The impact of functional neuroimaging studies to reveal endophenotypes and predisposition to development of mood disorders

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The serotonergic transmitter system is known to be involved in a large variety of psychophysiological functions, including feeding, mood, aggression and pain. Serotonin is also a critical neurotransmitter in the generation and regulation of emotional behaviour and it plays a prominent role in the inhibition of impulses. The research presented in this lecture focuses on the neural bases of personality dimensions that predispose individuals to affective disorders, with special emphasis on the serotonergic neurotransmitter system.

We have for the first time demonstrated that the presence of a receptor or transporter is highly genetically determined. In support of this, several papers have now reported that the triallelic form of the polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) is associated with in vivo SERT binding in the brain. Recently, the 5-HTTLPR has been associated with seasonality in healthy individuals; we have corroborated and extended this finding and found that the number of daylight minutes at the time of scanning correlated negatively with SERT binding in the putamen and the caudate nucleus. Furthermore, in the putamen, we found a significant gene*daylight effect, such that there was a negative correlation between 5-HTT binding and daylight minutes in carriers of the short 5-HTTLPR allele, but not in homozygote carriers of the long allele. Our findings are in line with S-carriers having an increased response in neural circuits involved in emotional processing to stressful environmental stimuli, but here demonstrated as a endophenotype with dynamic changes in serotonin reuptake.

It is recognized that depression results from an interaction between genetic liability and environmental risk factors such as stressful life events. Different personality profiles are also considered as risk factors for affective disorder. In healthy individuals certain personality characteristics are linked to higher frontolimbic 5-HT₁A receptor binding. It has now been shown that elevated cortical 5-HT₁A and decreased serotonin transporter binding is present in subjects at high risk for developing mood disorders, by comparing regional 5-HT₁A receptor binding and serotonin transporter binding in twins at high risk to twins at low risk of developing mood disorders. High-risk individuals had a high correlation between neuroticism and frontolimbic 5-HT₁A receptor binding and secondly, that monozygotic twins at high risk have reduced SERT binding in dorsolateral prefrontal cortex similar to what has been observed in human postmortem studies of depressed patients.

References