

Taurine, a Natural LXRAgonist, May Promote Amyloid Beta Clearance in the Brain

There is recent evidence that taurine can serve as an agonist for the LXRAgonist nuclear receptor (but not LXRBeta) in human macrophages; taurine interacts directly with LXRAgonist, and dose-dependently increases the expression of various genes transcriptionally responsive to LXRAgonist, including ABCA1, ABCG1, ApoE, and LXRAgonist itself.¹ The authors note that such expression would be expected to promote reverse cholesterol transport from foam cells, and that this may help to explain why dietary taurine exerts anti-atherogenic effects in rodents.²⁻⁶ The agonist activity of taurine for LXRAgonist is not as potent as that of the synthetic agonist TO-901317, but taurine has the advantage of being available and clearly safe; moreover, it does not promote triglyceride synthesis in the liver because it suppresses the nuclear translocation of SREBP-1 via an independent mechanism.¹

A number of studies show that LXRAgonist aid the microglial clearance of fibrillar amyloid beta, reducing brain amyloid plaque in transgenic mouse models of Alzheimers and of traumatic brain injury.⁷⁻¹³ This effect is dependent on apoE induction in neighboring astrocytes, and likely also requires ABCA1 induction in these cells; hence, lipidated apoE, primarily of astrocytic origin, may play a key cofactor role in promoting microglial phagocytosis of amyloid beta fibrils.¹³ ApoE induction may also aid brain clearance of oligomeric amyloid beta by promoting its export to the cerebrospinal fluid.¹⁴ Importantly, astrocytes are known to express both LXRAgonist and the membrane taurine transporter.^{13, 15-19} Analogously, the RXRAgonist bexarotene has recently been reported to promote microglial clearance of amyloid beta in an AD mouse model – an effect contingent on induction of apoE in astrocytes.²⁰ RXRAgonist partners with either LXRAgonist or PPARgamma in apoE induction. LXRAgonist agonists can also antagonize microglial activation induced by LPS or fibrillar amyloid beta;⁸ however, it is not clear whether LXRAgonist specifically can mediate this effect, and the inhibitory impact of LXRAgonist on the hepatic acute phase response is mediated by LXRBeta.²¹

These considerations suggest that taurine supplementation might have potential for promoting clearance of amyloid beta in AD mouse models, and possibly clinically as well. It would be of interest to test this in AD mouse models. Whether taurine might work in a complementary fashion with bexarotene to promote apoE induction could also be examined.

Surprisingly, there do not appear to be any published studies that have examined taurine loading in rodent models of Alzheimer's. However, there is recent evidence in mice that long term taurine supplementation can have a favorable impact on the cognitive decline associated with "healthy aging" in rats; this effect appears to reflect improved survival or preserved function of certain GABAergic interneurons in the forebrain.^{22, 23} In light of its safety, low cost, and ready availability - and its likely favorable impact on vascular health - supplemental taurine may have excellent practical potential for slowing the onset or progression of Alzheimer's if in fact it can promote microglial amyloid beta clearance in the human brain. Moreover, if it does indeed work in a complementary fashion with bexarotene, taurine could be used for primary prevention, with bexarotene added to the regimen if the early onset of Alzheimer's is detected.

References

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