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ORIGINAL ARTICLE

Links between psychopathological symptoms and cortical thickness in men with severe alcohol use disorder: A Magnetic Resonance Imaging study

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Abstract

Background: Anxiety and depression are psychopathological states frequently co-occurring with severe alcohol use disorder (SAUD). These symptoms generally disappear with abstinence but may persist in some patients, increasing the relapse risk.

Methods: The cerebral cortex thickness of 94 male patients with SAUD was correlated with symptoms of depression and anxiety, both measured at the end (2–3 weeks) of the detoxification treatment. Cortical measures were obtained using surface-based morphometry implemented with Freesurfer.

Results: Depressive symptoms were associated with reduced cortical thickness in the superior temporal gyrus of the right hemisphere. Anxiety level was correlated with lower cortical thickness in the rostral middle frontal region, inferior temporal region, and supramarginal, postcentral, superior temporal, and transverse temporal regions of the left hemisphere, as well as with a large cluster in the middle temporal region of the right hemisphere.

Conclusions: At the end of the detoxification stage, the intensity of depressive and anxiety symptoms is inversely associated with the cortical thickness of regions involved in emotions-related processes, and the persistence of the symptoms could be explained by these brain deficits.

KEYWORDS
abstinence, alcohol use disorders, anxiety, cortical thickness, depression

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1 | INTRODUCTION

The brain, like most organs, is vulnerable to damage from excessive alcohol consumption. A large body of evidence documents damages to the peripheral and central nervous system in individuals with severe alcohol use disorder (SAUD).[1-3]

An accelerated global shrinkage (i.e., atrophy) of the brain is one of the most common findings in neuroimaging, with repeated observations of white and gray matter reduction, particularly in the cerebellum, insula, and frontal/temporal regions.[4-8]

One way to explore these brain changes is to measure cortical thickness (CT). CT corresponds to the metric distance between corresponding points located on the pial and white matter boundaries of the neocortex. It ranges from 1 to 4.5 mm depending on brain regions with an average of about 2.5 mm, and is part of cortical volume, together with cortical surface area and degree of gyrification.[9,10] A reduction in CT has been observed with sustained alcohol abuse[11-15] and has been associated with relapse.[12]

At a behavioral level, SAUD is often accompanied by depressive and anxious symptoms.[16-18] Some authors explain this association by the self-medication hypothesis asserting that alcohol may alleviate unpleasant or negative mood states.[19-21] A better understanding of comorbid mood disorders is particularly important for SAUD patients attempting to quit, as they may increase relapse risk. Patients reporting high depressive/anxiety symptoms in addition to SAUD may have specific structural damage and answers may be found through exploration of neurological correlates of mood disorders in these patients.

Structural deficiencies and alterations in CT have been widely described in mood disorders. Studies of major depressive disorders, generalized anxiety disorder, and social anxiety (Kühn et al., 2011; Abdallah et al., 2012; Syal et al., 2012; Frick et al., 2013; Strawn et al., 2014; Molent et al., 2018; Suh et al., 2019) have reported frontal and temporal neuroanatomical alterations.[22-28]

Very few studies have assessed the structural brain-imaging substrates of mood collateral symptoms in patients with SAUD. Two brain imaging studies have addressed the comparison between SAUD patients with and without another established psychiatric diagnosis.[29,30] These studies only considered diagnosed psychopathological comorbidities, thus offering no insights into the influence of the more common subclinical depression or anxious states (i.e., mild or moderate symptoms without a formal psychiatric diagnosis).

The present study aims to measure cortical ribbon thickness in a population of SAUD patients in relation to depressive and anxious symptoms measured during the detoxification phase. This phase is of particular importance: inpatients with high levels of depressive and/or anxiety symptoms at the beginning of detoxification often experience a sharp decline in symptoms within 2–4 weeks of abstinence.[31-36] A minority of patients however have persistent symptoms. Our aim is therefore to explore the cerebral correlates of the intensity of mood-related symptoms presented at the end of the detoxification program, namely 2–3 weeks after the day of admission. Based on the available findings in SAUD and demonstrated cortical thinning in mood disorders, we expect to find substantial thickness reductions associated with comorbidities.

Previous studies have taken a dichotomous approach in focusing on the presence or absence of diagnoses of depression and anxiety, based on the ICD-10 or the Diagnostic and Statistical Manual of Mental Disorders (DSM, American Psychiatric Association, 2001).[37] Such an approach, however, does not reflect the clinical reality, in which mood disturbances should be placed on a continuum of severity rather than on a dichotomy, even low or moderate psychopathological symptoms being potentially related to brain impairments. In this study, therefore, we chose to study symptoms' intensity rather than the presence of a comorbid diagnosis.

