Oxidative stress in MECP2 duplication syndrome

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Rett syndrome (RTT) and MECP2 duplication syndrome (MDS) are neurodevelopmental disorders caused by alterations in the methyl-CpG binding protein 2 (MECP2) expression. A relationship between MECP2 loss-of-function mutations and oxidative stress has been previously documented in patients and murine models of RTT (1,2). To date, no data on oxidative stress have been reported for the MECP2 gain-of-function mutations in patients with MDS. In the present work, the pro-oxidant status and oxidative fatty acid damage in MSD was investigated (n=6) and compared to RTT (n=24) and healthy condition (n=12). Patients with MECP2 gain-of-function mutations showed increased oxidative stress marker plasma levels (plasma non-protein bound iron, F2-isoprostanes, and F4-neuroprostanes), as compared to healthy controls. Such increases were similar to those observed in RTT patients except for higher plasma F2-isoprostanes levels. Moreover, plasma levels of F2-isoprostanes were significantly correlated with the size of the amplified region.

For the first time MECP2 gain-of-function mutations are indicated to be linked to an oxidative damage and related clinical symptoms overlapping with those of MECP2 loss-of-function mutations. A finely tuned balance of MECP2 expression appears to be critical to oxidative stress homeostasis, thus shedding light on the relevance of the redox balance in the central nervous system integrity.

References

This work was supported by the Regione Toscana (Bando Salute 2009; “Antioxidants (ω-3 polyunsaturated Fatty Acids, lipoic acid) supplementation in Rett syndrome: A novel approach to therapy,” RT no. 142).