

DEFICIENT PURPOSEFUL USE OF FOREPAWS IN FEMALE MICE MODELLING RETT SYNDROME

De Filippis, Bianca^a, Musto, Mattia^a, Altabella, Luisa^b, Romano, Emilia^a, Canese, Rossella^b, Laviola, Giovanni^a.

^a*Behavioural Neuroscience Section, Dept. Cell Biology & Neuroscience, Istituto Superiore di Sanità, Roma, Italy;* ^b*Molecular and Cellular Imaging Section, Dept. Cell Biology & Neuroscience, Istituto Superiore di Sanità, Roma, Italy;*

Rett syndrome (RTT) is a rare neurodevelopmental disorder, characterized by severe behavioural and physiological symptoms. Mutations in the methyl CpG binding protein 2 gene (MECP2) cause more than 95% of classic cases. Motor abnormalities represent a significant part of the spectrum of symptoms affecting RTT patients and are the cause of a marked decreasing in the quality of their life. In the present study we investigated motor coordination and fine motor skill domains in MeCP2-308 mice, a validated RTT model. This was complemented by the in vivo magnetic resonance spectroscopy (MRS) analysis of metabolic profile in behaviourally-relevant brain areas. We focused our investigation on females, the most affected gender in RTT. MeCP2-308 heterozygous female mice (10-12 months of age) were impaired in tasks validated for the assessment of purposeful and coordinated forepaw use (Morag test and Capellini handling task). A fine-grain analysis of spontaneous behaviour in the home-cage also revealed an abnormal handling pattern when interacting with the nesting material, reduced motivation to explore the environment and increased time devoted to feeding in RTT mice. The brain MRS in vivo evaluation highlighted decreased levels of bioenergetic metabolites such as creatine and taurine in the striatal area in MeCP2-308 female mice compared to controls. Present results confirm behavioural and brain alterations previously reported in MeCP2-308 males and identify novel endpoints on which the efficacy of innovative therapeutic strategies for RTT may be tested.

De Filippis B, Musto M, Altabella L, Romano E, Canese R, Laviola G (2015). Deficient purposeful use of forepaws in female mice modelling Rett syndrome. *Neural Plasticity*, in press.