

ABSTRACT

Recent evidence suggests that deficient executive functions are fundamental to the cognitive deficits in Autism spectrum disorders (ASD). It has been suggested that individuals with ASD have disrupted neural connectivity including that in the frontal lobes that mediate executive functions. With reports of immunologic abnormalities in children with ASD, it is plausible that such abnormalities disrupt the neural connectivity in the brains of individuals with ASD. There is, however, relatively little empirical evidence to support the notion. This dissertation reports on three studies to examine whether the executive dysfunction in children with ASD is associated with their immunologic abnormalities and disordered neural connectivity.

In study one, the executive functioning of 19 high-functioning (HFA) and 19 low-functioning (LFA) children with ASD were compared to 28 children with normal development using a battery of neuropsychological tests. Results not only confirmed previous knowledge that children with ASD had significant executive dysfunctions compared with children with normal development, but also extended it to show that LFA children were significantly more impaired than HFA children. Study two built on this knowledge and examined whether immunological abnormalities are associated with the differential executive dysfunctions in 18 HFA and 19 LFA children. Results indicated that LFA children showed greater executive dysfunctions as well as higher

levels of total lymphocyte, T lymphocyte and suppressor/cytotoxic T lymphocyte levels than HFA children. In addition, executive dysfunctions were significantly associated with the three lymphocyte levels, lending support to the notion that immunological factors may play a role in the cognitive dysfunctions in individuals with ASD. Study three further examined whether the differential executive dysfunctions and immunologic levels in LFA and HFA children are associated with their neural connectivity. Results on 17 HFA and 14 LFA children showed that LFA children had significantly elevated theta coherence in the anterior network, as well as at the left *intra-hemispheric* and right-to-left *inter-hemisphere* connections than HFA children. LFA children also had significantly elevated immunologic level specifically in suppressor/cytotoxic T lymphocytes. Furthermore, the executive dysfunctions, disordered neural connectivity, and abnormal immunologic levels were found to be associated.

These findings have provided some initial evidence to support the notion that immunologic factors may play a role in causing neuronal damage in the anterior region of the brains of children with ASD, which is manifested in their disordered neural connectivity of that region, and their executive dysfunctions mediated by that same region.