NF-kB p50 knock-out mice as animal model of Autism

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Alterations in genes that regulate neurodevelopment can lead to cortical malformations, resulting in malfunction during postnatal life. Developmental disorders comprise diseases such as Down syndrome, schizophrenia, bipolar disorder, major depressive disorder, autism and epilepsy. Cortical malformations may result from abnormal neuronal proliferation, migration defects or abnormal formation of circuits/synaptogenesis. In this study, we evaluated whether mice lacking the NF-κB p50 subunit present alterations in cortical structure, with consequent behavioural impairments. We found that $p50^{-/-}$ mice at post-natal day 2 (P2) present an increase in radial glial cells, an increase in Reelin protein expression levels, other than a specific alteration in the cortical layering. Moreover, adult $p50^{-/-}$ mice display abnormal columnar organization in the somato-sensory cortex, with an increase in cell density, less neuropil space and a loss of linearity in the vertical organization of the minicolumns, a specific decrease in somatostatin- and parvalbumin-expressing interneurons, altered neurite orientation and a concomitant decrease in Synapsin I protein levels. Concerning behaviour, $p50^{-/-}$ mice, other than an increase in locomotor and exploratory activity measured in the open field test, present impairments in social behaviours, scored by means of the three chambered apparatus and the reciprocal social interaction test, with a reduction in social interaction. Finally, we tested the effect of Risperidone, an atypical antipsychotic drug used to treat irritability in autistic patients on $p50^{-/-}$ and wild type mice. Risperidone treatment improved the open field test performance of $p50^{-/-}$ mice, reducing both the distance travelled end the movement speed, decreasing hyperactivity. Together, these data provide new insight on the possibility of a link between altered function of NF-κB and the pathogenesis of neurodevelopmental disorders. We propose NF-kB p50 subunit-lacking mice as a new mouse model of autism.