**Table 1. Participant Demographics**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Probands | | HR-ASD | | HR-NoASD | | Group Comparison | | |
|  | n | % | n | % | n | % | X/t | df | p |
| **Sex** |  |  |  |  |  |  |  |  | <0.001a |
| Male (n,%) | 331 | 86.2 | 69 | 77.5 | 160 | 54.2 |  |  |  |
| Female (n,%) | 53 | 13.8 | 20 | 22.5 | 135 | 45.8 |  |  |  |
| **Child Race** |  |  |  |  |  |  |  |  | 0.568b |
| Asian (n,%) |  |  | 1 | 1.1 | 4 | 1.4 |  |  |  |
| Black (n,%) |  |  | 2 | 2.2 | 10 | 3.4 |  |  |  |
| More than one race (n,%) |  |  | 13 | 14.6 | 26 | 8.8 |  |  |  |
| White (n,%) |  |  | 71 | 79.8 | 249 | 84.4 |  |  |  |
| Missing (n,%) |  |  | 2 | 2.2 | 6 | 2.0 |  |  |  |
| **Maternal Education** |  |  |  |  |  |  |  |  | 0.371b |
| Less than college (n,%) | 126 | 32.8 | 26 | 40.4 | 90 | 30.5 |  |  |  |
| College degree (n,%) | 145 | 37.8 | 27 | 30.3 | 118 | 40.0 |  |  |  |
| Graduate degree (n,%) | 94 | 24.5 | 23 | 25.8 | 71 | 24.1 |  |  |  |
| Not answered (n,%) | 4 | 1.0 | 0 | 0.0 | 4 | 1.4 |  |  |  |
| Missing (n,%) | 7 | 1.8 | 2 | 2.2 | 5 | 1.7 |  |  |  |
| **Autistic Traits** | mean | SD | mean | SD | mean | SD |  |  |  |
| Proband SCQ Score (mean, SD) | 21.27 | 5.59 | 22.44 | 5.23 | 20.93 | 5.65 | -2.20 | 134 | 0.029a |
| Sibling ADOS Severity Score (mean, SD) |  |  | 5.86 | 1.88 | 1.61 | 0.99 | -20.43 | 102 | 0.001a |

aTesting for significant differences in distributions (Chi Square), or mean scores (t-tests) for HR-ASD vs. HR-NoASD unless otherwise noted.

bTesting for significant differences in distributions using Fisher’s Exact Test for HR-ASD vs HR-NoASD due to small counts (no X/t or df)

**Table 2. Correlations Between Infant Brain Phenotypes and Proband ASD Trait Level**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | HR-ASD | | | | | HR-NoASD | | | | |
|  | n | r | 95% CI | P value | FDR P value | n | r | 95% CI | P value | FDR P value |
| **TSA** |  |  |  |  |  |  |  |  |  |  |
| 6 months | 33 | 0.28 | (-0.07, 0.57) | 0.115 | 0.173 | 153 | -0.02 | (-0.18, 0.14) | 0.8 | 0.845 |
| 12 months | 39 | 0.40 | (0.1, 0.64) | 0.011 | 0.045 | 195 | -0.08 | (-0.22, 0.06) | 0.278 | 0.845 |
| 24 months | 46 | 0.41 | (0.14, 0.63) | 0.004 | 0.036 | 181 | -0.04 | (-0.18, 0.11) | 0.633 | 0.845 |
| **TCV** |  |  |  |  |  |  |  |  |  |  |
| 6 months | 44 | 0.31 | (0.02, 0.56) | 0.039 | 0.070 | 167 | -0.02 | (-0.17, 0.14) | 0.845 | 0.845 |
| 12 months | 39 | 0.36 | (0.05, 0.61) | 0.024 | 0.054 | 195 | -0.06 | (-0.19, 0.09) | 0.443 | 0.845 |
| 24 months | 48 | 0.35 | (0.07, 0.58) | 0.015 | 0.045 | 186 | -0.04 | (-0.18, 0.11) | 0.635 | 0.845 |
| **EA-CSF** |  |  |  |  |  |  |  |  |  |  |
| 6 months | 42 | -0.02 | (-0.32, 0.29) | 0.905 | 0.905 | 149 | -0.02 | (-0.18, 0.14) | 0.821 | 0.845 |
| 12 months | 39 | 0.16 | (-0.16, 0.46) | 0.319 | 0.359 | 183 | -0.07 | (-0.21, 0.08) | 0.372 | 0.845 |
| 24 months | 42 | 0.20 | (-0.11, 0.48) | 0.202 | 0.260 | 159 | -0.10 | (-0.25, 0.06) | 0.222 | 0.845 |

