EBioMedicine 21 (2017) 53–54

Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

Commentary

Common and Distinct Gray Matter Alterations in Social Anxiety Disorder and Major Depressive Disorder

Andreas Frick *

Department of Psychology, Uppsala University, Uppsala, Sweden
Department of Clinical Neuroscience, Karolinska Institutet, Stockholm, Sweden

Mood and anxiety disorders are impairing and costly psychiatric conditions with considerable comorbidity (Chartier et al., 2003) and pathophysiological overlap. In a study in this issue of *EBioMedicine*, Zhao and co-workers (Zhao et al., 2017) show that major depressive disorder (MDD) and social anxiety disorder (SAD) are associated with both common and specific abnormalities in brain morphology, further supporting the pathophysiological overlap between these disorders, but at the same time demonstrating that there are distinct brain mechanisms separating them. The authors reported common reductions in gray matter volume and/or cortical thickness in regions encompassing cortico-striato-thalamo-cortical circuitry and the salience and dorsal attention networks. MDD-specific alterations in cortical thickness were found in regions involved in visual processing and superior frontal cortex, and SAD patients had thinner pre- and postcentral cortices. All participants were medication-naïve, strengthening the conclusion that the gray matter alterations were related to the disorders and not biased by effects of pharmacological treatment.

Surprisingly, Zhao et al. (Zhao et al., 2017) did not replicate findings from large-scale and meta-analytic MDD studies of reduced cortical thickness in the ACC and insular cortex (Schmaal et al., 2017). Rather, the findings were in the opposite direction. This is also surprising given the recent report of reduced gray matter volume in these regions being a common neural substrate across a range of psychiatric disorders including MDD and SAD (Goodkind et al., 2015). The inconsistencies may probably be explained by many different factors including differences in study populations (e.g. non-comorbid and medication-naïve in Zhao et al.). We must also be open for the possibility of spurious findings given the relatively small sample size in Zhao et al., although the authors do safeguard against this as best as possible with a stringent statistical threshold.

The findings from Zhao et al. (Zhao et al., 2017) support the extension of neural models of SAD from fear circuitry and amygdala-centered models to models including additional brain regions and networks such as cortico-striato-thalamic-cortical circuitry and the salience and attention networks. Indeed, there is rather limited evidence of changes in amygdala volume in the SAD literature. It should also be noted that the findings from previous studies investigating gray matter alterations in SAD are mixed and no clear picture has emerged (Brühl et al., 2014). We recently applied pattern recognition on voxel-wise regional gray matter volume (Frick et al., 2014) and found that accurate separation of patients with SAD from healthy controls could only be achieved from the pattern of gray matter volume from the whole brain, not specific regions. Based on these results and the highly variable findings from previous studies using univariate methods, we proposed that gray matter alterations in SAD are best described as diffuse and widespread. However, it should be noted that studies on gray matter alterations in SAD, including our own, have often been small, with only few studies including more than 40 patients, and that the results may further be confounded by methodological heterogeneity, previous medication, and comorbidity. In this respect, the paper by Zhao et al. (Zhao et al., 2017) represents a welcome contribution to the field by investigating two different aspects of brain structure in the same individuals and only including non-comorbid and treatment-naïve patients.

The impact of neuroimaging on clinical psychiatric practice has been very limited, and this will most probably be true also for the study by Zhao et al. However, this might be about to change, as in recent years, machine learning pattern recognition techniques applied to neuroimaging data has produced some interesting findings, including that brain scans may be useful for discriminating between psychiatric disorders (Orrù et al., 2012; Pantazatos et al., 2014) and predict who will respond to treatment (Fu et al., 2013; Månsson et al., 2015). If these findings stand the test of replication and validation in independent samples, clinicians might soon order MRIs to be used in diagnosis and treatment selection. The distinct pattern of gray matter alterations in MDD and SAD found by Zhao et al. (Zhao et al., 2017) indicates that these disorders would be separable by automatic methods, with the caveat that the present results are based on group-level comparisons and not on the individual patient level.

It is not uncommon that patients with SAD develop depressive symptoms, or vice versa, that patients with MDD develop social anxiety symptoms. Taking this into consideration, the current non-comorbid sample may be less representative of the larger population of MDD and SAD patients. Despite the high degree of comorbidity between MDD and SAD, there is a dearth of longitudinal neuroimaging studies, and the chicken-or-egg question of brain alterations in mood and anxiety disorders is still unanswered. By applying a developmental perspective, future studies could examine putative differential trajectories leading to the two diagnostic categories of MDD and SAD and when in the process common and distinct gray matter abnormalities present.

DOI of original article: http://dx.doi.org/10.1016/j.ebiom.2017.06.013.
* Corresponding author at: Department of Psychology, Uppsala University, Box 1225, SE-751 42 Uppsala, Sweden.
E-mail address: andreas.frick@psyk.uu.se.

http://dx.doi.org/10.1016/j.ebiom.2017.06.021

Disclosure

The author declared no conflicts of interest.

