

## **Acetylcholine-dopamine balance hypothesis: an update**

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### **Abstract**

The breakdown of the balance between acetylcholine and dopamine in the striatum causes a variety of neurological diseases. Physiologically action commands popped up in the cerebral cortex trigger a conditional pause response in the firing of the tonically active cholinergic interneurons in the striatum through the thalamo- and corticostriatal pathways. The pause response is made possible by a concomitant increase of firing frequency of the dopaminergic neurons, which dramatically increases the release of dopamine only in the projection areas of the cholinergic interneurons when the release of acetylcholine stops during the pause response. This facilitates the synaptic efficacy of the striatal medium spiny projection neurons in the areas, which enables an execution of action commands with an improvement of signal-to-noise ratio. Deviation from the balance in either direction would hamper proper functioning of the cortico-basal ganglia-thalamocortical loop circuits. In Parkinson's disease dopamine depletion blocks autoinhibition of acetylcholine release through muscarinic autoreceptors, thereby leading to excessive acetylcholine release which eventually prunes spines of the indirect pathway projection neurons of the striatum and thus interrupts information transfer from motor command centers in the cerebral cortex.

**Keywords:** acetylcholine, dopamine, Parkinson's disease, basal ganglia

## **The molecular mechanism of bone and joint destruction in rheumatoid arthritis**

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Rheumatoid arthritis (RA) is a chronic inflammatory disorder characterized by invasive synovial hyperplasia associated with localized and generalized bone loss. Proliferation of the synovial cells leads to pannus tissue that invades the bare area between cartilage and bone, finally resulting in progressive bone and joint destruction in the affected joints. There is accumulating evidence that osteoclasts, the primary cells responsible for bone resorption, are involved in bone and joint destruction in RA. Preventing joint destruction is one of the most challenging issues in treating patients with RA. The recent elucidation of the various intracellular signaling pathways in osteoclasts has brought a tremendous understanding of the pathophysiology of inflammatory bone loss, and has heightened expectation of a novel intervention. We here highlight the molecular mechanism of bone and joint destruction in RA and the role of intracellular signaling pathways in osteoclastogenesis and mature osteoclast function. We also describe the recent trials on inhibitor drug and anti-cytokine therapies of arthritic joint disease targeting osteoclasts.

**Key words:** bone resorption, osteoclasts, RANKL, synovium, T cells

## **Proteomic analysis of the dementia with mass spectrometry.**

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The analysis of the protein of human sample is necessary and indispensable to research the disease. The information obtained by analyzing each disease brings an important finding to the clarification. However, the system that can analyze a very small amount protein is necessary because the human sample is valuable and limited. It is a proteomics research with the mass spectrometry for one of the most effective methods to do these now. In this review, it explains the type of mass spectrometry, the pretreatment to the analysis, and the method of identifying the protein about an indispensable mass spectrometer for the analysis of the protein. In addition, how the mass spectrometry is used for the research of dementia is outlined.

**Key words:** proteomics, mass spectrometry, dementia, Alzheimer's disease