2 | MATERIALS AND METHODS

2.1 | Participants

We recruited 94 individuals with SAUD from the full-time alcohol detoxification unit of the Cliniques Universitaires Saint-Luc, Brussels, Belgium. Patients had abstained from alcohol consumption for 14–18 days before being tested. Inclusion criteria were to meet the DSM-5 criteria for SAUD, based on the clinical assessment of the principal investigator (PDT) and being fluent in French. Exclusion criteria consisted of having history of addictive, psychiatric, neurological, or physical disorder that could influence brain morphology except for nicotine dependence. Participants could also not have a contraindication for magnetic resonance imaging (MRI). All participants gave a written informed consent. The present study is based on a reanalysis of data collected previously and that have already given rise to other publications, unrelated to the topic of the current one.[38-40]

2.2 | MR data acquisition and processing

Three-dimensional anatomical heavily T1-weighted images were acquired from a 3 T Achieva, Philips Healthcare scanner with a 32-channel phased array head coil. Patients, instructed to remain still, were positioned comfortably in the coil and fitted with soft earplugs. The 3D sequence consisted of a gradient echo sequence with an inversion prepulse (Turbo Field Echo) acquired in the sagittal plane using the following parameters: TR/TE/flip angle = 9.1 ms/4.6 ms/8°, 150 slices, slice thickness = 1 mm, in-plane resolution = $0.81 \times 0.95\,mm^2$ (acquisition) reconstructed in $0.75 \times 0.75\,mm^2$, FOV = $220 \times 197\,mm^2$, acquisition matrix = 296 × 247 (reconstruction 3202), SENSE factor = 1.5 (parallel imaging). The whole brain was measured and segmented by completing the FreeSurfer image analysis pipeline (http://surfer.nmr.mgh.harvard.edu) using a set of automated sequences to reconstruct the cortical surface. The final segmentation (i.e., morphometry and surface data) is based on both a subject-independent probabilistic atlas and subject-specific measured values. The atlas

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is built from a training set comprising a set of 40 participants whose brains (surfaces or volumes) were labeled by hand (Dale et al. 1999; Fischl et al., 2002, 2004).[41-43] After completion of the pipeline, each segmentation was visually inspected, and any geometric inaccuracies were corrected. Only small skull strip errors were found and corrected before running the data through the pipeline again.

2.3 | Measurement of depressive and anxious symptoms

Depression was assessed with the French translation of the abbreviated version of the Beck Depression Inventory (BDI). It is a 13-item form (Beck and Beck, 1972), with each item having four option responses, scored 0, 1, 2, or 3.[44] The item's content includes sadness, pessimism, sense of failure, dissatisfaction, guilt, self-dislike, self-harm, social withdrawal, indecisiveness, distorted body image, work difficulty, fatigue, and loss of appetite. The patient score is the sum of the score obtained to each item. Higher scores indicate greater depressive severity. It is recommended to use the cutoff score of 9 to detect patients with high levels of depressive symptoms.[45]

To measure anxiety, we used the State–Trait Anxiety Inventory (STAI; (Spielberger, 1983)[46]; for the French version, (Bruchon-Schweitzer and Paulhan, 1993).[47] It is a self-reported questionnaire divided into two 20-item subsections measuring state and trait anxiety, respectively. Each item has four option responses, scored 1, 2, 3, or 4. We only used the state subsection (how one feels at the moment) in this study. Higher scores indicate greater anxiety severity. A threshold score of 40 is generally used to determine a clinical level of anxiety.[48]

2.4 | Statistical analyses

Descriptive statistics are presented as the mean ± SD. We used Pearson's correlation coefficient to measure the linear association between depression and anxiety scores. Whole brain analyses were undertaken using a GLM to identify the brain regions for which cortical thickness were significantly associated with depression and anxiety. FreeSurfer's Qdec was used to perform correlations between cortical thickness and depression and anxiety-related symptoms' scores with age being controlled as covariate. All results were corrected for multiple comparisons using a Monte Carlo simulation thresholded at 1.3 ($p < 0.05$).

3 | RESULTS

3.1 | Clinico-demographics

The 94 participants were men with a mean age of 47.3 ± 11.2, a mean depression score of 7.5 ± 5.7 and a mean anxiety score of 39.4 ± 12.8. 35% ($N = 33$) of patients showed scores above the cutoff score for depression and 44% ($N = 41$) showed scores above the cutoff score for anxiety. We found a significant positive correlation between scores of anxiety and depression ($r = 0.661$, $p < 0.001$) (see Figure 1).

3.2 | Surface-based analyses

3.2.1 | Correlation between cortical thickness and depression

In the right hemisphere, cortical thickness was significantly and negatively associated with depression in a large cluster in the superior temporal area, with a temporal peak and going through the transverse area (see Figure 2 and Table 1). No significant correlation was found between cortical thickness and depression in the left hemisphere.

3.2.2 | Correlation between cortical thickness and anxiety

In the right hemisphere, cortical thickness was significantly and negatively linked with anxiety in a large cluster in the middle temporal area going from the supramarginal through the superior temporal and transverse with part of the middle pole and temporal pole (see Figure 3 and Table 1). In the left hemisphere, cortical thickness significantly and negatively correlated with anxiety in three regions: (1) the rostral middle frontal region with the pars opercularis, orbitalis and triangularis, (2) the inferior temporal region with mostly the gyrus fusiform lingual and the parahippocampic region, (3) the supramarginal, post-central, superior temporal, transversal temporal area (see Figure 4 and Table 1).

