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REVIEW

Williams syndrome: recent advances in our understanding of cognitive, social and psychological functioning

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Purpose of review
Since the last review of Williams syndrome in *Current Opinion* (2001) there have been many advances in knowledge about the cognitive, social and psychological impairments that characterize the disorder. The present review focuses on current research in these areas.

Recent findings
Williams syndrome is associated with a wide range of cognitive, linguistic, social and other difficulties. When young, these deficits may appear relatively mild – for example, many children are highly sociable and talkative – but with age the impact of these difficulties becomes more evident. Thus, inappropriate social behaviours can significantly increase the risk of social exclusion and vulnerability to abuse. Their superficially good speech can lead to educational and other services failing to understand the true extent of impairments or the need for specialist support. Mental health problems, especially related to anxiety, often become an increasing challenge from adolescence onwards.

Summary
The core difficulties associated with Williams syndrome have a cascading effect on many areas of development over time. However, specialist provision is rare and intervention trials are almost nonexistent. Longitudinal research is needed to identify factors associated with cognitive, social and emotional problems and to develop more effective ways of minimizing and treating difficulties.

Keywords
developmental problems, developmental trajectories, Williams syndrome

INTRODUCTION

Williams syndrome is a rare genetic disorder, estimated to affect between 1 in 7500 and 1 in 20 000 live births, caused by a hemizygous sporadic microdeletion of 26–28 genes on chromosome 7q11.23. Although the physical phenotype is remarkably consistent across the world [1], there are variations in behavioural phenotype and brain structure/function [2]. The condition typically results in deletion of one copy of the *Elastin* gene and elastin deficiency is associated with many of the characteristic physical features, including cardiovascular disease, connective tissue abnormalities and the distinguishing facial physiognomy. Other problems include infantile hypercalcaemia, renal tract abnormalities, gastrointestinal problems, strabismus, short stature, sensory processing impairments (especially hypersensitivity to sounds) and premature ageing [3▪▪]. Williams syndrome is also associated with cognitive, language and social impairments and behavioural and emotional problems, and difficulties in these latter domains are the focus of the present review.

COGNITIVE ABILITIES AND STYLES OF LEARNING

The majority of individuals with Williams syndrome has mild to moderate intellectual disability [intelligence quotient (IQ) 30–70], with verbal IQ generally being higher than nonverbal. There are no apparent

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KEY POINTS

- Although the sociability of young children with Williams syndrome is often considered a positive asset, lack of understanding of social situations can lead to problems of social rejection, abuse or victimization as they grow older.
- The superficially good expressive language of individuals with Williams syndrome often gives a very misleading impression of their true level of capacity and may result in their being deprived of appropriate support.
- Mental health problems, especially anxiety, present major difficulties for many individuals but research on how best to treat psychiatric disorders is very limited.
- Despite the many cognitive, social, emotional and behavioural problems associated with Williams syndrome there is a lack of research on interventions that might help to minimize the impact of these difficulties on daily life.

sex differences in IQ [3▪▪] and scores remain relatively stable over time [4▪▪], although the discrepancy between verbal and nonverbal skills may increase with age. Current research confirms earlier findings on profiles of relative strengths and weaknesses. Thus, there tend to be particular difficulties in visuo-spatial skills (visuo-spatial learning and construction ability, visuo-spatial memory and visual discrimination), sensory motor processing and executive function (behavioural inhibition and planning ability) [5▪]. There are also attentional difficulties, which may be connected with the auditory hyper-responsiveness and distractibility that is characteristic of Williams syndrome [6]. In contrast, many individuals show relative strengths in verbal short-term memory and language. Musical ability is another skill associated with Williams syndrome and this, too, may be related to heightened auditory sensitivity. However, a systematic review of musical ability in Williams syndrome [7▪▪] suggests that musical aptitude is highly variable and strengths tend to be related more to a heightened interest and emotional responsiveness to music rather than formal musical skills.

