Journal of Affective Disorders Reports 10 (2022) 100435

Contents lists available at ScienceDirect

Journal of Affective Disorders Reports

journal homepage: www.sciencedirect.com/journal/journal-of-affective-disorders-reports

Research Paper

Hippocampal volume and parahippocampal cingulum alterations are associated with avoidant attachment in patients with depression

Tobias Bracht [a,b,*], Niklaus Denier [a,b], Meret Wallimann [a,b], Sebastian Walther [a,b], Nicolas Mertse [a,b], Sigrid Breit [a,b], Andrea Federspiel [a,b], Roland Wiest [b,c], Leila Soravia [a,b]

[a] Translational Research Center, University Hospital of Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland
[b] Translational Imaging Center (TIC), Swiss Institute for Translational and Entrepreneurial Medicine, Bern, Switzerland
[c] Institute of Diagnostic and Interventional Neuroradiology, University of Bern, Bern, Switzerland

ARTICLE INFO

Keywords:
Depression
Attachment
Hippocampus, Cingulum
White matter
Diffusion tensor imaging

ABSTRACT

Background: Insecure attachment style (anxious and avoidant) predisposes to the development of depression and has been linked to hippocampal alterations in healthy individuals. However, it is unclear if there are alterations of the hippocampus and the parahippocampal cingulum (PHC) in patients with depression.
Methods: Forty-eight patients with major depressive disorder and 18 healthy controls underwent MP2RAGE and diffusion-weighted magnetic resonance imaging. Attachment characteristics were assessed with the revised adult attachment scale. Patients were classified into subgroups with low (anxious: $n = 27$; avoidant: $n = 21$) and high (anxious: $n = 20$; avoidant: $n = 28$) attachment characteristics. Bilateral PHC were reconstructed using manual tractography. Hippocampal volumes, mean fractional anisotropy and mean diffusivity (MD) in bilateral PHC were compared between attachment subgroups and healthy controls.
Results: Patients had higher scores of anxious and avoidant attachment, which were associated with depression severity. Patients with high avoidance had decreases in hippocampal volumes in comparison to patients with low avoidance. Furthermore, patients with high avoidance had increased MD in bilateral PHC in comparison to patients with low avoidance and in comparison to healthy controls.
Limitations: Assessment of attachment characteristics may be influenced by cognitive biases due to depressive symptoms
Conclusions: High attachment avoidance in patients with depression is associated with volume reductions in the hippocampus and impaired PHC-microstructure.

1. Introduction

The ability to form meaningful relationships is a crucial aspect of life. Psychological research has shown that people with a secure attachment style are more committed to their relationships (Segal and Fraley, 2015), more capable to adapt to stressful events (Jayamaha et al., 2017), and report fewer depressive symptoms (Bowlby, 1969; Bradford et al., 2017). Attachment Theory offers one framework to explain these findings (Mikulincer and Shaver, 2007). According to this theory, every human being has an innate need to attach to others. As this attachment behaviour can regulate our affective states by seeking comfort and thus regain a feeling of security, it can be seen as a self-regulation strategy (Mikulincer and Shaver, 2007). Therefore, dysfunctional attachment strategies, which derive from unresponsive parenting, to name one example, can have a profound effect on psychological functioning. This is supported by consistent evidence, reporting that insecurely attached children and adults are at greater risk of developing a mental illness (Colonnesi et al., 2011; Groh et al., 2017), particularly depression (Dagan et al., 2018; Zheng et al., 2020).

Research on attachment behaviour usually differentiates between two dimensions of insecure attachment, namely anxious and avoidant attachment (Picardi et al., 2005; Ravitz et al., 2010; Zheng et al., 2020). Anxious attachment is characterized by a strong desire for closeness, manifesting in distress due to preoccupation with the availability of others. Therefore, it is linked to increased stress levels and is consistently associated with depressive symptoms (Zheng et al., 2020). Avoidant

* Corresponding author at: University Hospital of Psychiatry and Psychotherapy, University of Bern, Translational Research Center, Bolligenstrasse 111, 3000 Bern 60, Switzerland.
E-mail address: tobias.bracht@upd.unibe.ch (T. Bracht).

https://doi.org/10.1016/j.jadr.2022.100435
Received 26 April 2022; Received in revised form 20 August 2022; Accepted 14 November 2022
Available online 15 November 2022

attachment is related to discomfort with closeness and maintenance of independence. Avoidant individuals prefer to keep emotional distance and use deactivating strategies to deal with distress. Since these strategies, e.g., emotional suppression and distraction, prevent them from resolving their emotional issues, it is also related to depression vulnerability (Zheng et al., 2020).

Attachment behaviour is complex and therefore underlying circuits may involve networks mediating incentive motivation, certain forms of emotional responding and regulation, and various social behaviours such as proximity seeking and separation distress (Coan, 2008). Animal studies have shown that early attachment experiences may influence the development of the brain, resulting in permanent structural and functional alterations (Jackowski et al., 2011; Moriceau and Sullivan, 2005). For example, a disrupted maternal-infant dyadic can cause a hippocampal volume reduction in non-human primates (Jackowski et al., 2011). This points to a particularly pronounced role of the hippocampus, which forms episodic memory of events with emotional significance (Phelps, 2004), processes that in turn impact on attachment behaviour (Coan, 2008). The parahippocampal cingulum (PHC) links the hippocampus with occipital, parietal and frontal areas brain areas, such as the cingulate gyrus (Jones et al., 2013; Lin et al., 2021). These connections form a network that is crucial for secure attachment behaviour (Serra et al., 2015).

Cross-sectional magnetic resonance imaging (MRI) studies in healthy individuals repeatedly demonstrated associations between attachment styles and brain structure and function (Long et al., 2020). Most studies found that anxiously attached individuals show increases in activation in response to emotional stimuli in limbic areas (e.g. in the amygdala and in the parahippocampal gyrus). In contrast, individuals with avoidant attachment show decreased activations in limbic areas and increased activation in areas involved in cognitive control (e.g. the prefrontal cortex (PFC)) (Long et al., 2020; Nasiriavanaki et al., 2021; Vrticka et al., 2012; Vrticka and Vuilleumier, 2012). In line with findings of increased functional activation patterns some structural MRI-studies point to volume increases in limbic areas in anxiously attached individuals (e.g. in the insula and the amygdala (Acosta et al., 2018; Schneider-Hassloff et al., 2016)). However, other groups found that anxious attachment is associated with volume and cell density decreases in limbic structures such as the anterior cingulate gyrus, the anterior temporal pole and the hippocampus (Benetti et al., 2010; Quirin et al., 2010; Zhang et al., 2018). Individuals with avoidant attachment show decreases of volume and density in the hippocampus and the parahippocampal gyrus as well (Quirin et al., 2010; Zhang et al., 2018). Diffusion weighted MRI studies also suggest a role of the hippocampal complex for attachment characteristics. Secure attachment was associated with increased fractional anisotropy (FA) in the PHC (Serra et al., 2015). Another study found that avoidant attachment is associated with increase in mean diffusivity (MD) in the amygdala and on a trend level in the hippocampus (Rigon et al., 2016). These findings support the assumption that attachment behaviour is associated with white matter microstructure of the hippocampal complex and its connection pathways.

Hippocampal volume reduction is also one of the most commonly reported brain alterations in depression (Arnone et al., 2012; Sheline, 2011). This also applies for the PHC, a major connection pathway of the hippocampus. The PHC has a specific role for motor behaviour, and for emotion and memory processing (Bracht et al., 2016; Dalboni da Rocha et al., 2020), which are processes that are critical to both depression pathophysiology (Bracht et al., 2015a; Dillon and Pizzagalli, 2018; Walther et al., 2019) and attachment style (Sutin and Gillath, 2009). PHC-microstructure is associated with genetic variants in depression and there are remission related neuroplastic processes in the PHC (Bracht et al., 2015a; Doolin et al., 2019; Han et al., 2017; Won et al., 2016). These findings suggest that both patients with depression and individuals with insecure attachment have structural alterations of the hippocampus and the PHC. To date, research on neuronal correlates of adult attachment has focused mainly on healthy individuals (Long et al., 2020). Only one functional MRI (fMRI) study examined neuronal correlates of attachment in a group of females with depression reporting overlapping activations in the cortico-striato-thalamic circuits of affect regulation for insecure attachment and depression (Galynker et al., 2012). However, no study has been conducted to investigate the relationship between attachment styles in depression and structural brain measures of the hippocampus and its connection pathways.

It was the aim of this study to investigate associations between insecure attachment, depression severity and structural alterations of the hippocampus and the PHC. We hypothesized that (I) patients with depression have higher anxious and avoidant attachment than healthy controls (II) high attachment anxiety and avoidance is associated with higher depression severity in patients with depression (III) high attachment anxiety and avoidance is associated with reduced volume of the hippocampi and with reduced white matter microstructure (decreased FA and increased MD) in the PHC in patients with depression (Benetti et al., 2010; Quirin et al., 2010; Zhang et al., 2018).

2. Methods

2.1. Participants

Forty-eight patients with depression were recruited at the in- and outpatient clinic of the University Hospital of Psychiatry and Psychotherapy in Bern, Switzerland. The study sample includes participants of previous reports (Bracht et al., 2022; Mertse et al., 2022). Inclusion criteria were current diagnoses of a major depressive disorder according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and age between 18-65 years. Diagnoses was made by the treating psychiatrist and based on the Mini International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998). Exclusion criteria were psychiatric comorbidities and personality disorders, as assessed with the MINI and the Structured Clinical Interview for DSM-IV Axis II (SCID-II) (Wittchen et al., 1997). The 21-item Hamilton rating scale for depression (HAMD) (Hamilton, 1967) and the 21-item self-report Beck Depression Inventory (BDI-II) (Beck et al., 1996) were used to assess depression severity. Handedness was assessed with the Edinburgh Handedness Inventory (Oldfield, 1971). One patient had to be excluded from diffusion weighted MRI analyses because the left PHC could not be reconstructed successfully.

Eighteen healthy controls were matched for age and gender. Inclusion criteria were the absence of any present or past psychiatric disorder as assessed with the MINI and the SCID-II screening questionnaires. Subclinical depressive symptoms were assessed with the HAMD and the BDI-II. Further exclusion criteria for all participants were claustrophobia, neurological disorders or contraindications to perform an MRI. Written informed consent was obtained from all subjects and the study was approved by the local cantonal ethics committee (KEK-number: 2017-00731).

2.2. Assessment of adult attachment style

All participants were assessed with the revised adult attachment scale (AAS-R) (Schmidt et al., 2016). The AAS-R is a German self-report measure with 18 items to assess basic dimensions of attachment. It is available in two versions, one for romantic relationships and one for close personal relationships in general, from which the latter was used. The AAS-R distinguishes between three different forms of attachment: closeness, trust and anxiety. Each scale is composed of six items, which range from one (*not at all characteristic of me*) to five (*very characteristic of me*). Consequently, high scores represent a high expression of the characteristic in each dimension. The measures trust and closeness have a substantial theoretical overlap and both represent avoidance (low scores of closeness and trust represent high avoidance). As in the initial discriminatory analysis of the AAS closeness was superior to trust to

indicate the avoidant style we chose the closeness scale to measure avoidant attachment (Collins and Read, 1990).

2.3. Attachment subgroups

The patient group was divided into two subgroups (low and high) for anxious and avoidant attachment. AAS-R test scores were converted into standardized stanine scores using age- and gender-specific norm values (stanine values, percentile ranks) based on a population-representative survey of the German population ($N = 2510$) (Schmidt et al., 2016). For categorization of anxious attachment, the AAS-R anxiety scale was used. The low category included patients with low to average stanine-scores of 1-7, representing the lower 89% of the population. The high category comprised patients with stanine scores above seven, indicating a score in the 89th percentile or above. For grouping of avoidant attachment, the AAS-R closeness scale was used. The low avoidance group comprised patients with average to high closeness stanine scores ranging from 3-9, representing the upper 89% of the population. The high avoidance group was defined with a closeness stanine score under three, representing the 11th percentile. Thus, every MDD patient was assigned to two different attachment groups (anxiety and avoidance) depending on the individual scoring on each scale. Low grouping of anxiety and avoidance represents high attachment functioning, whilst high grouping of anxiety and avoidance represents low attachment functioning. Stanine distribution of patients and controls and overlap between patients categorized with low and high characteristics of anxiety and avoidance are shown in the supplementary material (see supplementary Fig. 1, supplementary Table 3).

2.4. MRI data acquisition

A 3-Tesla Magnetom Prisma scanner (Siemens, Erlangen, Germany) with a 64-channel head and neck coil was used for data acquisition. A bias-field corrected MP2RAGE sequence with two gradient echo images (INV1 and INV2) and a T1-weighted image (UNI) was used to acquire high-contrast T1-weighted images with the following parameters: 256 Slices, FOV = 256 × 256, 256 × 256 matrix, 1 × 1 × 1 mm^3 isotropic resolution, TR = 5000 ms, TE = 2.98 ms, TI = 700 ms and T2 = 2500 ms. Diffusion weighted images (DWI) were measured along 64 directions using a spin-echo echo-planar sequence using the subsequent parameters: 64 × b = 1000 s/mm2, 1 × b = 0 s/mm2, 60 Slices, FOV = 269 × 269, 128 × 128 matrix, 2.2 × 2.2 × 2.2 mm3 isotropic resolution, TR = 6200 ms, TE = 69 ms.

2.5. Volumetry of the hippocampus

For segmentation and calculation of bilateral hippocampal volumes we used *HD-BET* for brain extraction (INV1 volumes) and *DL+DiReCT* for hippocampal segmentation (UNI volumes) (Rebsamen et al., 2020) (Isensee et al., 2019).

2.6. Data analyses

2.6.1. Diffusion weighted MRI

FSL 6.0 (http://www.fmrib.ox.ac.uk/fsl/) and FSL-BET was used for robust brain extraction (-R option). Due to the noisy background of MP2RAGE UNI images, brain extraction was performed using INV2-images as input and applying the derived binary mask to the UNI-image. Diffusion-weighted imaging (DWI)-MRI scans were processed using ExploreDTI 4.8.6 (Leemans et al., 2009) and in as described in previous publications (Bracht et al., 2021, 2019; Denier et al., 2020). First, a correction for subject motion was performed by co-registering the DWI-images to the b0-image (Leemans and Jones, 2009). Second, an EPI correction for eddy current distortions and field inhomogeneities was executed warping the motion corrected DWI-images to the brain extracted MP2RAGE image (Wu et al., 2008). Third, whole-brain deterministic tractography was performed applying a diffusion tensor model (Basser et al., 1994). Fractional anisotropy (FA) < 0.2 and angle threshold > 45 degrees were used as termination criteria. The PHC has been reconstructed as suggested by Jones et al. ("restricted PHC") (Jones et al., 2013) and in line with our previous publications (Bracht et al., 2016, 2015a): Two "AND-ROIs" were drawn on horizontal sections of the colour coded first eigenvector-fractional anisotropy (FEFA) images. One ROI was placed at the height of the most ventral section of the splenium. The second ROI was placed four slices above. A "NOT--gate" was placed on a coronal section five slices posterior to the rostro-caudal midpoint of the body of the corpus callosum. Spurious fibres that do not correspond to known anatomy were eliminated using further NOT gates. FA and MD were averaged across the tract (see Fig. 1).

2.7. Statistical analyses

The Statistical Package for Social Sciences SPSS 27.0 (SPSS, Inc., Chicago, Illinois) was used for data analyses. Dimensional demographic variables between groups were compared using two-sample t-tests. Categorical variables were compared using χ^2 tests.

To investigate group differences of volumes of bilateral hippocampi and white matter microstructure in the PHC we first compared hippocampal volume, FA in the PHC and MD in the PHC between all patients and healthy controls. Three separate mixed-model ANCOVAs with the between subject factor group (patients vs. healthy controls), the within subject factor hemisphere (left vs. right), and the covariates age and sex were calculated for the dependent variables hippocampal volume, FA and MD. Separate ANCOVAs have been used to avoid multicollinearity due to high correlations between FA and MD.

Second, volumes of the hippocampi, FA in the PHC and MD in the PHC were compared between controls and patients with low and high attachment anxiety and between controls and patients with low and high attachment avoidance. Accordingly, three separate mixed-model ANCOVAs with the between subject factor group (low attachment anxiety, high attachment anxiety, and healthy controls), and three separate mixed-model ANCOVAs with the between subject factor group (low attachment avoidance, high attachment avoidance, and healthy controls) were calculated with the within subject factor hemisphere (left vs. right), the covariates age and sex and the dependent variables hippocampal volume, FA and MD. Level of significance was set at $p < 0.05$ for the analysis of hippocampal volume. Given that both FA and MD investigate white matter microstructure, a Bonferroni correction for multiple comparisons was applied resulting in $p < 0.025$ (0.05/2).

Post hoc mixed-model ANCOVAs with the within subject factor hemisphere and the covariates age and gender were used to compare dependent variables with a significant main effect between patient subgroups and healthy controls. For post hoc group comparisons between two patient subgroups, depression severity (total HAMD-21) was included as an additional covariate. Effect sizes were reported using η^2 (Olejnik and Algina, 2003).

To investigate associations between depression severity and attachment characteristics Spearman correlations between HAMD-total scores, anxious attachment (AAS-R: anxiety total score), and avoidant attachment (AAS-R: closeness total score) have been calculated for the patient group. Further exploratory Spearman correlations were calculated for the patient group between anxious attachment (AAS-R: anxiety total score), avoidant attachment (AAS-R: closeness total score), HAMD-scores, and imaging parameters (volumes of hippocampi, FA in the PHC, MD in the PHC) (see supplementary Table 2).

3. Results

Patients and controls did not differ regarding age, gender and handedness. All but six patients were on antidepressive medication at the time of the MRI-scan. Comparing patients with controls, patients had

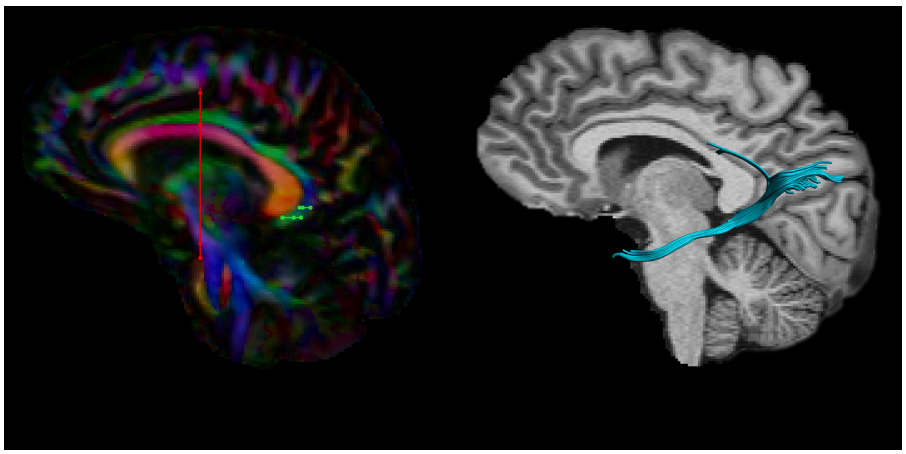

Fig. 1. Single-subject reconstruction of the parahippocampal cingulum.
Regions of interest AND-gates are displayed in green; the NOT-gate is displayed in red. The parahippocampal cingulum is visualized in light blue.

higher scores in the subscales of attachment avoidance (AAS-R: closeness) and higher scores in the subscale of attachment anxiety (AAS-R: anxiety) (Table 1). Distribution of patient classification into attachment style subgroups was as follows: low anxious attachment ($n = 28$), high anxious attachment ($n = 20$); low avoidant attachment ($n = 21$), high avoidant attachment ($n = 27$). All controls had low anxious attachment characteristics. Sixteen controls had low avoidant attachment characteristics and two controls had high avoidant attachment characteristics (see supplementary material Tables 1 and 3 and supplementary Fig. 1). Higher depression severity (total score HAMD-21) was associated with higher attachment anxiety (AAS-R: anxiety) ($r = 0.363$, $p = 0.011$) and with higher attachment avoidance (AAS-R: closeness) ($r = -0.385$, $p = 0.007$) in the patient group (see Fig. 2).

Comparing hippocampal volume and white matter microstructure (FA and MD) between all patients with depression and healthy controls there were no significant group differences (see Table 2). Comparing avoidant attachment subgroups (low, high) and healthy controls there were significant group main effects for volume of the hippocampus ($\eta^2 = 0.104$) and for MD ($\eta^2 = 0.176$) but not for FA in the PHC. Anxious attachment subgroups and healthy controls did not differ regarding hippocampal volume, FA or MD in the PHC (see Table 3).

Significant group main effects of mixed-model ANCOVAS (see Table 3) comparing healthy controls with patient subgroups of avoidance were followed up with post hoc ANCOVAs. Results were driven by patients with high avoidance, in the way that they had decreased hippocampal volume in comparison to patients with low avoidance ($F(1, 43) = 5.73$, $p = 0.021$, $\eta^2 = 0.118$) but not in comparison to healthy controls ($F(1, 41) = 0.11$, $p = 0.74$). Patients with low avoidance did not differ from healthy controls regarding hippocampal volume ($F(1, 40) = 1.76$, $p = 0.20$). Patients with high avoidance had increased MD in the PHC in comparison to patients with low avoidance ($F(1, 42) = 6.93$, $p = 0.012$, $\eta^2 = 0.142$), and in comparison to healthy controls ($F(1, 41) = 9.34$, $p = 0.004$, $\eta^2 = 0.186$). Patients with low avoidance did not differ from healthy controls regarding MD ($F(1, 37) = 0.16$, $p = 0.688$) (see Fig. 3).

Table 1
Socio-demographic and clinical variables for patients and controls.

