CHRONIC STRESS ACCELERATES AGING INDUCED COLLATERAL DYSFUNCTION IN C57BL6 MOUSE MODEL OF HIND LIMB ISCHEMIA

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Background: Aging is a major vascular risk factor. Chronic stress is associated with impaired endothelial function. We hypothesized that chronic stress accelerates aging induced collateral dysfunction in mouse model of hind limb ischemia.

Methods: 20 month-old C57Bl6 mice were subjected to chronic stress, either cold stress (CS) or social defeat stress (SS), with non-stressed animals serving as controls. CS entailed mice being placed for 1 hour per day in a cage containing 1 cm of iced water for 4 weeks, while the age matched controls were not stressed. In SS, for 20 days mice were housed in a food and liquid deprived wired box placed inside an aggressor's (AG) cage for 6 hours/day, and were exposed to the AG 3 times/day for 1 minute, or for up to 10 attacks. The control mice were housed in a food and liquid deprived environment for 6 hours without the AG's proximity. 2 days after the end of the stress protocol, femoral artery ligation (FAL) was performed. Laser Doppler perfusion imaging was used to access blood flow recovery at days 0, 7, 14, 21 and 28. A barrier test was used to evaluate the behavioral effects on days 1 and 28, and a foot appearance and use score were measured on day 5 in the SS models.

Results: CS and SS were associated with impaired blood flow recovery after FAL (p<0.002 & p<0.05 respectively). SS mice had higher use scores (p<0.001) and a strong trend for appearance score, both indicative of ischemia-induced impairment. SS mice also displayed more avoidance and freezing motion to the AG (both fear responses) and grooming (anxiogenic marker) compared to the control.

Conclusion: Chronic stress accelerates aging hind limb collateral dysfunction in 20 month old C57Bl6 mice following FAL as demonstrated by impaired blood flow recovery in two different types of stress.