Title: Longitudinal Assessment of Intellectual Abilities of Individuals with Williams Syndrome: Bayesian Multilevel Modeling

Authors: Vitor Neves Guimarães[1], Subhadip Pal[1], Caroline Greiner de Magalhães[1], and Carolyn B. Mervis[1]

Introduction: Williams syndrome (WS) is a rare neurogenetic developmental disorder caused by a hemizygous microdeletion on chromosome 7q11.23. A previous longitudinal study of 40 children and adolescents with WS (Mervis et al., 2012) found that Verbal, Nonverbal, and IQ Composite standard scores (SSs) on the Kaufman Brief Intelligence Test-2 (KBIT-2; Kaufman & Kaufman, 2004) were stable over the age range of 4 – 17 years, with average performance in the borderline range. In addition, maternal education level had a significant impact on Verbal SS and IQ Composite intercepts. The current study extends the previous study by adding 81 participants and increasing the number of observations for most of the original participants.

Method: Participants were 121 individuals with genetically-confirmed classic length WS microdeletions (M_{grand} = 9.50 years, SD_{grand} = 3.44, $Range_{grand}$: 5.55–21.60, 61 females), 40 of whom had been included in Mervis et al. (2012). Thirty of the latter (75%, 17 females) had at least one additional testing point (*Mdn* = 5, Range: 1–8). Each participant was assessed a minimum of four times at intervals of at least 11.5 months (*Mdn* = 5 assessments, Range: 4–12), over a period of 2.99 – 13.98 years (*Mdn* = 7.07 years). KBIT-2 Verbal SS, Nonverbal (Reasoning) SS, and IQ Composite were used to measure intellectual abilities and were centered around the population mean of 100 (σ = 15). Chronological age was centered around the sample grand mean of 9.50 years. Maternal education levels were dichotomized based on whether or not the participant's mother had a bachelor's degree, with a total of 97 (78%) having this credential. Three sets of multilevel Bayesian linear models were fitted with intellectual ability measures as outcome variables: one set of unconditional, or growth-only models, and two sets of conditional, or growth by maternal education level-only models and growth by maternal education level and participant sex models. Weakly informative Normal and sample-based Student *t* priors were used to fit Gaussian and Student *t*-family models. Models were compared and selected using the Widely Applicable Information Criterion (WAIC) and Leave-one-out technique (LOO).

Results: All models showed good convergence ($\hat{R}$ = 1.00). Student *t*-family models yielded better results according to both the WAIC and LOO criteria. In addition, the conditional growth by maternal education and participant sex models showed a better fit for the data and are the only ones reported here for the sake of brevity. All models explained small amounts of variance: R^2 = .090 (*SD* = .01, IQR: .07 – .10) for Verbal SS, R^2 = .055 (*SD* = .01, IQR: .03 – .05) for Nonverbal SS, and R^2 = .077 (*SD* = .01, IQR: .06 – .08) for IQ Composite.

Posterior estimated mean Verbal SS at age 9.50 years for participants whose mother did not have a bachelor's degree was 74 (Intercept = -25.53, *SD* = 1.50, 95% *Credible Interval (CI*) [-28.46, -22.54]) with an estimated annual growth of -.26 (*SD* = .36, 95% *CI* [-.96, .42]). The posterior mean difference due to maternal bachelor's degree for Verbal SS was 5.68 points (*SD* = 1.68, 95% *CI* [2.30, 8.98]) with an annual growth of -.32 (*SD* = .40, 95% *CI* [-1.11, .46]). Mean Nonverbal SS at age 9.50 years was 76 (Intercept = -23.69, *SD* = 1.72, 95% *CI* [-26.98, -20.41]) with an estimated annual growth of -.03 (*SD* = .40, 95% *CI* [-.81, .78]) for no maternal bachelor's degree. The posterior mean difference due to maternal bachelor's degree for Nonverbal SS was 4.27 points (*SD* = 1.90, 95% *CI* [.65, 7.93]) with an annual growth of -.14 (*SD* = .46, 95% *CI* [-1.08, .74]). Mean IQ Composite SS at age 9.50 years was 72 (Intercept = -28.69, *SD* = 1.63, 95% *CI* [-31.34.79, -24.90]) with an annual growth of -.15 (*SD* = .25, 95% *CI* [-.90, .58]) for no maternal bachelor's degree. Posterior mean difference for maternal bachelor's degree was 5.71 points (*SD* = 1.81, 95% *CI* [2.16, 9.19]) with an annual growth of -.29 (*SD* = .43, 95% *CI* [-1.15, .58]). No significant sex effects were identified.

Discussion: Consistent with previous findings (Mervis et al., 2012), posterior distributions for all intellectual ability measures were within the borderline disability range. In addition, the posterior estimates for the effect of age (i.e., regression slopes) were not statistically significant, suggesting that SSs remained stable over the age range from 4 – 18 years for all dependent variables. Significant posterior mean differences attributed to maternal education were found for all three dependent variables: Verbal SS, Nonverbal SS, and IQ Composite SS. This pattern of findings is consistent with prior findings for typically developing children. The lack of significant change in SSs over time in a relatively large sample over a median of 7.07 years, combined with the finding of

no significant differences as a function of participants' sex, indicates that the KBIT-2 is an appropriate measure of intellectual ability for studies of children and adolescents with WS that include a wide age range of participants within the same sample.

References: Kaufman, A.S. & Kaufman, N.L. (2004). *Kaufman Brief Intelligence Test–Second Edition*. Circle Pines, MN: AGS Publishing

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[1]University of Louisville