	Patients ($n = 48$)	Controls ($n = 18$)	p
Age (years)	43.2 ± 11.8	41.6 ±13.9	0.641
Gender (male)	54.2%	55.6%	0.92
Handedness (right, left, ambidextrous)	(89%, 5.5%, 5.5%)	(84%, 11%, 5%)	0.79
Duration of depressive episode (months)	12.5 ± 11.3	n/a	n/a
Number of depressive episodes	3.4 ± 4.0	n/a	n/a
HAMD-21	21.8 ± 4.9	0.4 ± 0.8	<0.001
BDI	28.9 ± 9.1	1.8 ± 2.6	<0.001
AAS-R: closeness	17.8 ± 5.1	26.2 ± 3	<0.001
AAS-R: anxiety	18.0 ±7	10 ± 3	<0.001
SSRI	20.8%	n/a	n/a
Dual antidepressants	41.7%	n/a	n/a
Tricyclic antidepressants	18.8%	n/a	n/a
Lithium	35.4%	n/a	n/a

Abbreviations: HAMD-21: Hamilton rating scale for depression; BDI: Beck Depression Inventory; AAS-R: revised adult attachment scale; SSRI: selective serotonin reuptake inhibitors.

4. Discussion

This study investigated associations between insecure attachment styles, depression severity, volumes of the hippocampi and microstructure of the PHC. Patients with depression had significantly higher attachment avoidance and higher attachment anxiety than healthy controls. Depression severity was correlated with the two attachment domains (high attachment avoidance and anxiety). Patients with high attachment avoidance had smaller hippocampi than patients low attachment avoidance. In addition, patients with high attachment avoidance had higher MD in the PHC in comparison to patients with low attachment avoidance and in comparison to healthy controls. Volumes of hippocampi and white matter microstructure in the PHC did not differ between all patients with depression and healthy controls and between subgroups of anxious attachment.

As expected insecure attachment was more pronounced in patients with depression than in controls and was associated with depression severity, which is in line with previous studies (Dagan et al., 2018; Zheng et al., 2020). Even though attachment styles are moderately stable over time, meaningful change in these styles can be linked to a change in understanding of personal and interpersonal experiences (e.g. perception of oneself and others such as increases in self-esteem and perceptions of social support), which leads to increases in security over time (Cozzarelli et al., 2003). Longitudinal studies show that early attachment relationships are significant predictors of fear and anxiety (Warren et al., 1997), as well as depression (Armsden et al., 1990; Kobak et al., 1991) in later childhood and adulthood. Furthermore, attachment styles are related to the quality of attachment to close others (Muris et al., 2001). Low quality of attachment in turn is associated with lower perceived social support, smaller and less satisfying support networks, and higher emotion dysregulation (Marganska et al., 2013), which are well known risk factors for the development of depression (Anders and Tucker, 2000).

Patients with depression and high avoidance had smaller hippocampi than patients with depression and low avoidance. Hippocampal

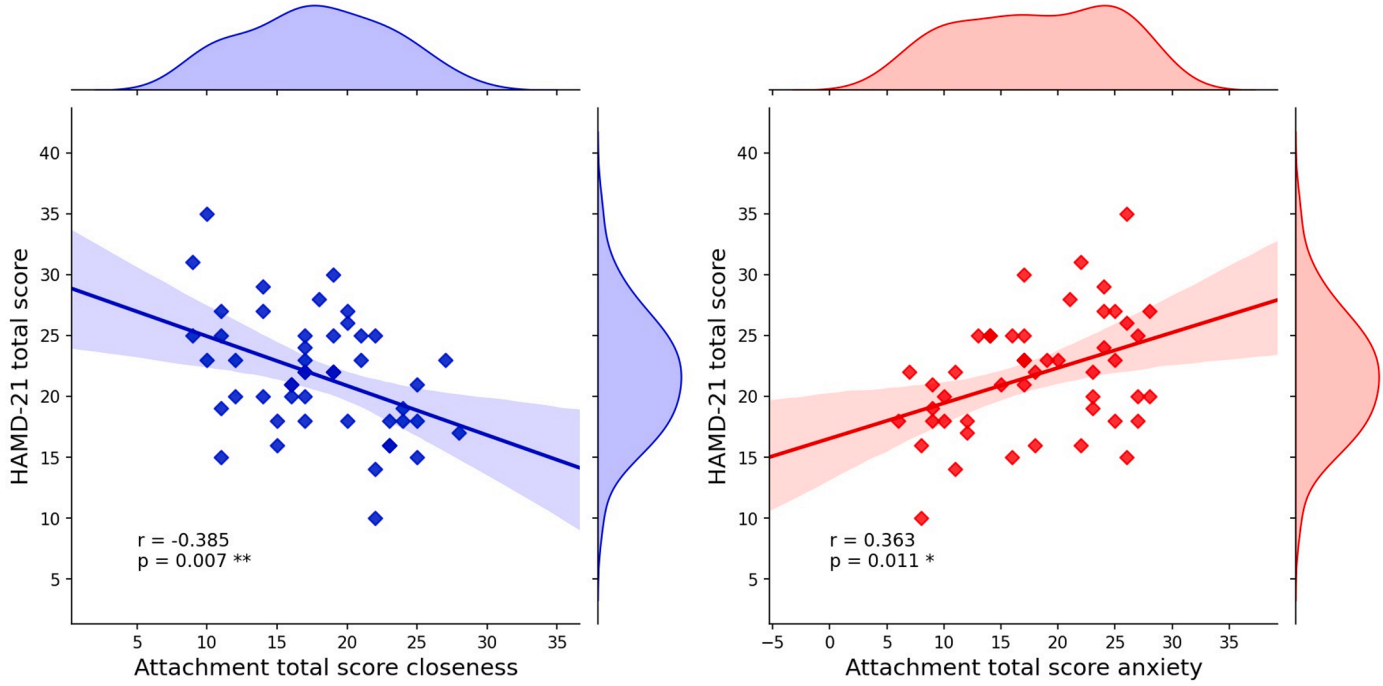

Fig. 2. Associations between depression severity and attachment characteristics.

Table 2
Group comparisons between all patients with depression and healthy controls.

	Main effect group	Main effect hemisphere	Group x hemisphere
Hippocampal volume	F (1, 62)=0.47 $p = 0.50$	F (1, 62)=1.52 $p = 0.22$	F (1, 62)=0.45 $p = 0.50$
Fractional anisotropy (FA)	F (1, 61) =0.25, $p = 0.691$	F (1, 61) = 0.94, $p = 0.336$	F(1, 61) = 1.86, $p = 0.178$
Mean diffusivity (MD)	F (1, 61) = 2.70, $p = 0.11$	F (1, 61) = 2.71, $p = 0.11$	F(1, 61) =0.47, $p = 0.50$

Table 3
Results of mixed-model ANCOVAS comparing healthy controls with patient subgroups of avoidance (AAS-R: closeness) and anxiety (AAS-R: anxiety).