Recent studies have also begun to identify different styles of learning in Williams syndrome. For example, learning by elementary school children was enhanced if they were allowed delays between tasks to consolidate memory and learning [8▪] The performance of young adults on a visuo-motor computer task was significantly improved if participants first observed someone else completing the task rather than learning by trial and error [9▪]. Difficulties with tasks that involved remembering the location of a reward could also be minimized if adults were required to perform a fixed motor response to obtain the reward [10].

ADAPTIVE BEHAVIOUR

A recent systematic review [11▪▪] confirms that adaptive function in Williams syndrome is significantly lower than among same age peers. No consistent sex differences were identified but domain profiles varied with age. Thus, among children and adolescents, scores for socialization and communication tended to be higher than scores on the personal/daily living skills domain. For adults, scores tended to be highest for socialization and lowest for communication. However, there is some inconsistency among studies with respect to domain profiles as well as heterogeneity within samples [12]. The reported relationship between IQ and adaptive behaviour also varied between studies. In some, IQ scores were higher than adaptive behaviour scores; in others, adaptive behaviour scores were higher, and in others there was no difference. Similarly, although some studies suggested that adaptive behaviour improves with age, others reported stability and others a decline [4▪▪,11▪▪].

LANGUAGE

Although language is considered a relative strength in Williams syndrome, language profiles are typically very uneven. In general, receptive language is more delayed than expressive or written language, whereas social-pragmatic use of language is particularly impaired compared with lexical, phonological, syntactical and morphological skills. Findings also vary according to the ages of the samples studied [13,14]. For example, over time, morphological errors tend to become more evident [15] and the gap between expressive and receptive language may increase [16▪,17▪▪]. With age, some individuals become poorer at taking the listener's knowledge into account and they have continuing difficulties in monitoring their output and organization of discourse [18]. As in many other developmental disorders, poorer pragmatic language in Williams syndrome is associated with greater impairments in social functioning and higher levels of behavioural disturbance [19▪▪]. Moreover, the relatively good expressive skills of many individuals can give a very misleading impression of their true level of understanding, or capability in other domains.

SOCIAL FUNCTIONING

The highly social nature of young children with Williams syndrome is one of their most positive

traits and across the age-span the condition is characterized by an intense drive for social interaction [20▪]; a desire to form affectionate bonds with others [21▪], and increased empathy [22▪]. However, understanding of the 'rules' governing social interactions is often significantly impaired. Moreover, deficits in social cognition, and the discrepancy between social understanding and the desire for social contact, tend to increase with age. Older children and adults have difficulties making and sustaining friendships and frequently experience peer rejection, social victimization, bullying and abuse [23▪,24▪]. The social vulnerability of people with Williams syndrome also tends to increase with age and greater independence. In one study, over 80% of young American adults with Williams syndrome were reported to use the Internet daily, mostly without supervision [25▪]. However, they were poor at recognizing the potential dangers of online networking; they shared large amounts of identifiable information, and often took risks such as giving out bank details or agreeing to meet with strangers [20▪,25▪]. Poor social understanding is also evident in experimental studies. For example, compared with typically developing peers, children with Williams syndrome had difficulties identifying story characters' concealed intentions and thoughts, and were more likely to want to befriend a character who had been revealed as having negative motives [26▪].

Social-cognitive mechanisms

The ability to understand others' mental states is essential for successful social interactions and difficulties in Theory of Mind are often proposed as underlying the social-pragmatic deficits in Williams syndrome. Although young children with Williams syndrome perform relatively well on tasks of emotional understanding, they were poorer than same-age peers on false belief tasks [27▪,28▪]. Visually presented ToM tasks also seem to be particularly challenging, suggesting that difficulties processing basic social-perceptual cues may affect social understanding [29▪,30▪]. For example, preschoolers with Williams syndrome were able to follow a partner's gaze toward an object of interest, but they looked at that object for less time than typical peers [31▪], indicating that they may lack understanding of the meaning of their partner's gaze.