4 | DISCUSSION

We examined the cerebral correlates of the degree of depression and anxiety-related symptoms presented 2 weeks after detoxification admission day among patients with SAUD.

Firstly, we confirmed that most patients, at the end of the detoxification stage, presented sub-clinical levels of depression and anxiety. It should be noted that the assessment and MRI were performed between days 14 and 18, when the patients were not any longer under the effects of benzodiazepines but had already received at least 5/6 sessions of brief psychodynamic psychotherapy.[49] It is likely that these interventions contributed to improvements in symptomatology. We also observed a strong correlation between the reported anxiety and depression levels. This relationship was not surprising as symptoms of anxiety and depression often coexist.[50] High rates of comorbidity between anxiety and depressive disorders have been explained in several ways including the fact that symptoms of depression and anxiety represent different outward manifestations of the same

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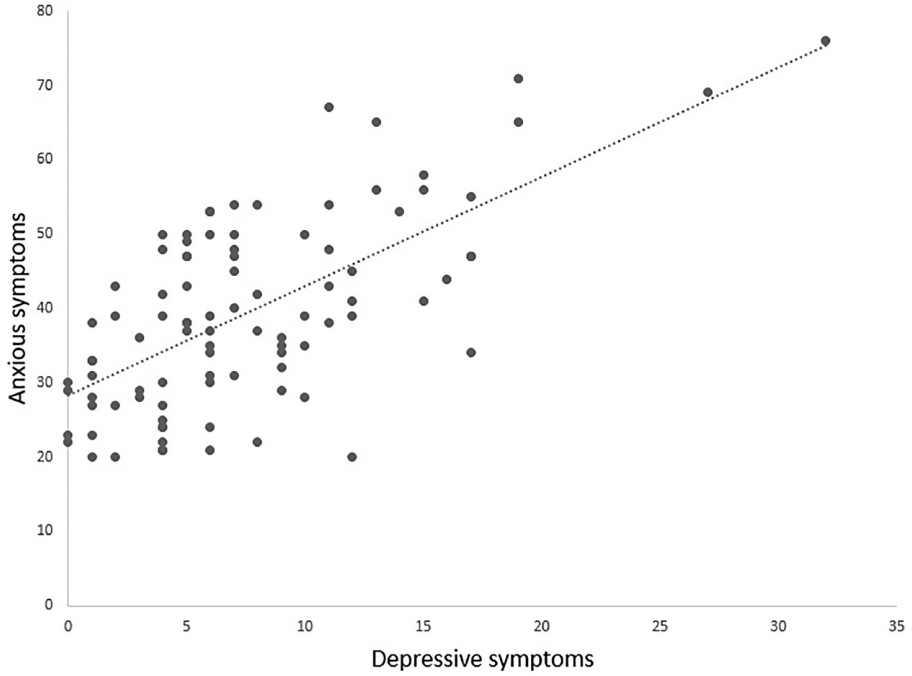

FIGURE 1 Scatter plot of anxiety scores [State–Trait Anxiety Inventory (STAI)] by depression scores [the Beck Depression Inventory (BDI)].

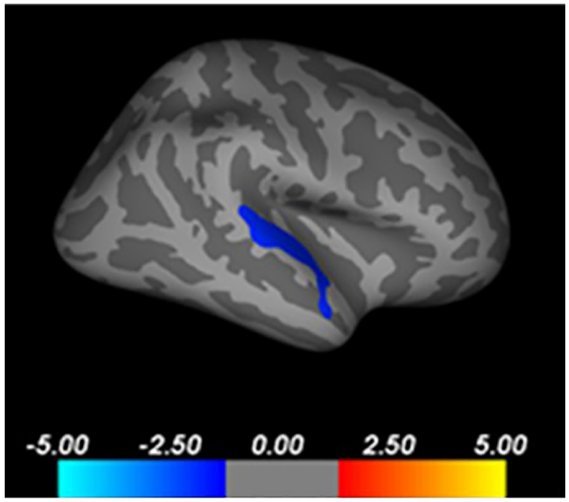

FIGURE 2 Brain areas of the right hemisphere in which cortical thickness was found negatively correlated with the current level of depression. Correction for multiple comparisons using Monte Carlo simulation ($p < 0.05$).

underlying cause[51] or that anxiety may predispose to depression and vice versa.[52]

At the brain level, we firstly observed that, in the right hemisphere, the higher the score in depressive symptoms measured by the Beck Depression Inventory, the thinner the cortical ribbon in the superior temporal gyrus. Numerous studies have shown that this region of the brain, centrally linked to emotional processing, shows morphological changes in patients suffering from major depression (MDD).[53,54] Takahashi et al[55] in particular, have shown that its volume is inversely correlated with the score at the Beck Depression Inventory in MDD patients. At the functional level, Yang et al[56] found that patients with MDD exhibit weaker neural responses to rewards in the superior temporal gyrus than healthy controls. The correlation only found with the right hemisphere is consistent with the dominance of this hemisphere in the processing of unconscious negative emotions which has long been described in the neuropsychological and neuroimaging literature.[57-60] A cortical thinning of the lateral aspect of the right hemisphere has even been proposed as an endophenotype for MDD by Peterson and Weissman.[61] Specifically as regard to the superior temporal gyrus, its reduced volume only in the right hemisphere has been linked to suicide in various psychiatric disorders[62] and in particular in adolescents with MMD or resistant depression with a history of suicide attempts.[63,64] The latter authors suggested that a reduced volume of the right superior temporal gyrus could constitute a structural neural marker of abnormalities in the evaluation of socio-emotional information.

