

# SUPPLEMENTARY MATERIAL

FOR THE MANUSCRIPT

## **Similar cortical but not subcortical gray matter abnormalities in women with posttraumatic stress disorder with versus without dissociative identity disorder**

**Sima Chalavi, PhD <sup>a</sup>, Eline M. Vissia, MSc <sup>a</sup>, Mechteld E. Giesen, MSc <sup>a</sup>,  
Ellert R.S. Nijenhuis, PhD <sup>b</sup>, Nel Draijer, PhD <sup>c</sup>, Gareth J. Barker, PhD <sup>d,e</sup>,  
Dick J. Veltman, PhD <sup>c</sup>, Antje A.T.S. Reinders, PhD <sup>a,f,\*</sup>**

<sup>a</sup> Department of Neuroscience, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands

<sup>b</sup> Top Referent Trauma Center Mental Health Care Drenthe, Assen, The Netherlands

<sup>c</sup> Department of Psychiatry, VU University Medical Center, Amsterdam, The Netherlands

<sup>d</sup> King's College London, Institute of Psychiatry, Department of Neuroimaging, London SE5 8AF, United Kingdom

<sup>e</sup> Center for Neurodegeneration Research, King's College London, United Kingdom

<sup>f</sup> Department of Psychosis Studies, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom

\* Corresponding author

**Correspondence to:**

Antje A.T.S. Reinders, PhD

Department of Psychosis Studies

Institute of Psychiatry (IoP)

King's College London

De Crespigny Park, PO Box 40

London SE5 8AF

United Kingdom

E-mail: a.a.t.s.reinders@gmail.com(preferred); a.a.t.s.reinders@kcl.ac.uk

Tel: +44 (0)20 7848 0966

Fax: +44 (0)20 7848 0287

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### **Supplementary Material 1: All-PTSD vs. HC comparisons**

In our study, both DID-PTSD and PTSD-only groups shared the diagnosis of PTSD.

Therefore, we further merged these patient groups into one larger group, referred to as “All-PTSD”, in order to investigate the common morphological features of PTSD.

We found that in comparison with HC, All-PTSD patients had significantly smaller volumes of the whole-brain and bilateral hemispheres, total and bilateral frontal and temporal, and total and left insula superparcels (eTable 1 and eFigure1). Furthermore, significant differences between All-PTSD and HC were found in cortical surface area of the whole brain and right hemisphere, total and bilateral frontal, right temporal, and total and left insula superparcels (eTable 1). With regard to cortical thickness, compared with HC, All-PTSD group had significantly smaller cortical thickness of the left hemisphere and left parietal, temporal and occipital superparcels (eTable 1). Moreover, volumes of the total and right hippocampus and left accumbens area differed significantly between All-PTSD and HC groups (eTable 2). Excluding the subgroup with only adult traumatizing events from the All-PTSD group (total remaining N=28) resulted in a smaller total ( $p=0.006$ ), left ( $p=0.022$ ) and right ( $p=0.004$ ) hippocampal volume as compared with HC.

### **Supplementary Material 2: Morphological analysis of parcels within the superparcels**

The results as presented in the main manuscript are based on a gross assessment of the cortical GM of the superparcels (Woodward et al., 2009). We reduced the number of measurements extracted from FreeSurfer to satisfy the assumption for multiple comparison correction by the creation of whole-brain and unilateral superparcels. These supplementary material present the additional analyses which were performed on the individual parcels within each superparcel in order to investigate which brain regions were driving the cortical GM differences for each GM measure superparcel (i.e. volume, surface-area and thickness) between posttraumatic stress disorder (PTSD) patients with a dissociative identity disorder (DID-PTSD), PTSD patients without DID (PTSD-only) and healthy controls (HC). Every

superparcel is presented in a separate table: eTable 3 presents the individual areas within the frontal superparcel, eTable 4 presents the individual areas within the parietal superparcel, eTable 5 presents the individual areas within the temporal superparcel, eTable 6 presents the individual areas within the occipital superparcel, and eTable 7 presents the individual areas within the insular superparcel. For every individual area cortical GM volume, surface-area and thickness are presented.

### **Supplementary Material 3: Medication effect**

It has been reported that the use of typical antipsychotics, anti-epileptics or antidepressants can change the neuroanatomy of the brain (Chakos et al., 1994; Gur et al., 1998; Massana et al., 2005; Scherk and Falkai, 2006; Vermetten et al., 2003). In order to ascertain that the GM volumetric findings (reported in Table 2-3 of the main manuscript) were genuine and not due to the use of psychiatric medications, we repeated the statistical analyses after excluding the DID-PTSD or PTSD-only patients with current or past histories of psychiatric medications use. The results are reported in eTables 8-19.

