S 22-4

HYPERPROLACTINEMIA AND OSTEOPOROSIS

Nateetip Krishnamra

Department of Physiology, and Consortium for Calcium and Bone Research (COCAB), Faculty of Science, Mahidol University, Bangkok, Thailand

Hyperprolactinemia from pituitary adenoma, from taking certain neuroleptic drugs, or prolonged lactation have been found to be associated with decreases in bone density and bone mass. This associaton has often been explain in term of estrogen deficiency secondary to hyperprolactinemia. However, the fact that some hyperprolactinemic men exhibited bone loss and some hyperprolactinemic women developed osteoporosis even with regular menses led to the speculation that prolactin itself might have a direct action on bone metabolism. The idea later received supports from reports of prolactin receptors in human osteosarcoma cell lines and primary cultures of mouse osteoblasts. Furthermore, prolactin receptor knockout mice had a decrease in bone formation rate and bone mineral density, which led to a hypothesis that prolactin was required for normal bone formation and maintenance of bone mass (Clement-Lacroix et al. 1999). In contrast Coss and his group (2000) reported an inhibitory effect of phosphorylated prolactin on alkaline phosphatase activity in osteoblasts which resulted in reduced calvarial bone and endochondral ossification. Our previous work showed that although exogenous prolactin accelerated bone turnover in both young and adult rats, long term prolactin led to bone gain in young and bone loss in adult rats. In lactating rats, high circulating levels of prolactin had the same stimulatory effect on the *in vivo* bone turnover with a net loss of bone calcium (Lotinun et al, 2003). Our recent studies in human osteosarcoma cell line MG-63 and human fetal osteoblast (hFOB) showed the presence of prolactin receptors and an inhibitory effect of prolactin on the activity and mRNA expression of alkaline phosphatase, an enzyme marker of osteoblast activity. MG-63 cells responded to prolactin by decreasing differentiation and increasing the RANKL/OPG ratio, an index of bone resorption. In contrast, hFOB responded with increased differentiation, increase in osteocalcin mRNA expression and decrease in RANKL/OPG ratio. The mechanisms underlying the differential responses of bone cells to prolactin are under investigation.

*This work was supported by Senior scholar research grant (RTA 4780008) from the Thailand Research Fund, research grant (BT-B-01-MG-14-4804) from the National Center for Biotechnology and Genetic Engineering, and the Faculty of Science, Mahidol University.

DPS 1

QUANTITATIVE ULTRASTRUCTURAL ANALYSIS OF SYNAPTIC CONNECTIONS ON TRIGEMINAL MOTOR AND MESENCEPHALIC NEURONS

Yong Chul Bae

Department of Oral Anatomy and Neurobiology, School of Dentistry, Kyungpook National University, Daegu, Korea

Neurons communicate with each other at the synapse. Elucidation of synaptic connection and related neurotransmitters at the specific neural circuits of trigeminal motor system is crucial for understanding central mechanism for rhythmical jaw movement. we have investigated synaptic connectivity i) on somata of jaw closing (JC) motoneurons and ii) of trigeminal mesencephalic (Vmes) neurons during postnatal development when ingestive behavior change from sucking to chewing, and iii) of JC muscle spindle afferents within the trigeminal motor nucleus (Vmo) that is involved in jaw jerk reflex. These studies were performed by injection of HRP into the corresponding muscles or single axon or somata, by postembedding immunocytochemistry with serial ultrathin sections, and by image analysis program with electron microscopy. Mean length and synaptic covering percentage of boutons forming synapse with JC motoneurons significantly increased during postnatal development. Among the inhibitory bouton types, proportions of GABA and glycine immunoreactive bouton types was similar in neonatal JC motoneurons. Boutons immunoreactive for glycine alone, however, significantly increased and became predominant bouton type during postnatal development. Somata of masseteric Vmes neuron in adult rats showed synaptic contact with boutons immunoreactive for GABA alone, glycine alone, both GABA and glycine, and for glutamate. Bouton immunoreactive for GABA was most prevalent types among the inhibitory bouton types. Synaptic covering percentage (total proportion of cell membrane covered by boutons) of the apposed boutons were 6.6±3.9%. Synaptic covering percentage, packing density of boutons and proportion of each immunoreactive bouton types did not show significant change during development. Bouton size and ultrastructural parameters related to neurotransmitter release of boutons on Vmes neuron somata were similar to boutons presynaptic to primary afferents. Most (86%) of the analyzed masseteric group Ia boutons showed simple synaptic cotact with 1 or 2 neuronal profiles in the Vmo. They formed fewer axoaxonic contact (35.6%) compared to group Ia boutons of hind limb muscle (86~100%). Distribution range and size of Ia boutons was limited and small in the trigeminal system compared to in the spinal system. Our data suggest that the distinct synaptic connectivities in the trigeminal motor system is closely related to masticatory jaw movement distinguished from spinal motor system.