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The social phenotype of Williams syndrome

Anna Järvinen[1,2], Julie R Korenberg[3] and Ursula Bellugi[1]

Williams syndrome (WS) offers an exciting model for social neuroscience because its genetic basis is well-defined, and the unique phenotype reflects dimensions of prosocial behaviors. WS is associated with a strong drive to approach strangers, a gregarious personality, heightened social engagement yet difficult peer interactions, high nonsocial anxiety, unusual bias toward positive affect, and diminished sensitivity to fear. New neurobiological evidence points toward alterations in structure, function, and connectivity of the social brain (amygdala, fusiform face area, orbital-frontal regions). Recent genetic studies implicate gene networks in the WS region with the dysregulation of prosocial neuropeptides. The study of WS has implications for understanding human social development, and may provide insight for translating genetic and neuroendocrine evidence into treatments for disorders of social behavior.

Addresses
[1] Laboratory for Cognitive Neuroscience, the Salk Institute for Biological Studies, La Jolla, CA, USA
[2] Brain and Mind Laboratory, Department of Biomedical Engineering and Computational Science, Aalto University School of Science, Espoo, Finland
[3] Center for Integrated Neuroscience and Human Behavior, and Department of Pediatrics, University of Utah, Salt Lake City, UT, USA

Corresponding author: Bellugi, Ursula (bellugi@salk.edu)

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Introduction

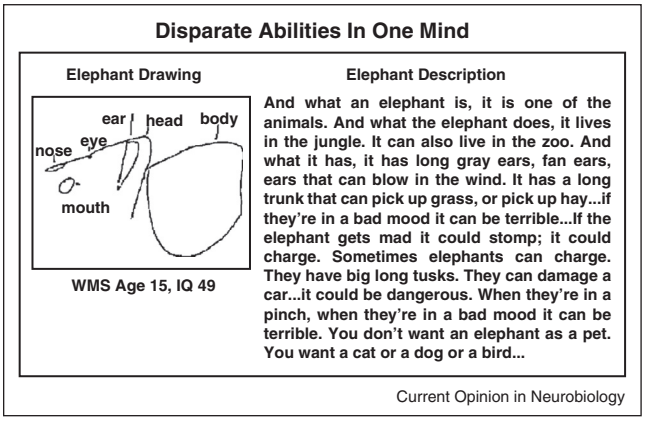
Williams syndrome (WS) is a multisystem disorder [1] characterized by a distinctive social profile that holds promise for understanding the underlying neurogenetic systems that provide meaning for human social interaction. Resulting from a hemizygous deletion of ~25 genes on chromosome 7q11.23 [2••], a unique and robust behavioral characteristic of WS is an increased social drive particularly toward strangers [3,4], manifesting as a strength in processing social over nonsocial stimuli, engaging language, increased social gaze, and empathic, friendly, and emotional personality [2••,5••,6]. This profile stands against a backdrop of strikingly uneven profile of cognitive functions, with profoundly impaired visual-spatial processing [7] (Figure 1). The neuropsychiatric profile is associated with mean IQ of approximately 50–60, with a typically higher verbal than performance IQ [1,8]. One fascinating aspect of the WS social phenotype is that, unlike for visual-spatial processing with impaired functions across the board, the haploinsufficiency resulting from the gene deletion leads to a profile characterized by intriguing dissociations, or strengths and weaknesses (e.g. overly friendly with a difficulty in making friends; socially fearless but anxious; positive affect with maladaptive behaviors). In this sense, the WS gene deletion provides a unique model system to begin to relate single/clustered genes to specific alterations at the phenotypic level, with the ultimate potential of advancing our understanding of human social behavior at multiple levels.

This review focuses on capturing the nature of the unique WS social profile by outlining its major features at the level of behavior, followed by recent advances in the study of brain and genes. While the literature on the WS social phenotype has been building up for some time, the syndrome is emerging newly into focus and gaining new interest due to a recent surge of neurobiological evidence suggesting a consistent profile of brain structure and function underlying the social profile. Subsequently, the studies have provided critical new information about the 'social brain', paving the way for WS to serve as a 'prototype model' of social functioning that will allow new insight into understanding the biological basis of aspects of human social behavior in the future. We finish by addressing entirely new directions in molecular genetics suggesting dysregulation of prosocial neuropeptides in the overly social phenotype of WS, thereby implicating the study of WS prosocial behavior to encompass neuroendocrinology for the first time.

