Roles of Estrogen Receptor 1 (*Esr1*) in Auditory Function and Balance in Mice

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Background

It is well-documented that biological sex influences hearing in humans. In general, women display better high-frequency hearing compared to men at most ages. Research also shows that auditory function is diminished following menopause, suggesting that estrogen may play a key role in influencing hearing. In this study, we tested the hypothesis that estrogen receptor 1 (ESR1) is essential for the maintenance of normal hearing and balance using wildtype (WT) and *Esr1* knockout (*Esr1* KO) mice on a normal-hearing CBA/CaJ mice background.

Methods

To investigate the roles of *Esr1* in cochlear development and maintenance of normal hearing in mice, we performed auditory brainstem response (ABR) tests, distortion product otoacoustic emission (DPOAE) tests, and rotarod balance performance tests in male and female WT and *Esr1*-KO mice at 3 month of age. Two-way ANOVA with Bonferroni's multiple comparisons test was carried out using GraphPad Prism 10 to analyze ABR threshold, DPOAE amplitude, and DPOAE threshold. Unpaired two-tailed student's t-tests were used to analyze rotarod performance.

Results

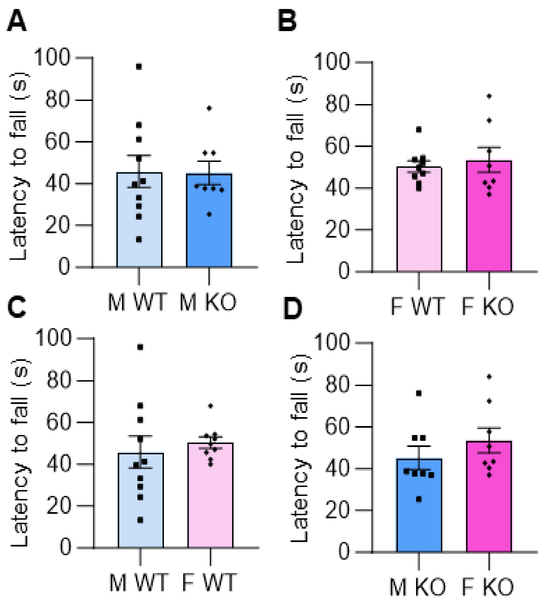

Figure 1. Assessment of rotarod performance. A-D, Rotarod balance performance was assessed by measuring latency to fall (s) in male and female WT and *Esr1* KO mice at 3 months of age; M WT (n=10), M KO (n=9), F WT (n=10), F KO (n=8). Data are shown as means ± SEM. Unpaired two-tailed Student's t-test was performed.; M WT, male wildtype; F WT, female wildtype; M KO, male *Esr1* knockout; F KO, female *Esr1* knockout.

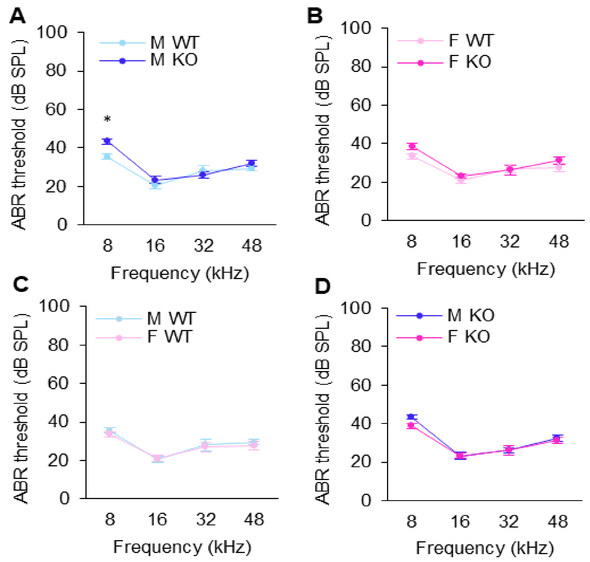

Figure 2. ABR threshold. ABR thresholds (A-D) were measured with tone burst stimuli at 8, 16, 32, and 48 kHz in male and female WT and *Esr1* KO mice at 3 months of age; M WT (n=10), M KO (n=9), F WT (n=10), F KO (n=8). Data are shown as means ± SEM; Two-way ANOVA with Bonferroni's multiple comparisons tests was performed. *, P < 0.05; ABR, auditory brainstem response; M WT, male wildtype; F WT, female wildtype; M KO, male *Esr1* knockout; F KO, female *Esr1* knockout.

