

Social and behavioral development of girls and women with Turner syndrome

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Abstract. Research on the behavioral characteristics of girls and women with Turner syndrome has identified an increased risk for learning disabilities as well as social and behavioral problems (poor concentration, immaturity, anxiety) that typically present during childhood and adolescence. Most adult women with Turner syndrome, however, are emotionally stable, living self-sufficient lives. This chapter will summarize findings on the social and behavioral development of girls and women with Turner syndrome consider the mechanisms underlying these patterns, and present strategies for assuring optimal psychosocial development and adjustment. © 2006 Published by Elsevier B.V.

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1. Introduction

Research on the behavioral characteristics of girls and women with Turner offers a unique opportunity to explore the association between identifiable alterations in genetic make-up and both neurocognitive and behavioral development. This chapter will summarize findings on the social and behavioral development of girls and women with Turner, consider the underlying mechanisms, and discuss implications for clinical care.

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2. Cognitive development

While the prevalence of mental retardation in women with Turner syndrome is just slightly higher (8–10%) than that in the population at large [1], numerous studies have documented the presence of a cognitive impairment or learning disability that particularly affects nonverbal perceptual motor and spatial skills [2]. Deficits in visual–spatial organization, social cognition, non-verbal problem solving and psychomotor functioning have been identified [3]. Studies have also documented weaknesses in nonverbal memory [4], executive function [5] and attentional abilities [2].

Approximately 70% of individuals with Turner syndrome experience these learning disabilities to some degree although there is considerable variation among individuals [2,6]. These deficits translate into problems with mathematics [7,8], directional sense, driving and multitasking as well as related problems in social functioning [1–3]. Difficulty with spatial and math skills appear early but problems with reading comprehension may surface as academic demands become more complex.

3. Social and behavioral development across the lifespan

3.1. Childhood

During infancy, parents most commonly report problems in relation to motor (gross motor 39%, fine motor 59%) and language delays (37%), and feeding problems (71%) [9]. As girls with Turner syndrome move into their early school years, concerns about increased activity level, poor concentration and immaturity begin to appear along with parental observations of limited peer relationships [10,11].

At this time, the cognitive disabilities associated with Turner syndrome begin to play a more central role in behavioral adjustment. Many girls present with symptoms of attention deficit hyperactivity disorder (ADHD). On tests of attentional skills, girls with Turner syndrome demonstrate deficits in inhibitory control but do not have difficulty sustaining or focusing attention [2,5]. On assessments of executive functioning, difficulties with distraction, planning [5], and both short-term recall and working memory [4] are reported. Weaknesses in these core cognitive skills contribute to the ADHD behavioral pattern observed and may play a role in the social immaturity and peer problems noted by parents and teachers [10].

3.2. Adolescence

During adolescence, inattention, immaturity, social isolation and anxiety appear to be the most common problems [3,11–13]. Higher rates of ADHD compared to contrast groups of adolescent girls have been documented [12]. The pattern of ADHD observed in adolescent girls with Turner syndrome is distinguished by many signs of social immaturity. Parents of adolescent girls with Turner syndrome also endorsed more anxiety and depression [13] than observed among girls in the normative sample. Problems with anxiety in girls with Turner syndrome can be expressed as shyness, a preoccupation with keeping things in order and a lack of flexibility in terms of change in routines. Learning or cognitive deficits may underlie

these social difficulties as some studies have found that females with Turner syndrome may misinterpret, or fail to recognize, facial expressions and body language [14] although observational studies have not yet substantiated this finding [15].

Girls and adolescents with Turner syndrome also endorsed a less positive sense of self-concept when compared to girls with short stature and normative samples. Lowered ratings on self-concept reflect concerns in the social arena, predominantly [3,10,]. A recent study of 50 young women, with final heights within the normal range, treated with growth hormone during childhood assessed social and behavioural functioning at age 18. The investigators found no evidence of behavioural problems but self-esteem and attitudes about their bodies were less positive among the girls with Turner syndrome than for their peers [16].

3.3. *Adulthood*

Psychological studies of adult women with Turner syndrome have addressed questions about academic and work achievement, interpersonal relationships, emotional difficulties and quality of life. Most adults with Turner syndrome report reasonable levels of satisfaction in employment and social life [17–19]. Survey data from a number of studies of adult women reveal excellent education and occupation achievement but some delays in reaching milestones associated with adult development, such as marriage or living independent of parents [17,19]. Some women are employed at an occupational level below that predicted by education [17]. This may reflect the long-term impact of early learning disabilities, some of which do persist into adult life [20]. One recent study of quality of life found that problems in school accounted for 25% of the variance in well-being among adult women with Turner syndrome [21].

Survey studies have also explored the social and emotional functioning of adult women with Turner syndrome [17–19]. Adult women with Turner syndrome report lower self-concept similar to that found in child and adolescent groups. However only health status was significantly associated with self-concept, accounting for 28% of the variance [17]. One study of a small sample of 22 adult women, found that 86% reported that their “self-esteem needed improvement” and 72% endorsed being “sometimes depressed” [18]. Depressed mood was most commonly associated with regrets about infertility. These women reported having had few friends during adolescents but none was socially isolated as an adult.

Most women with Turner syndrome report heterosexual sexual orientation but many have a delayed pattern of dating and initiation of sexual relationships [17]. Past reports of prevalence rates for psychiatric diagnoses among women with Turner syndrome range from 2% to 10% (Sybert, unpublished data). However, a recent study of 100 women with Turner syndrome found that 52% met criteria for a present or past episode of depression [22]. The women with Turner syndrome in this sample had higher lifetime rates of depression than community based samples but their rates were similar to contrasts groups recruited from gynecological clinics.

