# Proton spectra in aged rats: correlation with learning abilities

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## Introduction

Aging is associated with neuronal death, loss of synapses and dendritic pruning resulting in memory impairment and cognitive decline. The aim of our study was to determine metabolic changes in the hippocampus during aging in rats with distinct spatial learning abilities.

## Materials and Methods

Ten Wistar male rats aged 22 months and six Wistar male rats aged 4 months underwent functional testing and magnetic resonance spectroscopy (MRS). Functional test: The rats were tested in a Morris water maze (MWM) (1) 8 times per day for 5 consecutive days. Rats were divided into two groups according to their performance in the MWM test (good learner- mean latency <=38 s, bad learners - mean latency > 38 s). MRS: Animals were then scanned by a 4.7 T Bruker MR spectrometer with a home-made surface coil. 1H spectra were measured using a modified single voxel STEAM sequence (with selective CHESS pulses for water suppression), with short echo time (TE=3 ms) and repetition time TR=5000 ms. The volume of interest was approximately 35 $mm^3$ to cover both hippocampi (Figure 1). Spectra (Figure 2) were evaluated using the LCModel (2) to obtain absolute metabolite concentrations in laboratory units.

## Results

The results obtained in the MWM test showed four old rats to be bad learners (mean latency 51.1 ± 8.3 s) and four old rats together with all the young rats to be good learners (mean latency 29.7 ± 3.4 s). The concentration of water-soluble choline (Cho) significantly increased in aged rats, but there were no differences between the rats with good and bad learning abilities. Creatine metabolites (Cr) showed no differences between young and aged rats but significantly differences between bad and good learners. We observed a clear trend for changes in glutamate (Glu), inositol (Ins) and N-acetyl aspartate (NAA) concentrations. The Glu concentration decreased in aged rats, with a significant difference between young rats and aged bad learners. In contrast, Ins concentration increased, and the changes were significant between young and old rats and between young and bad learners. The NAA concentration in aged rats decreased, with the greatest decrease seen in the group of rats with bad learning ability, but the differences were not statistically significant. We did not observe any changes in taurin (Tau) concentration. The absolute concentrations of selected metabolites in young and aged rats are summarized in Table 1. A typical 1H MR spectrum of the hippocampus of an old rat is shown in Figure 2.

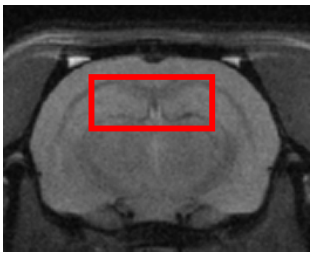

Figure 1. A typical MR image of a rat brain that served as a localizer for MR spectroscopy. The red rectangle shows the location of the hippocampus.

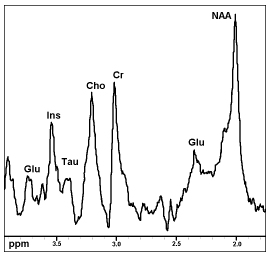


Figure 2. A proton spectrum of an aged rat hippocampus.

| | Cho (mM) | Cr (mM) | Glu (mM) | Ins (mM) | Tau (mM) | NAA (mM) |
|---|---|---|---|---|---|---|
| Young number =6 | 1.7±0.1 | 8.3±0.4 | 9.4±0.8 | 3,4±0.2 | 5.4±0.7 | 9.2±0.9 |
| Old good learners number=4 | 2.1±0.1 | 8.8±0.2 | 8.3±1.5 | 4.5±0.5 | 5.3±0.6 | 8.3±0.9 |
| Old bad learners number =6 | 1.9±0.1 | 6.9±0.9▪ | 7.3±0.6+ | 4.6±0.7+ | 5.5±0.7 | 7.7±0.7 |
| All old number =10 | 2.1±0.1* | 7.7±0.6 | 7.7±0.7 | 4.6±0.4* | 5.4±0.5 | 7.9±0.5 |

Table 1. Absolute concentrations of selected metabolites in the hippocampus. Data are expressed as mean ± S.E.M. Significant differences (two-tailed t-test, $p < 0.05$) between young and old rats are marked with asterisks, between good and bad learners with a box, and between young rats and bad learners with a cross.

## Discussion and Conclusion

The increased concentration of choline and the lower NAA concentration in the aged rat hippocampus is in agreement with published results (3). The changes in Glu, Ins, Cr and NAA concentrations in aged rats compared to young rats were higher in bad learners than in good learners. In addition to a decrease in NAA, a putative neuronal marker, due to the loss of neurons in the aged rat hippocampus, the concentration of creatine, a marker of metabolic activity (4), may be considered as sign of learning disability because it was significantly lower in rats with poor learning ability (compared to good learners).

## References

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