

Functional imaging genetics of neural circuits for social cognition

Speaker: Andreas Meyer-Lindenberg
National Institute of Mental Health, NIH

Social skills are essential for survival in primates and are likely a driving force in brain evolution. However, little is known about specific genetic influences on social behavior and the neural circuits that mediate them. Dr. Meyer-Lindenberg has been applying different neuroimaging techniques to investigate those influences in humans. Particularly, he has studied participants with Williams syndrome (WS) -caused by an infrequent microdeletion of some 28 genes on chromosome 7q11.23-, which show a unique hypersociability combined with increased non-social anxiety. Using fMRI, he found reduced amygdala activation in individuals with WS for threatening faces but increased activation for threatening scenes, relative to matched normal controls. Furthermore, activation and interactions of prefrontal regions linked to amygdala, especially orbitofrontal cortex, were abnormal, suggesting a genetically controlled neural circuitry for regulating human social behavior. Dr. Meyer-Lindenberg has also studied the effects of prosocial neuropeptides, such as oxytocin, on this circuit. Oxytocin is a key mediator of complex emotional and social behaviors that increases trust in humans, suggesting amygdala involvement. He found that compared to placebo, oxytocin potently reduces activation of the amygdala in healthy males exposed to fear-inducing visual stimuli, and disrupts connections to brainstem regions implicated in autonomic and behavioral manifestations of fear. These results indicate that human amygdala function is strongly modulated by oxytocin and provides a potential rationale for therapeutic strategies in disorders associated with abnormal amygdala function, such as social phobia or autism. Individuals with the short allele of the serotonin transporter gene (5-HTTLPR S) have reduced expression of the transporter and appear to be at higher risk for developing depression following stressful life events. Recently, Meyer-Lindenberg and collaborators showed gray matter volume reductions in the subgenual cingulate region of 5-HTTLPR S carriers and functional uncoupling of anterior cingulate-amygdala connections necessary for extinction of negative affect. These findings provide a model for the effect of interactions between genetic risks and environmental stress in a specific neural circuit implicated in depression. Finally, Dr. Meyer-Lindenberg presented his MRI investigations on a large sample of healthy human volunteers looking at brain effects of a common functional polymorphism that also impacts on the 5-HT system, and has been previously associated with impulsive aggression (allelic variation in the X-linked monoamine oxidase A [MAOA] gene). He found that compared with the high expression allele, subjects carrying the low expression allele –associated with increased risk of violent behavior- showed changes in limbic circuitry for emotion regulation and cognitive control that may be involved in the association of MAOA with impulsive aggression. These data suggest neural systems-level effects of X-inactivation in human brain, and point toward potential targets for a biological approach toward violence. To conclude, Dr. Meyer-Lindenberg seeks to convince the audience that “social imaging genetics” is a feasible enterprise that can use single gene mechanisms and small deletion syndromes to help understand what underlies complex social behavior and its neuronal correlates in human brain.