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The Social Phenotype of Williams Syndrome

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Abstract

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 non-social 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.

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 non-social stimuli, engaging language, increased social gaze, and empathic, friendly, and emotional personality [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 [8, 1]. One fascinating aspect of the WS social phenotype is that, unlike for visual-spatial processing

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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- and other reports, event related potentials (ERP), and more recently psychophysiology) has revealed increased appetitive drive toward social engagement and heightened approachability towards 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, 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 [16, 5**] 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 vs. 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 of our program of studies has been to examine the variability and consistency of social-affective behavior of WS from a developmental perspective. As described later, it is particularly useful to examine the heterogeneity in social behavior in WS through the prism of genetic and neural variance. One part of this effort at the behavioral level included creating a new measure designed to tap onto central issues in quantifying social and affective behavior characteristic of WS, entitled The Salk Institute Sociability Questionnaire (SISQ) [3, 20, 21]. The SISQ has been widely used to examine social behavior across the lifespan, cultures, and populations (WS, autism, Down syndrome, and typical development) [3, 20, 21]. Our data from over 200 individuals with WS of ages 1-52 years on the SISQ consistently show that individuals with WS are characterized by higher global sociability and approachability toward strangers as compared to any control group. Moreover, the WS group is associated with reduced variability with respect to social-affective behaviors relative to the comparison groups. Thus, the distinctiveness of the social behavior in WS appears to be intimately linked to their engagement with, and approachability toward, unfamiliar people. Indeed, the relative homogeneity of the etiology of WS together with the diminished variability with respect to social behavior lends the syndrome ideally to the study of genotype-phenotype relations with respect to social-affective behavior.

The social behavior of individuals with WS is however often inappropriate and is accompanied by marked deficits in social skills, such as difficulties in social adjustment, social judgment, with an inflexible, repetitive, and pragmatically insensitive social repertoire [22, 23, 24]. This paradoxical profile has been characterized as an excessive desire to approach others, an overly friendly and engaging personality, coupled with an inability to sustain friendships, with particular difficulties in peer relations. Combined with limitations in intellectual, cognitive, and motor functions [1], the excessively friendly social profile of

WS predisposes such individuals to social vulnerability, such as risk of social isolation, difficulties in employment, bullying, abuse, and erratic relationships [25]. In addition, it is noteworthy that the characteristic social-emotional behavior of WS also coexists in the context of diagnostically significant anxiety disorders [26, 27, 23] as well as specific attentional difficulties [24, 26]. The distinct paradoxes and dissociations of the WS social profile, including the anxieties, may be accountable by the level of intellectual function. Taken together, WS behavior includes a nuanced spectrum of distinct socially positive and maladaptive behaviors, which are unlike those seen in typical extraversion, and imply the dysregulation of multiple brain circuits.

Salience of faces

Given that abnormalities in the perception and responsivity to faces are primary contributors to social dysfunction, studies have begun to address the increased attention to faces in WS, and its relation to the “hypersocial” phenotype. Individuals with WS exhibit a significant interest in face stimuli across development (Figure 2) [13, 20], and spend more time focused on faces than on non-social stimuli [28]. Subsequently, WS is characterized by a dissociation such that those with the syndrome show better processing of social than non-social affective stimuli [29, 30], which may result from the early bias toward social information, leading to enhanced processing of such stimuli at the expense of non-social information. Recently, eye tracking studies have quantified the earlier observations of the remarkable early attentional bias toward faces [5**, 13, 20] showing that individuals with WS fixate longer on faces [14, 15] and eyes [31] than controls, and once fixated, they show delays in disengaging [31, 32].

A new line of research for WS focusing on autonomic nervous system responsivity has suggested that atypically low general arousal level [33] may contribute to the exaggerated eye contact in individuals with WS [34]. At the same time, WS is associated with increased heart rate reactivity and a lack of electrodermal habituation to faces, indexing increased arousal to such stimuli [30]. Thus, a lack of habituation to faces may be linked to the increased affiliation and attraction to faces characterizing the syndrome, as face stimuli may appear unusually novel to individuals with WS.

