Differences between Boys and Girls in the Development of Neuroanatomical Functional Connectivity underlying Intelligence found using Bayesian Connectivity Analysis

V. J. Schmithorst[1], and S. K. Holland[1]

[1]Radiology/Pediatric Brain Imaging, Children's Hospital Medical Center, Cincinnati, Oh, United States

Introduction

Previous studies have shown that women possess a greater association between white matter properties and intelligence [1-2] as compared to men. A recent functional MRI (fMRI) study [3] showed a developmental aspect to this sexual dimorphism. Girls displayed an increasing association with age of intra (left)-hemispheric functional connectivity with intelligence, while the opposite effect was shown in boys. To investigate a possible effect with regard to inter-hemispheric functional connectivity the task of narrative processing, shown to recruit bilateral networks [4], is used in conjunction with a recently published Bayesian methodology for modeling functional connectivity [5] modified to test for between-groups differences.

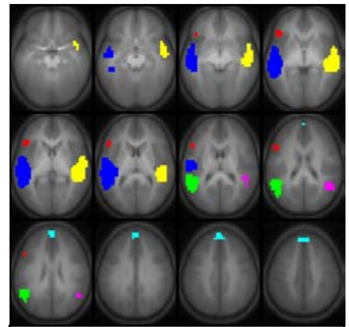

Figure 1. Regions with significant (p < 0.05, corrected) correlation of full-scale IQ with functional activation from a narrative comprehension task with in a cohort of 303 normal children ages 5-18. Images in neurological orientation.

Materials and Methods

fMRI data were obtained from 303 normal children (151M, 152F) ages 5-18 on a Bruker 3T Medspec scanner. EPI-fMRI scan parameters were: TR/TE = 3000/38 ms, BW = 125 kHz, FOV = 25.6 X 25.6 cm, matrix = 64 X 64, slice thickness = 5 mm. The fMRI paradigm was a 30 second on-off block design. One story, read by an adult female speaker, was presented during the task period. During the control period, pure tones of 1 s duration were presented at unequal intervals of 1–3 s. The fMRI data were analyzed using a random-effects General Linear Model (GLM). fMRI time courses were extracted from each subject from all regions found with a significant correlation of functional activation with full-scale IQ (Figure 1).

The Bayesian methodology for connectivity analysis [5] was modified for the specific analyses desired for this study. From each fMRI timecourse Y a vector of binary values A is constructed according to whether elevated activity occurs during the narrative comprehension period: $A = I(Y > c\ \sigma)$ where σ is the standard deviation of the residuals from a GLM performed on each individual timecourse. A data-driven method was utilized to select a value of c = 0.626 to maximize the selectivity of the indicator function. For each pair of ROIs a and b in each subject s the joint activation frequencies z are derived as:

$$z_{1s} = \sum_{m=1}^{M} I(A_{asm} = 1, A_{bsm} = 1),\ z_{2s} = \sum_{m=1}^{M} I(A_{asm} = 1, A_{bsm} = 0),\ z_{3s} = \sum_{m=1}^{M} I(A_{asm} = 0, A_{bsm} = 1),\ z_{4s} = \sum_{m=1}^{M} I(A_{asm} = 0, A_{bsm} = 0)$$

where m denotes all time points during the narrative comprehension epochs, and I is the indicator function. The multinomial likelihood of the data is:

$$p(z \mid \theta) \propto \prod_{s=1}^{S} \prod_{i=1}^{4} \theta_{is}^{z_{is}} \text{ where } \theta_{1s} = P(A_{asm} = 1, A_{bsm} = 1), \theta_{2s} = P(A_{asm} = 1, A_{bsm} = 0), \theta_{3s} = P(A_{asm} = 0, A_{bsm} = 1), \theta_{4s} = P(A_{asm} = 0, A_{bsm} = 0).$$