The intensity of reported anxious symptoms was related to CT in four different brain areas. In the left hemisphere, 1-the rostral middle frontal region with the pars opercularis, orbitalis and triangularis, 2-the inferior temporal region with mostly the gyrus fusiform lingual and the parahippocampic region and 3-a region including the supramarginal, post-central, superior temporal, and transversal temporal regions. In the right hemisphere, it was associated with a cluster in the middle temporal area going from the supramarginal through the superior temporal and transverse with part of the middle pole and temporal pole.

In addition to the previously mentioned role of the superior area of the temporal pole in emotion regulation, these are the same regions that are engaged in tasks related to Theory of Mind (ToM)

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TABLE 1 Cortical thickness brain areas associated with depression and anxiety in SAUD subjects.

			Talairach coordinates[a]			
Variables	**Max[b]**	**Size (mm)[c]**	***X***	***Y***	***Z***	**Brain area**
Anxiety	−2.530	1436	35	−2	−23	Right middle temporal
	−3.98	1424	−42.5	−54.6	−18.8	Left inferior temporal
	−3.275	908	−53.8	21.4	16.7	Left rostral middle frontal
	−3.058	1159	−57.6	−26.3	27.4	Left supramarginal
Depression	−2.960	1056	65.2	−17	3	Right superior temporal

[a]The Talairach coordinates of the maximum.

[b]The maximum −log10 (p value) in the cluster. The − sign is because the correlation is negative.

[c]Surface area (mm) of the cluster.

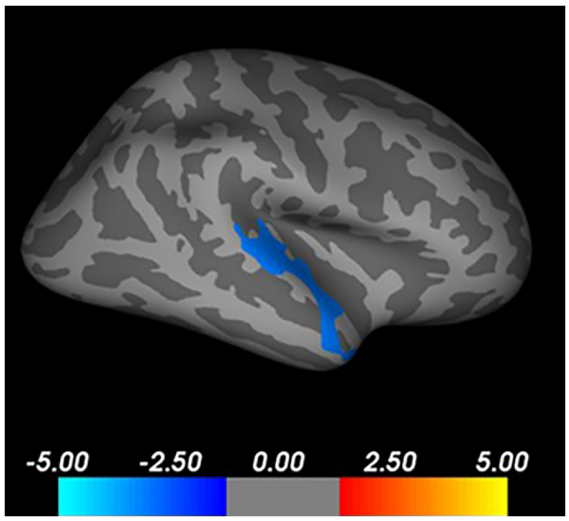

FIGURE 3 Brain areas of the right hemisphere in which cortical thickness was found negatively correlated with the current level of anxiety. Correction for multiple comparisons using Monte Carlo simulation ($p < 0.05$).

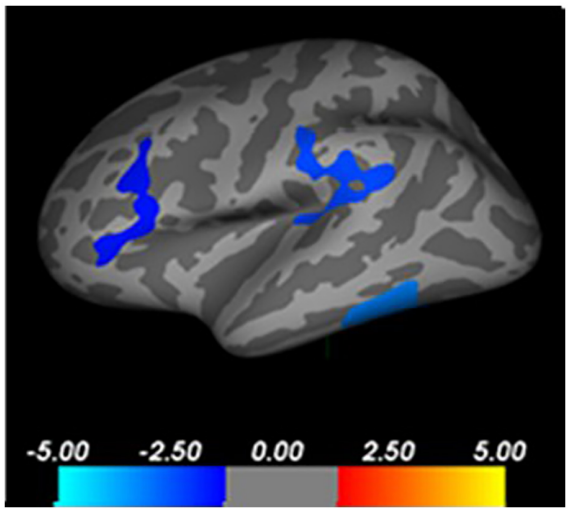

FIGURE 4 Brain areas of the left hemisphere in which cortical thickness was found negatively correlated with the current level of anxiety. Correction for multiple comparisons using Monte Carlo simulation ($p < 0.05$).

(for reviews, see Ref. [65-68]), that is, the ability to attribute mental states to other people. fMRI studies have shown that ToM demanding tasks are linked to activation of the prefrontal cortex (MPFC), temporo-parietal junction (TPJ) (an area at the border of parietal and posterior temporal lobes), superior temporal sulcus as well as temporal poles and amygdala.[69] Studies conducted in people with SAUD have shown impairments in ToM abilities[70] leading to a reduction in the quality of social interactions.[71-73] These difficulties could underlie the phenomenon of self-medication with alcohol in SAUD individuals when confronted with negative affect and sensitive interpersonal situations.[74]

In conclusion, our study shows that at the end of the detoxification stage, the intensity of depressive and anxiety symptoms is associated with reduced cortical thickness of regions involved in emotions-related processes. It suggests that in the minority of patients in whom depressive and anxious symptoms persist, alterations in cortical thickness are observed and these alterations are located in exactly the same regions as those found in patients suffering from severe depression or anxiety alone. This could mean that anxiety and depressive symptoms are transient and not associated with brain changes in the majority of SAUD patients but those in whom symptoms persist present brain alterations in regions known to be impacted in individuals with a diagnosis of depression and/or anxiety.

