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NEURODEVELOPMENT

Isolation reduces myelination

> re-introducing isolated mice to a social environment did not reverse the effects

Experiences early in life can have long-lasting effects on the brain. For example, studies in animals and children have shown that early social isolation is associated with white matter alterations. The mechanisms underlying these changes are not well understood, but a new study shows that in mice, social isolation during a critical post-weaning period impairs prefrontal cortex (PFC) function and reduces myelination in the PFC by altering oligodendrocyte neuregulin 1 (NRG1)–receptor tyrosine kinase ERBB3 signalling.


STOCKBYTE

Makinodan *et al*. housed male mice in isolation, in standard housing conditions or in enriched environments from postnatal day 21 (P21) onwards. On P50, isolated mice showed reduced social interaction and working memory, both of which involve the PFC, compared with control and environmentally enriched mice. In addition, myelin was thinner, oligodendrocyte morphology was less complex and expression of myelin genes was reduced on P65 in the PFC of isolated mice. Interestingly, social isolation from P21 to P35 was sufficient to establish these effects, whereas isolation from P35 to P65 was not. Moreover, re-introducing isolated mice to a social environment did not reverse the effects. Together, this points to a critical period for appropriate PFC myelination.

NRG1–ERBB signalling has a role in oligodendrocyte maturation, and the authors showed that mice in which *Erbb3* expression in oligodendrocytes was reduced at the beginning of the critical period phenocopied socially isolated mice, whereas there were no effects if it was reduced after the critical period. This suggests that NRG1–ERBB3 signalling in the PFC is required for normal myelination. Social isolation from P21 to P35 did not affect the expression of *Erbb2*, *Erbb3*, *Erbb4*, *Nrg2* or *Nrg3* in the PFC. However, it decreased type III NRG1 mRNA levels — the NRG1 isoform that is mainly expressed in the PFC.

The effects of severe social neglect in childhood are well known, and this study shows that some of them may be induced by altered NRG1–ERBB3 signalling during a critical period of prefrontal myelination.

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ORIGINAL RESEARCH PAPER Makinodan, M. *et al.* A critical period for social experience-dependent oligodendrocyte maturation and myelination. *Science* **337**, 1357–1360 (2012)