The emotional phenotype

Studies of basic emotion processing have revealed a markedly uneven profile in WS, with decreased recognition of negative social signals within both visual and auditory domains by such individuals [e.g., 35], which has been hypothesized to contribute to the increased approachability and inappropriate social engagement [36]. However, this combines with a distinct attentional and processing bias toward positive social stimuli [17], and a preserved ability to process positive affect [29, 35, 37]. Reflecting the positive bias, individuals with WS also tend to perceive unfamiliar faces abnormally positively [4]. In contrast, individuals with WS show difficulties in attending to [18] and recognizing [17] angry faces, and demonstrate delays in identifying negative facial expressions [38].

An important aspect of the WS emotional profile pertains to reports of increased emotional responsivity, including enhanced empathic display and reaction [5**, 13]. Specifically,

increased emotional reactions in individuals with WS have been described in relation to their interactions with other people [12, 16] and the experience of music [39]. Evidence suggests that there are two systems for empathy: a basic perceptually-based emotional contagion system (involving the mirror neuron system), and a more advanced cognitive perspective-taking system. Studies have already established that individuals with WS show difficulties in cognitive aspects of empathy, e.g., theory of mind, which is not surprising given their level of cognitive function. Thus, the characteristic profile of WS of increased emotional reactivity and social affiliation in the context of poor social intelligence is mirrored by relatively less severely impaired social-perceptual aspects of "theory of mind", as indexed by performance in standard emotion processing tasks as compared to the more profound impairments in the higher-order social-cognitive functions, as indexed by performance in mentalizing tasks [see 12]. This pattern of processing has resulted in the postulation of the dual-component model of theory of mind [12]. Interestingly, in children with WS, difficulties in interpreting social dynamics in ambiguous situations, i.e., in the context of the social attribution task, correspond to deficits in reciprocity in real-life social interactions [40]. Taken together, this suggests that performance of individuals with WS on artificial theory of mind tasks may translate to aberrant social skills in real-life settings.

Emotional functioning thus represents an another area characterized by "peaks and valleys" of ability within the WS social profile, and raises questions regarding the underpinnings of this behavior, such as, whether the unusual emotional reactivity characterizing WS may be associated with over-activity in the traditional empathy or mirror neuron system circuits. A recent study with potential implications for mirror neuron system function found that individuals with WS perform below mental age level in tasks tapping on the understanding of motor acts (the "what" aspect not involving intention). At the same time, their understanding of a motor intention (the "why" aspect implicating intention reading) is mental age appropriate [41]. This may provide insight into the empathic functions in WS.

Taken together, studies have revealed a profile of "dissociations" characterizing the WS social phenotype: the overdrive for social interaction and increased emotional responsivity on one hand, and clear limitations in social intelligence and related cognition on the other, raising intriguing questions regarding the pathways resulting in the characteristic profile. The bulk of behavioral literature sets the stage for the quest for the neurobiological and genetic underpinnings of the WS social phenotype.

The social brain

While the bulk of neurobiological literature on WS indicates diffuse abnormalities in the social brain [42**], at the same time, it paints a picture of brain structure and function that closely mirrors the excessively social and emotional behavioral profile of WS. Specifically, data are beginning to suggest that socially relevant structures are disproportionately enlarged in WS [42**, 43]. Conversely, there are both structural and functional alterations in the dorsal visual processing stream [43, 44]. Reflecting the increased use of language for social purposes [16, 5**] described earlier in relation to the WS personality, larger volumes of the ventral-orbital prefrontal region have been associated with greater use of social-affective language in individuals with WS [45]. Moreover, new evidence of language-associated brain

activity patterns as measured by event related potentials (ERP) reveals that individuals with WS show the largest, and those with autism the smallest, N400 ERP component [46*], which in healthy individuals indexes sensitivity to the semantic aspects of language. The N400 amplitude correlates with approachability in individuals with WS only, suggesting that the atypical neural processing of language may be instrumental to their social drive [47]. Thus, neurobiological studies are beginning to uncover neural correlates underlying aspects of the social-emotional phenotype of WS.

