Neuroscience Campus Amsterdam

# Neuroimaging sex differences in gray and white matter structure

[1,2]D. van 't Ent,[1,2]A. den Braber,[3]D. Stoffers, [4]K. Linkenkaer-Hansen,[1]D.I. Boomsma,[1]E.J.C. De Geus

[1]Dept Biological Psychology, VU university [2]Neuroscience Campus Amsterdam; [3] Dept of Sleep and Cognition, NIN, Amsterdam, [4] Dept of Integrative Neurophysiology, Center for Neurogenomics and CognitiveResearch, Neuroscience Campus Amsterdam, VU University, The Netherlands

## Introduction

Men have an approximately 9-12% larger brain volume, but imaging studies on sex differences in brain structures have reported inconsistent results (e.g. the corpus callosum larger in females: Lacoste-Utamsing, 1982, larger in males: Sullivan, 2001, or of similar size: Bishop, 1997. This might be due suboptimal matching for e.g. age, or family background. In addition, previous studies generally focussed on a single structural measure. We investigated sex differences in regional gray matter volume, white matter volume and white matter directionality in 87 matched male-female pairs.

## Methods

### Participants (Table 1, top):

42 Dizygotic Opposite Sex (DOS) twin pairs and 45 carefully matched male-female pairs

### Neuroimaging data :

Structural T1-weighted sMRI and DTI.

### Data Analysis :

Sex differences in regional gray and white matter volume were assessed by Voxel Based Morphometry (VBM-SPM8: Wellcome Dept of Imaging Neuroscience, London, UK). Sex differences in white matter directionality were assessed by comparing fractional anisotropy (FA) using tract-based spatial statistics (TBSS: FSL software package, FMRIB, Oxford, UK).

### Statistics :

Paired sample t-tests between males and females ($p < 0.05$, FDR corrected)

Table. 1

| | *matched pairs* | | | | | *DOS pairs* | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | males (n=45) | females (n=45) | df | t-value | p-value | males (n=45) | females (n=45) | df | t-value | p-value |
| **Demography** | | | | | | | | | | |
| Age | 31.8±7.6 | 32.0±7.5 | 44 | -0.72 | .476 | 29.9 ±10.5 | 29.9 ± 10.5 | | | |
| Educational attainment (% low/middle/high) | 13.3/26.7/60.0 | 8.9/35.6/55.6 | 2 | 1.05 | .592 | 2.4/31.0/66.7 | 7.1/31.0/61.9 | 2 | 1.07 | .584 |
| **Global brain measures** | | | | | | | | | | |
| Gray Matter | 749.4 ± 50.4 | 666.3 ± 56.4 | 44 | 8.62 | <.001 | 761.2 ± 68.9 | 661.0 ± 48.2 | 41 | 11.63 | <.001 |
| White Matter | 533.1 ± 42.0 | 473.3 ± 44.6 | 44 | 7.85 | <.001 | 532.6 ± 50.0 | 466.5 ± 39.5 | 41 | 12.00 | <.001 |
| Total Intracranial Volume | 1544.2 ± 110.9 | 1365.0 ± 117.3 | 44 | 8.82 | <.001 | 1557.1 ± 132.7 | 1355.4 ± 101.0 | 41 | 12.67 | <.001 |
| Mean Fractional Anisotropy | .297 ± .012 | .292 ± .011 | 44 | 2.96 | .005 | .289 ± .010 | .287 ±.008 | 41 | 1.12 | .269 |

## Results

### Global brain measures (Table 1, bottom):

In both samples, total gray, white matter and intracranial volume were larger in males. Mean FA was also enlarged in males in the matched sample, but not the DOS sample.

### Regional GM volume (VBM corrected for TIV and age):

Across all pairs and separately in the matched and DOS samples we found enlarged volumes in men for hypothalamus, putamen/globus pallidus and rostral midbrain (Fig 1).

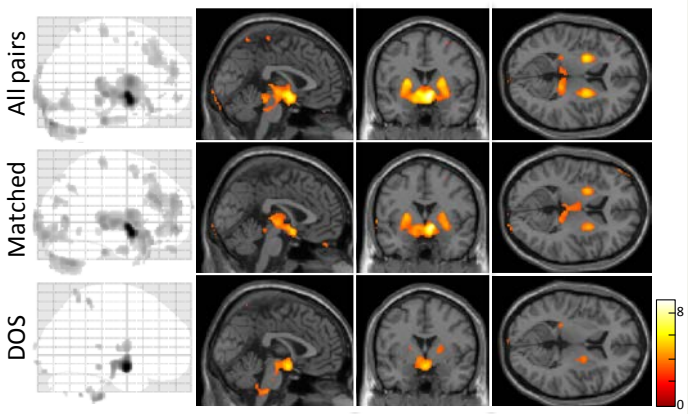


Fig. 1: color bar indicates t-values

GM volume enlargement in females was noted in a number of small clusters restricted to cortical areas (Fig. 2), with largest statistical significance in left insula, and cingulate regions. The left insula finding was not replicated in the matched sample.

