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Sex differences in brain structure in opposite sex twin pairs

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Introduction

Sex differences in human brain anatomy are of increasing interest, especially since it is believed that behavioural differences between males and females might be directly related to dissimilarities in brain structure.

In studies on sex differences in the human brain there have been considerable inconsistencies with regard to the anatomical structures involved. The lack of systematic matching for age, family environment, and genetic background may be partly blamed for the variable findings.

The present study investigates sex differences in brain structure using opposite sex twin pairs which are very well matched, not only for age, but also for their early developmental environment and part of their genetic make-up.

Methods

Participants: 24 opposite sex twin pairs (mean age (SD): 29 (9.71)) were selected from the Netherlands Twin Registry (Boomsma et al., 2006).

MRI acquisition and preprocessing: Of each twin, whole brain structural T1 weighted MR scans were collected (3.0 T Philips Intera Scanner). Gray matter structures were analyzed using the voxel based morphometry (VBM) toolbox in SPM8. MR images were first segmented into gray matter, white matter and cerebrospinal fluid. Subsequently the gray matter segmentations were normalized to a group template using the Diffeomorphic Anatomical Registration Through Exponential Lie algebra (DARTEL) algorithm in SPM8, and then warped from DARTEL space to the standard Montreal Neurological Institute brain.

Statistical analysis: A paired t-test, was performed on the modulated gray matter compartments to find gray matter regions of significant volume difference (adjusted for total intracranial volume) in males compared to females. Statistical results were considered significant at $p < 0.05$, FDR corrected.

Results

Global brain volume

Men exhibited significantly larger total intracranial volumes (TIV), gray matter (GM) and white matter (WM) compared to women. Means, standard deviations and t-statistics for global brain volume measures are presented in Table 1.

Measure	Sex	Mean (SD)	T-value	df	p-value
TIV	M	1534.67(151.65)	8.324	23	<.001
	F	1338.75(108.92)			
GM	M	752.49(79.86)	7.464	23	<.001
	F	655.35(54.76)			
WM	M	522.81(54.01)	7.873	23	<.001
	F	458.85(39.75)			

Table 1 Mean (SD) for global brain measures. T-statistics are reported at P<0.05, FDR-corrected. M=males, F=females

Regional brain volume (adjusted for total intracranial volume)

GM enlargements in male twins compared to their female co-twins (fig. 1) : Male twins exhibited relatively increased gray matter for the hypothalamus.

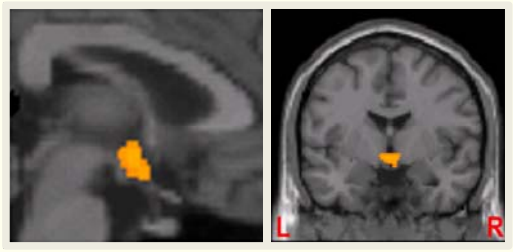

Figure 1 Regional volume increase in male twins compared to their female co-twins

GM enlargements in female twins compared to their male co-twins (fig. 2): Female twins exhibited relatively increased gray matter for the parahippocampal *(figure 2A)*, dorsolateral prefrontal *(figure 2B)* and orbitofrontal cortex *(figure 2C)*.

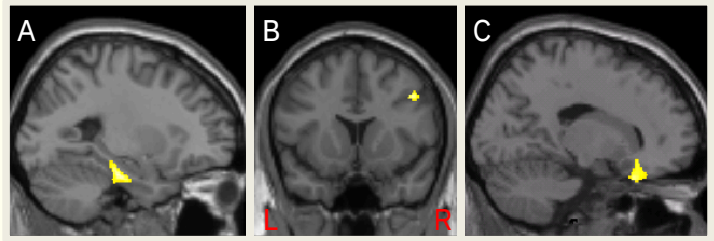

Figure 2 Regional volume increase in female twins compared to their male co-twins

Conclusions

As expected, we found that total brain size and intracranial volume are generally larger in men compared to women. Furthermore, after correcting for global brain volume differences, we observed several regional sexual dimorphisms.

Sex differences for the hypothalamus, hippocampus and orbitofrontal cortex have been reported earlier, and our findings therefore provide further support for their involvement. On the other hand, for other brain areas reported previously, such as the amygdala and caudate nucleus, we could not confirm significant sex effects (Lenroot al., 2010).

Our results underline the importance of using carefully matched subjects when studying sex differences of the brain. Brain sex differences are a rich source of information for understanding the behavioural differences that exist between males and females and are also highly important to consider in studies on the neurobiology of neuropsychiatric disorders, especially those that differ in prevalence or symptoms between men and women.

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