Long-term survival study showing aging effect on the sensory function of peripheral nervous system in rats using fMRI/fcMRI under 9.4 Tesla

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Introduction

The aging process affects both CNS function and peripheral nerve function. In humans, this process changes the sensorimotor function significantly and also limits cognitive function [1]. However, the aging effect on the peripheral nervous system (PNS) is not well studied. It is well documented that the PNS in constantly reformed by environmental factors. Thus comparison across human groups can be challenging since the PNS could be affected by different factors. Due to the fact that it is challenging to follow the same patient over a significantly long aging period, use of internal controls is not an option in human aging studies. The rat becomes an excellent surrogate for aging studies due to the short life span and high similarity to the PNS structure of humans. fMRI and fcMRI were carried out in the same group of animals in this study to reveal the aging effect in the PNS-CNS system at 1month (young rat), 3 months (adult rat) and 5 months (senile rat).

Materials and Methods

Animal preparation: Seven Sprague-Dawley rats (weighting 150±5g) were used. The right side median nerve was exposed on all animals and a microelectrode was placed onto the nerve trunk. The incision was then closed. Electrodes connections were place in a subcutaneous pocket for later access. An infusion of Dexdomitor (0.1mg/kg/hr) was given during the fMRI scan. The animals were scanned with a Bruker 9.4Tesla 30cm animal scanner. An electrical stimulation of 10Hz, 0.5mA, 1ms was applied to stimulate the median nerve. A block design was used. All physiological parameters were monitored and maintained within normal range.

fMRI/fcMRI parameters and data analysis: MRI data was acquired using a gradient-echo EPI sequence. FOV=3.5cm, TR=2s, TE=19 ms, matrix size 96 x 96, slice thickness 1mm. Each rat was scanned twice for resting-state and median-nerve stimulation data. The scan results were registered to the same template. fcMRI was analyzed using the seed-voxel technique. For each animal, the seed was chosen from the BOLD fMRI activation from median nerve stimulation. A band-pass filter of 0.01Hz-0.1Hz was used. The fcMRI data was smoothed with a FWHM kernel of 0.5mm. Multiple comparisons were done to determine the threshold. The Fisher Z transform was applied to all fcMRI data. For group analysis, individual results were acquired first and then averaged to provide representative group results. Analysis was done on all 10 slices.

Results

Median nerve stimulation usually activates 3-4 slices in the brain covering about 3 mm in the sagittal direction. The middle slice is displayed here to illustrate the experimental results. Figure 1(A) shows the BOLD fMRI test of median nerve stimulation at all time points. Localized S1FL (primary sensory area of forelimb) activation is seen on the side of the brain contralateral to stimulation. This location remains constant across the experiment period. Voxel analysis was done and the results are shown in Figure 1(B). As the rat brain develops from young age (1 month post-op) to mature age (3-5 month post-op), the S1FL representation of median nerve expands significantly. There is no statistical significant difference between the adult age with the senile age. Figure 2 shows fcMRI of the sensory network in the cortex using a seed-voxel from the corresponding median nerve BOLD fMRI activation. The fcMRI results are fairly consistent across time points. fcMRI signals from different hemisphere are separated from each other covering in the S1FL cortex, leaving blank gaps in the cingulate cortex of both hemispheres. The result shows that as the animal grows from young to adult, a more spread sensory network develops in the cortex. The network shrinks as the animals become senile.. However, the older animals show stronger inter-voxel correlations. The overall trend in the fcMRI test correlates with the fMRI test.

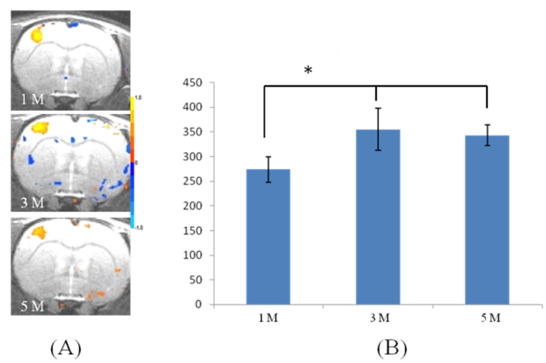

Fig.1 (A) BOLD fMRI S1FL activation of right median nerve stimulation at 1, 3 and 5 months post-operatively. (B) Voxel analysis showing significant expansion of median nerve representation area within S1FL in mature rat (3, 5 month) comparing to young rat (1 month)

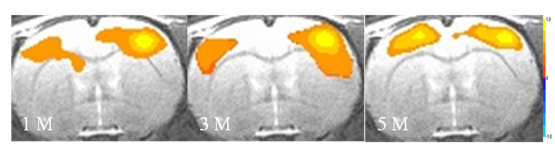

Fig.2 fcMRI showing sensory network in S1FL using seed from BOLD fMRI median nerve stimulation scans. 3month time point shows the widest distribution of the network, and the 5 month time point shows the strongest inter-voxel correlation.

Conclusion and Discussion

The results from both fMRI and fcMRI demonstrate a common trend of the aging process in the sensory system. From the result, we found that the sensory network peaks at the adult age. When individual animal grows from young age into adult age, the sensory network spreads out and as the animal enters senile age, the same network shrinks. This finding correlates well with the biological feature of the animal that the cognitive function is the best at adult age. On the other hand, fcMRI shows a stronger inter-voxel correlations which might indicates that in the senile age, despite the fact that the sensory network shrinks, the network works more efficiently than at a younger age. More work needs to be done on the fcMRI network analysis to further prove this hypothesis.

Reference 1. Karen Z.H Li, Hlman Lindenberger. Relations between aging sensory/sensorimotor and cognitive functions. Neuroscience & Biobehaviral Reviews. 2002: 26. 777-783.