**Table 3. Longitudinal Model Results for Primary Variablesa**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Estimate | 95% CI | df | P value |
| **TCV Model** |  |  |  |  |
| Proband SCQ | -907.389 | (-2519.59, 704.81) | 292 | 0.269 |
| Proband Sex - Female | -2099.07 | (-25120.67, 20922.53) | 292 | 0.858 |
| Sibling Sex - Female | -75402.5 | (-92391.04, -58413.95) | 292 | <0.001 |
| Sibling Group - HR-NoASD | -127931.864 | (-219393.21, -36470.52) | 292 | 0.006 |
| Group x Proband SCQ | 6147.958 | (2253.39, 10042.52) | 292 | 0.002 |
| **TSA Model** |  |  |  |  |
| Proband SCQ | -66.435 | (-168.5, 35.63) | 266 | 0.201 |
| Proband Sex - Female | 406.645 | (-1142.03, 1955.32) | 266 | 0.606 |
| Sibling Sex - Female | -4725.86 | (-5816.15, -3635.57) | 266 | <0.001 |
| Sibling Group - HR-NoASD | -7928.76 | (-14409.55, -1447.97) | 266 | 0.017 |
| Group x Proband SCQ | 384.939 | (107.51, 662.37) | 266 | 0.007 |

aReference groups for sex and sibling diagnostic group are female, and HR-NoASD, respectively.

**Figure 2. Brain Phenotypes Trajectories from 6 to 24 months in HR-ASD Infants**

Least squares (LS) means of total CV, total SA, and right middle occipital gyrus SA are plotted at 6, 12, and 24 months for HR-ASD siblings split by proband SCQ group (SCQ ≥ 21 = SCQ-High; SCQ < 21 = SCQ-Low). HR-ASD infants with probands with elevated ASD traits have enlarged total SA and regional SA in the right middle occipital gyrus, and greater total CV at 12 and 24 months compared to HR-ASD infants with probands with lower levels of ASD traits. LS means are adjusted for proband and sibling age and sex. Percent differences between groups are reported where significant (\*P < .05, \*\*P < .01, \*\*\*P < .001) along with adjusted Cohen’s d effect size estimates. Error bars represent 95% confidence intervals around LS means.



**Table 4. Sibling brain phenotypes and ASD severity, social skills at 24-months**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | 24-month ADOS Severity Score | | | 24-month CSBS  Social Composite | | | 24-month Vineland Socialization | | |
|  | n | r | p | n | r | p | n | r | p |
| **TCV** |  |  |  |  |  |  |  |  |  |
| 6 months | 235 | 0.18 | 0.007 | 195 | -0.18 | 0.01 | 227 | -0.19 | 0.005 |
| 12 months | 250 | 0.20 | 0.002 | 218 | -0.18 | 0.007 | 247 | -0.19 | 0.003 |
| 24 months | 254 | 0.15 | 0.017 | 220 | -0.18 | 0.007 | 251 | -0.15 | 0.02 |
| **TSA** |  |  |  |  |  |  |  |  |  |
| 6 months | 203 | 0.21 | 0.003 | 178 | -0.20 | 0.008 | 197 | -0.28 | <.001 |
| 12 months | 249 | 0.17 | 0.008 | 216 | -0.17 | 0.01 | 245 | -0.18 | 0.004 |
| 24 months | 244 | 0.11 | 0.07 | 215 | -0.13 | 0.04 | 241 | -0.16 | 0.01 |