Title: Parent of Origin, Age and Sex Effects on the Intellectual and Behavioral Phenotype of Children with Williams Syndrome

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Introduction: Williams syndrome (WS) is caused by a hemizygous deletion of chromosome 7q11.23. Children with WS exhibit a characteristic personality profile of striking social approach/disinhibition alongside considerable anxiety. They also exhibit a characteristic profile of cognitive abilities with a relative strength in expressive vocabulary and considerable weakness in visuospatial construction. It has been hypothesized that the parent of origin (PoO; the parent who contributed the chromosome containing the deletion) affects the intellectual and behavioral phenotype associated with WS via a paternal imprinted gene bias for GTF2I, one of the deleted genes. Reduced GTF2I expression in WS has been suggested to mediate oxytocin reactivity, resulting in higher oxytocin levels among children with WS. Crespi and Procyshyn (2017) posit that higher levels of oxytocin resulting from maternally derived deletions (maternal PoO) lead to increased social approach and anxiety, higher expressive vocabulary ability, and more severe visuospatial impairment.

Method: All participants had genetically confirmed classic-length deletions of the WS region and ranged in age from 4 to 17 years (M ≈ 10 years). The number of participants varied according to the dependent variable. The Differential Ability Scales-II (DAS-II; Elliott, 2007) was administered to 203 participants (105 girls) to assess intellectual abilities. In addition to the General Conceptual Ability score (GCA; similar to IQ), analyses were completed on standard scores (SSs) for the core clusters: Verbal, Nonverbal Reasoning (NVR), and Spatial. The Peabody Picture Vocabulary Test–4 (PPVT-IV; Dunn & Dunn, 2007) and the Expressive Vocabulary Test–2 (EVT-2; Williams, 2007) were administered to 206 participants (107 girls) as measures of receptive and expressive vocabulary respectively. Parents of 245 participants (123 girls) completed the Scales of Independent Behavior–Revised (SIB-R; Bruininks, Woodcock, Weatherman, & Hill, 1996) as an assessment of their child’s adaptive behavior skills. In addition to the Broad Independence SS, analyses were completed on SSs for all component domains: Motor Skills, Personal Living Skills, Social Interaction and Communication Skills, and Community Living Skills. For these assessments, MS = 100 and SD = 15 for the general population. Parents of 116 participants (62 girls) completed the Social Responsiveness Scale–2 (SRS-2; Constantino, 2012) from which the Social Motivation scale T-score was examined (M = 50, SD = 10). Parents of 249 participants (125 girls) completed a modified parent-report version of the Multidimensional Personality Questionnaire (MPQ; Tellegen, 1985), from which the Williams syndrome Personality Profile (WSPP) score was calculated as outlined in Klein-Tasman and Mervis (2003). PoO of the deletion was determined from parent and child blood samples by molecular genetic methods. All statistical analyses included PoO and biological sex as between-subjects factors and maternal education (a proxy for socioeconomic status) and chronological age (CA) as covariates. Due to the number of statistical tests conducted, the alpha level was set at p < .01.

Results: Multivariate analyses of covariance (MANCOVAs) were conducted to determine the effects of PoO and sex while controlling for CA and maternal education on the core clusters of the DAS-II and the domains of the SIB-R. Likewise, univariate analyses of covariance (ANCOVAs) were conducted on the DAS-II GCA, SIB-R Broad Independence SS, PPVT-4 SS, EVT-2 SS, SRS-2 Social Motivation T-score, and MPQ WSPP score. A significant effect of CA [F(3, 195) = 13.53, p < .001, η² = .17] was found on the linear combination of the DAS-II core cluster SSs. Follow-up univariate ANCOVAs revealed that NVR SS decreased slightly but significantly with CA (p = .002) but no CA effects were present for Verbal SS (p = .68) or Spatial SS (p = .09). Significant effects of CA [F(4, 236) = 18.67, p < .001, η² = .24] and sex [F(4, 237) = 6.08, p < .001, η² = .09] were found on the linear combination of the SIB-R domains. Follow-up univariate ANCOVAs found Personal Living SS increased slightly but significantly with CA (p = .004) and Community Living SS decreased slightly but significantly with CA (p = .004). In addition, Personal Living SS was higher for girls than boys (p < .001). Girls also earned higher Broad Independence SSs than boys [F(1, 239) = 7.81, p = .006, η² = .03]. No significant effects were found in the analyses of DAS-II GCA, PPVT-4 SS, EVT-2 SS, Social Motivation scale T-score, or WSPP score.

Discussion: We did not find any evidence of genomic imprinting bias corresponding with PoO of the WS deletion. In other words, intellectual and behavioral abilities do not differ on average between children who inherited the deletion from their mother or children who inherited the deletion from their father. Very few effects of CA or sex were found. Implications of these results will be addressed.

References/Citations: