

## Abstract EFAS/DGA 2007

### Effects of Prolonged Gacyclidine Intracochlear Perfusion on cochlear function and histology in Guinea Pigs

Wenzel, G.I. <sup>1</sup>, Lim, H.H. <sup>1</sup>, Warnecke, A. <sup>1</sup>, Stoever, T. <sup>1</sup>, Lobl, Th. <sup>2</sup>, Schloss, J. <sup>2</sup>, Schwab, B. <sup>1</sup>, Lenarz, Th. <sup>1</sup>

<sup>1</sup> Hals-Nasen-Ohrenklinik der Medizinischen Hochschule Hannover, <sup>2</sup>NeuroSystec

**Introduction** Gacyclidine is a highly specific NMDA receptor antagonist with neuroprotective properties. In animal studies, administration of gacyclidine (adsorbed to Gelfoam) into the round window niche as well as a bolus injection suppressed salicylate-induced tinnitus. Since one method for tinnitus treatment in humans could be a chronic intracochlear perfusion and the majority of candidates for this would be hearing patients, we sought to assess whether prolonged administration of gacyclidine would compromise hearing performance in an animal model.

**Methods** Guinea pigs were implanted with osmotic pumps that delivered either 0.5µL/h of 0.3 mM gacyclidine and or Ringer solution (control group) for 9 days via a catheter inserted through the round window membrane. The concentration and rate of drug delivery were selected to provide a dose that was substantially higher than is expected for tinnitus control in humans. Frequency-specific ABRs (1-40 kHz, 10-80 dB SPL in 10dB steps) were recorded before implantation and compared with those obtained after drug administration. After the last ABR recording the animals were sacrificed, the cochleae harvested, fixed in 4% PFA and stained with Rhodamine-Phalloidin. Whole mount preparations were then analyzed under fluorescent microscopy.

**Results** No significant changes in ABR thresholds were observed suggesting that prolonged administration of gacyclidine for tinnitus treatment should be safe in terms of hearing preservation. There were no significant differences in hair cell loss between gacyclidine or Ringer infused ears and contralateral ears ( $p < 0.05$ ).

**Conclusions** Prolonged intracochlear administration of gacyclidine for tinnitus treatment seems to be safe in terms of hearing preservation and hair cell loss in guinea pigs. Further studies investigating the toxicological effects of different dosages and durations are under way to ensure the safety of the drug for long-term human use and to warrant clinical trials.

