Selected references – Patrick Fisher

Fisher, P. M. & Hariri, A. R. (2013). Identifying serotonergic mechanisms underlying the corticolimbic response to threat in humans. *Philosophical Transactions of the Royal Society.B: Biolological Sciences, 368,* 20120192.
Notes: A corticolimbic circuit including the amygdala and medial prefrontal cortex (mPFC) plays an important role in regulating sensitivity to threat, which is heightened in mood and anxiety disorders. Serotonin is a potent neuromodulator of this circuit; however, specific serotonergic mechanisms mediating these effects are not fully understood. Recent studies have evaluated molecular mechanisms mediating the effects of serotonin signalling on corticolimbic circuit function using a multi-modal neuroimaging strategy incorporating positron emission tomography and blood oxygen level-dependent functional magnetic resonance imaging. This multi-modal neuroimaging strategy can be integrated with additional techniques including imaging genetics and pharmacological challenge paradigms to more clearly understand how serotonin signalling modulates neural pathways underlying sensitivity to threat. Integrating these methodological approaches offers novel opportunities to identify mechanisms through which serotonin signalling contributes to differences in brain function and behaviour, which in turn can illuminate factors that confer risk for illness and inform the development of more effective treatment strategies
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Fisher, P. M., Holst, K. K., Mc, M. B., Haahr, M. E., Madsen, K., Gillings, N. et al. (2012). 5-HTTLPR status predictive of neocortical 5-HT4 binding assessed with [1)C]SB207145 PET in humans. *NeuroImage, 62,* 130-136.
Notes: Serotonin (5-HT) is a neuromodulator affecting myriad aspects of personality and behavior and has been implicated in the pathophysiology of affective disorders including depression and anxiety. The 5-HTTLPR is a common genetic polymorphism within the promoter region of the gene coding for the serotonin transporter such that the S allele is associated with reduced transcriptional efficacy compared to the L allele, potentially contributing to increased serotonin levels. In humans, this genetic variant has been linked to inter-individual variability in risk for affective disorders, related aspects of personality and brain function including response to threat. However, its effects on aspects of serotonin signaling in humans are not fully understood. Studies in animals suggest that the 5-HT 4 receptor (5-HT(4)) shows a monotonic inverse association with long-term changes in serotonin levels indicating that it may be a useful measure for identifying differences in serotonergic neurotransmission. In 47 healthy adults we evaluated the association between 5-HTTLPR status and in vivo 5-HT(4) receptor binding assessed with [(11)C]SB207145 positron emission tomography (PET). We observed a significant association within the neocortex where [(11)C]SB207145 binding was 9% lower in S carriers compared to LL homozygotes. We did not find evidence for an effect of season or a season-by-5-HTTLPR interaction effect on regional [(11)C]SB207145 binding. Our findings are consistent with a model wherein the 5-HTTLPR S allele is associated with relatively increased serotonin levels. These findings provide novel evidence supporting an effect of 5-HTTLPR status on serotonergic neurotransmission in adult humans. There were no indications of seasonal effects on serotonergic neurotransmission