An important limitation of our study is that we did not have data for all participants on indices of SAUD severity, which prevented us from controlling for this variable in the correlations and should be considered for future studies. The cross-sectional nature of our study does not allow to draw any conclusions on the temporality of the links, but it can be hypothesized that regardless of the origin of the cortical thinning, the improvement in anxiety and depression after detoxification may be impeded by brain deficits in these regions.

For future studies, it would be interesting to conduct a multishell diffusion or DTI study on the anatomical connections between the regions we have highlighted and the limbic regions, known as a hub of emotional processing. In particular, the uncinate fasciculus, a major tract connecting the rostral part of the prefrontal cortex (PFC)

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to the amygdala,[75] is associated with the processing of emotional expressions[76] and its abnormalities have been associated with several psychiatric disorders.[77] Its exact function remains poorly understood, however, and deserves further investigation in the context of alcohol-related emotional disorders.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the conception or design of the work, or the acquisition, analysis, or interpretation of data for the work. GP, PdT, and PM drafted the work, and all authors revised it critically for important intellectual content. All authors gave final approval of the version to be published, and all authors agreed to be 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.

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CONFLICT OF INTEREST STATEMENT

Authors do not have any conflict of interest.

DATA AVAILABILITY STATEMENT

The dataset for this manuscript is not publicly available because the data used are from different experimenters without sharing agreement and because consent had only been obtained from participants for participation in the study and not to share data with third parties. MRI data are person-specific and therefore are not anonymous. However, the cortical thickness files by region (i.e., Destrieux and Desikan-Killiany Atlases) can be made available upon request depending on the situation and after consultation and approval by the other investigators and parties involved.

ETHICS STATEMENT

Approval of the research protocol by an Institutional Reviewer Board: The protocol for this research project was submitted to and approved by the Biomedical Ethics Commission of the Université Catholique de Louvain (Belgium) and it conforms to the provisions of the Declaration of Helsinki.

Informed consent: All informed consent was obtained from the subjects before engaging in the experimental procedures.

Registry and the Registration No. of the Study/Trial: N/A.

Animal Studies: N/A.

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REFERENCES

1. Oscar-Berman M, Marinkovic K. Alcoholism and the brain: an overview. Alcohol Res Health. 2003;27(2):125–33.
2. Suzanne M, Kril JJ. Human alcohol-related neuropathology. Acta Neuropathol. 2014;127(1):71–90.
3. Zahr NM, Kaufman KL, Harper CG. Clinical and pathological features of alcohol-related brain damage. Nat Rev Neurol. 2011;7(5):284–94. https://doi.org/10.1038/nrneurol.2011.42
4. Bühler M, Mann K. Alcohol and the human brain: a systematic review of different neuroimaging methods. Alcohol Clin Exp Res. 2011;35(10):1771–93. https://doi.org/10.1111/j.1530-0277.2011.01540.x
5. Carlen P, Wortzman G, Holgate R, Wilkinson D, Rankin JC. Reversible cerebral atrophy in recently abstinent chronic alcoholics measured by computed tomography scans. Science. 1978;200:1076–8. https://doi.org/10.1126/SCIENCE.653357
6. Kubota M, Nakazaki S, Hirai S, Saeki N, Yamaura A, Kusaka T. Alcohol consumption and frontal lobe shrinkage: study of 1432 non-alcoholic subjects. J Neurol Neurosurg Psychiatry. 2001;71(1):104–6. https://doi.org/10.1136/jnnp.71.1.104
7. Maes M, Vandoolaeghe E, Degroote J, Altamura C, Roels C, Hermans P. Linear CT-scan measurements in alcohol-dependent patients with and without delirium tremens. Alcohol (Fayetteville, N.Y.). 2000;20(2):117–23.
8. Schroth G, Naegele T, Klose U, Mann K, Petersen D. Reversible brain shrinkage in abstinent alcoholics, measured by MRI. Neuroradiology. 1988;30(5):385–9.
9. Fischl B, Dale AM. Measuring the thickness of the human cerebral cortex from magnetic resonance images. Proc Natl Acad Sci USA. 2000;97(20):11050–5.
10. Hogstrom LJ, Westlye LT, Walhovd KB, Fjell AM. The structure of the cerebral cortex across adult life: age-related patterns of surface area, thickness, and gyrification. Cereb Cortex. 2013;23(11):2521–30. https://doi.org/10.1093/cercor/bhs231
11. Bae S, Kang I, Lee BC, Jeon Y, Cho HB, Yoon S, et al. Prefrontal cortical thickness deficit in detoxified alcohol-dependent patients. Exp Neurobiol. 2016;25(6):333–41. https://doi.org/10.5607/en.2016.25.6.333
12. Durazzo TC, Tosun D, Buckley S, Gazdzinski S, Mon A, Fryer SL, et al. Cortical thickness, surface area, and volume of the brain reward system in alcohol dependence: relationships to relapse and extended abstinence. Alcohol Clin Exp Res. 2011;35(6):1187–200.
13. Fortier CB, Leritz EC, Salat DH, Venne JR, Maksimovskiy AL, Williams V, et al. Reduced cortical thickness in abstinent alcoholics and association with alcoholic behavior. Alcohol Clin Exp Res. 2011;35(12):2193–201.
14. Momenan R, Steckler LE, Saad ZS, van Rafelghem S, Kerich MJ, Hommer DW. Effects of alcohol dependence on cortical thickness as determined by magnetic resonance imaging. Psychiatry Res. 2012;204(2):101–11. https://doi.org/10.1016/j.pscychresns.2012.05.003
15. Tomasi DG, Wiers CE, Shokri-Kojori E, Zehra A, Ramirez V, Freeman C, et al. Association between reduced brain glucose metabolism and cortical thickness in alcoholics: evidence of neurotoxicity. Int J Neuropsychopharmacol. 2019;22:548–59. https://doi.org/10.1093/ijnp/pyz036
16. Foulds JA, Douglas Sellman J, Adamson SJ, Boden JM, Mulder RT, Joyce PR. Depression outcome in alcohol dependent patients: an evaluation of the role of independent and substance-induced depression and other predictors. J Affect Disord. 2015;174:503–10. https://doi.org/10.1016/j.jad.2014.11.052
17. Raimo EB, Schuckit MA. Alcohol dependence and mood disorders. Addict Behav. 1998;23(6):933–46. https://doi.org/10.1016/S0306-4603(98)00068-9

