Biochemical characteristics of inflammation in CDKL5-Rett syndrome: plasma protein patterns and effects of ω-3 PUFAs

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The cyclin-dependent kinase-like 5 (CDKL5) gene is known to be responsible for the rare early onset seizures variant (ESV) of Rett syndrome (RTT), a severe neurodevelopmental disorder mainly associated with sporadic *de novo* mutations in the methyl-CpG binding protein 2 (*MECP2*) gene. An emerging role for inflammation has been recently reported in *MECP2* mutations-related (1,2). To date, no information regarding the inflammatory protein response for *CDKL5*-RTT is available. Here, we evaluated plasma protein patterns in *CDKL5*- and *MECP2*-RTT ω-3 PUFAs before and after ω-3 polyunsaturated fatty acids (PUFAs) supplementation, both compared to healthy controls.
Our findings evidenced an increased expression of positive acute-phase response (APR) proteins in *CDKL5*-RTT as well as *MECP2*-RTT (i.e., alpha-1-antitrypsin, alpha-1B-glycoprotein and fibrinogen alpha chain). However, *CDKL5* proteins related to components of the innate immune system (i.e., complement component 3 end CD5 antigen-like) showed distinctive trends. Detectable APR changes in *CDKL5*-RTT were present to a lower degree as compared to *MECP2*-RTT, while immunoglobulins (i.e., Ig alpha-1-chain C region and Ig mu chain C region) and the anti-inflammatory agent inter-alpha-trypsin inhibitor were increased to a similar degree in both *CDKL5*- and *MECP2*-RTT. Omega-3 PUFAs partially counterbalanced the observed pro-inflammatory status. In conclusion, *CDKL5*-RTT shows a sub-inflammatory state with distinctive features as compared to *MECP2*-RTT.

References

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