Biological mechanisms

Hypersociability in Williams syndrome is also attributed to various biological mechanisms. These include a common polymorphism within the *GTF2I* gene (General transcription factor II-I), which is found within the Williams syndrome microdeletion and is associated with decreased threat-related amygdala reactivity in response to social stimuli [32▪▪,33▪]. Reduced *GTF2I* expression or activity, leading to oxytocin dysregulation, may also be associated with the high sociability and empathy, and low social anxiety found in Williams syndrome [34▪▪,35▪]. It has also been proposed that hypersociability in Williams syndrome may be linked to a paternally imprinted gene bias to GTF21 expression, whereby individuals seek increased attention and psychological resources from others, although this theory requires confirmation [34▪▪].

IMPLICATIONS FOR INTERVENTION

Despite many studies on cognitive, language and social profiles in Williams syndrome, there is a lack of research on interventions or on ways of minimizing problems. Although it is suggested [35▪] that better understanding of the strengths and difficulties associated with Williams syndrome could help to improve educational provision and social inclusion, there is little evidence of 'syndrome-specific' adaptations to teaching in schools. Children with Williams syndrome are less likely to be placed in mainstream school than children with autism or Down syndrome, and access to inclusive education decreases further from junior to secondary school [36▪]. The majority of children with Williams syndrome are also reported by parents to have no additional specialist educational provision (for speech, learning, physical or mental health difficulties) [37]. Nevertheless, the studies reviewed here suggest a number of potential strategies to enhance learning. Eye-tracking experiments with Williams syndrome toddlers [31▪] indicate that they attend more to novel than repetitive stimuli and also that those who respond most to new stimuli have better developed social skills. The same research group [30▪,38▪▪] highlights similarities in social-cognition difficulties between Williams syndrome and autism spectrum disorders (ASD) and proposes that many of the social-cognitive interventions developed for young children with ASD might have similar benefits for those with Williams syndrome. In the classroom, providing shorter lessons with more frequent breaks could help to improve memory, consolidate learning, avoid fatigue and optimize performance [8▪]. Task performance in older children and adults could be enhanced by active demonstration of correct responses, rather than learning by trial and error [9▪], and/or by teaching specific rules to achieve success [10]. It is also suggested [5▪] that early intervention to improve functional visual and motor skills could improve adaptive behaviour and social

integration more generally. Other authors have highlighted the need for more research into how the affinity for music in Williams syndrome might be better utilized to improve motivation and attention and reinforce learning [7▪▪].

With respect to language, there are no substantive, controlled trials of interventions that might help to improve conversational skills [16▪,18]. Even in special schools, many children with Williams syndrome do not receive additional speech and language therapy [36▪] possibly because their apparently good expressive skills lead to an assumption that no specialist language input is required. However, one small scale, noncontrolled study [17▪▪] found that even a very brief intervention appeared to improve young people's narrative discourse and conversation.

Developing interventions to reduce social vulnerability, together with education and guidance, from an early age, about 'stranger danger' are also essential [20▪,25▪,39▪]. It is becoming increasingly important, too, to develop programmes that teach Internet safety. Improving ToM skills by focusing on children's emotional awareness, using explicit instructions and working with teachers and parents in natural contexts may help to optimize social competence and understanding [28▪]. Social skills groups, too, could potentially benefit young people with Williams syndrome but to date there has been no systematic evaluation of their effectiveness. However, a brief social education programme for adults with Williams syndrome was reported to lead to improvements in social knowledge [24▪].

