



XYY Syndrome

First description and alternative names

XYY syndrome (47, XYY); YY Syndrome; Jacob's syndrome. The first case of XYY syndrome was reported as an incidental finding by Adam Sandberg and colleagues in 1961.

Genetics and molecular biology

The majority of cases of XYY syndrome are due to a paternal non-disjunction during meiosis II, following a normal meiosis I; a few cases resulting in an additional Y chromosome. In some cases it arises during early embryogenesis in a post-zygotic mitotic error, in which case it can result in a 46,XY/47,XYY mosaic form (Robinson & Jacobs, 1999).

Incidence/prevalence

The prevalence of 47,XYY is currently estimated at approximately 1/1000 males. As it is typically not associated with marked phenotypic characteristics it is frequently underdetected. Most people with XYY are not diagnosed or diagnosed late.

Physical features and natural history

Physical phenotypic differences associated with XYY syndrome are usually mild. Hypertelorism, macrodontia, pes planus, central adiposity, clinodacty have been described (Bardsley,2014, Lalatta,2012). Speech delay is common. Delayed development of motor skills (such as sitting and walking), weak muscle tone (hypotonia), hand tremors or other involuntary movements (motor tics), and behavioral and emotional difficulties are also frequent. Boys have increased growth velocity during childhood, and adult height is usually increased approximately 7cm above what is expected. The tall stature is explained by the presence of additional copies of the SHOX gene (and possibly also other genes related to stature) in subjects with 47,XYY. A severe cystic acne may develop during adolescence. Asthma prevalence is significantly greater in XYY than in the general population (Bardsley,2013)

Puberty, testicular function and fertility are usually normal (only a trend to macroorchidism has been signaled in early puberty), whereas boys with Klinefelter syndrome (KS) experience testicular failure.

Behavioural and psychiatric characteristics

Individuals with XYY syndrome are at increased risk for behavioural problems and psychiatric disorders. There is a high rate of diagnosis of Attention Deficit Disorder,(more marked than in KS) and increased risk of problems with distractibility, impulsivity and difficulties with temper management. Problems with social relatedness are also common. Individuals with XYY have been reported as having

increased scores on measures of autistic spectrum disorders (ASD) symptoms. Prenatal diagnosis was associated with higher cognitive function and less likelihood of an ASD diagnosis (Ross, 2013). Further, expression of NLGN4Y, a gene that may be involved in synaptic function, is increased in boys with XYY vs. XY controls, and the level of expression correlates with more severe autism symptom score (Ross, 2015)

The prevalence of XYY syndrome among psychiatric patients is approximately **3 times** that of the general population prevalence. Psychiatric diagnoses are more common in boys diagnosed postnatally and are often the reason these boys had karyotype evaluation (Bardsley, 2013). Risk for psychosis is high in XYY men (Verri, 2008).

Jacob (1965) described that the XYY chromosome abnormality was about 20 times greater in frequency in the inmate population than in non-incarcerated population. Recently a large study in persons with KS and 47,XYY covering all diagnosed individuals in Denmark demonstrates that persons with 47,XYY and KS are convicted of a number of specific offenses more frequently than the back, however the increased crime rate may be partly or fully mediated by poor socioeconomic conditions (Stockholm et al 2012).

Neuropsychological and neurological characteristics

XYY syndrome is usually associated with normal to slightly diminished cognitive function as measured with IQ; verbal IQ may be more affected than performance IQ. XYY males underachieve despite their social background. Many boys require speech therapy and special education. Reading may be particularly affected. Educational performance may be more adversely affected than what would be expected based on IQ measures alone. Difficulties with attention and impulse control are frequently reported.

XYY condition is associated to higher risk for seizures; focal epilepsy and an electroclinical pattern characterized by focal spike and waves, similar to benign focal epilepsy has been described in XYY boys (Torniero, 2010)

Neuroimaging

Male with XYY show increased total gray matter (GM) and white matter (WM) volume (Bryant, 2012)-

Increased grey matter may be the result of reduced synaptic pruning, leading to altered synaptic function and perhaps increased seizure risk. (Bardsley, 2014).

Voxel MRI documented recently that boys with XYY have lesser WM in the frontal region combined with an increase in GM in the right insula, whereas increased WM and reduced GM were observed in the superior parietal, postcentral and occipital regions (Lepage, 2014). These results may be due to overexpression of genes either in the homologous region on the X and Y chromosome or alternatively of male specific genes located on the Y chromosome (ibidem)

Available guidelines for behavioural assessment/treatment/management

Current recommendations usually include neuropsychological assessment and early intervention for learning disorders or behavioral problems.

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Annapia Verri, April 2016

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