Gregarious personality, affiliative drive, and compromised social relationships

Studies of children and adults with WS highlight strikingly consistent and unique patterns of behavior both at the cognitive level [6] and in terms of sociability [5••]. The social behavior in WS also appears distinct from typical uninhibited behavior [9•]. Accumulating evidence utilizing an array of methodologies (questionnaires, observations, experiments, self-reports and other reports, event related potentials (ERP), and more recently psychophysiology) has revealed increased appetitive drive toward social engagement and heightened approachability toward strangers as some of the core features of the WS social phenotype [3,4,10,11]. Individuals with WS typically demonstrate an overly friendly, affectionate, engaging,

Figure 1



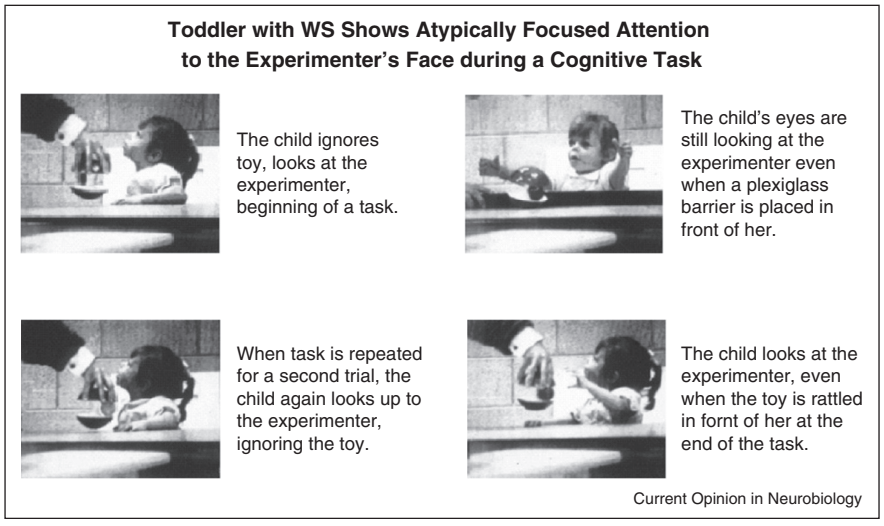
Peaks and valleys of cognitive ability: dissociation of visual-spatial and language (social) functions in WS.

and socially disinhibited personality [6,12]. An empirically derived personality profile of WS has been constructed based on the Children's Behavior Questionnaire (CBQ) and the Multidimensional Personality Questionnaire (MPQ), reflecting Rothbart's psychobiological approach to temperament and Tellegen's Three-Factor Model of personality, respectively [6]. The findings showed that the personality characteristics that distinguished individuals with WS from those with intellectual disabilities of mixed etiology with 96% sensitivity and 85% specificity included a lack of shyness and high empathy. In addition, individuals with WS were uniquely gregarious, people-oriented, visible, tense, and sensitive/anxious. The characteristic WS sociability may further be characterized by an attraction to strangers [4], a propensity to direct eye contact [13] and a bias toward focusing on the faces and eyes [14,15], abnormally expressive language [16], a penchant for positive affect, evident in both receptive and expressive functions [5••,17], and insensitivity to negative emotional signals [18], suggesting social fearlessness. The profound interest in unfamiliar people is observable from infancy (Figure 2), and is exhibited also by the lack of separation/stranger anxiety shown by children with WS when separated from their parents [19••].

The excessive sociability of WS encompasses the domain of language. Reilly and colleagues [5••,16] analyzed narratives of individuals with WS, Down syndrome, specific language impairment, focal lesions, and age-matched typical controls for social-affective language and formal grammatical competence. Social-affective language characteristics pertain to language reflecting the narrator's attitude or perspective, including attributing emotions or motivations to characters, using intensifiers (really, very, so) and sound effects, direct quotes, and character speech, and tools for 'hooking' the listener's attention. While individuals with WS significantly exceeded all other populations tested in their use of socially engaging language, their level of grammatical competence was similar to those with specific language impairment [15]. This robust finding has been replicated across development and across different cultures in WS [5••]. In addition to language, the effect of WS hypersociability is also evident cross-culturally [20], even though at the same time, culture subtly mediates the genetic expression of social behavior in WS (American versus Japanese, French, and Italian).

The increased sociability has been observed with remarkable consistency in WS across different measures and ages, as the broad literature to date attests. A central focus

Figure 2



A preoccupation with a stranger (experimenter) by a child with WS interferes with task administration.