Society for the Study of Behavioural Phenotypes
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SSBP Information Sheet

VELO-CARDIO-FACIAL SYNDROME

Alternative names: Deletion 22q11 syndrome, Sedlackova syndrome, DiGeorge syndrome, Shprintzen syndrome, Conotruncal anomaly face syndrome.

Incidence / prevalence: It is the most frequent known interstitial deletion found in man and occurs in approximately 1 in 4000 live births (1).

Genetics / aetiology: Most individuals with VCFS are found to have an interstitial deletion of approximately 3 million bases pairs although smaller deletions have also been reported. In a minority of individuals, no deletion can be detected. In a recent development, several groups have reported that the T-box transcription factor gene Thxl is responsible for the cardiovascular defects found in VCFS using a mouse model of the disease (2-4)

Physical phenotype: The usual features are a characteristic facial appearance (a long face, small ears with over-furled helices, upslanting eyes, a widened nasal bridge with a prominent nasal tip and a small mouth), cleft palate and br cleft lip and congenital heart disease (particularly conotruncal heart defects). It is important to stress that there is considerable variability of expression of the phenotype, even within members of the same family. In addition to the usual physical features, over 100 other physical features of the syndrome have also been reported.

Psychiatric/behavioural disorder: Several common temperamental features have been described in studies of children and adolescents with VCFS including behavioural excitation, an exaggerated response to threatening stimuli, and an enduring fearfulness of painful situations. (5)In addition, children with VCFS are reported to have poor social interaction skills, a bland affect with minimal facial expression, attentional difficulties and high levels of anxiety and depression (5-6). As the first cohort of children with VCFS was followed into adolescence and early adulthood, evidence began to accumulate for a high prevalence of major psychiatric disorder in these individuals. Specifically, several studies have reported high rates of bipolar disorder (64%), attention deficit disorder (ADDIADHD)(36%) and psychosis (10-30%) (7-9). In a large series of VCFS adults, Murphy and colleagues (1999) found that VCFS individuals have very high rates of psychosis (30%), the majority of which was schizophrenia (25%) (10)

Neuropsychological deficits: Early reports of children with VCFS described language abnormalities including immature language usage, poor development of numeric skills and significant impairments in reading and spelling (11). In a study of 37 VCFS children, Swillen and colleagues (1997) reported a wide variability in intelligence ranging from moderate learning disability to average intelligence with a mean full-scale IQ (FSIQ) of approximately 70 12 Forty-five per cent of individuals (n = 17) had a learning disability, the vast majority (82%) of which was mild. Similarly, Moss and colleagues (1999) reported that the mean FSIQ of their sample of 33 children and adults was 71, with 17 (52%) of their sample demonstrating learning disability (13) VCFS individuals with a familial deletion are found to have a lower mean FSIQ than individuals with a de novo (non-inherited) deletion (12)

A specific neuropsychological profile has also been described in children with VCFS with verbal IQ exceeding performance IQ on tests of general intellectual functioning (12-13) This discrepancy may relate to difficulties in planning ability, visuospatial ability and non-verbal reasoning in addition to deficits in novel reasoning and concept formation.

Brain structural abnormalities: Most structural neuroimaging studies of VCFS individuals have been qualitative and report the presence of a small cerebellum (3 6%), white matter hyperintensities (27 - 90%) and developmental midline anomalies such as cavum septum pellucidum and cavum vergae (40-45%) (14) The few quantitative neuroimaging studies that have been performed report relatively reduced volumes of total brain, left parietal lobe grey matter and right cerebellar white matter volumes but increased volumes of both frontal lobes, mid-sagittal corpus callosum areas and enlarged Sylvian fissures (15) Unfortunately, these studies have been limited by small sample sizes, the absence of appropriately IQ-matched control groups and studies have only involved VCFS children. In a quantitative neuroimaging study of VCFS adults, van Amelsvoort and colleagues (2001) reported that, compared to an age and IQ-matched control group, VCFS adults exhibited widespread differences in white matter bilaterally and regional specific differences in grey matter in left cerebellum, insula, frontal and right temporal lobes. (14)

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