Additional ERP evidence suggests that in WS, relatively good behavioral performance on tasks of face processing is sustained by abnormal brain activity. For example, on a facial identity judgment task, while age-matched individuals with WS and typical controls showed similar behavioral performance, individuals with WS relative to controls showed abnormal ERP activity within the first 200 ms post-stimulus [48], namely a smaller N100 component and a markedly larger N200 (both index perceptual and attentional processes in healthy individuals) (Figure 3). The abnormally large N200 in WS is thought to reflect increased attention to faces. Since the small N100/large N200 pattern has not been observed in any other population studied (e.g., typical development, autism, specific language impairment), in either adults or children, this pattern is likely to reflect a WS specific ERP signature indexing increased attention to human faces [48]. Additionally supporting the interest in processing faces, magnetic resonance imaging (MRI) studies have revealed greater grey matter thickness and density of the fusiform gyrus in individuals with WS relative to typical controls [42**, 43]. The volume of the fusiform face area (FFA) is also enlarged in WS, with the functional volume correlating positively with face processing accuracy [49*]. The disproportionately large FFA in WS may reflect abnormally rapid specialization and development of the face sensitive regions of the FFA due to the robust attentional bias toward such stimuli beginning in early childhood [42**].

The overly sociable and emotional aspect of the WS phenotype is captured by findings showing that WS is associated with enlarged total amygdala volume relative to typical controls [43], and this correlates with ratings of approachability in response to images of facial expressions of unfamiliar people [50]. Further, individual differences in amygdala response to social threat has also been linked to approachability toward unfamiliar people in WS [51]. Functional MRI (fMRI) studies indicate that individuals with WS show reduced amygdala and orbitofrontal cortex (OFC) activation in response to threatening faces as compared to typical controls [36, 52]. Additionally, recent combined ERP and fMRI evidence shows that while brain responses to negative facial expressions are attenuated in WS, neural activity to happy faces is enhanced as compared to typical [52]. Combined, these findings may thus be linked to the insensitivity to negative social signals, abundance of positive affect, and bias toward attending and processing of positive emotion characterizing individuals with WS. Meyer-Lindenberg et al. [36] also reported aberrant amygdala-prefrontal interactions in WS during the processing of threatening faces, which was hypothesized to relate to the non-social anxiety, diminished social fear, and increased affiliation characterizing the syndrome.

An important brain structure linked to empathy, emotional responsiveness, and personality is the insula [53]. A recent study reported a global reduction in dorsal anterior insula volume,

together with compromised connectivity between the insula, amygdala, and OFC, in individuals with WS [54*]. Moreover, structural and functional alterations in the anterior insula predicted the extent to which the participants displayed the distinct hypersocial, empathic, and anxious WS personality, suggesting a genetic insula-mediated mechanism underlying the social-behavioral phenotype of WS. Taken together, the neurobiological literature is providing important clues with respect to potential substrates underpinning the unique dimensions of the WS social profile outlined earlier at the behavioral level. However, the evidence also raises questions, such as whether the insatiable drive for social interaction may be related to alterations in the reward regions/circuits of the brain in WS, and whether the increased attraction and attention to faces may be associated with enhanced OFC-FFA connectivity in WS, which will require disentanglement in future studies.

Genetics and hints toward new directions

Despite being a highly heritable disorder of social dysfunction, the genetic underpinnings of autism remain largely unknown [55*], and thus direct genotype-phenotype correlations are highly elusive. By contrast, the well-documented hemizygous deletion of ~25-28 genes on chromosome 7q11.23 that results in WS [2**] is present in ~98% of diagnosed individuals. The social profiles of WS and autism characterized by hypersociability and social avoidance respectively may appear at the first glance as polar opposites, suggesting that parallel study of the disorders may be particularly informative and attractive in an effort to unravel the neurogenetic bases of social function. However, as phenotypes are by a definition a collection of behavioral symptoms, and because their developmental trajectories are a mixture of environmental and biological influences, linkages with genetic data in the context of cross-syndrome comparisons are not straightforward. This highlights the fact that elucidating the genetic bases of social-affective behaviors is a formidably complex task, which however is now becoming possible to tackle.

In WS, focusing on the effects of the specific genes on behavior, a major avenue for addressing gene-behavior relationships involves characterizing the rare ~2% of diagnosed individuals associated with genetic variance from the typical deletion. Korenberg and colleagues [3] reported an important case whose deletion spares GTF2I but not GTF2IRD1, and this participant shows atypical social behavior for WS by appearing socially inhibited, i.e., shy, with severely compromised visual-spatial abilities. This evidence implicates the deletion of GTF2IRD1 and GTF2I in the network of genes and transcription factors underlying WS sociability and cognition.

Thus, although such studies are still scarce, the comparison of the characterizations of individuals with full deletions with those of the cases with atypically sized deletions is helping to parse the WS phenotype by highlighting the contributions of specific genes to observed behavior [2**, 3]. In a recent example, Karmiloff-Smith and colleagues [56] reported two small deletion cases, a female with 24 genes deleted sparing the four telomeric genes in the WS region, and a male with only the four telomeric genes deleted. Although both cases exhibited social deficits, the male showed an autistic-like socially inhibited profile, whereas the social behavior of the female resembled that typically observed in WS, including low levels of shyness and increased positive affect. At the same time, relative to

the full deletion WS profile, detailed neurocognitive assessments of the two cases revealed complex, divergent and convergent patterns of function, highlighting the challenging nature of genotype-phenotype studies.

A new research strategy attempting to understand the genetic mechanisms associated with complex disorders such as autism and WS has focused on copy number variants (CNVs). Here, a well-defined cluster of genes deleted or duplicated along a chromosome is studied in disorders of, e.g., social function, to pinpoint both discrete and interacting genes impacting brain development and organization.

As opposed to autism, given the strength and consistency of the hypersocial phenotype in WS, the relatively small cluster of dosage-sensitive genes deleted in WS appears vital for social-emotional and visual-spatial functions. A recently identified 7q11.23 duplication syndrome is associated with separation anxiety disorder and/or social phobia; features that are not only typically absent, but contrary in individuals with WS [19**]. Interestingly, spontaneous duplication of the 7q11.23 has recently also been linked to autism [55*]. As WS and autism present highly contrasting profiles of social motivation and social-interactive behavior, this further suggests both the dosage-sensitivity and significance of these genes in social behavior. Consistent with this notion, an association between variants in GTF2I and profound social impairments and increased repetitive behaviors was recently reported in autism [57].

Some of the WS region genes have been studied in knock out mice although the application of animal models to the understanding of human disease is not straightforward [56]. In one study, two mutant lines of mice were generated with deletions of the region syntenic to the human WS region [58*]. Elevated sociability and fear response characterized the proximal deletion line missing genes from GTF2I to LIMK1, whereas cognitive deficits were associated with the distal deletion line lacking genes from LIMK1 to FKBP6. As several key behaviors characterizing the WS phenotype were successfully replicated in mice, the animal model may provide important clues regarding the genes and gene networks related to complex neurobehavioral mechanisms in humans.

An exciting experimental study published this year by Korenberg et al. provided powerful new clues with respect to the effects of specific genetic information deleted in WS on neuroendocrine function in individuals with WS. Critically focusing on the endogenous as opposed to exogeneous exposure to neuropeptides, this study leads to the hypothesis that dysregulation of prosocial neuropeptides may underlie the increased social-affective behavior in WS [59**]. Oxytocin (OT) and arginine vasopressin (AVP) are thought to play a key role in human social behavior; e.g., exogeneous exposure to OT has been associated with increased eye contact, trust, and sensitivity to others' emotion [60**], although there still remains controversy surrounding the effects of OT and AVP in humans. OT is suggested to impact social-emotional behavior by acting upon distributed limbic and paralimbic regions; however, the neuropeptide targets and central neural circuits are unknown in humans [61, 62]. Most notably, OT modulates the fear response by acting upon the amygdala by attenuating its activation and its connectivity with the brainstem [62]. In contrast to studies using intranasal OT, Dai et al. [59**] sought to determine the potential

effects of altered baseline and/or release levels on social behavior using WS as a model. The study reported increased basal OT levels and peak release of both OT and AVP in response to positive emotional (favorite music) and negative physical (cold) stimulation in individuals with WS relative to typical controls. In WS, baseline OT level further correlated positively with approach, but negatively with adaptive social behaviors. This is the first powerful data implicating a biological mechanism that may underlie the paradox of increased social affiliation coupled with poor social relationships, anxiety, and some other social disturbances in WS. This new evidence raises questions of whether the increased release of OT and AVP may act on specific amygdalar regions to contribute toward increased eye contact, approachability, and attention to faces in WS; whether endogenous variation of OT and AVP may be implicated in aspects of the altered social-emotional behavior characterizing WS; and whether the WS gene deletion may be linked to disturbances in the release of both OT and AVP. Taken together, the diverse strands of evidence discussed in this article distinguish WS as an attractive candidate for an integrated approach toward elucidating the neural and genetic determinants of human social behavior (Figure 4). Fascinating clues integrating cross-level data are just beginning to emerge from WS [59**] and autism [61], which will be central to the novel efforts of elucidating the neuroendocrinology of the social brain.

