## ACOUSTICS2008/3392 Tuning curves derived from auditory brainstem responses point to a defect in outer hair cells of hypothyroid mice

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Based on an analysis of ABR derived tuning curves, recent reports suggest that the mechanics of passive transduction in hypothyroid mice, although delayed developmentally, eventually become indistinguishable from normal animals, whereas the mechanics of active transduction remain grossly abnormal throughout life, raising the possibility that the outer hair cell system is at least partially responsible for abnormalities observed in mutant animals. Moreover, results of in vitro studies have shown that although OHCs are electromotile, they appear unable to withstand extensive voltage excursions in the whole cell voltage clamp environment; i.e., they appear fragile. These data led us to question the structural integrity of the OHC lateral wall in hypothyroid mice. Preliminary studies suggest that the cortical cytoskeleton is abnormal in at least some regions of the OHC lateral wall and preliminary confocal immunofluorescence images of the constituent proteins, f-actin and  $\alpha$ -II spectrin, suggest that spectrin is either absent or expressed in very low levels in the cytoskeleton of OHCs harvested from the hypothyroid progeny of Tshr mutant dams. We suggest that a cytoskeletal defect involving the f-actin cross-linking protein, spectrin, might compromise the efficient transfer of force along the long axis of OHCs, effectively diminishing the power of active amplification.