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Letter to the editor

Olfactory deficits in deletion syndrome 22q11.2

Deletion syndrome 22q11.2 (DS22q11) is a high risk factor for psychosis and dopaminergic dysregulation due to haploinsufficiency of the Catechol-O-Methyl-Transferase gene (*COMT*) is suggestive to underlie the increased disposition to neuropsychiatric disorders (Bassett et al., 2007; Boot et al., 2008; Debbané et al., 2006). Olfactory function is modulated by dopaminergic neurotransmission in the olfactory bulb and alterations in olfactory perception have consistently been identified in neuropsychiatric disorders that have been related to dysregulation in the dopamine system, such as Parkinson's disease, attention deficit-/hyperactivity disorder and schizophrenia (Mesholam et al., 1998; Moberg et al., 2006; Romanos et al., 2008). Deficient olfactory identification has previously been reported in children with DS22q11 (Sobin et al., 2006) and the Met allele of *COMT* negatively affected the performance of olfactory identification in 18 adults with DS22q11 (Bassett et al., 2007). Whereas the reported alterations in olfactory identification involve activation of higher cortical areas such as the orbitofrontal cortex, early processes of olfactory function (sensitivity and discrimination) primarily related to function of the olfactory bulb and piriform cortex have yet not been assessed in DS22q11 (Brand, 2006). Hypothesizing that disturbance of the dopaminergic system is reflected by alterations in olfactory function we further investigated early processes of olfaction (sensitivity and discrimination) in DS22q11. We applied a validated olfactory testing instrument ("Sniffin Sticks", Burghart Instruments, Wedel, Germany) assessing olfactory sensitivity, discrimination and identification in 27 non-psychotic children and adolescents with DS22q11 and 27 healthy controls. Details on the procedure and validation on the Sniffin Sticks have been published elsewhere (Hummel et al., 2007). Groups did not differ significantly in age and gender, but did differ in regard to IQ (Table 1). We recruited patients during family meetings organized by the self-help group "KIDS-22q11 e.V.". The study was approved by the Ethics Committee of the University of Wuerzburg (study number 130/07). All participants and their legal guardians gave informed, written consent. Participants were screened for neuropsychiatric disorders via Child Behavior Checklist (Achenbach, 1991) and further instruments assessing intelligence, ADHD and depressive symptoms. Parents filled in a questionnaire retrieving anamnestic data on previous somatic and psychiatric diagnoses. None of the participants was using nicotine. None of the controls exceeded the clinical threshold of the CBCL.

We identified global olfactory deficits in the DS22q11 group with high effect sizes for all three olfactory domains; controlled by analyses of covariance IQ differences between groups did not confound our results ($F>4.72$; $df=1,51$; $p<.03$). Results remained significant when adjusting for age, sex, velopharyngeal insufficiency, otorhinolaryngologic problems, psychiatric comorbidity, methylphenidate medication or clinical scores (CBCL, ADHD, and depression) ($F>4.72$; $df=1,49$; $p<.04$), except for the CBCL overall score regarding olfactory sensitivity ($F=1.77$; $df=1,49$; $p=.19$). Correlation analyses of CBCL with sensitivity indicated a significant association in the group of patients ($r=-.417$; $n=25$, $p=.04$), but not in controls ($r=0.017$; $n=27$; $p=0.93$). Higher CBCL total scores were associated with diminished olfactory sensitivity in patients supporting the notion that higher levels of psychopathology are associated with more pronounced alterations in the olfactory system in DS22q11.

Converging evidence implies disturbed olfactory function as a salient feature of neuropsychiatric disorders, such as schizophrenia, possibly related to dopamine metabolism. We hypothesized that altered dopaminergic neurotransmission in DS22q11 affected olfactory performance and expected to find impairments in all olfactory domains. Our current finding further supports previous evidence implicating dopaminergic dysregulation in aberrant olfactory function. Based on the assumption that the dopamine system is dysregulated and may be one causal factor for the high incidence of psychosis in DS22q11, olfactory dysfunction may be a promising candidate as a biomarker of increased psychiatric vulnerability in the syndrome.

Table 1
Sample characteristics of patient and control sample matched for age and sex. Olfactory function [Sniffin Sticks scores] and statistics for both samples (mean scores ± standard deviations).

	Patients	Controls	Student t-test/χ^2/ (Cohen's d)
N	27	27	–
Age [years; months] (age range)	10;5 ± 2;7 (6;6–16;4)	11;0 ± 1;11 (8;5–17;0)	T = 0.81; df = 52; P = .42
Sex (f/m)	8/19	7/20	$\chi^2 = 0.09$; df = 1; P = .76
IQ	80 ± 17	107 ± 12	T = 6.55; df = 52; P < .01
CBCL (total t-score)	64.08 ± 9.05 (n = 25)	48.67 ± 5.38	T = −7.54; df = 50; P < .01
General ADHD symptoms[a]	1.00 ± 0.51 (n = 24)	0.30 ± 0.23 (n = 26)	T = −6.37; df = 48; P < .01
Depressive symptoms[a]	48.96 ± 9.95 (n = 26)	42.89 ± 8.00	T = −2.45; df = 51; P = .02
Sensitivity	5.19 ± 3.36	8.41 ± 2.39	T = 4.05; df = 52; P < .01 (1.102)
Discrimination	8.44 ± 2.46	11.22 ± 1.95	T = 4.61; df = 52; P < .01 (1.254)
Identification	8.78 ± 2.74	11.30 ± 1.90	T = 3.93; df = 52; P < .01(1.070)

[#]Cohen's d above 0.8 indicates a high clinical or practical relevant effect.
[a] Measured by the "Fremdbeurteilungsbogen für ADHS" and "Depressionsinventar für Kinder und Jugendliche", references available upon request.

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