

Tourettesyndrome: From the clinical picture to neuroimaging studies

Foredrag torsdag d. 1.2. kl. 15.30-16.30 i auditorium 93 på Rigshospitalet af dr. med. Kirsten Müller-Vahl

Kirsten R Müller-Vahl, Department of Clinical Psychiatry and Psychotherapy, Medical School Hannover, Carl-Neuberg-Str. 1, D-30625 Hannover, Germany, Telephone: +49-511-5323167, Fax: +49-511-5323187, e-mail: mueller-vahl.kirsten@mh-hannover.de

Gilles de la Tourette-Syndrome (Tourette-Syndrome, TS) is a complex neuropsychiatric spectrum disorder characterized by multiple waxing and waning motor and one or more vocal tics, onset before age 21. In many cases behavioral problems are associated. Dopamine receptor antagonists are considered the first-line pharmacotherapy for tics.

Between 1995 and 2004 we investigated 480 patients attending our TS outpatient department. Tic severity (STSS) was very mild to moderate in more than 2/3 of patients, marked to very severe in less than 1/3. Associated behavioral symptoms were seen in the majority of patients: obsessive-compulsive behavior (OCB) (80.0%), anger control problems (61.5%), self-injurious behavior (44.5%), attention deficit disorder (42.9%), anxiety disorder (37.5%), hyperactivity (30.8%), mood disorder (25.6%), sleeping problems (23.3%), and addiction (12.3%). The mean comorbidity score was 2.7. 12.7% had a "TS only". STSS and comorbidity score correlated significantly.

Pathologically there is strong evidence that structural disturbances of the basal ganglia and cortical frontal areas are involved. However, findings from in vivo imaging studies have provided conflicting results. We investigated 19 unmedicated men with "TS only" and 20 male control subjects using voxel-based morphometry (VBM) and voxel-based magnetization transfer imaging (MTI) to investigate differences in grey (GM) and white matter (WM). Our results demonstrated reduced GM volumes in the left caudate nucleus, the cingulate gyrus, the left postcentral gyrus, and different frontal cortices. For WM volumes, there were changes in right and left frontal areas, and the medial corpus callosum. Using MTI reductions in frontal cortices and the right cingulate gyrus were seen. These data further support the hypothesis of an involvement of cortico-striato-pallido-thalamo-cortical circuits in TS pathology.

Pathophysiologically increased dopaminergic neurotransmission has been hypothesised to play a role in the pathophysiology of TS. We investigated striatal dopamine transporter binding in 12 TS patients using SPECT and 123I-beta-CIT. We found significantly higher relative striatal activity ratios in TS compared to normal controls. In addition, we found decreased specific radiotracer binding to serotonin transporters (SERT) of the hypothalamus midbrain region in TS patients with OCB. Moreover, a negative correlation between the severity of OCB and the degree of SERT binding was detected. Our results, therefore, suggest not only an involvement of the dopaminergic system in TS pathology, but also an impairment of the serotonergic system.

References.

Müller-Vahl KR. The treatment of Tourette's syndrome: current opinions. *Expert Opin Pharmacother* 2002;3:899-914

Müller-Vahl K, Makowski L, Geomelas M, Emrich H, Kolbe H. Klinische Symptome des Tourette-Syndroms: eine prospektive Studie bei 480 Patienten. *Aktuelle Neurologie* 2005;32:S147.

Müller-Vahl KR, Berding G, Brücke T, Kolbe H, Meyer GJ, Hundeshagen H, Dengler R, Knapp WH, Emrich HM. Dopamine transporter binding in Gilles de la Tourette-Syndrome. *J Neurol* 2000;247:514-520

Müller-Vahl KR, Meyer GJ, Knapp WH, Emrich HM, Gielow P, Brucke T, Berding G. Serotonin transporter binding in Tourette Syndrome. *Neurosci Lett*. 2005;385(2):120-5.

Peschel T, Kaufmann J, Dengler R, Bodammer N, Emrich H, Müller-Vahl K. In vivo Neuropathologie bei Patienten mit Tourette-Syndrom: Ergebnisse von voxelbasierter Morphometrie, Magnetisierungstransfer und Diffusions-Tensor-Imaging. *Aktuelle Neurologie* 2005;32:S147.