RESEARCH SUMMARY

Amygdala-Hippocampal Connectivity Changes During Acute Psychosocial Stress: Joint Effect of Early Life Stress and Oxytocin.
Fan, Y., Petske, K., Feeser, M., Aust, S., Pruessner, J.C., Boker, H., Bajouj, M. And Grimm, S. *Neuropsychopharmacology* (2015), 40, 2736-2744.

The amygdala is a distinct neuro-anatomical structure located deep in the temporal lobes of the brain; one of its functions is to process emotional information and it is the core fear centre of the brain. There are left and right amygdalae in the brain. The hippocampus is a sea-horse-shaped structure in the left and right medial temporal lobe of the brain; it responds to, and processes, stress information. Long-term traumatic stress is associated with atrophy of the hippocampus and as the cells die it reduces in size. The hippocampus contains a high density of glucocorticoid receptors. The amygdala is located next to one end of the hippocampus. Both the amygdala and hippocampus are believed to work in concert for processing emotion, fear and stress.

Early life stress (ELS) is a cumulative reaction to adverse social experiences; these can be physical, sexual, and emotional abuse (EA) as well as physical neglect experienced in early life. ELS leads to a dysregulation of cortisol handling, and to psychosocial stress in later adult life. Oxytocin is a neuropeptide hormone that facilitates trust and attachment between individuals. It modulates the human fear response and has a calming effect.

This study had two aims: 1) to analyse the effect of experimental stress-induced changes in the amygdala connectivity; 2) to investigate the effect of ELS and oxytocin on stress-induced amygdala functional connectivity. Connectivity can be understood as the nerve pathways between different regions in the brain (e.g. between the amygdala and the hippocampus); they are analogous to patterns of wiring in a computer between the electronic input, the processors, the memory, and the output devices; amygdala functional connectivity to the hippocampus is comparable with a computer instruction from a processor that activates an output device e.g. a printer.

31 males with ages between 21-37 years were finally selected from a sample of 541 males. The study method used double-blind, placebo-controlled, within-subject cross-over tests for observing the effect of oxytocin given intranasally – this means that each individual tested received both treatments, i.e. both oxytocin and placebo, and neither they, or their ‘testers’ knew what they were receiving. Psychosocial stress was performed through challenging mental arithmetic tests. Cortisol samples were obtained from the saliva of the subject before and after the psychosocial stress. The brain functional connectivity pattern for the amygdala was measured using fMRI (functional Magnetic Resonance Imaging). All results were analysed statistically to identify statistically significant differences.

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An important point to stress is that EA (emotional abuse) in this population sample shows a graded increase from a low of 5 units to a high of 23 units of measurement of the degree of self-assessed abuse. In many previous papers by contrast, EA is simply divided only into two groups: those without abuse, compared with those who had been abused. The results in this paper showed that with the placebo controls (no oxytocin treatment), as the measure of EA increased in the population sample, there was a stronger stress-induced functional connectivity between the amygdalae and hippocampus. In contrast, with oxytocin administration there was no significant correlation between EA and stress-induced changes between the amygdala and the hippocampus. Similarly, as the cortisol stress response increased, the stress-induced-connectivity shift between the right amygdala and the right hippocampus decreased during oxytocin treatment but not with the application of the placebo.

In summary, the changed functional connectivity in the amygdala and hippocampus caused by psychosocial stress, in those who received high emotional abuse in childhood, is not reduced by oxytocin. In other words, the normal stress-reducing effect of oxytocin is cancelled out by high early life stress. What the experiment shows is that in people who had high levels of emotional abuse in early life, and who were subjected to psychosocial stress as adults, their brain-coping mechanisms were resistant to the action of the natural stress-modulator oxytocin. Dr P M Dean

Website: http://www.whataboutthechildren.org.uk
What About The Children? (***WATCh?***)**:** Company No. 5252973 - Reg. Charity No. 1108816
Registered Office: Feldon House, Chapel Lane, Newbold on Stour CV37 8TY **Tel:** 0845 602 7145