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Titolo	A SINGLE PRENATAL EXPOSURE TO POLY I:C INCREASES SUSCEPTIBILITY TO EPILEPSY IN THE ADULT OFFSPRING [Tesi di dottorato]
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Sommario	In the last years, evidence accumulated showing a direct connection between brain inflammation and neurodevelopmental disorders such as autism and schizophrenia. Epilepsy and seizures episodes, in particular, are associated to enhanced brain inflammation, while the activation of the immune response consequent to infections strongly increases the risk of seizures. By using the Poly I:C (polyinosinic-polycytidylic acid) mouse model of maternal immune activation (MIA), we demonstrated that a single administration at gestational day 9 (GD9) is able to affect the glutamate-GABA equilibrium in the offspring through a long-lasting deregulation of the chloride transporter KCC2 at cortical level, resulting in an alteration of the hyperpolarizing action of GABA, which endures at mature stages, as highlighted by the increased seizure susceptibility. Furthermore, mice injected with Poly I:C during adult life show no differences in susceptibility to kainate-induced seizures respect to control mice, thus providing the evidence that the increased susceptibility to seizures following prenatal Poly I:C exposure is the consequence of a neurodevelopmental process. We also provide the proof-of-concept that KCC2 expression abnormality and its deleterious physiological consequences can be prevented by dietary maternal

	supplementation with MgSO4, already known to reduce inflammation at the maternal-fetal interface. Notably, the increased binding of the two master regulators of neuronal genes expression, REST and MeCP2, on KCC2 promoter, suggests a possible epigenetic mechanism involved in the regulation of KCC2 expression following inflammation in the mother. Thus, maternal immune activation, through pro-inflammatory cytokines, may lead to epigenetic modifications responsible for KCC2 dysregulation and the consequent pathological outcomes, as suggested also by in vitro experiments.
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