Dynamic Chiropractic

CHIROPRACTIC (GENERAL)

Receptors and Neurotransmitters: Capturing Lightning in a Bottle

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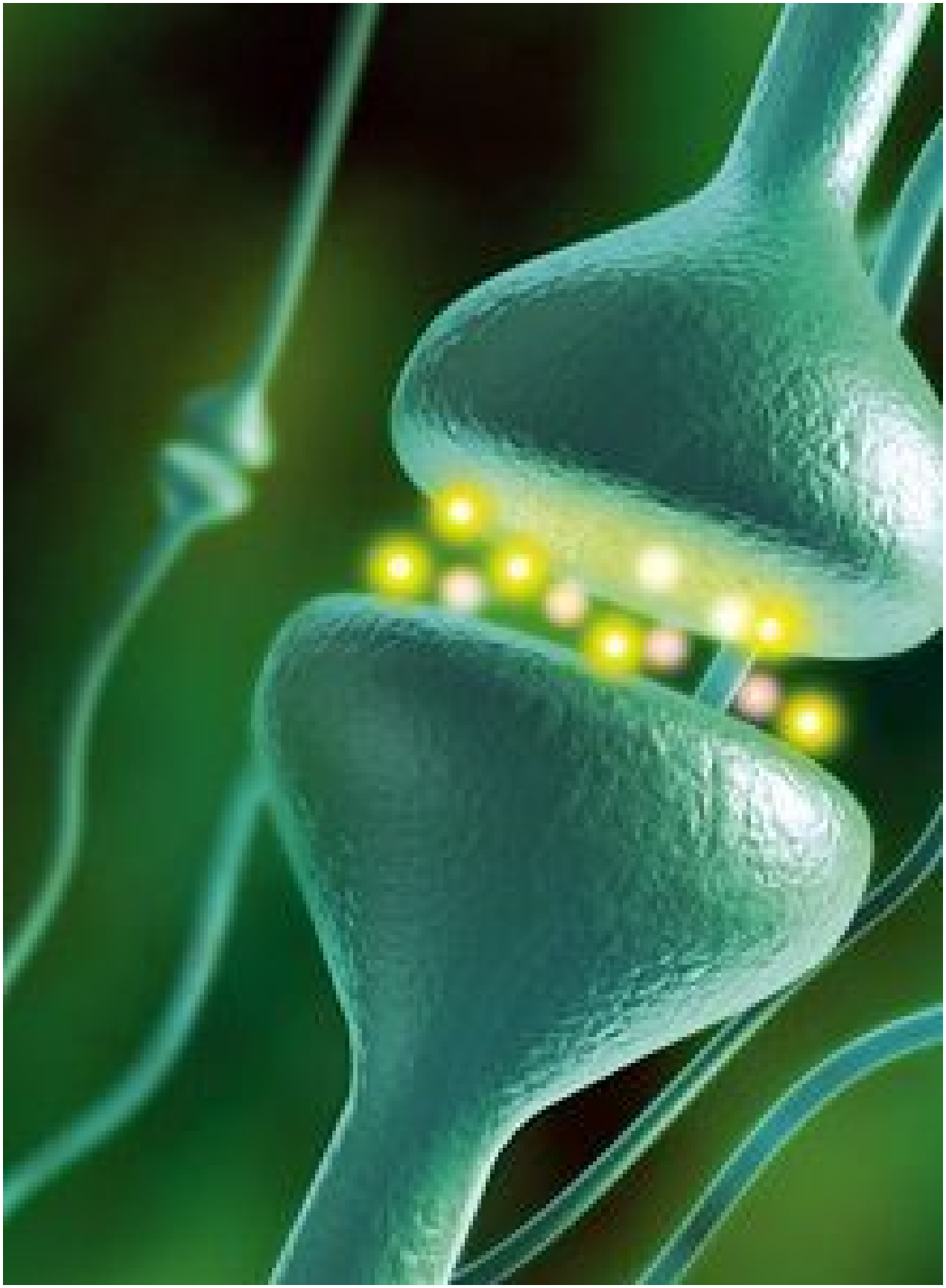
History shows us that the research process can be both exhilarating and humbling: exhilarating in that such breakthrough discoveries as radiation, vulcanization or penicillin have changed the course of history and reaped countless benefits to mankind; humbling in that a trivial or imperfectly crafted question can sometimes deliver a result that more closely resembles a dope slap than a knockout blow. It takes a carefully crafted, well-thought-out research question to yield a result that is more than obvious or downright insulting in the lack of meaningful information that it delivers. Put another way, in the immortal words of Mark Twain when describing precise writing: "The difference between the almost right word & the right word is really a large matter - it's the difference between the lighting bug and the lightning."[1]

And so, when it comes to chiropractic research, I'm taking this space to bring such a more focused and vital research question into the limelight. I'm expanding upon an important example of the chemistry that pervades the neurological principles which occupy the epicenter of chiropractic theory, a topic I discuss in an upcoming article.[2] Specifically, I'm drilling down to the agent responsible for both receiving and regulating the chemical agents which pass from neuron to neuron in neurotransmission.