References

Brühl, A.B., Delsignore, A., Komossa, K., Weidt, S., 2014. Neuroimaging in social anxiety disorder—a meta-analytic review resulting in a new neurofunctional model. Neurosci. Biobehav. Rev. 47:260–280. http://dx.doi.org/10.1016/j.neubiorev.2014.08.003.

Chartier, M.J., Walker, J.R., Stein, M.B., 2003. Considering comorbidity in social phobia. Soc. Psychiatry Psychiatr. Epidemiol. 38:728–734. http://dx.doi.org/10.1007/s00127-003-0720-6.

Frick, A., Gingnell, M., Marquand, A.F., Howner, K., Fischer, H., Kristiansson, M., Williams, S.C.R., Fredrikson, M., Furmark, T., 2014. Classifying social anxiety disorder using multivoxel pattern analyses of brain function and structure. Behav. Brain Res. 259: 330–335. http://dx.doi.org/10.1016/j.bbr.2013.11.003.

Fu, C.H.Y., Steiner, H., Costafreda, S.G., 2013. Predictive neural biomarkers of clinical response in depression: a meta-analysis of functional and structural neuroimaging studies of pharmacological and psychological therapies. Neurobiol. Dis. 52:75–83. http://dx.doi.org/10.1016/j.nbd.2012.05.008.

Goodkind, M., Eickhoff, S.B., Oathes, D.J., Jiang, Y., Chang, A., Jones-Hagata, L.B., Ortega, B.N., Zaiko, Y.V., Roach, E.L., Korgaonkar, M.S., Grieve, S.M., Galatzer-Levy, I., Fox, P.T., Etkin, A., 2015. Identification of a common neurobiological substrate for mental illness. JAMA Psychiatry 72:305–315. http://dx.doi.org/10.1001/jamapsychiatry.2014.2206.

Månsson, K.N.T., Frick, A., Boraxbekk, C.-J., Marquand, A.F., Williams, S.C.R., Carlbring, P., Andersson, G., Furmark, T., 2015. Predicting long-term outcome of internet-delivered cognitive behavior therapy for social anxiety disorder using fMRI and support vector machine learning. Transl. Psychiatry 5, e530. http://dx.doi.org/10.1038/tp.2015.22.

Orrù, G., Pettersson-Yeo, W., Marquand, A.F., Sartori, G., Mechelli, A., 2012. Using support vector machine to identify imaging biomarkers of neurological and psychiatric disease: a critical review. Neurosci. Biobehav. Rev. 36:1140–1152. http://dx.doi.org/10.1016/j.neubiorev.2012.01.004.

Pantazatos, S.P., Talati, A., Schneier, F.R., Hirsch, J., 2014. Reduced anterior temporal and hippocampal functional connectivity during face processing discriminates individuals with social anxiety disorder from healthy controls and panic disorder, and increases following treatment. Neuropsychopharmacology 39:425–434. http://dx.doi.org/10.1038/npp.2013.211.

Schmaal, L., Hibar, D.P., Sämann, P.G., Hall, G.B., Baune, B.T., Jahanshad, N., Cheung, J.W., van Erp, T.G.M., Bos, D., Ikram, M.A., Vernooij, M.W., Niessen, W.J., Tiemeier, H., Hofman, A., Wittfeld, K., Grabe, H.J., Janowitz, D., Bülow, R., Selonke, M., Völzke, H., Grotegerd, D., Dannlowski, U., Arolt, V., Opel, N., Heindel, W., Kugel, H., Hoehn, D., Czisch, M., Couvy-Duchesne, B., Rentería, M.E., Strike, L.T., Wright, M.J., Mills, N.T., de Zubicaray, G.I., McMahon, K.L., Medland, S.E., Martin, N.G., Gillespie, N.A., Goya-Maldonado, R., Gruber, O., Krämer, B., Hatton, S.N., Lagopoulos, J., Hickie, I.B., Frodl, T., Carballedo, A., Frey, E.M., van Velzen, L.S., Penninx, B.W.J.H., van Tol, M.-J., van der Wee, N.J., Davey, C.G., Harrison, B.J., Mwangi, B., Cao, B., Soares, J.C., Veer, I.M., Walter, H., Schoepf, D., Zurowski, B., Konrad, C., Schramm, E., Normann, C., Schnell, K., Sacchet, M.D., Gotlib, I.H., MacQueen, G.M., Godlewska, B.R., Nickson, T., McIntosh, A.M., Papmeyer, M., Whalley, H.C., Hall, J., Sussmann, J.E., Li, M., Walter, M., Aftanas, L., Brack, I., Bokhan, N.A., Thompson, P.M., Veltman, D.J., 2017. 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 22:900–909. http://dx.doi.org/10.1038/mp.2016.60.

Zhao, Y., Chen, L., Zhang, W., Xiao, Y., Shah, C., Zhu, H., Yuan, M., Sun, H., Yue, Q., Jia, Z., Zhang, W., Kuang, W., Gong, Q., Lui, S., 2017. Gray matter abnormalities in non-comorbid medication-naive patients with major depressive disorder or social anxiety disorder. EBioMedicine http://dx.doi.org/10.1016/j.ebiom.2017.06.013.