In sum, the findings across behavioural studies suggest that girls with Turner syndrome show a delay in terms of social and emotional development but that most adult women with Turner syndrome are emotionally stable and living self-sufficient lives as independent productive adults.

4. Causal mechanisms

Efforts to understand what leads to the behavioural patterns that characterize girls and women with Turner syndrome have investigated the role of genetic, hormonal and environmental factors on the neurocognitive development of these women.

4.1. Genetic factors

There is some evidence that different karyotypes may be associated with specific cognitive and behavioural outcomes. For instance, the risk for mental retardation is highest in individuals with a marker chromosome (66%) or a ring (X) chromosome (30%) [23], while learning disabilities are more common in girls and women with 45,X karyotype than individuals with mosaicism [10]. In relation to behavioural profiles, Rovet reports [3] found that girls with isochromosomes had most social problems, while those with other rearrangements of the X chromosomes were at greatest risk for both social and behavioural problems and those with mosaic karyotypes had the lowest risk of either social or behavioural problems.

Haploinsufficiency of specific genes has been hypothesized as causing the physical and behavioral features found in Turner syndrome [24]. While some of the phenotype of Turner syndrome may be due to the effect of X-chromosome aneuploidy in the blastocyst prior to X-inactivation, there may also be features that result from later lack of expression of genes in the pseudoautosomal regions of the second X chromosome that usually escape X-inactivation. These genes may be necessary for “normal functioning” [36,37]. Ross et al. [25] demonstrated that visuospatial ability was poor in those females missing a specific region of the short arm of the X chromosome that ordinarily escapes X inactivation. These findings, along with those related to physical features of Turner syndrome [23], support the hypothesis that the genes in the noninactivated areas may play an important role in phenotypic expression.

Imprinting, differential outcomes based on whether the individual’s intact X chromosome comes from the mother or the father, may also play a role in the cognitive and behavioural phenotype. Skuse et al. [26] found more social problems in girls with Turner syndrome whose X was maternally derived than those with a paternal X, as well as differential patterns of cognitive impairments. However, elevated rates of ADHD have been reported in girls with Turner syndrome with no association between IQ scores and parental origin of the X chromosome [27].

4.2. Hormonal factors

Lack of exposure to typical level of ovarian hormones, both estrogens and progesterones, may contribute to behavioral patterns observed in Turner syndrome. Ross et al. [28–30] found that estrogen replacement was associated with some improvement in visual perceptual and motor planning, speed of motor and cognitive processing and memory function but did not improve visuospatial performance. Androgen exposure was associated with some improvement in working memory but had no effects on verbal abilities, spatial cognition or executive function [30]. A recent study of adult women

suggests greater social anxiety and depression in both women with Turner syndrome and premature ovarian failure [31]. Finally, studies of growth hormone therapy suggest positive effects on behaviour with improvements in self-esteem, and socialization but no clear effects on overall cognitive function [32,33].

4.3. Neurocognitive factors

Initial positron emission scanning (PET) and magnetic resonance studies have revealed right posterior region disparities (e.g. volume differences) and parietal lobe abnormalities when comparing individuals with Turner syndrome and female controls [34,35]. Findings of temporal lobe differences including disproportionately reduced right hippocampal volume and larger left amygdala gray matter may relate to the memory and social cognition deficits noted in Turner syndrome [34].

Recent research using fMRI techniques documents parietal lobe and prefrontal cortex differences which are consistent with visual motor problems [36]. When presented with math problems, girls with Turner syndrome demonstrated wider activation in the frontal and parietal regions than controls but evidenced less activation with more complex problems [37]. The investigators hypothesized that girls with Turner syndrome may partially compensate for executive dysfunction by activating additional prefrontal cortex regions involved in inhibition, attention and working memory.

There is a growing body of evidence to suggest a chromosomally determined process of neurocognitive development, which, in turn, affects cognitive, social and behavior development in individuals with Turner syndrome. Skusse and colleagues [14,38] have explored one possible pathway by which neurocognitive deficits could affect social function, in a series of investigations of the ability of women with Turner syndrome to accurately interpret facial affect. This 'cognitive' inability to read and respond effectively to facial affective cues may then result in social and behavioral deficits.

4.4. Environmental factors

Although there is growing support for a biologically based causal model, environmental factors must also be considered. Individuals with Turner syndrome face many challenges. Short stature and lack of spontaneous puberty alter their developmental course even if treated. Many experience overprotection by family and ridicule from peers [39]. They must overcome learning disabilities, manage an array of associated medical concerns and cope with issues related to fertility.

5. Implications for care

In closing while most adult women with Turner syndrome appear to be well adjusted areas of social, emotional and behavioral vulnerability present particularly during the childhood and adolescent years. Strategies to enhance social and behavioural development include: (1) individual cognitive testing at the onset of school with ongoing attention to need for additional assessment or tutoring to keep up with grade level expectations; (2) coaching to assure active social involvement especially during the middle and high school

years; (3) preparing for emancipation and successful transition into the working world with age appropriate expectations for participation in chores, social activities and jobs outside the home; (4) educational planning early high school so that girls who have significant learning problems can be guided appropriately including how to qualify for accommodations as needed at the college level.

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