Using flat priors, the posterior (Dirichlet) distribution is $p(\theta \mid z) \propto \prod_{s=1}^{S} \prod_{i=1}^{4} \theta_{is}^{z_{is}}, \sum_{i=1}^{4} \theta_{is} = 1 \forall s$. The conditional joint activation probability $P(A_{asm} = 1 \mid A_{bsm} = 1) = \theta_1 / (\theta_M + \theta_1), \theta_M = MAX(\theta_3, \theta_2)$ is used as a measure of overall connectivity. Sampling from the posterior distributions of θ, a three-way ANCOVA with a dependent variable of the joint activation probability and independent variables of sex, age, and IQ is performed. Bayesian posterior inferences are then drawn from the posterior distributions of the regression coefficients for sex-X-IQ interaction and sex-X-IQ-X-age interaction. To account for a possible confound regarding task performance, a connection was deemed significant only if the posterior probability was P>0.99 from an analysis including only the subset of 259 subjects whose performance on a post-scan recall test was better than chance (p < 0.02), and the posterior probability was P > 0.95 for an analysis including all subjects.

Results and Discussion

Six regions were found (Figure 1) with a significant correlation of IQ with functional activation: the superior temporal gyrus (Wernicke's areas) bilaterally (blue, yellow), the posterior superior temporal gyrus bilaterally (green, magenta), the superior medial frontal gyrus (cyan), and the left inferior frontal gyrus (Broca's area; red). Significant sex-X-IQ interactions (girls > boys) were seen for the functional connectivity of Wernicke's areas (both hemispheres) to the left posterior superior temporal gyrus (Figure 2, left). Significant sex-X-IQ interactions (boys > girls) were seen for the functional connectivity of Broca's area to Wernicke's areas and the right posterior superior temporal gyrus (Figure 2, middle). A significant three-way sex-X-age-X-IQ interaction (girls > boys) was seen for the functional connectivity of Wernicke's areas (both hemispheres) with the right posterior superior temporal gyrus (Figure 2, right). Girls thus show greater reliance on connectivity between Wernicke's areas and the posterior superior temporal gyrus (with a developmental effect seen in the right hemisphere), while boys show greater reliance on feed-forward and feed-back connectivity between Broca's area and auditory processing regions. These results are consistent with previous studies showing sex-related differences in posterior language areas for higher-order semantic processing at the sentence level [6], and more spatially distinct networks for phonological and lexical-semantic processing in males [7].

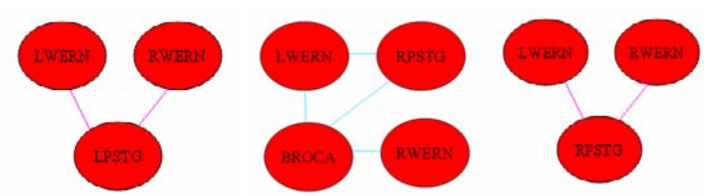

Figure 2. Functional connectivity diagrams showing: sex-X-IQ interaction (girls>boys; left), sex-X-IQ interaction (boys>girls; middle), sex-X-IQ-X-age interaction (girls>boys; right). (Abbreviations: LWERN = Left Wernicke's area; RWERN = Right Wernicke's area; BROCA = Broca's area; RPSTG = Right Posterior Superior Temporal Gyrus; LPSTG = Left Posterior Superior Temporal Gyrus).

Conclusion

A Bayesian methodology for the investigation of functional connectivity was modified to test for between-groups differences in a cohort of over 300 normal children performing a narrative comprehension task. Our results suggest that the previously-hypothesized greater reliance in girls with age on functional connectivity for intelligence is modulated by specific information processing demands.

References

[1] Haier RJ et al., *Neuroimage*, 25, 230, 2005. [2] Jung RE et al., *Neuroimage*, 26, 965, 2005. [3] Schmithorst VJ & Holland SK, *Neuroimage*, 31, 1366, 2006. [4] Schmithorst VJ et al., *Neuroimage*, 29, 254, 2006. [5] Patel RS et al., *Hum Brain Mapp*, 27, 267, 2006. [6] Kansaku K et al., *Cereb Cortex*, 10, 866, 2000. [7] Pugh KR et al., *Brain*, 119, 1221, 1996.