As we expected, after excluding patients with a history of using psychiatric medications, the effects became less significant which can be due to the reduced statistical power. Important exceptions were the increase in statistical significance of the total (DID-PTSD vs. HC) and left (DID-PTSD vs. HC; DID-PTSD vs. PTSD-only) cortical surface area of the parietal superparcels after the exclusion of patients with a history of using anti-depressants and the increase in the statistical values of the total, left and right caudate volumes (DID-PTSD vs. HC; DID-PTSD vs. PTSD-only) after excluding patients with a history of antipsychotics or anti-epileptics. The latter analysis also revealed a strong increase in statistical significance of the total, left and right hippocampal volumes (DID-PTSD vs. PTSD-only).

We also investigated whether our finding of larger dorsal-striatal volumes could have been due to the usage of antipsychotics exposure, which has been previously suggested (Dazzan et al., 2005). Only 3 (out of seventeen) DID-PTSD patients had been exposed to

antipsychotics, and when the analyses were repeated after excluding these three patients, we found if anything an even more robust enlargement of bilateral caudate volume in DID-PTSD patients compared to both HC and to PTSD-only patients. We also found that differences in hippocampal volume remained unchanged or became even more marked when DID-PTSD patients with a history of using antipsychotics and anti-epileptics were excluded from the analysis.

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**eTable 1a. Statistical results for cortical volume (mm<sup>3</sup>) for All-PTSD vs. HC comparison**

| Superparcels              | Measure | Total/<br>side | All-PTSD to HC comparison |               |  |
|---------------------------|---------|----------------|---------------------------|---------------|--|
|                           |         |                | Mean (SD)                 |               | t-test: <i>P</i> Value (Effect size <sup>^</sup> ) |
|                           |         |                | All-PTSD (n=33)           | HC<br>(n=28)  | All-PTSD vs. HC                                    |
| Whole-brain <sup>§</sup>  | volume  | total          | 449276(36752)             | 468430(28543) | <b>&lt;0.001**</b> (-0.59)                         |
|                           |         | left           | 224161(18105)             | 234336(14676) | <b>&lt;0.001**</b> (-0.62)                         |
|                           |         | right          | 225115(18758)             | 234094(14003) | <b>0.002**</b> (-0.55)                             |
| Frontal <sup>‡</sup>      | volume  | total          | 168497(16793)             | 176665(10572) | <b>&lt;0.001**</b> (-0.60)                         |
|                           |         | left           | 84507(7927)               | 88555(5548)   | <b>&lt;0.001**</b> (-0.60)                         |
|                           |         | right          | 83989(8930)               | 88110(5173)   | <b>0.001**</b> (-0.58)                             |
| Parietal <sup>&amp;</sup> | volume  | total          | 122701 (8404)             | 126517 (9795) | 0.078 (-0.42)                                      |
|                           |         | left           | 60872 (4373)              | 63019 (5287)  | 0.052 (-0.44)                                      |
|                           |         | right          | 61829 (4214)              | 63497 (4702)  | 0.155 (-0.37)                                      |
| Temporal <sup>#</sup>     | volume  | total          | 101188 (8969)             | 105858 (7498) | <b>0.004**</b> (-0.57)                             |
|                           |         | left           | 50667 (4491)              | 53209 (3967)  | <b>0.002**</b> (-0.60)                             |
|                           |         | right          | 50521 (4559)              | 52648 (3719)  | <b>0.014*</b> (-0.51)                              |
| Occipital <sup>£</sup>    | volume  | total          | 43710 (4404)              | 45340 (4850)  | 0.22 (-0.35)                                       |
|                           |         | left           | 21739 (2325)              | 22552 (2541)  | 0.28 (-0.33)                                       |
|                           |         | right          | 21971 (2222)              | 22788 (2513)  | 0.22 (-0.35)                                       |
| Insula                    | volume  | total          | 13178 (1017)              | 14047 (1042)  | <b>0.001**</b> (-0.84)                             |
|                           |         | left           | 6374 (544)                | 6999 (446)    | <b>&lt;0.001**</b> (-1.26)                         |
|                           |         | right          | 6803 (586)                | 7048 (704)    | 0.23 (-0.38)                                       |

eTable 1b (continue). Statistical results for cortical surface area (mm<sup>2</sup>) for All-PTSD vs. HC comparison

