phobia itself and not to the presence of concurrent personality disorders.

Eighteen subjects with social phobia and 18 controls were investigated with positron emission tomography and the radiolabeled serotonin precursor, [3-11C]-5-HTP (5-HTP). Individuals with social phobia demonstrated proportionally lower regional relative whole-brain accumulation of 5-HTP in areas of the frontal and temporal cortices as well as the striatum, but higher accumulation in the cerebellum. This suggests that there are imbalances in presynaptic serotonin function in individuals with social phobia, although this could only be confirmed in men, and not in women.

By means of a postal survey, distributed to 2000 randomly selected individuals, social phobia in Sweden was found to be common, with a point prevalence of 15.6%.

Importance of serotonin-related candidate genes for human behaviour

Jonas Melke
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Family and twin studies have been consistent in demonstrating that genetic factors are involved in the etiology of most major psychiatric disorders, as well as in various normal personality traits. Mostly due to the efficacy of serotonin-acting drugs, such as selective serotonin reuptake inhibitors (SSRI) and tricyclic antidepressants (TCA), the neurotransmitter serotonin has been implicated in a variety of common psychiatric disorders, including depression, a spectrum of anxiety disorders and premenstrual dysphoria; moreover, some studies have suggested that also personality is influenced by serotonin.

The overall purpose of the studies presented in this thesis was to explore the possible influence of a variety of serotonin-related genes on: 1) normal personality traits, 2) eating behavior, and 3) two psychiatric disorders known to respond markedly to SSRIs, i.e. panic disorder and premenstrual dysphoria.

Observations show: 1) a previously suggested association between a promoter-region polymorphism (5-HTTLPR) in the serotonin transporter gene (SERT) and anxiety-related personality traits could be further substantiated. This relationship was observed in middle-aged women assessed with the personality questionnaire Karolinska Scales of Personality. 2) A recently identified polymorphism in the gene encoding the serotonin receptor 5-HT3 (HTR3A) was found to be associated with the personality trait harm avoidance, as assessed with the Temperament and Character Inventory. This association was observed in two independent samples of middle-aged women recruited from the normal population. 3) A functional effect of the 5-HTTLPR was supported by investigating the association between genotype and the expression of the serotonin transporter in human platelets. 4) An amino acid substitution (Cys23Ser) in the gene encoding the serotonin receptor 5-HT2C (HTR2C), was found to be associated with weight loss, and possibly also with anorexia nervosa, in teenage girls. 5) In association studies, polymorphisms in several serotonin-related genes were investigated in panic disorder patients and patients with premenstrual dysphoria. None of the investigated polymorphisms was found to be associated with these disorders.

Our results lend support for an involvement of the SERT gene in the regulation of anxiety-related personality traits. The observed association between the HTR3A polymorphism and harm avoidance supports the notion that this personality trait is influenced by serotonin, and suggests that this influence may partly be mediated by 5-HT3 receptors. Our finding that the Cys23Ser polymorphism in the HTR2C could be associated with weight loss supports the suggested influence of this receptor subtype on eating behavior. The positive findings regarding personality traits contrast to the lack of association between serotonin-related genes and psychiatric disorders, such as panic disorder and premenstrual dysphoria. Tentatively, this discrepancy suggests that, for evolutionary reasons, it is less likely for a single common polymorphism to be of major importance for the etiology of psychiatric disorders, than for a normal trait that is not the subject of evolutionary pressure.

Thoughts and what gets in-between

Jan Nielsen
Doctoral dissertation, Department of Psychology, Faculty of Health Science, University of Copenhagen, Copenhagen, Denmark

This Ph.D. dissertation—a part of The Copenhagen Prodromal Study—is a theoretical and empirical investigation of the relation between formal thought disorder and the schizophrenic spectrum. The main thesis of the dissertation is that through formal thought disorder one obtains a better demarcation and identification of schizophrenic states, and that formal thought disorders are particularly valuable as indicators