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, F_2-isoprostanes, and F_4-neuroprostanes), as compared to healthy controls. Such increases were similar to those observed in RTT patients except for higher plasma F_2-isoprostanes levels. Moreover, plasma levels of F_2-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

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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).