

Cortical Volume Abnormalities in Post Traumatic Stress Disorder: an ENIGMA-PTSD Working Study Mega Analysis

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Introduction: Posttraumatic stress disorder (PTSD) affects millions of people globally and is characterized by intrusive memories of a traumatic event, avoidance of trauma-related circumstances, hyper arousal, and negative alterations in mood and cognition (1,2). Previous studies of PTSD report volume abnormalities in multiple regions of the cerebral cortex. However, findings are inconsistent and few address the possibility that PTSD abnormalities may be associated with PTSD symptom severity (3,4,5). Some evidence points to reduced volumes in emotion-related prefrontal limbic, insular, parietal, occipital, and temporal regions (6,7,8). However, these findings remain tentative, possibly due to small sample sizes (9). A better understanding of brain abnormalities that underlie PTSD is needed to help develop more effective treatments.

Objectives: This project's objective was to perform a large multi-cohort mega-analysis to systematically examine all cortical regions for volumetric abnormalities in PTSD patients.

Methods: High resolution T1-weighted brain sMRI scans from 11,690 individuals were acquired by 39 sites worldwide using the standardized protocols developed by ENIGMA. Each hemisphere was divided into 34 cortical regions of interest (ROIs). The measured volumes of these 68 ROIs were used to perform several analyses. After controlling for mean intracranial volume (ICV), a mixed effects model mega-analysis of individual subject data from all cohorts was used to test for: (a) cortical volume differences in each ROI between PTSD and control groups and (b) an association between cortical volume and PTSD severity.

Results: After aggregating and analyzing regional volumes data from 2169 PTSD patients and 8391 controls without PTSD, results indicated significant reductions in volume of 41 of the 68 cortical regions in PTSD patients compared to controls (standardized coefficients = -0.166 to -0.063, FDR corrected P values < 0.048). The regions with, on average, significantly smaller volumes were found in the insular, cingulate, frontal, occipital, temporal, and parietal regions of

the brain. 11 of these 41 regions (Left and right lateral orbitofrontal gyri (LOFG), right rostral middle frontal gyrus, left and right pars orbitalis gyri, right pars triangularis gyrus, left bankssts gyrus, left and right middle temporal gyri, left and right superior parietal gyri (SPG)) were also significantly negatively correlated with PTSD severity (standardized coefficients = -0.094 to -0.060, FDR corrected P values < 0.044).

Conclusion: These results show an association between PTSD and smaller cortical volumes in prefrontal regulatory regions as well as in broader emotion and sensory processing cortical regions. The significant findings for bilateral LOFG and SPG support current thinking on deficits in emotion neurocircuits in PTSD and mirrors previous conclusions about the involvement of sensory processing brain circuits in the pathophysiology of PTSD.

References

1. Kessler, R.C., Aguilar-Gaxiola, S., Alonso, J., Benjet, C., Bromet, E.J., Cardoso, G., Degenhardt, L., de Girolamo, G., Dinolova, R.V., Ferry, F., Florescu, S., Gureje, O., Haro, J.M., Huang, Y., Karam, E.G., Kawakami, N., Lee, S., Lepine, J.P., Levinson, D., Navarro-Mateu, F., Pennell, B.E., Piazza, M., Posada-Villa, J., Scott, K.M., Stein, D.J., Ten Have, M., Torres, Y., Viana, M.C., Petukhova, M.V., Sampson, N.A., Zaslavsky, A.M., Koenen, K.C.. *Trauma and PTSD in the WHO World Mental Health Surveys*. Eur J Psychotraumatol, 2017. **8**(sup5): pp. 1353383. Doi:10.1080/20008198.2017.1353383
2. Rytwinski, N.K., Scur, M.D., Feeny, N.C., Youngstrom, E.A. *The cooccurrence of major depressive disorder among individuals with posttraumatic stress disorder: a meta-analysis*. J Trauma Stress, 2013. **26**: pp. 299–309.
3. Richert, K.A., Carrion, V.G., Karchemskiy, A., Reiss, A.L. *Regional differences of the prefrontal cortex in pediatric PTSD: an MRI study*. Depress Anxiety, 2006. **23**: pp. 17–25.
4. Starcevic, A., Postic, S., Radojicic, Z., Starcevic, B., Milovanovic, S., Ilankovic, A., Dimitrijevic, I., Damjanovic, A., Aksić, M., Radonjic, V. *Volumetric Analysis of Amygdala, Hippocampus, and Prefrontal Cortex in Therapy-Naive PTSD Participants*. Biomed Res Int, 2014. **2014**: pp. 10.1155/2014/968495. Doi:10.1155/2014/968495
5. Lindauer, R.J., Vlieger, E.J., Jalink, M., Olf, M., Carlier, I.V., Majoie, C.B., Den Heeten, G.J., Gersons, B.P. *Effects of psychotherapy on hippocampal volume in out-patients with post-traumatic stress disorder: a MRI investigation*. Psychol Med, 2005. **35**: pp. 1421–31. Doi:10.1017/S0033291705005246
6. Eckart, C., Stoppel, C., Kaufmann, J., Tempelmann, C., Hinrichs, H., Elbert, T., Heinze, H.-J., Kolassa, I.-T. *Structural alterations in lateral prefrontal, parietal and posterior midline regions of men with chronic posttraumatic stress disorder*. J Psychiatry Neurosci, 2011. **36**(3): pp. 176–86.
7. Woodward, S.H., Schaer, M., Kaloupek, D.G., Cediell, L., Eliez, S. *Smaller Global and Regional Cortical Volume in Combat-Related Posttraumatic Stress Disorder*. Arch Gen Psychiatry, 2009. **66**(12): pp. 1373–82. Doi:10.1001/archgenpsychiatry.2009.160
8. De Bellis, M.D., Keshavan, M.S., Frustaci, K., Shifflett, H., Iyengar, S., Beers, S.R., Hall, J. *Superior temporal gyrus volumes in maltreated children and adolescents with PTSD*. Biol Psychiatry, 2002. **51**(7): pp. 544–52. Doi:10.1016/s0006-3223(01)01374-9
9. Liberzon, I., Wang, X., Xie, H. *Brain structural abnormalities in posttraumatic stress disorder and relations with sleeping problems*. In: Vermetten, E., Germain, A., Neylan, T.C., editors. *Sleep and combat-related post traumatic stress disorder*. New York, NY, USA: 2018, Springer-Verlag. pp. 145–68.