Regulation of the endocannabinoid receptor CB1 level and synaptic plasticity in prefrontal cortex of food restricted rats

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Endocannabinoids (eCB) regulates appetite and feeding behavior acting on different brain areas including the prefrontal cortex (PFC). To further investigate the role of the eCBs in the feeding behavior we evaluated the expression level and localization of the CB1 in neurons of the PFC of rats exposed to food restriction (FR, food availability to a 2-h period daily for 3 weeks) by immunohistochemistry and electrophysiological studies. The amount of CB1 receptor immunostaining was significantly decreased 1 h before food presentation, compared to controls; such reduction was still observed during the consumatory phase, but it was no longer apparent 1 h after food removal. Given that in the PFC CB1 are predominantly expressed by a specific subtype of perisomatic GABAergic interneurons, the CCK-containing basket cells, and that their axon target the perisomatic region of pyramidal neurons, we therefore analyzed the changes in CB1 density induced by FR in CCK-positive neurons as well as their co-localization with GAD65 at presynaptic GABAergic terminals. Double immunostaining for CB1 and CCK resulted decreased during the anticipatory phase, 1 h before food presentation, did not change during the consumatory phase, returning to control values 1 h after food removal. Co-localization density of CB1 and GAD65 was very similar to that observed for CB1 and CCK, resulting significantly reduced during the anticipatory and consumatory phase, respectively, but not longer altered 1 h after food removal. We next analyzed the basal properties of $GABA_A$ receptor–mediated sIPSCs recorded in voltage-clamped (–65 mV) pyramidal neurons in slices of the PFC obtained from FR and control rats. Moreover we next analyzed the basal properties of $GABA_A$ receptor–mediated sIPSCs recorded in voltage-clamped (–65 mV) pyramidal neurons in slices of the PFC obtained from FR and control rats. These electrophysiological studies have shown that CB1 agonist WIN 55,212-2 reduced the frequency of GABA-induced sIPSCs in PFC pyramidal neurons of control rats, with this effect being diminished in FR rats during the anticipatory phase before food presentation. Together our data indicate that FR induced changes in the expression level of CB1 receptor in rats may alter the activity of excitatory synapses suggesting that feeding restriction may exert an effective action strong impact on PFC synaptic plasticity.