

EFFECTS OF CALORIC RESTRICTION (CR) ON NMDA/AMPA RECEPTORS AND MULTIPLE SPINE BOUTON (MSB) SYNAPSES IN HIPPOCAMPAL CA1 ACROSS LIFESPAN

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Aging in rodents is associated with impaired performance on hippocampal dependent cognitive tasks. Synapses play an essential role in neural processing and compromised synaptic function may contribute to cognitive impairment in old rats. Caloric restriction (CR), which retards the progression of aging-related diseases, also has been reported to ameliorate deficits in the synaptic function of old animals. The present study investigated whether CR affects glutamate receptors and synapses in hippocampal CA1 across lifespan. Hippocampal CA1 from young (10 months), middle aged (18 months), and old (29 months) *ad libitum* fed (AL) and CR (N=8/group) Fischer 344 X Brown Norway rats was prepared for Western blot analysis of synaptophysin and of NMDA (NR1, NR2A, NR2B) and AMPA (GluR1, GluR2) receptor subunits that are critical for synaptic plasticity. In addition, CA1 stratum radiatum from another 6 rats per group was processed for electron microscopic analysis of multiple spine bouton (MSB) synapses. The prevalence of MSB synapses correlates positively with AMPA receptor levels as well as with physiological measures of synaptic efficacy. ANOVA revealed a significant effect of age on levels of the NR1, NR2A, NR2B, GluR1, and GluR2 subunits of glutamate receptors as well as of synaptophysin in CA1 of AL but not CR rats. In addition, the levels of all elements of synapse composition except GluR1 were lower in CR compared to AL rats for young but not middle aged or old groups. Stereological quantification of MSB synapses did not reveal an effect of either aging or diet on this synaptic subtype. In summary, the results indicate 1) aging-related declines in synaptic proteins in the absence of a loss of MSB synapses in hippocampal CA1 of AL rats but not CR rats and 2) lower levels of synaptic proteins in young CR compared to young AL animals.

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