	Main effect group	Main effect hemisphere	Group x hemisphere
AAS-R: closeness (volume)	F (2,61)=3.54 $p = 0.035$*	F (1,61)=1.56 $p = 0.22$	F (2,61)= 0.54 $p = 0.56$
AAS-R: anxiety (volume)	F (2,61)=1.36 $p = 0.26$	F (1,61)= 1.63 $p = 0.21$	F (2,61)= 0.24 $p = 0.79$
AAS-R: closeness (FA)	F (2, 60)=1.90 $p = 0.16$	F (1, 60)=0.60 $p = 0.44$	F (2, 60)=1.16 $p = 0.32$
AAS-R: anxiety (FA)	F (2, 60)=1.19 $p = 0.31$	F (1, 60)= 0.72 $p = 0.40$	F (2, 60)=0.92 $p = 0.41$
AAS-R: closeness (MD)	F (2,60)=6.41 $p = 0.003$**	F (1, 60)=2.55 $p = 0.12$	F (2, 60)=0.26 $p = 0.77$
AAS-R: anxiety (MD)	F (2, 60)=1.41 $p = 0.25$	F (1, 60)=2.75 $p = 0.10$	F (2, 60)=0.73 $p = 0.49$

Abbreviations: volume: volume of the hippocampi; FA: fractional anisotropy; MD: mean diffusivity; * $p<0.05$, ** $p < 0.01$.

volume reduction is a common finding in patients with depression that is influenced by chronicity and by duration of lifetime depression (Sheline, 2011; Videbech and Ravnkilde, 2004). Our results suggest that avoidant attachment characteristics, which were more pronounced in patients with depression than in healthy controls are another factor that affects hippocampal volume. This is consistent with findings of hippocampal volume reductions in healthy individuals with insecure attachment (Quirin et al., 2010; Zhang et al., 2018). In addition, patients with high avoidance had increased MD in the PHC in comparison to patients with low avoidance and to healthy controls. Our finding complements a previous DTI-study pointing to increased MD in the hippocampus in healthy individuals with avoidant attachment (Rigon et al., 2016). Increase in MD reflects increase in diffusion and may stem from loss of coherence of fibre tracts (e.g. loss of myelin), while FA may rather reflect axonal properties (Song et al., 2002). Given that we did not identify any alterations in FA in the PHC this may suggest alterations of myelin rather than alterations of axonal architecture. Nevertheless it is impossible to draw sub-compartment specific conclusions based on DTI-data (Jones and Cercignani, 2010).

Insecure attachment style leads to deficits in emotion regulation (Karreman and Vingerhoets, 2012; Marganska et al., 2013; van der Meer et al., 2015), which in turn may affect underlying brain networks including the hippocampus and the PHC (Jin and Maren, 2015; Shin et al., 2004). Hippocampal alterations and white matter microstructural alterations of temporal connection pathways may also stem from traumatic experiences in early childhood (Kribakaran et al., 2020; Olson et al., 2020; Soravia et al., 2022; Tendolkar et al., 2018), which is known to increase the risk of insecure attachment (Colonnesi et al., 2011; Groh et al., 2017). Furthermore, PHC microstructure is related to depression severity (Bracht et al., 2015a; Doolin et al., 2019), which was associated with insecure attachment characteristics in our study. Therefore, we controlled comparisons between patient subgroups for depression severity. Our results suggest an influence on hippocampal volume that is independent from the severity of the current episode. Thus, avoidant attachment characteristics may contribute to explain inconsistencies in findings of hippocampal volume reductions and PHC microstructure and should be considered in future analyses.

Subgroups with anxious attachment did not differ regarding hippocampal volume and PHC microstructure. It is possible that anxious attachment is associated with different structures (e.g. the amygdala). Phobic fears and experiences of paranoid threat have been linked to increases in activation the amygdala and to increased structural connectivity of amygdalar pathways (Bracht et al., 2014; Phan et al., 2006). Furthermore, anxious attachment has been associated with hyperactivation and volume increases of limbic structures including the

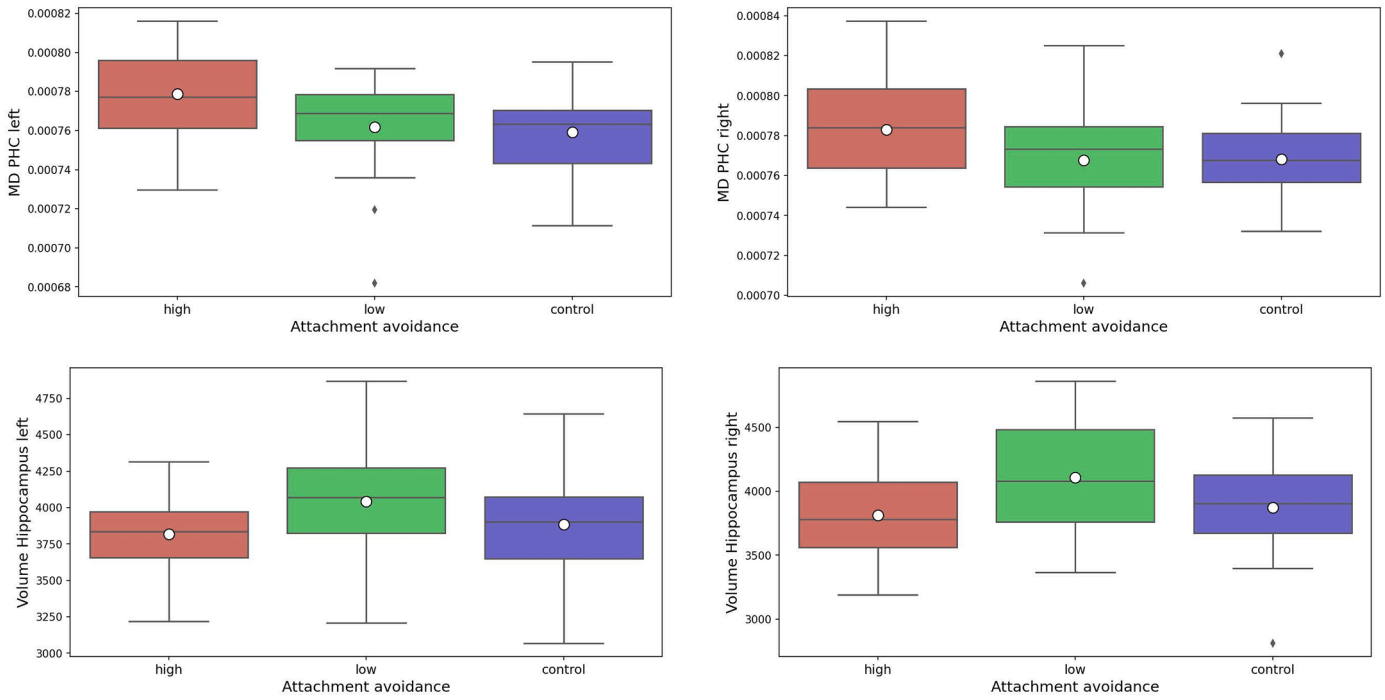

Fig. 3. Structural alterations of the hippocampi and the PHC in patients with high avoidance
Abbreviations: MD: mean diffusivity; PHC, parahippocampal cingulum. Patients with high avoidant attachment (red) have significantly higher MD than patients with low avoidant attachment (green) and healthy controls (dark blue). Hippocampal volumes of patients with high avoidant attachment have smaller hippocampi than patients with low avoidant attachment.

amygdala (Donges et al., 2012; Vrticka et al., 2012). Such volume increases and increases in structural connectivity may be masked due to the commonly observed structural impairments of limbic regions and pathways in patients with depression (Arnone et al., 2012; Bracht et al., 2015b; Sheline, 2011). In addition, we did not find any differences in PHC microstructure between all patients with depression and healthy controls. This highlights the need stratify patients into more homogeneous clinical subgroups to successfully link psychopathology to neurobiological alterations (Bracht et al., 2015b).

