

Abnormal visual evoked potentials, eye misalignment and visual acuity deficit in Rett syndrome: relationship with myelin oxidative damage

Joussef Hayek¹, Martina Zevolini², Bruno Natale², Cinzia Signorini³, Silvia Leoncini^{1,3}, Vincenzo Baranella⁴, Gloria Zollo^{1,3}, Lucia Ciccoli³, Jean-Marie Galano⁵, Camille Oger⁵, Thierry Durand⁵, Claudio De Felice⁶

¹ Child Neuropsychiatry Unit, University Hospital (AOUS), Policlinico “S. M. alle Scotte”, Siena, Italy; ² U.O.C. Oculistica, University Hospital AOUS Policlinico “S. M. alle Scotte”, Siena, Italy; ³ Department of Molecular and Developmental Medicine, University of Siena Siena, Italy; ⁴ Dipartimento di Scienze Mediche, Chirurgiche e Neuroscienze, University of Siena Siena, Italy; ⁵ Institut des Biomolécules Max Mousseron (IBMM), UMR 5247, CNRS/UM1/UM2/ENSCM, Montpellier Cedex 5, France; ⁶ Neonatal Intensive Care Unit, University Hospital, AOUS, Siena, Italy

Visual evoked potentials (VEPs) have been recently found to test cortical processing in MECP2-Rett syndrome (RTT), as an unbiased, quantitative biomarker to monitor brain function in RTT in the clinical setting (1). In the last few years our group has widely explored the role of oxidative stress (OS) in RTT(2). Aim of the present study was to assess VEPs, eye alignment and visual acuity in MECP2- and CDKL5-mutated RTT and their possible relationships with OS markers. A total of n=40 RTT patients (MECP2-RTT, n=34; CDKL5-RTT, n=6), as well as n=40 healthy age- and gender-matched controls participated to the study. We recorded pattern-reversal VEPs, and assessed visual acuity and eye alignment in RTT patients and controls. In addition, we evaluated plasma F₂-dihomo-isoprostanes, as a marker of brain myelin oxidative damage, using GC-NICI-MS/MS (3). Increased VEP latencies were detectable in 38.3% of MECP2-RTT and 66.6% of CDKL5-RTT patients (vs. 0% in controls, p<0.0001). Higher strabismus rates were evidenced in the RTT population (MECP2-RTT: 66.6%, CDKL5-RTT: 100%; controls: 2.4%, p<0.0001). A higher frequency esotropic (13.4%), exotropic (46.6%), and hypertropic (6.6%) strabismus was present in MECP2-RTT, while the eye misalignments observed in CDKL5-RTT patients were invariably of the exotropic type. Astigmatism (myopic, hyperopic or mixed) was detectable in the totality of the RTT patients. Refractive disorders were related to increased VEP latency. Plasma F₂-dihomo-isoprostanes were significantly higher in the examined RTT population (18.0±12.1 pg/mL vs. 1.1± 0.1, p=0.017).

A previously unrecognized relationship between visual alterations and myelin oxidative damage is present in RTT.

References

- 1 LeBlanc JJ et al. Visual evoked potentials detect cortical processing deficits in Rett syndrome. *Ann Neurol* 2015. In press. Doi: 10.1002/ana.24513.
- 2 De Felice C et al. Oxidative stress: a hallmark of Rett syndrome. *Future Neurology* 2015; 10 (3), 179–182.
3. De Felice C et al. F₂-dihomo-isoprostanes as potential early biomarkers of lipid oxidative damage in Rett syndrome. *J Lipid Res.* 2011;52(12):2287-97