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Immunohistological investigation of PPAR gamma and RXR alpha expression in brain tissue samples of living patients with severe traumatic brain injury

Vivien Skripek, Dr Ping Yip

Background: Traumatic brain injury (TBI) is a leading cause of death and chronic disability worldwide. The lack of effective therapeutic interventions can be attributed to a limited understanding of TBI's clinical pathophysiology, which halts potential molecular target discovery. Synthetic and natural agonists of peroxisome proliferator-activated receptors (PPAR) and retinoid X receptors (RXR) have shown to induce neuroprotection in several animal models of TBI. However, PPAR and RXR expression in the human cerebral cortex after TBI remains unexplored. The study aimed to characterise RXR alpha (RXRα) and PPAR gamma (PPARγ) expression levels and cell type-specificity in brain tissue from living severe TBI (sTBI) patients using immunohistochemistry.

Materials and methods: The brain tissues collected during surgical intervention at a median time of 5h post-injury were from three groups (n=7 per group) based on patients' Glasgow Outcome Scale Extended (GOS-E) scores at six months post-injury: GOS-E1-2 (dead or coma), GOS-E3-6 (moderate-severe disability), and GOS-E7-8 (mild disability).

Results: RXRα and PPARγ immunostaining were co-expressed with the neuronal marker NeuN, although RXRα occurred in a larger fraction of neurons than PPARγ. Only RXRα was present in astrocytes and CC1-positive oligodendrocytes. No PPARγ or RXRα expression was detected in microglia. Although no statistically significant difference was found in RXRα and PPARγ expression levels among the three groups, GOS-E7-8 showed a trend toward higher RXRα and PPARγ expression than GOS-E1-2. GOS-E3-6 had the highest RXRα expression, but the lowest PPARγ expression. Cortical layers 3-4 presented a negative association between neuronal soma size and RXRα expression, suggesting that RXRα is predominantly expressed in smaller neurons.

Conclusion: Our study indicated the presence of RXRα in neurons, astrocytes, and oligodendrocytes, as well as PPARγ in neurons in the brain tissue of sTBI patients, suggesting that acute administration of PPARγ and RXRα agonists could be effective neuroprotective drugs for TBI.