| Superparcels              | Total/<br>side | All-PTSD to HC comparison |                |   |
|---------------------------|----------------|---------------------------|----------------|---|
|                           |                | Mean (SD)                 |                | t-test: P Value (Effect size <sup>^</sup> ) |
|                           |                | All-PTSD<br>(n=33)        | HC<br>(n=28)   | All-PTSD vs. HC                             |
| Whole-brain <sup>s</sup>  | total          | 162377 (11993)            | 166157 (11612) | <b>0.042*</b> (-0.32)                       |
|                           | left           | 81098 (5965)              | 82813 (5722)   | 0.052 (-0.29)                               |
|                           | right          | 81279 (6055)              | 83344 (5917)   | <b>0.035*</b> (-0.34)                       |
| Frontal <sup>‡</sup>      | total          | 59057 (5156)              | 61592 (4019)   | <b>0.007*</b> (-0.45)                       |
|                           | left           | 29775 (2511)              | 29794 (2736)   | <b>0.017*</b> (-0.39)                       |
|                           | right          | 29732 (2666)              | 29666 (2678)   | <b>0.003**</b> (-0.51)                      |
| Parietal <sup>&amp;</sup> | total          | 46345 (3050)              | 46828 (3688)   | 0.31 (-0.14)                                |
|                           | left           | 22889 (1513)              | 23132 (1855)   | 0.24 (-0.14)                                |
|                           | right          | 23455 (1596)              | 23695 (1893)   | 0.41 (-0.14)                                |
| Temporal <sup>#</sup>     | total          | 31698 (2662)              | 32474 (2418)   | 0.053 (-0.31)                               |
|                           | left           | 16082 (1384)              | 16409 (1268)   | 0.12 (-0.25)                                |
|                           | right          | 15615 (1313)              | 16065 (1199)   | <b>0.024*</b> (-0.36)                       |
| Occipital <sup>£</sup>    | total          | 20401 (1914)              | 20669 (2489)   | 0.45 (-0.12)                                |
|                           | left           | 10208 (1004)              | 10314 (1270)   | 0.56 (-0.09)                                |
|                           | right          | 10192 (955)               | 10354 (1278)   | 0.37 (-0.15)                                |
| Insula                    | total          | 4424 (261)                | 4593 (366)     | <b>0.020*</b> (-0.54)                       |
|                           | left           | 2142 (143)                | 2304 (185)     | <b>&lt;0.001**</b> (-0.99)                  |
|                           | right          | 2282 (173)                | 2288 (230)     | 0.71 (-0.03)                                |



**eTable 1c (continue). Statistical results for cortical thickness (mm) for All-PTSD vs. HC comparison**

| Superparcels              | Total/<br>side | All-PTSD to HC comparison |               |                                 |
|---------------------------|----------------|---------------------------|---------------|---------------------------------|
|                           |                | Mean (SD)                 |               | t-test: P Value (Effect size ^) |
|                           |                | All-PTSD<br>(n=33)        | HC<br>(n=28)  | All-PTSD vs. HC                 |
| Whole-brain <sup>§</sup>  | total          | 168.92 (6.85)             | 171.38 (6.55) | 0.081 (-0.37)                   |
|                           | left           | 83.02 (3.29)              | 84.62 (3.33)  | <b>0.018*</b> (-0.48)           |
|                           | right          | 85.89 (3.70)              | 86.75 (3.40)  | 0.28 (-0.24)                    |
| Frontal <sup>‡</sup>      | total          | 65.60 (3.04)              | 66.24 (2.72)  | 0.23 (-0.22)                    |
|                           | left           | 32.57 (1.61)              | 32.76 (1.37)  | 0.55 (-0.12)                    |
|                           | right          | 33.02 (1.52)              | 33.48 (1.46)  | 0.078 (-0.30)                   |
| Parietal <sup>&amp;</sup> | total          | 33.53 (1.48)              | 34.09 (1.56)  | 0.088 (-0.37)                   |
|                           | left           | 16.86 (0.70)              | 17.21 (0.82)  | <b>0.032*</b> (-0.45)           |
|                           | right          | 16.67 (0.83)              | 16.88 (0.80)  | 0.23 (-0.26)                    |
| Temporal <sup>#</sup>     | total          | 51.27 (2.03)              | 52.06 (2.31)  | 0.091 (-0.37)                   |
|                           | left           | 25.24 (1.04)              | 25.79 (1.18)  | <b>0.024*</b> (-0.50)           |
|                           | right          | 26.03 (1.15)              | 26.28 (1.31)  | 0.37 (-0.20)                    |
| Occipital <sup>£</sup>    | total          | 15.18 (0.74)              | 15.55 (0.72)  | 0.089 (-0.50)                   |
|                           | left           | 7.52 (0.37)               | 7.74 (0.37)   | <b>0.040*</b> (-0.60)           |
|                           | right          | 7.67 (0.41)               | 7.81 (0.38)   | 0.22 (-0.37)                    |
| Insula                    | total          | 5.90 (0.28)               | 6.03 (0.34)   | 0.11 (-0.40)                    |
|                           | left           | 2.95 (0.15)               | 3.00 (0.19)   | 0.27 (-0.32)                    |
|                           | right          | 2.95 (0.16)               | 3.02 (0.17)   | 0.084 (-0.42)                   |

Abbreviations: HC=healthy controls; PTSD= posttraumatic stress disorder; DID=dissociative identity disorder patients.

