Normal amygdala morphology in dissociative identity disorder

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Summary
Studies investigating the structure of the amygdala in relation to dissociation in psychiatric disorders are limited and have reported normal or preserved, increased or decreased global volumes. Thus, a more detailed investigation of the amygdala is warranted. Amygdala global and subregional volumes were compared between individuals with dissociative identity disorder (DID: n = 32) and healthy controls (n = 42). Analyses of covariance did not show volumetric differences between the DID and control groups. Although several unknowns make it challenging to interpret our findings, we propose that the finding of normal amygdala volume is a genuine finding because other studies using this data-set have presented a mixture of increased and decreased subfield volumes caused a net result of normal global volumes.

Keywords
Subregions; global volume; DID; dissociation; FreeSurfer.

Method
Data from a total of 75 women (only female participants with DID volunteered) were collected. There were 32 female volunteers with DID and 43 healthy controls matched for age, gender, years of education and ethnicity. Data were collected in The Netherlands at the University Medical Centre in Groningen (UMCG) and the Amsterdam Medical Centre (AMC) and in Switzerland at the University Hospital in Zurich (UHZ). All participants gave written informed consent in accordance with the Declaration of Helsinki and as dictated by ethical requirements of the Medical Ethical Committees of UMCG (reference number: METC2008.211) and AMC (reference number: MEC09/155) and by the cantonal ethical commission of Zurich (Kantonale Ethikkommission Zürich; reference number: E-13/2008). All participants were given the right to withdraw and were fully debriefed in line with the ethical requirements of the Declaration of Helsinki.

Participants and data included in the current study are identical to those in the investigations of the hippocampus as a neurostructural biomarker of dissociation and whole-brain morphological studies. In sum: participants with DID were diagnosed by trained clinicians using the Structured Clinical Interview for DSM-IV Dissociative Disorders (SCID-D) and all had a comorbid diagnosis of PTSD or of PTSD in remission and other comorbidity as confirmed by participants and their personal therapists. The control group was recruited through local newspaper advertisements. Exclusion criteria for all participants included age outside the range of 18–65 years, pregnancy, systemic or neurological illness, claustrophobia, metal implants in the body and substance misuse. Additional exclusion criteria for the control group included the presence of dissociative symptoms and a history of trauma, past or current psychiatric disorders and medication use. Participants in the control group were required to have no or limited (somatoform) dissociative symptoms and potentially traumatising experiences.
Table 1: Descriptive statistics and analyses of covariance (ANCOVA) between participants with dissociative identity disorder (DID) and healthy controls on amygdala volume

|                         | Mean volume, mm³ (s.d.) | Between-group ANCOVA |
|-------------------------|-------------------------|-----------------------|
|                         | DID group (n = 32)       | Control group (n = 42) |
| Global amygdala         |                         |                       |
| Left                    | 1657.23 (151.45)        | 1706.07 (175.31)      |
| Right                   | 1700.45 (146.38)        | 1756.31 (166.70)      |
| Lateral nucleus         |                         |                       |
| Left                    | 614.83 (58.89)          | 629.21 (62.46)        |
| Right                   | 630.23 (45.38)          | 635.91 (58.79)        |
| Basal nucleus           |                         |                       |
| Left                    | 418.50 (45.49)          | 431.21 (45.05)        |
| Right                   | 423.26 (40.89)          | 438.64 (43.54)        |
| Accessory basal nucleus |                         |                       |
| Left                    | 254.66 (25.74)          | 264.97 (33.80)        |
| Right                   | 266.77 (29.35)          | 278.52 (31.83)        |
| Anterior amygdaloid area|                         |                       |
| Left                    | 52.48 (7.10)            | 53.32 (7.49)          |
| Right                   | 57.56 (8.87)            | 58.86 (8.57)          |
| Central nucleus         |                         |                       |
| Left                    | 46.81 (4.40)            | 46.42 (8.87)          |
| Right                   | 51.30 (7.86)            | 51.47 (8.04)          |
| Medial nucleus          |                         |                       |
| Left                    | 24.81 (5.76)            | 26.01 (8.25)          |
| Right                   | 28.49 (6.82)            | 28.97 (9.32)          |
| Cortical nucleus        |                         |                       |
| Left                    | 26.37 (3.93)            | 27.58 (5.76)          |
| Right                   | 29.37 (3.97)            | 30.23 (4.89)          |
| Corticoadymgdaloid transition |             | 0.253 (1.66) | 0.631 (0.04) | 0.524 |
| Left                    | 169.18 (16.92)          | 180.18 (21.38)        |
| Right                   | 177.85 (20.76)          | 187.25 (23.26)        |
| Paralaminar nucleus     |                         |                       |
| Left                    | 45.00 (5.24)            | 47.18 (4.88)          |
| Right                   | 45.61 (4.52)            | 46.46 (5.51)          |

P², partial eta squared.
α, 0.05 < P ≤ 0.1.

Volumetric analysis

Magnetic resonance imaging (MRI) data were collected using 3 T Philips whole-body scanners (Philips Medical Systems, Best, Netherlands) from centres in The Netherlands (AMC and UMC) and Switzerland (UHZ). An optimised T1-weighted anatomical MRI protocol for the three participating centres was used,11 three-dimensional magnetisation-prepared rapid gradient-echo imaging (3-D MP-RAGE), repetition time TR = 9.95 ms, echo time TE = 5.6 ms, flip angle 8°, voxel size 1 x 1 x 1 mm³, number of slices 160, total scan time 10 min 14 s. Ratios of DID to control participants were approximately equal across the centres and the number of participants per group did not differ across centres (χ² = 1.01, P = 0.603).

