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SUPPLEMENTARY INFORMATION

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Growing a social brain

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Supplementary Table 1: Evidence showing that social experience in early life shapes brain development

Level of Observation	Evidence	References
Receptors Expression	➢ The adult female offspring of increased licking/grooming rat mothers show increased Oestrogen Receptor alpha (ERα) expression in the medial preoptic area (MPOA) and are themselves high licking/grooming mothers. Moreover, the biological offspring of low licking/grooming mothers fostered at birth by high licking/grooming dams show increased ERα expression in the MPOA.	208
	➢ The adult offspring of increased licking/grooming rat mothers have increased glutamate receptor expression in the hippocampus	209
	➢ Offspring of high licking grooming rat mothers have reduced plasma adrenocorticotropic hormone (ACTH) and reduced corticosterone responses to acute stress. In the brain, they have increased glucocorticoid receptor expression in the hippocampus, and decreased corticotrophin releasing hormone expression in the hypothalamus.	210
	➢ Maternal care permanently alters pups' expression of gamma-Aminobutyric acid (GABA) benzodiazepine receptor in the medial and lateral amygdala, medial prefrontal cortex and hippocampus. Offspring of high licking/grooming rat mothers have increased expression of GABA benzodiazepine receptor and reduced stress reactivity.	211
	➢ The adult male offspring of increased licking/grooming rat mothers show increased amygdala vasopressin 1a receptor binding.	212
	➢ The adult female offspring of increased licking/grooming rat mothers show increased oxytocin receptor binding in the central nucleus of the amygdala and bed nucleus of the stria terminalis.	212
Epigenetics	➢ Maternal behaviour increases glucocorticoid receptor expression in the offspring by epigenetic modulations of increased histone acetylase transferase activity, histone acetylation and DNA demethylation.	213
	➢ Maternal behaviour in early life controls pup's long-lasting gene expression and by that "programs" her offspring function of certain receptors, hormones and neurotransmitters.	214-219

	➢ Post mortem analysis of human suicide victims who had been abused as children show they had more methyl groups on the glucocorticoid receptor gene, and decreased levels of glucocorticoid receptor mRNA in the hippocampus than did suicide victims who were not abused. ➢ Offspring of high licking grooming rat mothers have elevated dopamine receptor mRNA levels within the nucleus accumbens and increased conditioned place preference for a high-fat diet. ➢ The adult female offspring of increased licking/grooming rat mothers show increased oestrogen receptor alpha and beta mRNA levels within the MPOA of the hypothalamus. ➢ The adult offspring of increased licking/grooming rat mothers show increased oxytocin receptor mRNA levels within the MPOA	220 221 222 222
Neural Plasticity	➢ Brain-derived neurotrophic factor (BDNF) and Nerve growth factor (NGF) are neurotrophines and key players in brain development and plasticity. Rodents and non-human primates' studies show that neurotrophines are sensitive to stress of maternal separation. ➢ Maladaptive mothering alters neurotrophine levels, which impacts stress reactivity in adulthood. ➢ In rodents, rich social experience in infancy, with both maternal and peer interactions, increases neural plasticity, levels of BDNF and NGF in the hippocampus and hypothalamus, and the amount of social behaviours through adulthood. ➢ Postnatal sensory experience controls cortical development through activity-driven BDNF expression ➢ Typical, expected, postnatal experience is necessary for the emergence of normal patterns of neocortical organization. Animals reared in complex environments show enhancement in density of cortical synapses, increases in the number of brain support cells, and even augmentation of the complexity of the brain vascular system.	223 224 225 226
Cortical Growth and Folding in Newborns	➢ Accelerated cortical folding in the perinatal weeks depends on social auditory stimuli, and human language. ➢ Development of the auditory cortex in preterm infants will resemble their full-term infant counterparts if their incubators are equipped with	227 228

	recordings of their mothers' voices. ➢ Early experience with maternal voice has enduring effects on the developing auditory system and autonomic nervous system, with later social and emotional developmental implications.	229
Human Neuroanatomy	➢ Adults who experienced maltreatment as children showed significant grey matter volume reductions in the medial frontal gyrus, dorsolateral prefrontal cortex and anterior cingulate gyrus compared to their healthy counterparts, superior frontal gyrus and orbitofrontal cortex. ➢ Childhood maltreatment and abuse impact hippocampus volume and development in adulthood. ➢ Maternal support in early childhood predicts larger hippocampal volumes at school age. ➢ Positive parenting predicts structural development of adolescent amygdala (reduced growth) and accelerated thinning of the orbitofrontal cortex and anterior cingulate cortex.	230 231 232 233
Large-Scale Brain Networks Function	➢ Intrinsic networks like the default mode network, salience or control networks are not traceable at birth. They develop over years, while children grow within a social environment. ➢ Children with social-developmental deficits, such as in Autistic Spectrum Disorder, have aberrant default mode network connectivity is linked with severity of social impairments. ➢ Network analysis of resting-state fMRI and DTI tractography in ASD show reduced local and long-range functional connectivity. Moreover, the developmental trajectory of structural networks in children with ASD is altered.	234-238 239 240

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