

Imbalance of excitatory and inhibitory neural networks caused by pyrethroids or valproic acid; Relationship between gene expression and neuronal diseases

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The central nervous systems are stepwisely generated by the formation of correct neuronal networks, the development of which is promoted by receiving synaptic inputs at appropriate periods during the development of the brain. Therefore, an exposure of the brain to environmental chemicals or medicines during the development after birth would cause an abnormal formation of neuronal networks, resulting in the developmental disorders of the brain. Our recent study revealed that the expression of brain-derived neurotrophic factor (BDNF) gene was markedly induced by the treatment with deltamethrin, a pyrethroid insecticide, or valproic acid, an anti-convulsant drug in cultured neurons. Since BDNF plays a fundamental role in the expression of neuronal functions, it seems possible that these chemicals cause an inappropriate formation of neuronal networks and, hence, neuronal disorders. In support of this idea, it is well known that the administration of valproic acid to pregnant women results in an easy birth of autistic children. To elucidate the effect of deltamethrin or valproic acid on the development of the brain, we investigated the changes in gene expression induced by the exposure of cultured cells to these chemicals using Gene Chip System (Affymetrix). We found that the expression of genes, which encode proteins involved in excitatory or inhibitory synaptic transmission, were changed by the treatment either with valproic acid or deltamethrin, suggesting that these chemicals affect the balance of excitatory and inhibitory neurons. In this symposium, I would like to discuss the effect of deltamethrin and valproic acid on gene expression, and then relationship between gene expression and neuronal diseases.