\*\* Corrected for multiple comparisons

\* Uncorrected for multiple comparisons ( $P$ -value $\leq$ 0.05)

^ Cohen's d effect size

§ Sum of the cortical measurements of the five superparcels (Frontal, Parietal, Temporal, Occipital, Insula)

‡ Sum of the cortical measurements of the caudal and rostral middle frontal, lateral and medial orbitofrontal, pars opercularis, pars triangularis and pars orbitalis of the inferior frontal, paracentral, precentral, superior frontal, frontal pole, caudal and rostral anterior cingulate

& Sum of the cortical measurements of the superior and inferior parietal, postcentral, precuneus, isthmus and posterior cingulate, supramarginal.

# Sum of the cortical measurements of the superior, middle and inferior temporal, temporal pole, transverse temporal, banks of the superior temporal sulcus, parahippocampal, entorhinal, fusiform

£ Sum of the cortical measurements of the lateral occipital, cuneus, lingual, peri-calcarine

**eTable 2. Statistical results for subcortical volume (mm<sup>3</sup>) for All-PTSD vs. HC comparison**

| Superparcel             | Total/<br>side | All-PTSD to HC comparison |              |  |
|-------------------------|----------------|---------------------------|--------------|--|
|                         |                | Mean (SD)                 |              | t-test: <i>P</i> Value (Effect size <sup>^</sup> ) |
|                         |                | All-PTSD (n=33)           | HC (n=28)    | All-PTSD vs. HC                                    |
| Whole-brain             | total          | 53597 (4691)              | 54373 (2956) | 0.85 (-0.20)                                       |
|                         | left           | 26827 (2396)              | 27207 (1571) | 0.87 (-0.19)                                       |
|                         | right          | 26769 (2322)              | 27165 (1448) | 0.84 (-0.21)                                       |
| Hippocampus             | total          | 7804 (723)                | 8016 (709)   | <b>0.030*</b> (-0.30)                              |
|                         | left           | 3866 (355)                | 3951 (387)   | 0.085 (-0.23)                                      |
|                         | right          | 3938 (391)                | 4065 (353)   | <b>0.016*</b> (-0.34)                              |
| Amygdala                | total          | 3134 (328)                | 3150 (371)   | 0.96 (-0.05)                                       |
|                         | left           | 1561 (180)                | 1584 (198)   | 0.57 (-0.012)                                      |
|                         | right          | 1573 (170)                | 1565 (184)   | 0.67 (0.05)  |
| Caudate                 | total          | 7037 (1005)               | 7071 (632)   | 0.16 (-0.04)                                       |
|                         | left           | 3441 (500)                | 3439 (323)   | 0.13 (0.00)  |
|                         | right          | 3596 (518)                | 3631 (328)   | 0.22 (-0.08)                                       |
| Putamen                 | total          | 10408 (1379)              | 10764 (933)  | 0.96 (-0.31)                                       |
|                         | left           | 5313 (702)                | 5513 (469)   | 0.79 (-0.34)                                       |
|                         | right          | 5095 (694)                | 5251 (504)   | 0.86 (-0.26)                                       |
| Pallidum                | total          | 6072 (408)                | 3128 (301)   | 0.35 (-0.16)                                       |
|                         | left           | 1704 (256)                | 1740 (181)   | 0.72 (-0.17)                                       |
|                         | right          | 1368 (161)                | 1387 (146)   | 0.12 (-0.12)                                       |
| Nucleus<br>Accumbens    | total          | 1230 (202)                | 1323 (159)   | 0.10 (-0.52)                                       |
|                         | left           | 584 (86)                  | 647 (101)    | <b>0.031*</b> (-0.67)                              |
|                         | right          | 646 (131)                 | 676 (86)     | 0.51 (-0.28)                                       |
| Thalamus                | total          | 12735 (1229)              | 12791 (1047) | 0.32 (-0.05)                                       |
|                         | left           | 6303 (686)                | 6318 (556)   | 0.30 (-0.02)                                       |
|                         | right          | 6431 (567)                | 6473 (540)   | 0.40 (-0.08)                                       |
| Ventral<br>diencephalon | total          | 8172 (656)                | 8127 (520)   | 0.65 (0.08)  |
|                         | left           | 4054 (327)                | 4115 (312)   | 0.38 (0.15)  |
|                         | right          | 4118 (360)                | 4012 (241)   | 0.99 (0.01)  |

Abbreviations: HC=healthy controls; PTSD= posttraumatic stress disorder; DID=dissociative identity disorder patients.

\*\* Corrected for multiple comparisons

\* Uncorrected for multiple comparisons (*P*-value≤0.05)

<sup>^</sup> Cohen's d effect size