Abstract

There is growing evidence that pre-natal immune activation contributes to neuropsychiatric disorders. We will show that early post-natal immune activation resulted in profound impairments in social behavior, including in social memory in adult male mice heterozygous for a gene responsible for tuberous sclerosis complex (Tsc2+/-), a genetic disorder with high prevalence of autism. Interestingly, early post-natal immune activation did not affect either wild type (WT) or female Tsc2+/- mice. We demonstrate that these memory deficits are caused by abnormal mammalian target of rapamycin (mTOR)-dependent interferon signaling and impairments in microglia function. By mining the medical records of over 3 million children followed from birth, we show that the prevalence of hospitalizations due to infections in males (but not in females) is associated with future development of autistic spectrum disorders (ASD). Altogether, our results suggest the importance of synergistic interactions between strong early post-natal immune activation and mutations in ASD.