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Sialylation of Lactoferrin: a key player for neurodevelopment

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Lactoferrin (LF), a sialylated iron-binding glycoprotein consisting of multiple sialic acid (Sia) residues attached to N-linked glycan chains, and studies have shown that both the iron and Sia are crucial for early neurodevelopment and cognition.(1) However, there is limited knowledge of the impacts of the iron saturation and sialylation in LF molecule on the early neurodevelopment and cognition. Objectives of the study were to explore the impacts and mechanisms of iron saturation and sialylation in LF molecule on early neurodevelopment and cognition. Maternal dietary intervention with native bovine LF (Native-LF), iron-free bovine LF (Apo-LF), or Sia-free bovine LF (Desia-LF) at a dose of 0.60 g/kg body weight per day was administered throughout the lactation period. Offspring pups were assessed for anxiety, learning, and memory through behavioral tests before being euthanized on postnatal day 63. Brain hippocampal tissue was then analyzed for polysialic acid (polySia), a marker of neurodevelopment and neuroplasticity.(1) The study protocol was approved by the Xiamen University Animal Ethics Committee (AE1640102). Our results showed that Apo-LF pups exhibited a 1.32-fold increase in total distance travelled in the arena compared to both Native-LF and Desia-LF groups, with the overall difference among the groups being statistically significant in the open field test ($p = 0.008$). Additionally, the frequency of central area entries in the Apo-LF group was 2.00-fold higher than in Desia-LF pups ($p = 0.038$) and 1.3-fold higher than in Native-LF pups, with a significant overall difference ($p = 0.042$). No significant differences in total distance travelled or central area entries were observed between Native-LF and Desia-LF groups ($p > 0.05$). These results suggest that Apo-LF pups demonstrated better anti-anxiety behaviors than both Native-LF and Desia-LF pups. In the Morris water maze test, Apo-LF pups spent significantly more time in the target quadrant compared to both Desia-LF ($p = 0.019$) and Native-LF pups ($p = 0.0009$), indicating enhanced short-term memory. Additionally, Apo-LF pups exhibited greater polySia-NCAM expression ($1.2.95 \pm 0.048$) in the hippocampus, a marker associated with neuroplasticity and neurogenesis compared to both Native-LF and Desia-LF pups. We conclude that maternal supplementation with different types of lactoferrin during lactation supports improved learning and memory in offspring through distinct mechanisms, with sialylation playing a crucial role in neurocognitive development.

References

1. Chen Y, Wang B, Yang C *et al.* (2021) *Mol Nutr Food Res* **65**(8), e2001099.