## Vestibular effects of ionic and volume changes of inner ear fluid in an isolated preparation of a mouse labyrinth

*E.G. LaMont, R. Lim, R.J. Callister and A.M. Brichta , Hunter Medical Research Institute, School of Biomedical Science, The University of Newcastle, University Drive, Callaghan, NSW 2308, Australia.*

We have developed an *in vitro* preparation of the mouse inner ear to examine pharmacological and physiological features of balance (vestibular) transduction that cannot be easily addressed in whole animal or dissociated hair cell preparations. Having established the preparation's response to manipulation of the external (perilymphatic) compartment (Lee *et al.*, 2005), we have now begun investigating the effects of changing the internal (endolymphatic) compartment.

Mice were anaesthetized (ketamine 100 mg/kg, i.p.), decapitated, and the bony labyrinth was surgically isolated from the skull by removing, *in toto,* the petrous portion of the temporal bone. The tissue was placed into a recording chamber and maintained in Ringer's solution. Apertures were created in the bony labyrinth to access the underlying membranous ducts and nerve fibres. A bevelled, glass injecting pipette (10-15 μm tip diameter) was inserted into either the exposed endolymphatic or semicircular canal duct. The pipette was attached to a nanoliter injection pump that allowed us to introduce solutions of precisely controlled ionic concentrations and volumes into the duct. Sharp recording electrodes were used to impale individual primary afferent fibres in the anterior or horizontal ampullary nerves. Primary afferent action potential (AP) discharge was recorded during manipulation of endolymphatic composition and volume.

Our aim was to assess the effects of high potassium ($K^+$) concentration and increased volume on AP discharge, two factors thought to be associated with Ménière's disease. As might be expected, injections of high $K^+$ solution (200 mM KCl, 25 mM $KHCO_3$) into the semicircular canal duct caused a 4 to 5 fold increase in discharge rate ($n$ = 5). This was accompanied by diminishing AP amplitude as the afferent became depolarized. Within 15 s to 2 min after injection of high $K^+$ solutions, AP firing rate and amplitude returned to original levels, suggesting a return to prior conditions. While a majority (6 of 10) injections of 'normal' artificial endolymph (140 mM KCl, 25 mM $KHCO_3$) produced similar results to those seen with high $K^+$ solution, a few (4 of 10) injections of 'normal' endolymph resulted in decreases in discharge rate. We have begun to explore the potential mechanisms underlying these anomalous results and hypothesise that it is the location of the afferent terminal, within the neuroepithelium, that ultimately determines its response to endolymphatic volume changes.

Taken as a whole, our results suggest that: 1) we can affect afferent activity by altering the ionic composition of the endolymphatic compartment; and 2) volume changes play a significant role in modifying afferent activity.

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