Therapeutic effect of electroacupuncture in a p75 knockout mouse model of progressive hearing loss

Neurotrophin receptor p75 (p75NTR) knockout mice (p75(−/−) mice) provide a good animal model of progressive-onset hearing loss.1 Cell loss of the spiral ganglion neurons (SGNs) and hair cell degeneration at the basal turn of the cochlea are seen in p75(−/−) mice from 3 months of age. Furthermore, from 3 to 6 months of age, the hearing thresholds of p75(−/−) mice are gradually raised; and after 6 months of age, the mice mostly exhibit hearing loss.1 Several previous reports have indicated that electroacupuncture (EA) stimulation may improve subjective symptoms of tinnitus or hearing loss.2 3 However, the molecular mechanisms underlying the therapeutic effect of EA stimulation for hearing loss remain unclear. Thus, to determine whether EA stimulation is useful for the prevention of hearing loss, we used a p75(−/−) mouse model of progressive-onset hearing loss.

The Ting Gong (SI19; Small Intestine 19) and the Yifeng (TE17; Triple Energiser meridian 17) are

Figure 1 Haematoxylin and eosin (H&E) staining of cochleae from mice with and without electroacupuncture (EA) stimulation. (A) H&E staining of the organ of Corti in the basal turns from p75(+/+) mice, p75(+/−) mice (−EA) and p75(+/−) mice (+EA). Arrowhead: inner hair cells; arrow: outer hair cells. Scale bar: 50 μm. (B) H&E staining of the spiral ganglion neurons (SGNs) in the basal turns from p75(+/+) mice, p75(+/−) mice (−EA), and p75(+/−) mice (+EA). Scale bar: 50 μm. (C) Quantification of the numbers of SGNs in the apical, middle and basal turns of the cochleae from p75(+/+) mice, p75(+/−) mice (−EA), and p75(+/−) mice (+EA). Asterisks (*) indicate a significant increase in the numbers of SGNs. Student t test, *p=0.02, **p=0.001.

Acupuncture points commonly used to improve any kind of ear problem in Asian medical clinics—for example, hearing acuity and treating progressive hearing loss.23 We applied EA stimulation at SI19 and TE17 over 4 months (from 2 to 6 months of age). Acupuncture needles 0.16×4 mm were inserted perpendicularly as deep as 3–4 mm to the right and left of the SI19 and TE17 points, and electric stimulation of 1 Hz, 0.7 mA was performed twice a week for 30 min using a stimulator (Electrostimulator N-401; Ito Chotanpa Inc). Next, the mice were perfused transcardially with 50 mL of 4% paraformaldehyde solution under deep pentobarbital anaesthesia and the stimulated cochleae were dissected and post-fixed in 4% paraformaldehyde for 1 day. Thereafter, they were placed in a decalcifying solution (10% EDTA, pH 7.4) for 14 days. Paraffin-embedded 7 μm sections were then stained with haematoxylin and eosin. An Olympus BX50 microscope and a DP71 CCD digital colour camera unit (Olympus Co) was used for visual inspection and recording of images.

It was found that outer hair cells were lost and the organ of Corti was not present in the basal turns in the cochleae of the p75(−/−) mice without EA (−EA) at 6 months of age (figure 1A). However, the organ of Corti and outer hair cells remained normal in the p75(+/−) mouse who had received EA (+EA), as is the case with wild-type mice (p75(+/+) mice) (figure 1A). Furthermore, the numbers of SGNs in the middle and basal turns of the cochlea were significantly reduced in the p75(−/−) mice (−EA) (figure 1B,C). By contrast, EA-stimulated p75(−/−) mice retained the same number of SGNs in these regions (figure 1B, C). Previous reports indicated that neurotrophin receptor signalling is important to prevent the degeneration of SGNs.4–7 We showed that EA stimulation significantly increased the expression of receptor tyrosine kinases in the SGNs of p75(−/−) mice cochlea (figure 2). However, elucidation of the functional roles of EA stimulation on progressive hearing loss remains a primary goal of future research.

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