22q11.2 deletion and increased risk of schizophrenia in children and adolescents

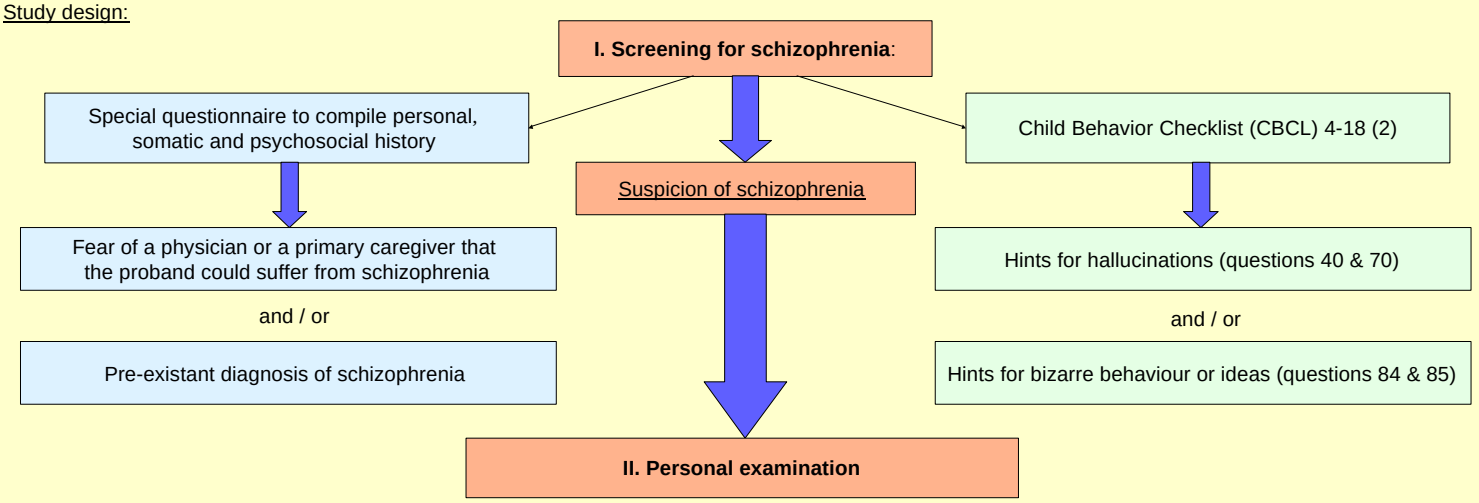
Wolfgang Briegel[1] und Marco Schneider[2]

[1]Department of Child and Adolescent Psychiatry and Psychotherapy, Leopoldina Hospital, Schweinfurt, Germany, e-mail: wbriegel@leopoldina.de;
[2]Department of Psychiatrie, Justus-Liebig-University, Giessen, Germany

Objective:
22q11.2 deletion [del.22q11.2] is the most frequent microdeletion in humans with an estimated occurrence of approximately 1 in 4,000 life births. Patients can show a variety of somatic symptoms, especially characteristic facial dysmorphia, congenital heart defects, thymic hypo- or aplasia, and velopharyngeal dysfunction with or without cleft palate. Developmental delays of psychomotor functions and language are very common, and about 40-50% of the affected individuals are mentally retarded (IQ < 70). Furthermore, the deletion seems to be one of the most important risk factors for schizophrenia. Until now, increased prevalence rates of this disorder have been well documented for adults, but not for children and adolescents with del.22q11.2 (1). Therefore, the aim of this study was to investigate whether there is an increased risk of schizophrenia for this age group.

Method:
Probands:
With support of the German 22q11.2 deletion syndrome foundation, KiDS-22q11, the primary caregivers of all known subjects aged 8-17 years (n=49) were anonymously asked to fill out questionnaires. The primary caregiver of another subject with del.22q11.2 could be recruited by an outpatient clinic.

Study design:



Statistical analysis:
CBCL-results were analyzed using SPSS 12.0 (Mann-Whitney-U-Test), statistical significance was defined as $p<0.05$.

Results:
Probands:
29 / 50 primary caregivers (58%) sent back filled-out questionnaires. The study comprises 8 females and 21 males aged 8 – 16 years (mean: 11.2 years). The deletion had been diagnosed in all patients by fluorescence in situ hybridization [FISH] (age range: 1 week –14 years).

Somatic problems:

Congenital heart defect	26/29	Immune deficiency	13/29
Velopharngeal insufficiency / cleft palate	11/29	Hearing loss	11/29
Seizures	9/29	Hypocalcemia	7/29

Areas of developmental delay:

Motor	20/29
Language and speech	18/29
Cognition	24/26 (missing data: 3)

I. Screening for schizophrenia:

14 year old boy with known schizophrenia ⟷ 14 year old boy with known schizophrenia, and 16 year old mentally retarded girl

Case report:
Paranoid schizophrenia; age of onset: 12 years; diagnosis of del.22q11.2 at the age of 14 years. No congenital heart defect, but typical facial signs of the deletion, and hypocalcemia.

CBCL 4-18 (2):
Significantly higher t-values could be found for these two probands when compared to the other subjects of this study for the subscales “withdrawn” ($p=0.005$), and “thought problems” ($p=0.010$).

II. Personal examination:
Only the 14 year old boy with already diagnosed paranoid schizophrenia could be examined personally. According to CASCAP-D (3) he showed: hyperexcitability; generalized anxiety; persisting optic halluzinations; and cognitive deficits despite of neuroleptic medication (quetiapine). Standardized testing (e.g. intelligence tests) could not be done because of the severity of his psychiatric disorder. He met ICD-10 criteria for a schizophrenic residuum.

Conclusions:
About 10% of schizophrenic disorders seem to have an onset before the age of 17 (4). Taking this into account, according to our results, the prevalence of schizophrenia among children and adolescents with del.22q11.2 could be 20 times as high as in the general age group. There are some limitations of this study: quite low response rate, missing representativeness, lack of objective informations about intellectual capacities of participants, and impossibility of personal examination of the second adolescent with a possible schizophrenic disorder. Nevertheless, the results of this study indicate that children and adolescents with del.22q11.2 should be carefully screened for symptoms of schizophrenia at regular intervalls.

References:
1. Briegel, W. & Cohen, M.: Das 22q11.2-Deletionssyndrom und seine Relevanz für die Kinder- und Jugendpsychiatrie. Z Kinder Jugendpsychiatr Psychother. 2004, 32(2),107-15
2. Achenbach, T.M.: Manual for the Child Behavior Checklist/4-18 and 1991 Profile. Burlington, VT: University of Vermont, Department of Psychiatry, 1991.
3. Döpfner, M., Berner, W., Flechtner, H., Lehmkuhl G. & Steinhausen, H.C.: Psychopathologisches Befund-System für Kinder und Jugendliche (CASCAP-D): Befundbogen, Glossar und Explorationsleitfaden. Göttingen: Hogrefe, 1998.
4. Remschmidt, H.: Zur Neurobiologie schizophrener Erkrankungen im Kindes- und Jugendalter. In: H. Remschmidt (Hrsg.): Schizophrene Erkrankungen im Kindes- und Jugendalter. Stuttgart-New York: Schattauer-Verlag, 2004.

Acknowledgement: The authors want to thank KiDS-22q11 and all parents who participated in this study.