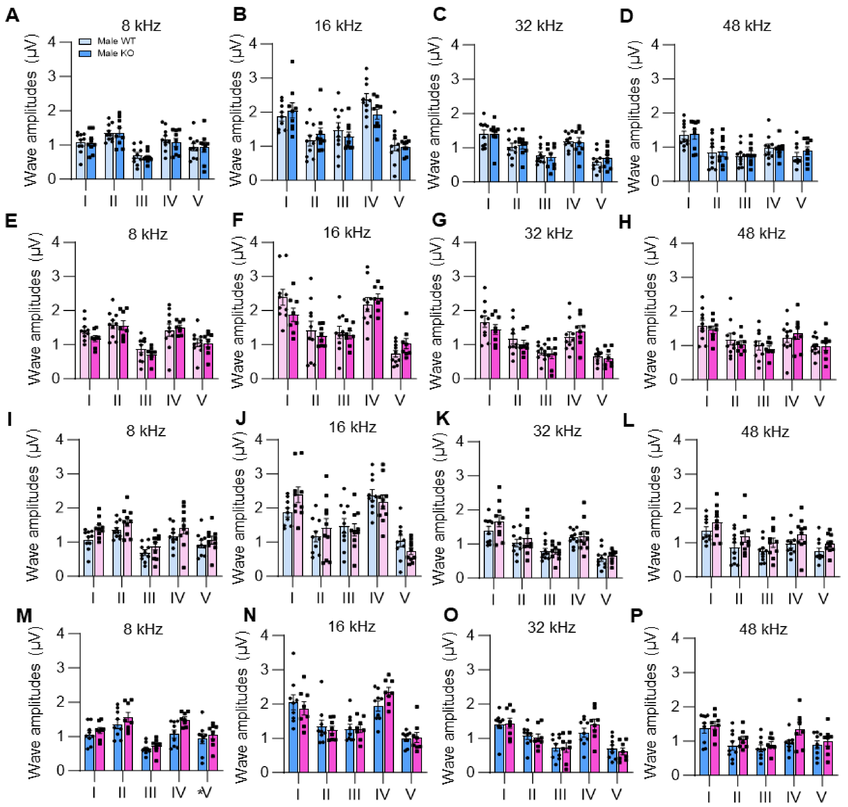

Figure 3. ABR Wave I-V Amplitude. ABR Wave I-V amplitudes (A-P) were measured at 8, 16, 32, and 48 kHz at 80 dB SPL in male and female WT and *Esr1*-KO mice at 3 months of age; M WT (n=10), M KO (n=9), F WT (n=10), F KO (n=8). Data are shown as means ± SEM; Two-way ANOVA with Bonferroni's multiple comparisons tests was performed. *, P < 0.05; ABR, auditory brainstem response; M WT, male wildtype; F WT, female wildtype; M KO, male *Esr1* knockout; F KO, female *Esr1* knockout.

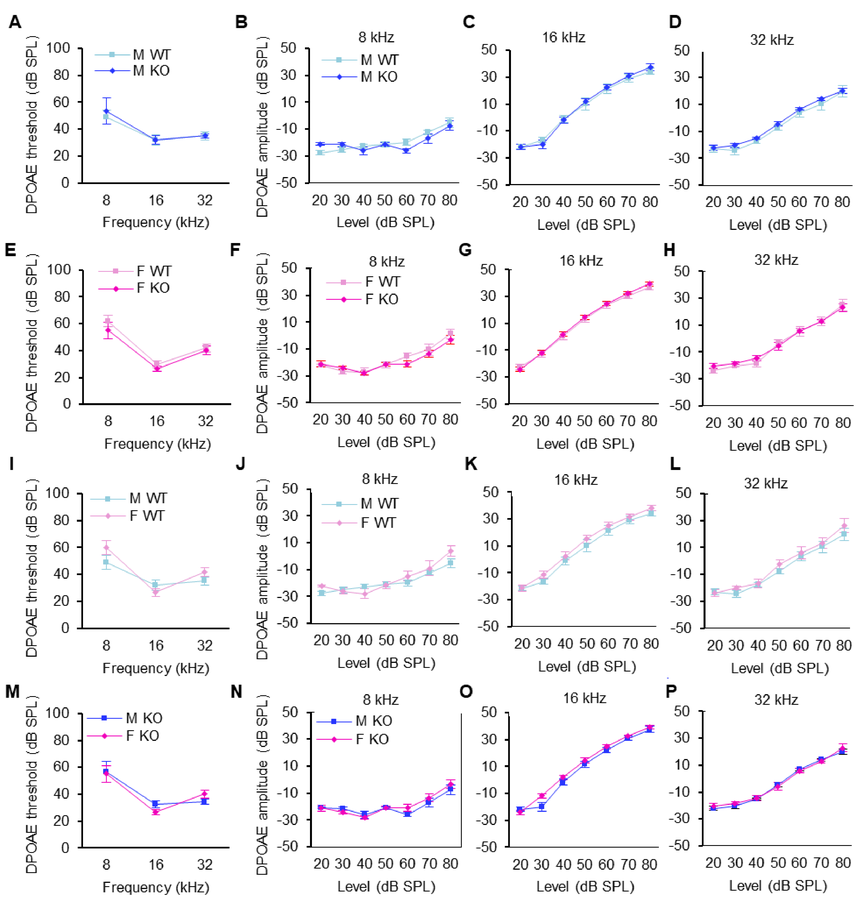

Figure 4. Assessment of outer hair cell function. DPOAE thresholds and amplitudes (A-P) were measured at 8, 16, and 32 kHz in male and female WT and *Esr1* KO mice at 3 months of age; M WT (n=10), M KO (n=9), F WT (n=10), F KO (n=8). Data are shown as means ± SEM. Two-way ANOVA with Bonferroni's multiple comparisons tests were performed. DPOAE, distortion product otoacoustic emission; M WT, male wildtype; F WT, female wildtype; M KO, male *Esr1* knockout; F KO, female *Esr1* knockout.

Conclusions

Contrary to our expectation, there were no significant differences in ABR thresholds, ABR wave amplitudes, DPOAE amplitudes and thresholds, or rotarod performance between WT and *Esr1* KO mice for both male and female at 3 months of age, suggesting that ESR1 is not essential for the maintenance of auditory and balance function in mammals.

Acknowledgments

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