Psychiatric disorders associated with 22q11.2 deletion syndrome

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Several psychiatric disorders have been associated with 22q11.2 deletion syndrome (22q11.2DS) also known as VeloCardioFacial Syndrome (VCFS) or Di George Syndrome. The identification of the cause of 22q11.2DS dates back to more than twenty years ago and since then, a substantial number of papers have been written on the association between VCFS and psychiatric disorders.[1]

The most frequent psychiatric disorders associated with 22q11.2DS are schizophrenia-like psychoses and their risk has been reported even up to 25 times than in general population. Among 22q11.2DS children, frequent diagnoses are autism-spectrum disorders and attention deficit/hyperactivity disorders, in adolescents and adults about 30% develop schizophrenia-like psychoses. The close association between 22q11.2DS and schizophrenia-like psychoses, has been considered as an excellent model to better understand brain dysfunction, social cognition, psychotic symptoms and cognitive and behavioral impairments.

The disease has similar prevalence and developmental patterns across countries. Data from an Israel and Switzerland large sample of 22q11DS, show that the average age at onset of schizophrenia-like psychoses ranges from19 to 26 years.[2] Moreover, psychotic-like symptoms were observed in almost one third of 22q11DS adolescents. Knowing the high risk for schizophrenia-like psychosis in 22q11.2DS subjects, the early identification of who will develop psychosis would be crucial for therapeutic programs. Antshel *et al.*,[3] in their 3-year follow-up study, showed that the most significant predictors of adolescent prodromal psychotic symptoms were parent ratings of odd/eccentric symptoms and lower performance on the perseverative errors at the Wisconsin Card Sorting Test.

When 22q11.2DS subjects with psychoses need a psychopharmacological treatment, the antipsychotic therapies need to bee carefully chosen, taking into account literature data on efficacy and tolerability. 22q11.2DS subjects seem to have a higher susceptibility to side effects when on antipsychotic therapies than subjects with psychotic disorders (without the 22q11.2DS). In the case report by Kontoangelos *et al*.[4], a severe acute dystonia was reported in a subject on a low dosage of Haloperidol and had a good tolerability to quetiapine. In an other very recent paper, Butcher *et al*.,[5] show that 22q11.2DS schizophrenia subjects are at higher risk for severe side effects when on Clozapine, although they had a good clinical response. Further data on clozapine and quetiapine efficacy in 22q11.2DS subjects with relapsing psychoses, are presented by Vorhoeven and Egger.[6] The two atypical antipsychotics in combination with valproic acid, seem more effective than other therapies in their treatment resistant patients' sample

The early-onset Parkinson's disease,[7] of the 22q11DS phenotype in older adults, is a relevant and clinically intriguing data. This phenotype has now been described in multiple case reports, suggesting that dopaminergic disruption in 22q11DS may be relevant to the expression of both psychosis and Parkinson's disease over the life span. These data may suggest a hypothetical explanation of the increased sensitivity to antipsychotics' side effects in 22q11.2DS subjects.

The data currently available on 22q11.2DS, are really promising for further comprehension of that fascinating subject of study which are psychoses and schizophrenia.

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