Conclusions

WS is associated with a clearly defined genetic basis, combined with an unusual, distinctive social phenotype, thereby providing an attractive model for the basis of a new approach to social neuroscience. Individuals with WS exhibit consistent and unique patterns of social behavior, characterized by an overly friendly, affectionate, engaging, and socially disinhibited personality particularly toward strangers, apparent cross-culturally, and through separable channels of communication, such as eye gaze and language. The neurobehavioral mechanisms linked to the WS social profile highlight parallel profiles of exaggerated/preserved function, suggesting alterations of the amygdala, FFA, and connectivity between brain regions subserving social-emotional processing, which confer to the WS social phenotype characterized by non-social anxiety, increased approachability, emotional responsivity, and empathy. Recent advances in molecular genetics have provided initial clues suggesting that the relatively small dosage-sensitive cluster of genes at 7q11.23 is implicated in social-affective functions, with the hemideletion characterizing WS resulting in overly social behavior, and interestingly, a duplication causing a socially withdrawn and anxious profile. A most intriguing new finding suggested the role of the WS gene deletion in the dysregulation of the prosocial neuropeptides, OT and AVP, for the first time, potentially implicating them in the altered social-emotional behavior of WS. This work underscores the need for future research to be directed on the mechanistic effects of OT and AVP on the social brain circuitry [60**, 61].

The diverse approaches described earlier in this article directed at unraveling the complex issues tapping onto genetics of social behavior have just commenced the journey toward elucidating the multidimensional nature of social behavior and its widespread disruptions in psychiatric disorders. Although not straightforward, the parallel study of WS and autism characterized by contrasting social phenotypes may be valuable in illuminating shared

neurogenetic mechanisms underlying social functions. In the long run, these efforts promise to provide insight into the neurodevelopmental mechanisms that shape human social abilities in general.

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for the uneven profile of abilities across, e.g., processing faces vs. mentalizing in individuals with WS, the authors propose that long-range connectivity patterns may follow a delayed trajectory with respect to short-range connectivity patterns in WS. In typical development, as the amount of information processed globally throughout a distributed network increases in the course of development, correspondingly, decreases in locally processed information are seen, reflecting strengthening of long-range connectivity and weakening of short-range connectivity over time.]

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implications for the interrelations between genetics, neural systems, and complex behavioral traits in humans.]

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Highlights

- WS serves as an excellent model for linking genes, neural systems and social phenotype.
- The key dimensions of WS sociability include increased approachability, attention to faces, and emotional responsivity.
- Hypersociability combines with altered structure and function of the social brain in WS.
- Genes at 7q11.23 are implicated in social-affective functions.
- The WS gene deletion is linked to dysregulation of prosocial neuropetides oxytocin (OT) and arginine vasopressin (AVP).

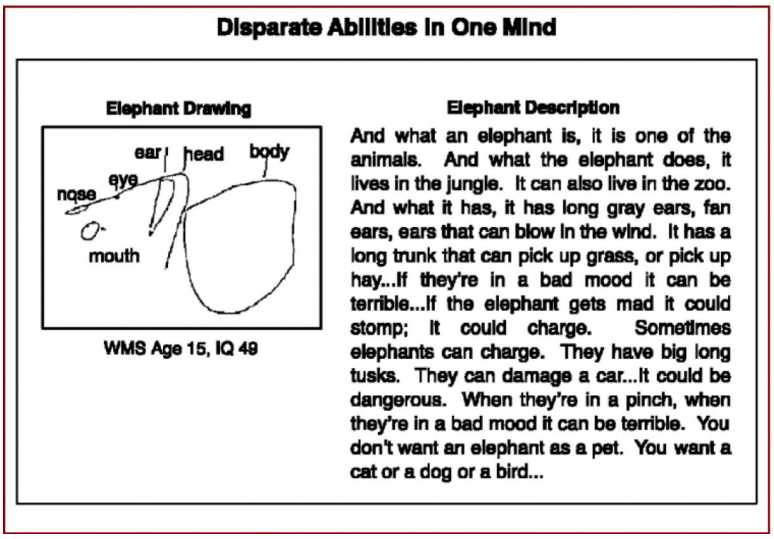

Figure 1.

