# Consequences of Post-Traumatic Stress Disorder on Cortical Thickness: an ENIGMA-standardized Mixed Effect Model Study Mega-Analysis

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**Background:** Post-traumatic stress disorder (PTSD) affects millions of people around the world (1). The condition is characterized by intrusive memories of the traumatic event(s), avoidance of trauma-related circumstances, hyperarousal, negative alterations in mood and cognition, and comorbidity with depression and other psychiatric conditions (2,3). Despite available pharmacological and behavioral treatments, personal suffering associated with PTSD along with persistent residual symptoms and functional impairments lead to significant financial and societal costs (4,5). Previous PTSD studies using structural magnetic resonance imaging (sMRI) report cerebral cortical gyrus thinning, however these results are inconsistent and unreliable. This may be attributed to an insufficient number of subjects in each individual study.

**Objective:** The goal of the current study was to utilize mega-analysis of data from many different sites and studies to produce more robust and reproducible results to help elucidate the impact of PTSD on the thickness of various cortical regions.

**Methods:** Data for T1-weighted high resolution sMRI of 68 cortical regions across both brain hemispheres were provided by contributing laboratories. Processing was completed using ENIGMA Consortium standardized protocols (6). A total of 11,801 subjects from 43 study sites globally were included. There were 2,466 PTSD (age=39.1±13.4, F/M=1,008/1,458) and 9335 control (age=48.1±14.1, F/M=4,485/4850) subjects across 57 and 55 cohorts, respectively. Current PTSD diagnosis was determined according to Diagnostic and Statistical Manual of Mental Disorders (DSM) IV or V criteria. A mixed effects model mega-analysis controlled for mean cortical thickness of individual subject data from all cohorts was used to test for gyral thickness differences between PTSD and control subjects. Differences in cortical thickness between PTSD subjects and control subjects who experienced a traumatic event but were not diagnosed with PTSD (trauma control) were also explored via these methods.

 

**Results:** When compared to their control counterparts, people diagnosed with PTSD were found to have significant cortical thinning of the left posterior cingulate gyrus and the right lingual gyrus. Also found was significant thinning of the right lingual gyrus when comparing PTSD to trauma control subjects. There were no significant changes found in any of the remaining cortical regions when comparing PTSD to general control or trauma control subjects.

**Conclusion:** Based on the results of this mega-analysis, PTSD has a significant effect on cortical thickness in multiple areas of the brain. These changes highlight the potential negative physiological effects that PTSD can have on people.

**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): p. 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. Spinhoven, P., Penninx, B.W., van Hemert, A.M., de Rooij, M., Elzinga, B.M. *Comorbidity of PTSD in anxiety and depressive disorders: prevalence and shared risk factors*. Child Abus Negl, 2014. **38**: pp.1320–30.

4. Kessler, R.C. *Posttraumatic stress disorder: the burden to the individual and to society*. J Clin Psychiatry, 2000. **61**(Suppl 5): pp. 4–12.

5. Andrews, G., Issakidis, C., Sanderson, K., Corry, J., Lapsley H. *Utilizing survey data to inform public policy: comparison of the cost-effectiveness of treatment of ten mental disorders*. Br J Psychiatry, 2004. **184**: pp. 526–33.

6. Wang, X., Xie, H., Chen, T., Cotton, A.S., Salminen, L.E., Logue, M.W., Clarke-Rubright, E.K., Wall, J., Dennis, E.L., O'Leary, B.M., Abdallah, C.G., Andrew, E., Baugh, L.A., Bomyea, J., Bruce, S.E., Bryant, R., Choi, K., Daniels, J.K., Davenport, N.D., Davidson, R.J., DeBellis, M., deRoon-Cassini, T., Disner, S.G., Fani, N., Fercho, K.A., Fitzgerald, J., Forster, G.L., Frijling, J.L., Geuze, E., Gomaa, H., Gordon, E.M., Grupe, D., Harpaz-Rotem, I., Haswell, C.C., Herzog, J.I., Hofmann, D., Hollifield, M., Hosseini, B., Hudson, A.R., Ipser, J., Jahanshad, N., Jovanovic, T., Kaufman, M.L., King, A.P., Koch, S.B.J., Koerte, I.K., Korgaonkar, M.S., Krystal, J.H., Larson, C., Lebois, L.A.M., Levy, I., Li, G., Magnotta, V.A., Manthey, A., May, G., McLaughlin, K.A., Mueller, S.C., Nawijn, L., Nelson, S.M., Neria, Y., Nitschke, J.B., Olff, M., Olson, E.A., Peverill, M., Phan, K.L., Rashid, F.M., Ressler, K., Rosso, I.M., Sambrook, K., Schmahl, C., Shenton, M.E., Sierk, A., Simons, J.S., Simons R.M., Sponheim, S.R., Stein, M.B., Stein, D.J., Stevens, J.S., Straube, T., Suarez-Jimenez, B., Tamburrino, M., Thomopoulos, S.I., van der Wee, N.J.A., van der Werff, S.J.A., van Erp, T.G.M., van Rooij, S.J.H., van Zuiden, M., Varkevisser, T., Veltman, D.J., Vermeiren, R.R.J.M., Walter, H., Wang, L., Zhu, Y., Zhu, X., Thompson, P.M., Morey, R.A., Liberzon, I . *Cortical volume abnormalities in posttraumatic stress disorder: an ENIGMA-psychiatric genomics consortium PTSD workgroup mega-analysis*. Mol Psychiatry, 2021. **26**(8): pp.4331–4343.

 