Paying Attention to Your Acetylcholine, Part 1

Structural Organization of Nicotinic Receptors

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Issue: Nicotinic cholinergic receptors exist in multiple forms in the brain and may be important in mediating diverse cognitive functions such as memory and attention.

Summary

The structure of nicotinic receptors has been elucidated. How these structures lead to specific functions will be discussed in BRAINSTORMS next month.

Take-Home Points

♦ There are 2 major classes of cholinergic receptors: nicotinic, which are stimulated by nicotine and act as gatekeepers for ion channels, and muscarinic, which are blocked by anticholinergic drugs and are linked to G proteins and second-messenger systems.

♦ Nicotinic receptors are composed of 5 types of subunits arranged around a central ion channel. These receptors have not only agonist binding sites for acetylcholine and nicotine, but also allosteric-modulating sites that can boost the actions of acetylcholine much like benzodiazepines boost the actions of GABA.

♦ Some nicotinic receptor subtypes may mediate attention and be potential targets for novel treatments of cognitive deficits in Alzheimer’s disease, schizophrenia, and other disorders.
Nicotinic Receptor

When 5 subunits are assembled, they constitute a complete nicotinic receptor, forming an ion channel in the middle. The secret to how nicotinic receptors mediate their different functions is the way they mix and match various combinations of their 5 subunits, with different mixtures in different parts of the brain as well as in different tissues, such as skeletal muscle and sympathetic ganglia.

Amino Acids and Subunits (α, β, γ, or δ) in Cell Membrane

Each subunit is a long string of amino acids that goes in and out of the neuron’s cell membrane 4 times, forming 4 transmembrane regions that correspond to the parts of the receptor within the membrane, but not to the tails and loops outside the membrane. The amino acid composition of this string varies to form different subunits (α, β, γ, or δ). There are even different types of α and β subunits that are very important in determining the functions they perform in the brain.

REFERENCES