Finally, this study has some limitations. First, demographic data on attachment were assessed with only one scale (AAS-R). Data on current and past romantic relationships and on aversive childhood experiences are not available (even though all participants were screened for post-traumatic stress disorder (PTSD), which was an exclusion criterion). Second, attachment characteristics were assessed during a depressive episode using a self-rating questionnaire. During a depressive state the world and relationships might be seen in a more realistic light (depressive realism model) or the negativity of depression might amplify the perception to see only the negative elements (cognitive distortion model). Research findings suggest that mild to moderate depression may better fit the depressive realism model, while more severe depression may better fit the cognitive distortion model. These fits are due to the impact of insight, which is heightened in mild to moderate depression but lessened in severe depression (Amador et al., 1994; Ghaemi, 2007; Markova and Berrios, 1992). In either way, cognitive biases during a depressive episode might influence the attachment assessment. To distinguish between state and trait characteristics, a repeated assessment of attachment style after successful treatment would have been necessary. Third, white matter microstructure may be influenced by depression severity (Bracht et al., 2015a). Therefore, comparisons between patient subgroups were controlled for depression severity. Fourth, the majority of patients was on antidepressants, which may have an impact on structural MRI-measures including white matter microstructure (Bracht et al., 2015b). Fifth, sample size of patient subgroups is small.

In conclusion, our results suggest that high attachment avoidance in patients with depression is associated with reduced hippocampal volume and reduced white matter microstructure in the PHC. Insecure attachment is an important risk factor for developing depression (Armsden et al., 1990; Kobak et al., 1991). Patients with depression and an avoidant attachment style may represent a neurobiological distinct subtype with structural alterations in the hippocampi and in the PHC, which may need distinct treatment approaches.

Role of funding source

This study received funding from the Robert Enke Foundation, from the Swiss Life Foundation and the Novartis Foundation for medical biological research. Tobias Bracht was funded by a grant from the Adrian et Simone Frutiger Foundation.

CRediT authorship contribution statement

Tobias Bracht: Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Niklaus Denier:** Conceptualization, Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Meret Wallimann:** Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Sebastian Walther:** Conceptualization, Formal analysis, Writing – review & editing. **Nicolas Mertse:** Data curation, Writing – review & editing. **Sigrid Breit:** Data curation, Formal analysis, Writing – review & editing. **Andrea Federspiel:** Methodology, Writing – review & editing. **Roland Wiest:** Writing – review & editing. **Leila Soravia:** Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing.

Declaration of Competing Interest

The authors declare that they have no conflict of interest

Acknowledgments

We thank Elmar Grosskurth, Viktoria Szabolcsi and Jakub Stefela for contributing to data acquisition.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jadr.2022.100435.