Data acquisition

Magnetic resonance imaging (MRI) data were collected using 3 T Philips whole-body scanners (Philips Medical Systems, Best, Netherlands) from centres in The Netherlands (AMC and UMC) and Switzerland (UHZ). An optimised T1-weighted anatomical MRI protocol for the three participating centres was used;11 three-dimensional magnetisation-prepared rapid gradient-echo imaging (3-D MP-RAGE), repetition time TR = 9.95 ms, echo time TE = 5.6 ms, flip angle 8°, voxel size 1 x 1 x 1 mm³, number of slices 160, total scan time 10 min 14 s. Ratios of DID to control participants were approximately equal across the centres and the number of participants per group did not differ across centres (χ² = 1.01, P = 0.603).

Statistical analysis

All analyses were performed using SPSS version 26 (www.ibm.com/uk-en/products/spss-statistics). Between-group differences in amygdala volumes for each hemisphere were tested with analyses of covariance (ANCOVA). Amygdala volumes acted as the dependent variable, group and centre as fixed categorical effects, and age and estimated TIV as continuous covariates. Group differences were investigated by comparing the estimated marginal means of the main effects with Bonferroni post hoc correction across all sub-regions and global volumes.

Results

Table 1 shows the descriptive statistics and the findings of the between-group analyses (ANCOVA) on amygdala global volumes and volumes of amygdala subregions. We did not find any significant differences between the DID and control groups for either the global amygdala volumes or for the volumes of amygdala subregions. There was only one trend showing decreased volume for the DID group, and that was in the left corticoamygdaloid transition area (F1,66 = 3.839, P = 0.054, η² = 0.05), with a mean decrease of 9.090 mm³.

Discussion

The current study confirms our previous finding of normal amygdala volumes in DID.14 Although the hippocampus is sensitive to excessive stress hormones, which may explain its decreased volumes in DID,1 the...
structure of the amygdala might be less sensitive to stress hormones than previously thought. Several unknowns add to the difficulty in interpreting our findings. They include the potential influence of different kinds of stress (e.g. attachment loss, physical abuse and emotional neglect), the sensitivity of the structure of the amygdala to the frequency and intensity of its activation and to ontogenetic developmental phases, and lifetime prefrontal inhibition of amygdala activation. The last, which is a potentially neuroprotective effect, might be more pronounced in individuals with DID, who predominantly function as one or more dissociative identities that successfully avoid emotional cues, which might relate to frequent prefrontal inhibition of amygdala activity. These unknowns all open pathways for future research.

The trend for decreased volume in the corticoamygdaloid transition area in our study might be due to scanner differences between the three centres as in the study by Morey and colleagues, they found that the covariates age and scanner were significant for the corticoamygdaloid transition area. Although we were careful to use identical scanner sequences at all three centres and included centre as a covariate, residual variance related to scanner differences in the corticoamygdaloid transition area cannot be excluded and could contribute to our finding of a trend. Age was the second covariate found in the study by Morey and colleagues to be significantly associated with amygdala volume. The effect of age on amygdala volumes in a sample of individuals with DID has been independently discussed for reported decreased amygdala volume. However, in the current study age is not a contaminating factor in the finding of normal amygdala volumes because the DID and control group were carefully matched (\(t(72) = -0.55, P = 0.581\)).

This short report is part of a sequence of brain imaging papers that originated from a multicentre collaboration between two centres in The Netherlands and one in Switzerland. We found that structural imaging can aid a diagnosis of DID, that there is no evidence for DID to be a neurodevelopmental disorder and that hippocampal subregion CA1 can be proposed as a biomarker for dissociative amnesia. The findings in these studies were all statistically significant, indicating that this data-set contains robust morphological aberration in relation to the diagnosis of DID and that normal amygdala volumes are a genuine finding. Therefore, we conclude that our previously reported normal amygdala volumes in DID are upheld under increased statistical power and after investigating the independent contributions of subregions of the amygdala to its global volume.

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**Author contributions**

All authors have approved the final version for publication and are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. A.A.T.S.R.: conceptualisation, data acquisition, funding acquisition, interpretation, methodology, project administration, resources, supervision, visualisation, writing – review and editing. L.I.: formal analysis, methodology, interpretation, software, visualisation, writing original draft and review and editing. Y.R.S. and S.C.: data acquisition, interpretation, methodology, project administration, software, writing – review and editing. S.C.: conceptualisation, data acquisition, formal analysis, interpretation, methodology, project administration, writing original draft and review and editing. E.R.S.N. and L.I.: conceptualisation, data acquisition, interpretation, methodology, writing – review and editing. D.V.: conceptualisation, funding acquisition, formal analysis, interpretation, supervision, writing – review and editing.

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**Declaration of interest**

D.J.V. and A.A.T.S.R. are members of the bPsych Open editorial board and did not take part in the review or decision-making process of this paper.

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**Data availability**

The data that support the findings of this study are available from the corresponding author on reasonable request.

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