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18. Smith JP, Randall CL. Anxiety and alcohol use disorders: comorbidity and treatment considerations. Alcohol Res. 2012;34(4):414–31.
19. Conger JJ. II. Reinforcement theory and the dynamics of alcoholism. Q J Stud Alcohol. 1956;17(2):296–305.
20. Robinson RJ. Comorbidity of alcohol abuse and depression: exploring the self-medication hypothesis. Iowa State University; 2007.
21. Tovmasyan A, Monk RL, Heim D. Towards an affect intensity regulation hypothesis: systematic review and meta-analyses of the relationship between affective states and alcohol consumption. PloS One. 2022;17(1):e0262670.
22. Kühn S, Schubert F, Gallinat J. Structural correlates of trait anxiety: reduced thickness in medial orbitofrontal cortex accompanied by volume increase in nucleus accumbens. Journal of Affective Disorders. 2011;134(1–3):315–9.
23. Abdallah CG, Coplan JD, Jackowski A, Sato JR, Mao X, Shungu DC, et al. Riluzole effect on occipital cortex: a structural and spectroscopy pilot study. Neurosci Lett. 2012;530(1):103–7.
24. Syal S, Hattingh CJ, Fouché JP, Spottiswoode B, Carey PD, Lochner C, et al. Grey matter abnormalities in social anxiety disorder: a pilot study. Metab Brain Dis. 2012;27:299–309.
25. Frick A, Howner K, Fischer H, Eskildsen SF, Kristiansson M, Furmark T. Cortical thickness alterations in social anxiety disorder. Neurosci Lett. 2013;536:52–5.
26. Strawn JR, Wegman CJ, Dominick KC, Swartz MS, Wehry AM, Patino LR, et al. Cortical surface anatomy in pediatric patients with generalized anxiety disorder. J Anxiety Disord. 2014;28(7):717–23.
27. Molent C, Maggioni E, Cecchetto F, Garzitto M, Piccin S, Bonivento C, et al. Reduced cortical thickness and increased gyrification in generalized anxiety disorder: a 3 T MRI study. Psychol Med. 2018;48(12):2001–10.
28. Suh JS, Schneider MA, Minuzzi L, MacQueen GM, Strother SC, Kennedy SH, et al. Cortical thickness in major depressive disorder: a systematic review and meta-analysis. Prog Neuropsychopharmacol Biol Psychiatry. 2019;88:287–302.
29. Sameti M, Smith S, Patenaude B, Fein G. Subcortical volumes in long-term abstinent alcoholics: associations with psychiatric comorbidity. Alcohol Clin Exp Res. 2011;35(6):1067–80.
30. Uhlmann A, Bandelow B, Stein DJ, Bloch S, Engel KR, Havemann-Reinecke U, et al. Grey matter structural differences in alcohol-dependent individuals with and without comorbid depression/anxiety—an MRI study. Eur Arch Psychiatry Clin Neurosci. 2019;269(3):285–94. https://doi.org/10.1007/s00406-018-0870-x
31. Brown SA, Inaba RK, Gillin JC, Schuckit MA, Stewart MA, Irwin MR. Alcoholism and affective disorder: clinical course of depressive symptoms. Am J Psychiatry. 1995;152(1):45–52. https://doi.org/10.1176/ajp.152.1.45
32. de Timary P, de Sousa Uva M, Denoël C, Hebborn L, Derely M, Desseilles M, et al. The associations between self-consciousness, depressive state and craving to drink among alcohol dependent patients undergoing protracted withdrawal. PloS One. 2013;8(8):e71560.
33. Foulds JA, Adamson SJ, Boden JM, Williman JA, Mulder RT. Depression in patients with alcohol use disorders: systematic review and meta-analysis of outcomes for independent and substance-induced disorders. J Affect Disord. 2015;185:47–59. https://doi.org/10.1016/j.jad.2015.06.024
34. Liappas J, Paparrigopoulos T, Tzavellas E, Christodoulou G. Impact of alcohol detoxification on anxiety and depressive symptoms. Drug Alcohol Depend. 2002;68(2):215–20. https://doi.org/10.1016/S0376-8716(02)00195-3
35. Petit G, Luminet O, Cordovil de Sousa Uva M, Zorbas A, Maurage P, de Timary P. Differential spontaneous recovery across cognitive abilities during detoxification period in alcohol-dependence. PloS One. 2017;12(8):e0176638. https://doi.org/10.1371/journal.pone.0176638
