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# Postnatal ependymogenesis occuring in wild-type *hyh* mice increases significantly in hydrocephalic *hyh* mice

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## Background

The hyh (hydrocephalus with hop gait) mouse carries a point mutation in alpha-SNAP protein and develops inherited hydrocephalus. Mutant mice are born with moderate hydrocephalus and a patent Sylvius aqueduct (SA). During the first postnatal week, SA obliterates and a severe hydrocephalus characterized by an enormous expansion of the dorsal third ventricle and of the collicular recess of the SA, develops. Interestingly, neither of these dilated cavities present spontaneous ventriculostomies. The aim of the present investigation was to elucidate some of the cellular phenomena occurring at the ventricular walls that allow such enormous ventricular dilatations.

## Materials and methods

Brains of wild type (non-hydrocephalic) and mutant (hydrocephalic) hyh mice were studied by light and transmission electron microscopy at various age intervals (PN-1 to PN-120). Proliferative activity, especially at the ventricular walls, was studied by PCNA (proliferative cell nuclear antigen) immunocytochemistry, and 5'-Bromo-2'-deoxyUridine (BrdU) labelling. BrdU protocols included pulse and cumulative labelling of postnatal animals, combined with short and long survival periods after the labelling.

## Results

In wild-type mice no BrdU-labelled or PCNA-positive cells were observed in the ependyma of the ventral walls of SA and third ventricle. However, proliferative cells were found in two discrete ependymal regions of the dorsal walls of the third ventricle (3Vd) and the SA (SAd). Here, proliferative activity continued at least during three weeks after birth. The localization, cytology and immunocytochemical properties indicate that both regions originate ependymal cells. Interestingly, in mutant (hydrocephalic) hyh mice, postnatal ependymogenesis occuring in 3Vd and SAd increased several fold.

## Conclusion

1. In non-hydrocephalic animals all ependymal cells lining the floor of the aqueduct are born during the fetal life; however, in the dorsal wall of the aqueduct and the roof of the third ventricle ependymogenesis continues during postnatal life. 2. In mutant mice, the hydrocephalic process triggers a dramatic increase of proliferative activity in these two ventricular regions letting them to expand without any disruption and, probably, allowing a longer survival. 3. In the cerebral aqueduct of hydrocephalic mice there are various ependymal lineages: one of them detaches, other proliferates while another neither detaches nor proliferates. Since all these ependymal populations are exposed to the same pressure and composition of the CSF, their differential response to the

hydrocephalic status can best be explained by their distinct genetic programme. Supported by Fondecyt 1030265-Chile to EMR, CONICYT and DID-UACH D-2005-12 to LFB, FIS PI030756 and FIS PI060423 to JMPF.

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