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High-energy diet alters intrinsic excitability in young hippocampal CA1 neurons: Gender-dependent responses to insulin

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Abstract:
Alarming increases in dietary fat intake and subsequent rises in obesity/insulin resistance/type II diabetes necessitate a focus on the effects of diet on normal physiological brain function and on cognitive performance. Rats trained in a passive-avoidance task exhibit enhanced memory retention 24 hr or more later when intrahippocampal insulin is administered immediately post-acquisition (Babri et al., 2007). Successful consolidation of many different learning tasks (e.g. inhibitory avoidance training or trace eye-blink conditioning) reduce Ca2+ dependent afterhyperpolarizations (AHPs) of hippocampal CA1 pyramidal neurons (Farmer & Thompson, 2012). Since successful learning of a task is accompanied by a reduction of AHPs (i.e. an increase in intrinsic excitability) and insulin enhances memory retention, we investigated the effects of a chronic high-energy diet, which can alter basal insulin, on measures of CA1 hippocampal neuron intrinsic excitability which regulate information transfer to hippocampal efferents: effects of diet and of insulin on post-burst afterhyperpolarizations.
Male and female young adult Long-Evans rats (4-6 mo) were fed from weaning either a control diet (14% fat, 64.8% carbohydrate, and 21.2% protein) or a high-energy diet (57.6% fat, 26.8% carbohydrate, and 15.6% protein) prior to brain slice preparation. The experimental high-energy diet was augmented with slow-digesting casein protein and medium-chain triglyceride polyunsaturated coconut oil to achieve the desired ratios. After slice preparation, in vitro current clamp recordings were made to assess post-burst AHPs, accommodation, and passive membrane properties. After baseline recordings, brain slices were perfused with insulin (0, 6, 12.5, 25, or 50 nM) and recordings were repeated.
Young control female CA1 neurons had smaller peak AHP amplitudes (~4.0 mV), both reduced medium AHPs (mAHPs) and reduced slow AHPs (sAHPs), and reduced accommodation (fired more spikes to a sustained depolarization), while on all these measures male control neurons were less intrinsically excitable. After 2 mo on chronic high energy diet, this gender-dependent profile was not only reversed, but intrinsic excitability of CA1 neurons from both genders was significantly reduced. Neurons from females on the high-energy diet had significantly larger mAHPs and sAHPs of longer duration and area than those from males, which were still significantly enhanced by the diet compared to controls. These neurophysiological changes, occurring within a relatively short time frame, could have significant cognitive consequences, which will be assessed in the next phase of our studies.