36. Schuckit MA, Smith TL, Danko GP, Pierson J, Trim R, Nurnberger JI, et al. A comparison of factors associated with substance-induced versus independent depressions. J Stud Alcohol Drugs. 2007;68(6):805–12. https://doi.org/10.15288/jsad.2007.68.805
37. American Psychiatric Association. DSM-5, Diagnostic and statistical manual of mental disorders, 5th edn., Washington D.C.: American Psychiatric Association; 2013. Vol. 21.
38. Maurage P, Joassin F, Philippot P, Heeren A, Vermeulen N, Mahau P, et al. Disrupted regulation of social exclusion in alcohol-dependence: an fMRI study. Neuropsychopharmacology. 2012;37(9):2067–75. https://doi.org/10.1038/npp.2012.54
39. Quoilin C, Dricot L, Genon S, de Timary P, Duque J. Neural bases of inhibitory control: combining transcranial magnetic stimulation and magnetic resonance imaging in alcohol-use disorder patients. Neuroimage. 2021;224:117435. https://doi.org/10.1016/j.neuroimage.2020.117435
40. Rolland B, Dricot L, Creupelandt C, Maurage P, De Timary P. Respective influence of current alcohol consumption and duration of heavy drinking on brain morphological alterations in alcohol use disorder. Addict Biol. 2020;25(2):e12751.
41. Dale AM, Fischl B, Sereno MI. Cortical surface-based analysis: I. Segmentation and surface reconstruction. Neuroimage. 1999;9(2):179–194.
42. Fischl B, Salat DH, Busa E, Albert M, Dieterich M, Haselgrove C, et al. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. Neuron. 2002;33(3):341–55.
43. Fischl B, Van Der Kouwe A, Destrieux C, Halgren E, Ségonne F, Salat DH, et al. Automatically parcellating the human cerebral cortex. Cereb Cortex. 2004;14(1):11–22.
44. Beck AT, Beck RW. Screening Depressed Patients in Family Practice. Postgraduate Medicine. 1972;52(6):81–85.
45. Furlanetto LM, Mendlowicz MV, Bueno JR. The validity of the Beck Depression Inventory-Short Form as a screening and diagnostic instrument for moderate and severe depression in medical inpatients. J Affect Disord. 2005;86(1):87–91.
46. Spielberger, CD. State-trait anxiety inventory for adults. 1983.
47. Bruchon-Schweitzer M, Paulhan I. Le manuel du STAI-Y de CD Spielberger, adaptation française. Paris: ECPA; 1993.
48. Gaudry E, Poole C. A further validation of the state-trait distinction in anxiety research. Aust J Psychol. 1975;27(2):119–25.
49. Lemma A, Target M, Fonagy P. Brief dynamic interpersonal therapy: a clinician's guide. OUP Oxford; 2011.
50. Maser JD, Cloninger C. Comorbidity of mood and anxiety disorders. American Psychiatric Association; 1990.
51. Hettema JM. What is the genetic relationship between anxiety and depression? American journal of medical genetics part C: Seminars in medical genetics. Hoboken: Wiley Subscription Services Inc, A Wiley Company; 2008. (Vol. 148(2), pp. 140–146).
52. Frances A, Manning D, Marin D, Kocsis J, McKinney K, Hall W, et al. Relationship of anxiety and depression. Psychopharmacology (Berl). 1992;106(1):S82–6.
53. Peng J, Liu J, Nie B, Li Y, Shan B, Wang G, et al. Cerebral and cerebellar gray matter reduction in first-episode patients with major depressive disorder: a voxel-based morphometry study. Eur J Radiol. 2011;80(2):395–9. https://doi.org/10.1016/j.ejrad.2010.04.006
54. Schmaal L, Hibar DP, Sämann PG, Hall GB, Baune BT, Jahanshad N, et al. Cortical abnormalities in adults and adolescents with major depression based on brain scans from 20 cohorts worldwide in the ENIGMA Major Depressive Disorder Working Group. Mol Psychiatry. 2017;22(6):900–9. https://doi.org/10.1038/mp.2016.60
55. Takahashi T, Yücel M, Lorenzetti V, Walterfang M, Kawasaki Y, Whittle S, et al. An MRI study of the superior temporal subregions in patients with current and past major depression. Prog Neuropsychopharmacol Biol Psychiatry. 2010;34(1):98–103.