References

Acosta, H., Jansen, A., Nuscheler, B., Kircher, T., 2018. A voxel-based morphometry study on adult attachment style and affective loss. Neuroscience 392, 219–229.
Amador, X.F., Flaum, M., Andreasen, N.C., Strauss, D.H., Yale, S.A., Clark, S.C., Gorman, J.M., 1994. Awareness of illness in schizophrenia and schizoaffective and mood disorders. Arch. Gen. Psychiatry 51, 826–836.
Anders, S.L., Tucker, J.S., 2000. Adult attachment style, interpersonal communication competence, and social support. Personal Relationsh. 7, 379–389.
Armsden, G.C., McCauley, E., Greenberg, M.T., Burke, P.M., Mitchell, J.R., 1990. Parent and peer attachment in early adolescent depression. J. Abnorm. Child Psychol. 18, 683–697.
Arnone, D., McIntosh, A.M., Ebmeier, K.P., Munafo, M.R., Anderson, I.M., 2012. Magnetic resonance imaging studies in unipolar depression: systematic review and meta-regression analyses. Eur. Neuropsychopharmacol. 22, 1–16.
Basser, P.J., Mattiello, J., LeBihan, D., 1994. Estimation of the effective self-diffusion tensor from the NMR spin echo. J. Magn. Reson. B 103, 247–254.
Beck, A.T., Steer, R.A., Brown, G., 1996. Beck Depression Inventory -II. APA PsyTests.
Benetti, S., McCrory, E., Arulanantham, S., De Sanctis, T., McGuire, P., Mechelli, A., 2010. Attachment style, affective loss and gray matter volume: a voxel-based morphometry study. Hum. Brain Mapp. 31, 1482–1489.
Bowlby, J., 1969. Attachment and Loss. Attachment. Attachment and Loss. Basic Books 1, New York.
Bracht, T., Horn, H., Strik, W., Federspiel, A., Razavi, N., Stegmayer, K., Wiest, R., Dierks, T., Muller, T.J., Walther, S., 2014. White matter pathway organization of the reward system is related to positive and negative symptoms in schizophrenia. Schizophr. Res. 153, 136–142.
Bracht, T., Jones, D.K., Bells, S., Walther, S., Drakesmith, M., Linden, D., 2016. Myelination of the right parahippocampal cingulum is associated with physical activity in young healthy adults. Brain Struct. Funct. 221, 4537–4548.
Bracht, T., Jones, D.K., Muller, T.J., Wiest, R., Walther, S., 2015a. Limbic white matter microstructure plasticity reflects recovery from depression. J. Affect. Disord. 170, 143–149.
Bracht, T., Linden, D., Keedwell, P., 2015b. A review of white matter microstructure alterations of pathways of the reward circuit in depression. J. Affect. Disord. 187, 45–53.
Bracht, T., Mertse, N., Walther, S., Ludi, K., Breit, S., Federspiel, A., Wiest, R., Denier, N., 2022. Link between structural connectivity of the medial forebrain bundle, functional connectivity of the ventral tegmental area, and anhedonia in unipolar depression. Neuroimage Clin. 34, 102961.
Bracht, T., Soravia, L., Moggi, F., Stein, M., Grieder, M., Federspiel, A., Tschumperlin, R., Batschelet, H.M., Wiest, R., Denier, N., 2021. The role of the orbitofrontal cortex and the nucleus accumbens for craving in alcohol use disorder. Transl. Psychiatry 11, 267.
Bracht, T., Viher, P.V., Stegmayer, K., Strik, W., Federspiel, A., Wiest, R., Walther, S., 2019. Increased structural connectivity of the medial forebrain bundle in schizophrenia spectrum disorders is associated with delusions of paranoid threat and grandiosity. Neuroimage Clin. 24, 102044.
Bradford, A.B., Burningham, K.L., Sandberg, J.G., Johnson, L.N., 2017. The association between the parent-child relationship and symptoms of anxiety and depression: the roles of attachment and perceived spouse attachment behaviors. J. Marital Fam. Ther. 43, 291–307.
Coan, J.A., 2008. Toward a neuroscience of attachment. Handbook of Attachment: Theory, Research, and Clinical Implications, 2nd Edition, pp. 241–256.
Collins, N.L., Read, S.J., 1990. Adult attachment, working models, and relationship quality in dating couples. J. Personal. Soc. Psychol. 58, 644–663.
Colonnesi, C., Draijer, E.M., Jan, J.M.S.G., Van der Bruggen, C.O., Bogels, S.M., Noom, M.J., 2011. The relation between insecure attachment and child anxiety: a meta-analytic review. J. Clin. Child. Adolesc. Psychol. 40, 630–645.
Cozzarelli, C., Karafa, J.A., Collins, N.L., Tagler, M.J., 2003. Stability and change in adult attachment styles: associations with personal vulnerabilities, life events. and global construals of self and others. J. Soc. Clinic. Psychol. 22, 315–346.
Dagan, O., Facompre, C.R., Bernard, K., 2018. Adult attachment representations and depressive symptoms: a meta-analysis. J. Affect. Disord. 236, 274–290.
Dalboni da Rocha, J.L., Bramati, I., Coutinho, G., Tovar Moll, F., Sitaram, R., 2020. Fractional anisotropy changes in parahippocampal cingulum due to Alzheimer's disease. Sci. Rep. 10, 2660.
Denier, N., Walther, S., Schneider, C., Federspiel, A., Wiest, R., Bracht, T., 2020. Reduced tract length of the medial forebrain bundle and the anterior thalamic radiation in bipolar disorder with melancholic depression. J. Affect. Disord. 274, 8–14.
Dillon, D.G., Pizzagalli, D.A., 2018. Mechanisms of memory disruption in depression. Trends Neurosci. 41, 137–149.
Donges, U.S., Kugel, H., Stuhrmann, A., Grotegerd, D., Redlich, R., Lichev, V., Rosenberg, N., Ihme, K., Suslow, T., Dannlowski, U., 2012. Adult attachment anxiety is associated with enhanced automatic neural response to positive facial expression. Neuroscience 220, 149–157.
Doolin, K., Andrews, S., Carballedo, A., McCarthy, H., O'Hanlon, E., Tozzi, L., Frodl, T., 2019. Longitudinal diffusion weighted imaging of limbic regions in patients with major depressive disorder after 6 years and partial to full remission. Psychiatry Res. Neuroimaging 287, 75–86.
Galynker, II, Yaseen, Z.S., Katz, C., Zhang, X., Jennings-Donovan, G., Dashnaw, S., Hirsch, J., Mayberg, H., Cohen, L.J., Winston, A., 2012. Distinct but overlapping neural networks subserve depression and insecure attachment. Soc. Cogn. Affect. Neurosci. 7, 896–908.
Ghaemi, S.N., 2007. Feeling and time: the phenomenology of mood disorders, depressive realism, and existential psychotherapy. Schizophr. Bull. 33, 122–130.
Groh, A.M., Fearon, P., Iljzendoorn, M., Bakermans-Kranenburg, M., 2017. Attachment in the early life course: meta-analytic evidence for its role in socioemotional development. Child Dev. Perspect. 11, 70–76.
Hamilton, M., 1967. Development of a rating scale for primary depressive illness. Br. J. Soc. Clin. Psychol. 6, 278–296.
Han, K.M., Won, E., Kang, J., Choi, S., Kim, A., Lee, M.S., Tae, W.S., Ham, B.J., 2017. TESC gene-regulating genetic variant (rs7294919) affects hippocampal subfield volumes and parahippocampal cingulum white matter integrity in major depressive disorder. J. Psychiatr. Res. 93, 20–29.
Isensee, F., Schell, M., Pflueger, I., Brugnara, G., Bonekamp, D., Neuberger, U., Wick, A., Schlemmer, H.-P., Heiland, S., Wick, W., Bendszus, M., Maier-Hein, K.H., Kickingereder, P., 2019. Automated brain extraction of multisequence MRI using artificial neural networks. Hum. Brain Mapp. 40, 4952–4964.
Jackowski, A., Perera, T.D., Abdallah, C.G., Garrido, G., Tang, C.Y., Martinez, J., Mathew, S.J., Gorman, J.M., Rosenblum, L.A., Smith, E.L., Dwork, A.J., Shungu, D. C., Kaffman, A., Gelernter, J., Coplan, J.D., Kaufman, J., 2011. Early-life stress, corpus callosum development, hippocampal volumetrics, and anxious behavior in male nonhuman primates. Psychiatry Res. 192, 37–44.
Jayamaha, S.D., Girme, Y.U., Overall, N.C., 2017. When attachment anxiety impedes support provision: the role of feeling unvalued and unappreciated. J. Fam. Psychol. 31, 181–191.
Jin, J., Maren, S., 2015. Prefrontal-hippocampal interactions in memory and emotion. Front. Syst. Neurosci. 9, 170.
Jones, D.K., Cercignani, M., 2010. Twenty-five pitfalls in the analysis of diffusion MRI data. NMR Biomed. 23, 803–820.
Jones, D.K., Christiansen, K.F., Chapman, R.J., Aggleton, J.P., 2013. Distinct subdivisions of the cingulum bundle revealed by diffusion MRI fibre tracking: implications for neuropsychological investigations. Neuropsychologia 51, 67–78.
Karreman, A., Vingerhoets, A.J., 2012. Attachment and well-being: the mediating role of emotion regulation and resilience. Personal. Individ. Differ. 53, 821–826.
Kobak, R.R., Sudler, N., Gamble, W., 1991. Attachment and depressive symptoms during adolescence: a developmental pathways analysis. Dev. Psychopathol. 3, 461–474.
Kribakaran, S., Danese, A., Bromis, K., Kempton, M.J., Gee, D.G., 2020. Meta-analysis of structural magnetic resonance imaging studies in pediatric posttraumatic stress disorder and comparison with related conditions. Biol. Psychiatry Cogn. Neurosci. Neuroimaging 5, 23–34.
Leemans, A., Jeurissen, B., Sijbers, J., Jones, D.K., 2009. ExporeDTI: a graphical toolbox for processing, analyzing and visualizing diffusion MR data. In: Proceedings of the International Society for Magnetic Resonance in Medicine 17th Annual Meeting April 18-24, 3536 Honolulu Hawaii.
Leemans, A., Jones, D.K., 2009. The B-matrix must be rotated when correcting for subject motion in DTI data. Magn. Reson. Med. 61, 1336–1349.
Lin, Y.H., Dhanaraj, V., Mackenzie, A.E., Young, I.M., Tanglay, O., Briggs, R.G., Chakraborty, A.R., Hormovas, J., Fonseka, R.D., Kim, S.J., Yeung, J.T., Teo, C., Sughrue, M.E., 2021. Anatomy and white matter connections of the parahippocampal gyrus. World Neurosurg. 148, e218–e226.
Long, M., Verbeke, W., Ein-Dor, T., Vrticka, P., 2020. A functional neuro-anatomical model of human attachment (NAMA): insights from first- and second-person social neuroscience. Cortex 126, 281–321.
Marganska, A., Gallagher, M., Miranda, R., 2013. Adult attachment, emotion dysregulation, and symptoms of depression and generalized anxiety disorder. Am. J. Orthopsychiatry 83, 131–141.
Markova, I.S., Berrios, G.E., 1992. The meaning of insight in clinical psychiatry. Br. J. Psychiatry 160, 850–860.
Mertse, N., Denier, N., Walther, S., Breit, S., Grosskurth, E., Federspiel, A., Wiest, R., Bracht, T., 2022. Associations between anterior cingulate thickness, cingulum bundle microstructure, melancholia and depression severity in unipolar depression. J. Affect. Disord. 301, 437–444.
Mikulincer, M., Shaver, P.R., 2007. Attachment in Adulthood: Structure, Dynamics, and Change. The Guilford Press.
Moriceau, S., Sullivan, R.M., 2005. Neurobiology of infant attachment. Dev. Psychobiol. 47, 230–242.
Muris, P., Meesters, C., Van Melick, M., Zwambag, L., 2001. Self-reported attachment style, attachment quality, and symptoms of anxiety and depression in young adolescents. Personal. Individ. Differ. 30, 809–818.
Nasiriavanaki, Z., Barbour, T., Farabaugh, A.H., Fava, M., Holmes, A.J., Tootell, R.B.H., Holt, D.J., 2021. Anxious attachment is associated with heightened responsivity of a parietofrontal cortical network that monitors peri-personal space. Neuroimage Clin. 30, 102585.
Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh inventory. Neuropsychologia 9, 97–113.

