A Novel Meta-analytic Technique Reveals the Neuroanatomy of Specific Language Impairment

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Specific Language Impairment (SLI) is a developmental language disorder that typically presents with grammatical deficits, often also accompanied by various other problems. Understanding the neural substrates of this disorder may lead to earlier diagnosis and treatment, and could also inform our understanding of acquired aphasias. However, no consensus has yet emerged from the growing literature investigating the neurobiology of SLI. We have proposed a brain-based hypothesis, the Procedural Deficit Hypothesis (PDH), which posits that SLI can largely be explained by abnormalities of brain structures that underlie the procedural memory system. Consistency across individuals in the core grammar deficits are explained by the consistent presence of anomalies in fronto-basal ganglia circuits, especially in Broca’s area and the caudate nucleus, which subserves grammar and its procedural memory substrates. In a prior qualitative review, we found evidence supporting the predictions of the PDH. However, such qualitative reviews can be biased and misleading due to the technical limitations of the approach. A rigorous quantitative meta-analysis of the neuroanatomy of SLI would provide a more accurate assessment of the literature, and could reveal finer-grained patterns. To quantitatively assess the neuroanatomical consistency of anomalies reported in prior studies of SLI, we developed and applied a new probabilistic meta-analysis technique, the Co-localization Likelihood Estimation (CLE) method, that incorporates advantageous features of various current techniques, and adds critical new capabilities well-suited to SLI and other developmental and adult-onset disorders.

CLE analysis is performed in three steps: (1) locations of anatomical or functional anomalies reported in published studies are coded, (2) For each location, a proportion of studies reporting anomalies among those investigating that location is calculated and weighted by the sample sizes of the studies, (3) A permutation significance test determines statistical significance of weighted proportions for each brain structure, accounting for differences in the number and sensitivity of studies examining each structure. We used CLE to analyze a database of 25 neuroanatomical studies of SLI, encompassing a total of 270 individuals with SLI and 265 typically-developing controls. The analysis showed that anomalies are detected at a greater than chance level only in frontal cortex (P=.005) and the basal ganglia (P=.002), and at lower chance in the cingulate cortex (P=.0002) and the diencephalon (P=.019). CLE-based one-way ANOVAs showed a significant effect of subregion within both frontal cortex (P=.029) and the basal ganglia (P=.020). Post-hoc CLE analyses within the basal ganglia revealed that the caudate is affected (P=.025), but not the lentiform nucleus. No single subregion of frontal cortex showed significant abnormalities in post-hoc tests. We were surprised by the lack of co-localization in Broca’s region, so we examined structural and functional anatomy studies separately. We found that functional (P=.015) but not structural (P=.46) anomalies in fact cluster in Broca’s region.

Overall, the results are largely consistent with the PDH, but further suggest that the caudate is the primary structure affected. The finding that Broca’s region was anomalous only in functional studies might be due to downstream functional effects of the caudate on Broca’s region.