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56. Yang XH, Huang J, Lan Y, Zhu CY, Liu XQ, Wang YF, et al. Diminished caudate and superior temporal gyrus responses to effort-based decision making in patients with first-episode major depressive disorder. Prog Neuropsychopharmacol Biol Psychiatry. 2016;64:52–9. https://doi.org/10.1016/j.pnpbp.2015.07.006
57. Bowers D, Blonder L, Feinberg T, Heilman K. Differential impact of right and left hemisphere lesions on facial emotion and object imagery. Brain. 1991;114(6):2593–609.
58. Bruder GE, Quitkin FM, Stewart JW, Martin C, Voglmaier MM, Harrison WM. Cerebral laterality and depression: differences in perceptual asymmetry among diagnostic subtypes. J Abnorm Psychol. 1989;98(2):177–86.
59. Deldin PJ, Keller J, Gergen JA, Miller GA. Right-posterior face processing anomaly in depression. J Abnorm Psychol. 2000;109(1):116–21.
60. Sato W, Aoki S. Right hemispheric dominance in processing of unconscious negative emotion. Brain Cogn. 2006;62(3):261–6.
61. Peterson BS, Weissman MM. A brain-based endophenotype for major depressive disorder. Annu Rev Med. 2011;62:461–74.
62. Sudol K, Mann JJ. Biomarkers of suicide attempt behavior: towards a biological model of risk. Curr Psychiatry Rep. 2017;19(6):1–13.
63. McLellan Q, Wilkes TC, Swansburg R, Jaworska N, Langevin LM, MacMaster FP. History of suicide attempt and right superior temporal gyrus volume in youth with treatment-resistant major depressive disorder. J Affect Disord. 2018;239:291–4. https://doi.org/10.1016/j.jad.2018.07.030
64. Pan LA, Ramos L, Segreti A, Brent DA, Phillips ML. Right superior temporal gyrus volume in adolescents with a history of suicide attempt. Br J Psychiatry. 2015;206(4):339–40.
65. Frith U, Frith C. The biological basis of social interaction. Curr Dir Psychol Sci. 2001;10(5):151–5.
66. Gallagher HL, Frith CD. Functional imaging of 'theory of mind'. Trends Cogn Sci. 2003;7(2):77–83.
67. Kapogiannis D, Sutin A, Davatzikos C, Costa P, Resnick S. The five factors of personality and regional cortical variability in the baltimore longitudinal study of aging. Hum Brain Mapp. 2013;34(11):2829–40. https://doi.org/10.1002/hbm.22108
68. Mitchell JP. Mentalizing and Marr: an information processing approach to the study of social cognition. Brain Res. 2006;1079(1):66–75.
69. Moriguchi Y, Ohnishi T, Mori T, Matsuda H, Komaki G. Changes of brain activity in the neural substrates for theory of mind during childhood and adolescence. Psychiatry Clin Neurosci. 2007;61(4):355–63. https://doi.org/10.1111/j.1440-1819.2007.01687.x
70. Onuoha RC, Quintana DS, Lyvers M, Guastella AJ. A meta-analysis of theory of mind in alcohol use disorders. Alcohol Alcohol. 2016;51(4):410–5.
71. D'Hondt F, Campanella S, Kornreich C, Philippot P, Maurage P. Below and beyond the recognition of emotional facial expressions in alcohol dependence: from basic perception to social cognition. Neuropsychiatr Dis Treat. 2014;10:2177.
72. Maurage F, de Timary P, Tecco JM, Lechantre S, Samson D. Theory of mind difficulties in patients with alcohol dependence: beyond the prefrontal cortex dysfunction hypothesis. Alcohol Clin Exp Res. 2015;39(6):980–8.
73. Maurage P, D'Hondt F, de Timary P, Mary C, Franck N, Peyroux E. Dissociating affective and cognitive theory of mind in recently detoxified alcohol-dependent individuals. Alcohol Clin Exp Res. 2016;40(9):1926–34.
74. Fein G. Commentary on Maurage et al., theory of mind difficulties in patients with alcohol dependence. Alcohol Clin Exp Res. 2015;39(7):1118–9.
75. Bissière S, Plachta N, Hoyer D, McAllister KH, Olpe H-R, Grace AA, et al. The rostral anterior cingulate cortex modulates the efficiency of amygdala-dependent fear learning. Biol Psychiatry. 2008;63(9):821–31.
76. Coad BM, Postans M, Hodgetts CJ, Muhlert N, Graham KS, Lawrence AD. Structural connections support emotional connections: uncinate Fasciculus microstructure is related to the ability to decode facial emotion expressions. Neuropsychologia. 2020;145:106562.
77. Jin J, Delaparte L, Chen HW, DeLorenzo C, Perlman G, Klein DN, et al. Structural connectivity between rostral anterior cingulate cortex and amygdala predicts first onset of depressive disorders in adolescence. Biol Psychiatry Cogn Neurosci Neuroimaging. 2022;7(3):249–55. https://doi.org/10.1016/j.bpsc.2021.01.012

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