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Age-dependent changes in gene expression and synaptic function in mouse auditory brainstem

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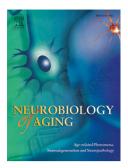
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## ACCEPTED MANUSCRIPT

1 Title: Age-dependent changes in gene expression and synaptic function in mouse auditory brainstem 2 Authors: Mahendra Singha, Pedro Miurab, Robert Rendena# 3 4 Affiliations: <sup>a</sup>Department of Physiology and Cell Biology, University of Nevada, Reno School of Medicine, Reno, NV 89557, USA. Department of Biology, University of Nevada, Reno, Reno, NV 89557, USA. 5 6 # Corresponding Author: 1664 N. Virginia St., Reno NV 89557. Email: rendenr@unr.edu. 7 8 **Abstract** Hearing acuity and sound localization are affected by aging and may contribute to cognitive dementias. 9 While loss of sensorineural conduction is well documented to occur with age, little is known regarding short-10 11 term synaptic plasticity in central auditory nuclei. Age-related changes in synaptic transmission properties 12 were evaluated at the mouse calyx of Held, a sign-inverting relay synapse in the circuit for sound localization, 13 in juvenile adults (one month old) and late-middle age (18-21 months old) mice. Synaptic timing and short-14 term plasticity were severely disrupted in older mice. Surprisingly, acetyl-l-carnitine (ALCAR), an 15 antinflammatory agent that facilitates mitochondrial function, fully reversed synaptic transmission delays in 16 aged mice to reflect transmission similar to that seen in juvenile adults. These findings support ALCAR 17 supplementation as an adjuvant to improve short term plasticity and potentially CNS performance in animals 18 compromised by age and/or neurodegenerative disease. 19 20 21 **Keywords**: neurotransmission; acetyl-l-carnitine; calyx of Held, aging, synaptic plasticity; electrophysiology 22 Abbreviations: SOC, superior olivary complex; MNTB, medial nucleus of the trapezoid body; ALCAR, 23 24 Acetyl-l-carnitine hydrochloride; EPSC, excitatory postsynaptic current 25 26 Declaration of conflicts of interest: none. 27 28

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