The Pharmacology of Auditory and Vestibular Systems

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Abstract

Pharmacologists are among the most recent basic medical scientists to apply themselves to the auditory and vestibular systems. They bring to the subject a fresh perspective and, uniquely, the ability to control biological processes through drugs. Interest in the auditory and vestibular systems among pharmacologists has focussed on: the **drug-sensitive** processes (primarily but not exclusively **neuro-transmission**); toxicology, and pharmacotherapy. Pharmacology holds the promise of shedding further light on auditory and vestibular function and ameliorating auditory and vestibular dysfunction.

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Pharmacology

The development of auditory and vestibular science has paralleled the development of other biomedical sciences in that it began with descriptions of form (anatomy) in which took root descriptions of function and the chemistry of function (physiology and biochemistry) and dysfunction (pathology). The 'new kid on the block' is Pharmacology which uses chemical manipulation of processes for further elucidation of those processes and for the correction or amelioration of dysfunction. Thus, Pharmacology, in contradistinction to its sister sciences, provides the capability of influence over function. Furthermore, its purview spans from the molecule to the clinic and all in between.

Areas of Research Interest: Current and Future

Neurotransmission

In order for drugs to exert such influence there must be drug-susceptible processes available. In the case of the nervous system, it is the neurotransmitter/modulators and their associated processes that have proved particularly drug-susceptible. Therefore, one approach to the establishment of the pharmacology and pharmacotherapy of auditory and vestibular systems is the elucidation of transmitter/modulator identities and their associated processes (i.e. synthesis, storage, release, action and termination of action). The neurotransmitter/modulators and their related processes are particularly valuable as sites of therapeutic drug action because they: command or are upstream of a host of intracellular reactions activated by the combination of the transmitter/modulator and its highly selective receptor, and they are, to some extent, localized to certain systems (e.g. dopamine in the basal ganglia).

The day of transmitter/modulator identification is rapidly closing. What has become clear from the pioneering identification studies is the complexity of the systems involved. In a relatively simple organ such as the semicircular canal, between the three major neural elements, the hair cell, the afferent and the efferent neurons there may be eight or more transmitters involved (i.e. acetylcholine, an excitatory amino acid, calcitonin-gene-related peptide, enkephalins, GABA, adenosine and perhaps histamine).

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The complexity is furthered by the existence of multiple receptors for these transmitter/modulators operating multiple second- and third-messenger systems. The job for the future in this area is fitting these systems into the dynamic mosaic of auditory and vestibular function.

A second approach to the pharmacology of the auditory and vestibular systems, as yet not widely used, would be to study and take advantage of the unique and relatively unique processes of the auditory and vestibular systems (i.e. transduction, the endocochlear potential, the intense secretory activity of the stria vascularis, the blood-labyrinthine barrier, the almost-unique affinity of the aminoglycoside antibiotics for the labyrinth) as sites of drug action with an eye toward producing drugs with great specificity and thereby, limited side effects.

Another approach to controlling a symptom such as vertigo which has many causes is to aim downstream of the cause at the common pathway over which the symptom is conducted. By interdicting the symptom at such a downstream site, causation becomes less important a factor in determining choice of therapy, but the therapy becomes symptomatically directed instead of causally directed. Specificity of drug action (i.e., designing or selecting a drug with actions only or especially in the vestibular pathway) may be had by aiming drugs at processes unique to the auditory and vestibular pathway. Such unique processes lie primarily in the inner ear and not in the central pathways. In its physiology the central pathways are like many other hierarchical central pathways. Because of this similarity in physiology, drugs aimed at the central pathways likely may affect nonauditory or non-vestibular structures and thus cause side effects. On the other hand, drugs aimed at some uniquely auditory or vestibular process (e.g. transduction) may gain specificity of action. If the process aimed at is upstream (i.e., inner ear processes), then selectivity is gained at the expense of broadness or inclusiveness of action. Here is the central problem in the pharmacotherapy of disorders of the inner ear: if one aims a drug downstream (i.e., at the central pathways), then one loses specificity or gains side effects.

Toxicology

Auditory and vestibular toxicology is another area of concern to pharmacologists. Toxicological studies often prove to be two-edged in that toxic mechanisms may be elucidated as well as made use of as in the relatively selective destruction of outer hair cells by the aminoglycoside antibiotics. As an example of making lemonade out of lemons, streptomycin and other aminoglycoside antibiotics are currently being applied directly to the vestibular labyrinth in cases of intractable vertigo. This procedure, called selective chemical vestibulectomy, appears to alleviate the vertigo without damaging cochlear structures when done appropriately. In this regard, an understanding of salicylate ototoxicity may likewise prove not only interesting and elucidative of inner ear processes but useful in some as yet unknown way.

Pharmacotherapy

Of the areas belonging to pharmacology, pharmacotherapy is most in need of help. It is currently empirical and often not rationally based. The encouragement of auditory and vestibular pharmacological research should help put the pharmacotherapy of these systems on a more rational footing.

A short list of dysfunctions possibly amenable to pharmacotherapy would include: deafness, vertigo, tinnitus and miscellaneous disorders such as the loss of speech discrimination in the elderly. These labyrinthine dysfunctions may be treated with drugs aimed at the uniquely labyrinthine processes listed above or perhaps some thought should be given to the possibility of local drug application which has proved so useful in ophthalmic pharmacotherapy.

New Techniques

Continuation of support for studies examining drug-susceptible processes is absolutely necessary. The audito-ry-vestibular field lags years behind its close cousin, vision, in this regard. But, in addition to the application of traditional techniques to traditional areas, we must bring new techniques to bear on the problems of the audi-tory-vestibular system. Advances in our understanding will ride on the backs of such techniques as hair cell isolation and culturing, patch-clamping, molecular genetics and the newer imaging techniques. For example, as we learn more about the structural heterology of transmitter/ modulator receptors, it may be possible to produce drugs of greater specificity by designing them to fit that very heterology.

Pharmacology by means of its major tools, drugs, is uniquely poised both to shed light on labyrinthine function and to ameliorate labyrinthine dysfunction.