MENTAL HEALTH

Many studies confirm the high risk of behavioural and emotional problems in Williams syndrome [3▪▪]. Among young children, attentional problems are the most frequent difficulties reported by parents and teachers [39▪]. Externalizing problems (oppositionality and aggression) and internalizing problems (anxiety and withdrawal) are also common [39▪,41▪,42▪], although rates of self-injurious behaviours are lower than in other genetic disorders [43]. A significant minority of children shows autistic-type disorders (social communication deficits, stereotyped and repetitive behaviours) [40,44▪]. By far the most commonly reported mental health problem in Williams syndrome, however, is anxiety. A systematic review [45▪] calculated that overall prevalence for anxiety disorder was 48%, with specific phobias (39%) and generalized anxiety disorder (10%) the main subtypes. Individuals with Williams syndrome had a four-fold increased risk of anxiety compared with individuals with heterogeneous intellectual disability and were at an elevated risk relative to the general population.

Most of these studies involve children or young adults and there is little research on trajectories of mental health over time. Existing studies examining changes with age are contradictory and indicate considerable variation [46▪▪,47▪,48]. A recent case study describes major depressive disorders and psychotic features in three adults with Williams syndrome, but there is no research on the overall prevalence of such disorders. There is also very little empirical evidence on how best to treat psychotic symptoms in this population [49▪].

Mechanisms associated with mental health problems in Williams syndrome

Research on factors associated with mental health problems in Williams syndrome has demonstrated a strong link between anxiety and impaired social functioning [50▪]. Studies also suggest that poor understanding of language and executive functioning deficits (in inhibition, attention and emotional control) are associated with increased anxiety [47▪,48]. Hyperacusis, too, may play a significant role [51▪▪]. Another potential mechanism, which has been increasingly linked with anxiety in both the general population and autism, is intolerance of uncertainty (IoU), a cognitive bias in which people negatively interpret uncertain events or situations [52]. A questionnaire-based study [51▪▪] of adolescents and adults with Williams syndrome found that both IoU and sensory hypersensitivity were significant predictors of anxiety severity, but with IoU seeming to play a more dominant role.

Although all these studies are important in identifying possible mechanisms underlying mental health problems in Williams syndrome, data are not based on direct assessments of psychological functioning. Moreover, the causal direction of the potential associations identified has yet to be ascertained. And, most importantly, there are currently no studies of the clinical implications of these findings for improving treatment, or prevention of anxiety in Williams syndrome.

RESEARCH LIMITATIONS

In most studies included in this review, samples are very small and often heterogeneous with respect to age and intellectual ability. Data tend to be based on indirect measures (questionnaires, self or parental reports, or analogue studies) rather than direct assessments, and there is almost no research on the lives of older adults or on trajectories of development from child through adulthood. There is also

relatively little research comparing the impairments in social cognition identified in Williams syndrome with other conditions, such as autism, in which similar deficits are present [53]. Greater focus on the similarities and differences between these conditions could provide more insight into the mechanisms underlying social or cognitive deficits, as well as having implications for possible interventions [30▪,38▪▪]. Finally, although several studies included in this review allude to the potential value of their findings for treatment, the lack of intervention studies is the greatest limitation of current research.

CONCLUSION

D'Souza and Karmiloff-Smith [54▪▪] propose that the genetic deletion in Williams syndrome affects basic level processes that have cascading effects on various domains over time. Lowered functional connectivity in significant brain networks may also affect subsequent information integration and cognition [55▪▪]. The present review confirms that many of the characteristics associated with Williams syndrome in childhood (enhanced sociability and expressive language) may later have a negative impact, as development in these domains becomes increasingly asynchronous with development in other areas. There now needs to be much greater focus on interventions to reduce social-communication difficulties and prevent them from becoming significant barriers to social inclusion in adolescence and adulthood. This requires:

(1) longitudinal research to identify early risk factors associated with later psychosocial and emotional problems,
(2) exploration of how the specific strengths of individuals with Williams syndrome might be used to moderate their difficulties in other areas,
(3) detailed examination of the relationships between multiple domains rather than targeting specific impairments, and
(4) investigating the benefits of therapies found to be effective in other conditions (such as autism) for improving social-communication and emotional problems in Williams syndrome.

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Conflicts of interest

There are no conflicts of interest.

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