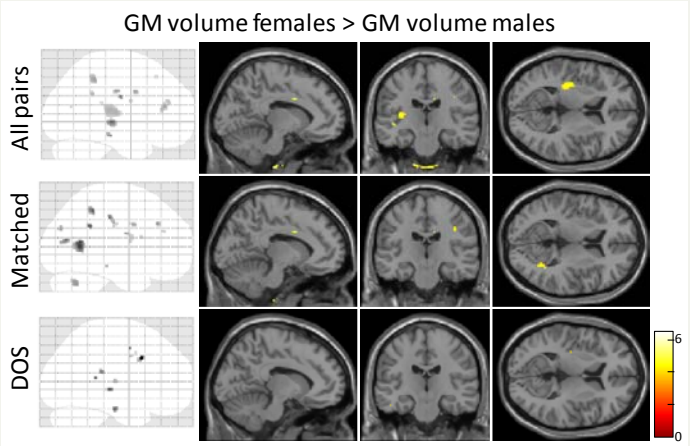


Fig. 2: color bar indicates t-values

### Regional WM volume (VBM corrected for TIV and age):

We found no significant sex differences for regional WM volume.

### DTI-FA (TBSS corrected for age):

Across all pairs and separately in the matched and DOS samples we found significantly larger FA values in males, for most fiber bundles (Fig. 3). Largest cluster significance was evident for the right and left anterior thalamic radiations. We found no significant FA enlargements for females.

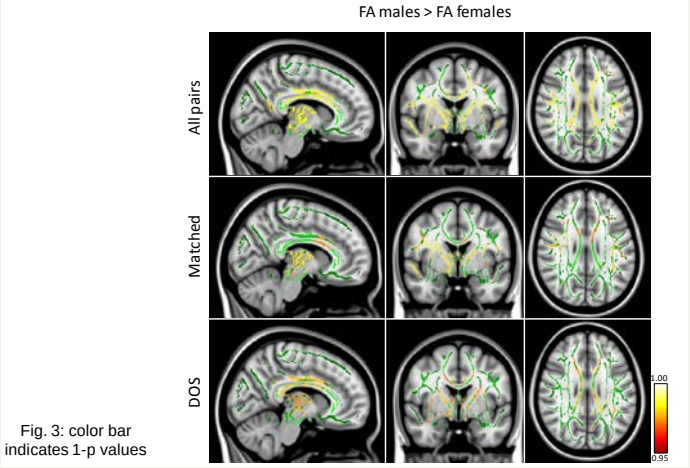


Fig. 3: color bar indicates 1-p values

## Conclusions

Men have larger GM volumes and higher FA in, or surrounding, subcortical structures. These are involved in the control of sexual and reproductive function (hypothalamus: Bao, 2010) and the programming and control of movement (putamen, globus pallidus, thalamus: Giedd, 1997; Peper, 2009) and have been associated with neuropsychiatric disorders more prevalent in males (tic disorders, schizophrenia: Shenton, 2001; Singer, 2003).

Women had larger gray matter volumes in brain regions involved in emotion and interoceptive awareness (insula, anterior cingulate: Sowell, 2007; Lv, 2010 ) and associated with neuropsychiatric disorders that have a higher prevalence in females (depression, anxiety disorders).

Sex differences provide a rich source of information for understanding behavioral differences between males and females and should always be considered in studies on the neurobiology of neuropsychiatric disorders that differ in prevalence or symptoms between the sexes.

References:

Bao, A.M. Neuroscientist, 2010, 16: 550-565; Bishop, K.M. Biobehavioral Reviews. 1997, 21: 581-601; Giedd, J.N. Progress in Neuro-Psychopharmacology & Biological Psychiatry, 1997, 8: 1185-1201; Lacoste-Utamsing, C. Science, 1982, 216: 1431-1432; Lv, B. Neuroimage, 2010, 53: 373-382; Peper, J.S. Psychoneuroendocrinology, 2009, 34: 332-342; Shenton, M.E. Schizophrenia Research, 2001, 49: 1-52; Singer, H.S. Brain Development, 2003, 25: S70-S84. Sowell, E.R. Cerebral Cortex,2007: 17: 1550-1560; Sullivan, E.V. Neurobiology of Aging, 2001, 22: 603-611.

VRIJE UNIVERSITEIT NEDERLANDS TWEELINGEN REGISTER

VU university medical center

VU University Amsterdam