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**Title:** Consequences of aging on the adaptative capacity of *Microcebus murinus* heart to stress

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**Mots clés :** heart rate regulation, automaticity impairment

**Introduction**

Aging is an important **risk factor** for cardiovascular disease. Regardless of lifestyle, aged people are subject to a decrease in maximal heart rate (HR) and in HR Variability (HRV). Mechanisms underlying the decrease in HR and HRV and the consequences on body physiology are still unclear.

**Objective**

Our objective is to study the effect of aging on the regulation of and its modulation by the neuronal environment that modulates HR in aged patients.

**Method**

To study HR and HRV, we used the small primate *Microcebus murinus* (ML), which generates 3 billion heartbeats in a lifetime, as humans (three times more than mice). To record cardiac activity, we developed a jacket to record surface ECGs in young (1–5 years) and aged (6–12 years) animals of both genders, under stressful condition and 3 hours after.

**Results**

First, we confirmed that HR was decreased 3 h post-stress vs. stress in young females (11.5%,  $P^* = 0.01$ ) and also in young males (great tendency: 8%,  $P = 0.06$ ). Conversely, no changes were observed in aged MLs ( $P = ns$ ) both genders. The analysis of the Coefficient of Variability of RR intervals (CVRR), which mainly reflects sympathetic tone, showed that under stress it was higher in aged vs. young MLs (46%,  $P^* = 0.03$ ), suggesting an impaired response to stress (loss of  $\beta$ -adrenergic regulation). Despite this difference, the CVRR was increased 3 h after stress in young (males, 80%,  $P^{***} = 0.0007$ ; females, 76%,  $P^* = 0.01$ ) and aged (males, 55%,  $P^* = 0.04$ ; females, 61%  $P^* = 0.03$ ) animals of both genders, compared with the stress condition, as expected. However, the Root Mean Square of Successive Differences between normal heartbeats (RMSSD), an index of the parasympathetic tone, was increased in young (males, 65%,  $P^* = 0.04$ ; females, 66%,  $P^* = 0.03$ ) but was unchanged in aged MLs (males, 23%;  $P = ns$ ; females, 40%,  $P = ns$ ), suggesting that the difficulty to recover from stress was related to an impaired vagal modulation in aged animals.

### Conclusion

Our results show that cardiac activity was not able to adapt to stress response due to aging through a  $\beta$ -adrenergic and vagal impairment. For the first time, these results pave the way to the understanding of why HRV decreases in aged patients.