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Nerve growth factor-promotes primary cilium assembly in cholinergic neurons from the human basal forebrain

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The primary cilium is a non-motile sensory antenna protruding from the surface of nearly all cells of the body, able to mediate the cellular response to extracellular signals. Although many of its functions remain to be clarified, it has been recently shown a role in neurogenesis [1]. In this study we evaluated the presence of the primary cilium in neurons isolated from the human fetal nucleus basalis of Meynert (*hf*nbM), a basal forebrain region crucially involved in the cholinergic transmission required for learning and memory. The *hf*nbM cells are characterized by the expression of cholinergic markers, such as choline acetyl transferase (ChAT) and also express the primary cilium, which, in basal conditions, was detected in the 17% of cells. It is known that nerve growth factor (NGF) supports survival, maintenance, connectivity and function of the brain cholinergic neurons. Indeed, we demonstrated that *hf*nbM cells respond to NGF in terms of proliferation, neurite formation and ChAT expression. Interestingly, NGF exposure significantly increased the percentage of ciliated cells (34.9%±1.8%). Given the known adverse effect of systemic chronic inflammation in the pathogenesis of neurodegenerative diseases, such as Alzheimer's disease, characterized by the loss of nbM neurons, we exposed our cells to tumor necrosis factor-α (TNF-α). We observed that TNF-α significantly reduced the number of ciliated cells (4.3%±2%). Our results strongly suggest for the first time that primary cilia may be involved in the NGF-driven maturation of human nbM cholinergic neurons and suggest that the deleterious effects of neuroinflammation may be linked to an altered formation of the primary cilium.

References

[1] Han et al. (2008) Hedgehog signaling and primary cilia are required for the formation of adult neural stem cells. Nat Neurosci 11:277-284.

Keywords
Nucleus basalis of Meynert, NGF, TNF-alpha, Alzheimer's disease