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

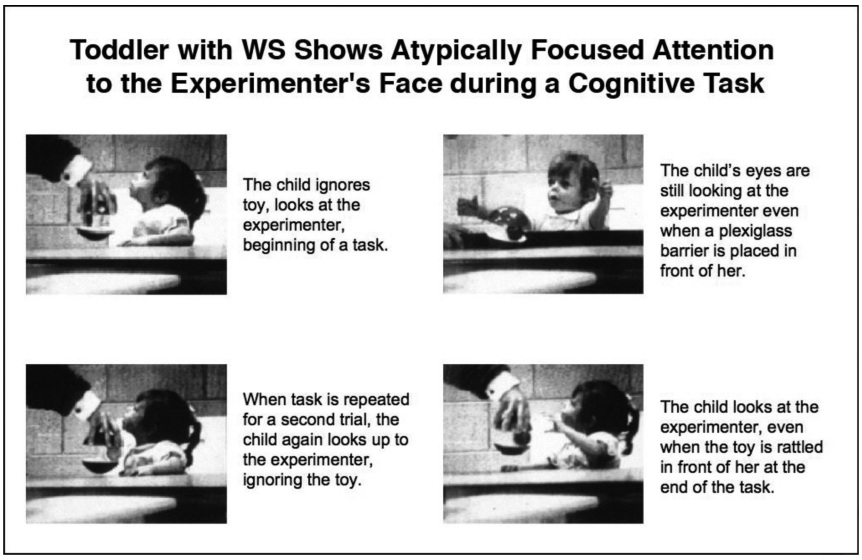

Figure 2.

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

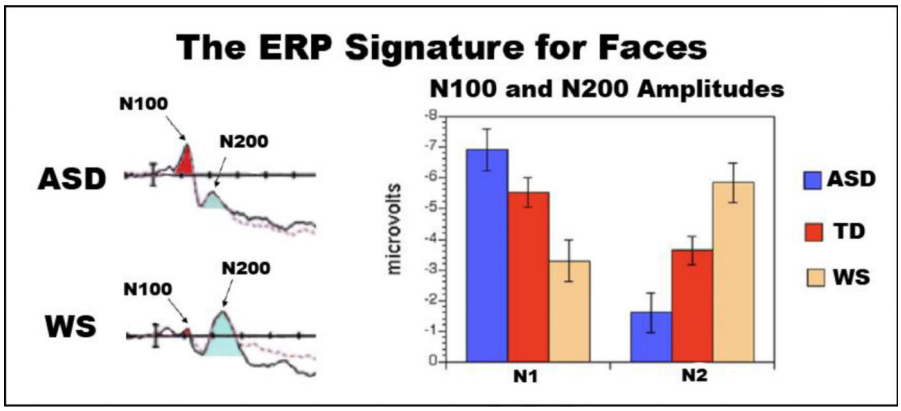

Figure 3.

ERP signature indexing converging profiles of attention to faces in WS (increased) and autism (decreased) relative to typical development (TD).

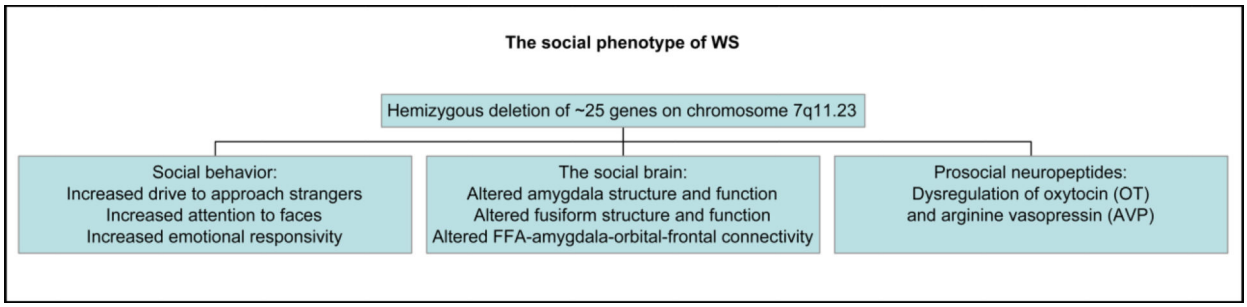

Figure 4.
Summary of the key dimensions of the social phenotype of WS.