That entity is the *receptor*, simply defined as any structure (a protein molecule) that receives and responds to an environmental stimulus. In neurology, that stimulus is a neurotransmitter and the response occurs in the form of an informative nerve impulse. Receptors function as agents of up- or down-regulation, depending upon the molecules to which they bind. In this fashion, the receptor becomes a veritable gatekeeper of neurotransmission. As such, its significance in afferent and

efferent nerve activity cannot be overemphasized.

A most compelling and dramatic example of this has been brought to us by a joint investigation in a mouse model conducted at the University of Rochester Medical Center, the Boston University School of Medicine and the National Institutes of Health.[3] Researchers found that adenosine, a nucleotide that is a building block of ATP and previously found to suppress pain through an A1 adenosine receptor,[4] is released during acupuncture in mice. Furthermore, the analgesic effect of acupuncture can be replicated by direct injection of an adenosine A1 receptor agonist. All of these effects are obliterated in knockout genetic strains of mice, which lack the adenosine A1 receptor. Finally, the pharmacologic inhibition of enzymes involved in adenosine degradation potentiate both the acupuncture-elicited increase in adenosine, as well as its antinociceptive effect.

All of these findings clearly demonstrate that (1) adenosine mediates the effects of acupuncture, and (2) interfering with adenosine breakdown may prolong the clinical effects of acupuncture. What this elegant series of experiments has shown us is that, at least for one type of acupuncture executed in an animal model, the analgesic effects most commonly attributed to acupuncture *have been packaged into a functional receptor for a neurotransmitter.* What if other analgesic effects attributed to all matter of health care interventions were similarly collapsible into the activity of one or more receptors? Simply put, to paraphrase the words of Mark Twain, lightning (instead of a lightning bug) will have been captured in a bottle.

Bringing receptor activity into the human realm is perhaps most persuasively demonstrated by the phenomenon of *insulin resistance,* responsible for the occurrence of non-insulin-dependent diabetes. The culprit in this disease for not being able to respond to insulin, needed for glycogen breakdown and the metabolism of glucose, is once again the receptor - for insulin. The molecular basis for this has been suggested to be the elevated serine/threonine phosphorylation of the major insulin receptor substrates, inhibiting their binding to a particular region of the insulin receptor and thus impairing their ability to undergo insulin-induced tyrosine phosphorylation. In this manner, further propagation of the insulin receptor signal is impaired.[5]

In a most informative weekend seminar I had the privilege of attending recently,[6] the presenting chiropractor pointed out that becoming familiar with neurotransmitters "blew his mind," with the effect of overturning the paradigm with which he viewed health care. In particular, he focused upon the chemical species that have been designated as neurotransmitters and how they function in the synapse. A critical component of the functional synapse is the postsynaptic neuron, which performs the function of neurotransmitter binding and the ensuing electrochemical response.

The means by which this function is accomplished is - once again - the receptor. The rate of firing can be controlled either by a hormone causing its own receptor site down-regulation (such as with acetyl choline receptor sites, called homotropic modulation) or interactions with factors other than the primary neurotransmitter itself (such as with the interactions of estrogen upon the dopamine receptor site, called heterotropic modulation).

Specifically, neurotransmitter binding affects hormone binding, and vice versa, in the following ways:

- Serotonin function is enhanced by estrogens in both men and women.
- Dopamine activity is enhanced by testosterone in men and by estrogens in women.
- Gamma-amino butyric acid (GABA) is enhanced by progesterone in both men and women.
- Acetylcholine is enhanced by testosterone in men and by estrogens in women.

Once again, the focus of all these cross-reactivities is the receptor. Because the receptor is mainly a high-molecular-weight protein, it needs to be studied by many of the same approaches as are taken in enzyme chemistry and regulation. This means that such phenomena as genetic deletions,[7] allosteric regulation and subunit analysis,[8] and the kinetics and specificities of binding to the substrate molecules (called ligands) to receptors[9] all become valuable tools for understanding the regulation of neurotransmission. In this manner, we will have not only clarified a number of basic mechanisms involved in neuroplasticity (of obvious interest to the chiropractic researcher), but also fulfilled Twain's criteria of capturing lightning in our creative minds and pursuits - to say nothing of in the laboratory itself.

References

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