

Poster number: MO 294

Age Effects on Regional Cerebral Blood Flow and Amygdala Activation in Response to Fear Stress

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Development & Aging

Abstract

Introduction

The aging process is generally characterized by the progressive loss of neuronal and physiological efficiency. One system that is impacted by the convergence of deficits in neuronal and physiological efficiency is the stress response system. Several reports suggest that during the aging process there are enhanced behavioral and neuroendocrine responses to stress. Recently, the exaggerated stress response observed during aging has been associated with increased phobias. Therefore the present studies were designed to explore cerebral blood flow changes responsible for metabolic support during neural signaling and the functional response associated with a fear eliciting stimulus (fox scent) in a rodent model of aging.

Methods

Young adult (3-6 months) and old (18-24 months) Fisher 344 male rats (300-400 grams) were imaged on a 4.7 Tesla imaging scanner under 2% isoflurane anesthesia. Anatomical images were acquired using the fast spin-echo pulse sequence (RARE) with TR = 2500 ms (90° flip angle), 8 echoes, TR effective TE = 10 ms, matrix = 256 x 256, FOV = 2.56 x 2.56 cm², and eight 1.5-mm slices.

Quantitative CBF was measured using the continuous arterial spin-labeling technique with four segmented gradient-echo EPI, with matrix = 128 x 128, FOV = 2.56 x 2.56 cm², TE = 15 ms, TR (90° flip angle), and eight 1.5-mm slices. Functional activation data was obtained using the fast spin-echo pulse sequence (RARE) with TR = 2.4 s, effective TE = 8 ms, matrix = 64 x 64, FOV 3.0 x 3.0 cm², and eighteen 1.0-mm slices, Repetition Number = 60.

MR Image analysis employed codes written in Matlab (MathWorks, Natick, MA) and STIMU software (Strupp, 1996). Analysis was performed on conservative ROIs avoiding brain-skull interface which were carefully drawn based on CBF maps and functional maps.

Results & Discussion

Figure 1 depicts mean CBF values in old and young male Fischer rats (n=4/each). Whole-brain CBF in old and young rats were 1.31 [plus/minus] 0.04 and 1.68 [plus/minus] 0.13 ml/g/min, respectively. Regional CBF differences between the two groups were statistically different (*P<0.05, **p<0.01). CBF was spatially heterogeneous with values in the hippocampus and cortex showing highest significant differences between the young and old groups.

Figure 2 represents the average percent change in positive BOLD signal intensity in the amygdala. The old animals exhibited a significant increase in BOLD activation in response to fox scent (*p<0.05).

Conclusions:

In this report significant changes in cerebral blood flow accompanied aging in several regions of interest. In spite of these decreases, there was enhanced BOLD activation in response to fear stimulus.

in the amygdala – a region central to the fear response- in the aged animals. We hypothesize that independent of observed changes in cerebral blood flow that accompanies the aging process, old animals can still mount a significant (if not exaggerated) response to life threatening stressors.

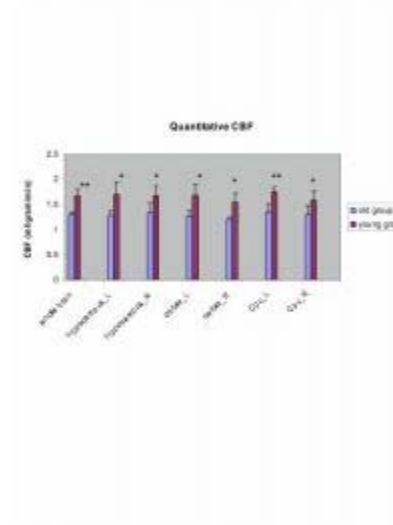


Figure 1

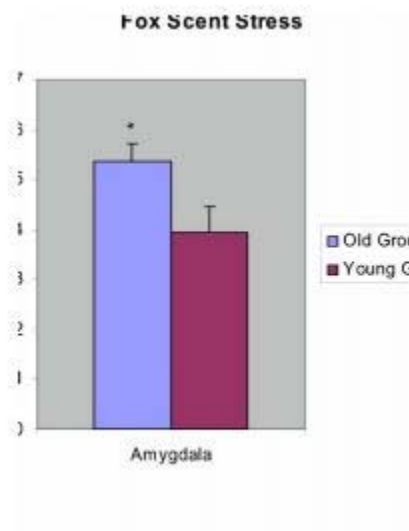


Figure 2

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