Olejnik, S., Algina, J., 2003. Generalized eta and omega squared statistics: measures of effect size for some common research designs. Psychol. Methods 8, 434–447.
Olson, E.A., Overbey, T.A., Ostrand, C.G., Pizzagalli, D.A., Rauch, S.L., Rosso, I.M., 2020. Childhood maltreatment experiences are associated with altered diffusion in occipito-temporal white matter pathways. Brain Behav. 10, e01485.
Phan, K.L., Fitzgerald, D.A., Nathan, P.J., Tancer, M.E., 2006. Association between amygdala hyperactivity to harsh faces and severity of social anxiety in generalized social phobia. Biol. Psychiatry 59, 424–429.
Phelps, E.A., 2004. Human emotion and memory: interactions of the amygdala and hippocampal complex. Curr. Opin. Neurobiol. 14, 198–202.
Picardi, A., Caroppo, E., Toni, A., Bitetti, D., Di Maria, G., 2005. Stability of attachment-related anxiety and avoidance and their relationships with the five-factor model and the psychobiological model of personality. Psychol. Psychother. 78, 327–345.
Quirin, M., Gillath, O., Pruessner, J.C., Eggert, L.D., 2010. Adult attachment insecurity and hippocampal cell density. Soc. Cogn. Affect. Neurosci. 5, 39–47.
Ravitz, P., Maunder, R., Hunter, J., Sthankiya, B., Lancee, W., 2010. Adult attachment measures: a 25-year review. J. Psychosom. Res. 69, 419–432.
Rebsamen, M., Rummel, C., Reyes, M., Wiest, R., McKinley, R., 2020. Direct cortical thickness estimation using deep learning-based anatomy segmentation and cortex parcellation. Hum. Brain Mapp. 41, 4804–4814.
Rigon, A., Duff, M.C., Voss, M.W., 2016. Structural and functional neural correlates of self-reported attachment in healthy adults: evidence for an amygdalar involvement. Brain Imaging Behav. 10, 941–952.
Schmidt, S., Muehlan, H., Brähler, E., 2016. Revised Adult Attachment Scale. Hogrefe.
Schneider-Hassloff, H., Straube, B., Jansen, A., Nuscheler, B., Wemken, G., Witt, S.H., Rietschel, M., Kircher, T., 2016. Oxytocin receptor polymorphism and childhood social experiences shape adult personality, brain structure and neural correlates of mentalizing. Neuroimage 134, 671–684.
Segal, N., Fraley, C., 2015. Broadening the investment model: an intensive longitudinal study on attachment and perceived partner responsiveness in commitment dynamics. J. Soc. Pers. Relationsh. 33, 581–599.
Serra, M., De Pisapia, N., Rigo, P., Papinutto, N., Jager, J., Bornstein, M.H., Venuti, P., 2015. Secure attachment status is associated with white matter integrity in healthy young adults. Neuroreport 26, 1106–1111.
Sheehan, D.V., Lecrubier, Y., Sheehan, K.H., Amorim, P., Janavs, J., Weiller, E., Hergueta, T., Baker, R., Dunbar, G.C., 1998. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J. Clin. Psychiatry 59 (Suppl 20), 22–33 quiz 34-57.
Sheline, Y.I., 2011. Depression and the hippocampus: cause or effect? Biol. Psychiatry 70, 308–309.
Shin, L.M., Shin, P.S., Heckers, S., Krangel, T.S., Macklin, M.L., Orr, S.P., Lasko, N., Segal, E., Makris, N., Richert, K., Levering, J., Schacter, D.L., Alpert, N.M., Fischman, A.J., Pitman, R.K., Rauch, S.L., 2004. Hippocampal function in posttraumatic stress disorder. Hippocampus 14, 292–300.
Song, S.K., Sun, S.W., Ramsbottom, M.J., Chang, C., Russell, J., Cross, A.H., 2002. Dysmyelination revealed through MRI as increased radial (but unchanged axial) diffusion of water. Neuroimage 17, 1429–1436.
Soravia, L.M., Denier, N., Moggi, F., Grieder, M., Federspiel, A., Tschuemperlin, R.M., Batschelet, H.M., Vollstadt-Klein, S., Wiest, R., Stein, M., Bracht, T., 2022. Reduced structural connectivity of the amygdala is associated with childhood trauma in adult patients with alcohol use disorder. Addict. Biol. 27, e13164.
Sutin, A.R., Gillath, O., 2009. Autobiographical memory phenomenology and content mediate attachment style and psychological distress. J. Couns. Psychol. 56, 351–364.
Tendolkar, I., Martensson, J., Kuhn, S., Klumpers, F., Fernandez, G., 2018. Physical neglect during childhood alters white matter connectivity in healthy young males. Hum. Brain Mapp. 39, 1283–1290.
van der Meer, L.B., van Duijn, E., Giltay, E.J., Tibben, A., 2015. Do attachment style and emotion regulation strategies indicate distress in predictive Testing? J. Genet. Couns. 24, 862–871.
Videbech, P., Ravnkilde, B., 2004. Hippocampal volume and depression: a meta-analysis of MRI studies. Am. J. Psychiatry 161, 1957–1966.
Vrticka, P., Bondolfi, G., Sander, D., Vuilleumier, P., 2012. The neural substrates of social emotion perception and regulation are modulated by adult attachment style. Soc. Neurosci. 7, 473–493.
Vrticka, P., Vuilleumier, P., 2012. Neuroscience of human social interactions and adult attachment style. Front. Hum. Neurosci. 6, 212.
Walther, S., Bernard, J.A., Mittal, V.A., Shankman, S.A., 2019. The utility of an RDoC motor domain to understand psychomotor symptoms in depression. Psychol. Med. 49, 212–216.
Warren, S.L., Huston, L., Egeland, B., Sroufe, L.A., 1997. Child and adolescent anxiety disorders and early attachment. J. Am. Acad. Child Adolesc. Psychiatry 36, 637–644.
Wittchen, H.U., Zaudig, M., Fydrich, T., 1997. Strukturiertes klinisches Interview für DSM-IV. Hogrefe, Göttingen.
Won, E., Kang, J., Kim, A., Choi, S., Han, K.M., Tae, W.S., Chang, H.S., Son, K.R., Greenberg, T., Joe, S.H., Lee, M.S., Ham, B.J., 2016. Influence of BclI C/G (rs41423247) on hippocampal shape and white matter integrity of the parahippocampal cingulum in major depressive disorder. Psychoneuroendocrinology 72, 147–155.
Wu, M., Chang, L.C., Walker, L., Lemaitre, H., Barnett, A.S., Marenco, S., Pierpaoli, C., 2008. Comparison of EPI distortion correction methods in diffusion tensor MRI using a novel framework. Med. Image Comput. Comput. Assist. Interv. 11, 321–329.
Zhang, X., Deng, M., Ran, G., Tang, Q., Xu, W., Ma, Y., Chen, X., 2018. Brain correlates of adult attachment style: a voxel-based morphometry study. Brain Res. 1699, 34–43.
Zheng, L., Luo, Y., Chen, X., 2020. Different effects of attachment anxiety and attachment avoidance on depressive symptoms: a meta-analysis. J. Soc. Pers. Relationsh. 37, 3028–3050.