4,5]

References

[1] Spets, D. et al. (2019). Different patterns of cortical activity in females and males during spatial long-term memory. *Neuroimage*. 199, 626-634. [2] Joel, D. et al. (2015). Sex beyond the genitalia: The human brain mosaic. *Proc Natl Acad Sci U S* A. 18(2): 115-126. [3] Jamalabadi, H., et al. (2016). Classification based hypothesis testing in neuroscience: Below-chance level classification rates and overlooked statistical properties of linear parametric classifiers. *Human Brain Mapping*. 27: 1842-1855. [4] Cahill, L. (2006). Why sex matters for neuroscience. *Nature Reviews Neuroscience*, 7, 477-484. [5] Andreano, J.M. & Cahill, L. (2009). Sex influences on the neurobiology of learning and memory. *Learn. Mem.16(4):248-266.*