Neurogenic Inflammation: Additional Points

William Meggs’s recent article, “Neurogenic Inflammation and Sensitivity to Environmental chemicals” (EHP 101:234–238), provides a useful introduction to a rapidly growing area of knowledge in physiology and posits a number of interesting hypotheses regarding the health effects of airborne chemicals. Some specific technical points, however, merit comment.

Meggs describes the common chemical sense as “a nasal sensation provoked by airborne chemicals” (p. 234, my emphasis). This statement is correct as far as it goes, but it neglects to mention that the trigeminal nerve also innervates the oral cavity and that ingested irritants (e.g., capsaicin, the irritant in hot peppers, and allyl isothiocyanate, the irritant in horseradish) trigger some of the same reflexes as inhaled irritants. Thus, so-called gustatory rhinitis involves rhinorrea, nasal congestion, and facial sweating after ingestion of “hot” (spicy) foods (1). As to whether the common chemical sense was only “recently separated” from olfaction as a sensory modality (p. 235), the 1990 study of odor and nasal pungency in anosmics cited by Meggs (2) is but the latest in a series stretching back over 80 years and utilizing various tools to separate the two sensory systems (3).

Neuropeptide release occurs in relation to other types of airway reflexes, some of which do, indeed, involve an efferent limb coming from the central nervous system, as portrayed in Meggs’s Figure 2. Gustatory rhinitis, for example, involves afferent trigeminal sensory fibers and efferent facial nerve cholinergic fibers and is blocked by the preadministration of atropine (1). In contrast to Figure 2, however, the axon reflex (whereby neuropeptides are released) is a primarily afferent process, involving release of neuropeptides from varicosities in sensory nerves (4). Thus, neuropeptide release can be thought of as a local, as opposed to a central, reflex. What is clear is that a complex interrelationship exists between local (neuropeptide-mediated) and central (adrenergic, cholinergic, and nonadrenergic/noncholinergic) airway reflexes. Each of these mechanisms, as well as mast-cell degranulation (atopy), is subject to various regulatory factors, ultimately influencing upper and lower airway reactivity to environmental stimuli.

Meggs briefly mentions the variety of neuropeptides documented in human airways (substance P, calcitonin gene-related protein, neurokinin A, and others), but then goes on to focus on the role of substance P. The relative distribution of neuropeptides and their physiological actions appear to vary across species, making generalizations difficult at this time (5). For example, whereas substance P promotes neurophil and eosinophil chemotaxis and adhesion, its role in mast cell function appears to be that of potentiating other stimuli, rather than as an independent stimulus for degranulation, as Meggs suggests (6).

One aspect of the relationship between neurogenic and immunogenic inflammation not touched upon in the article is the fact that individuals with a history of atopy seem to be at higher risk of reactivity to airborne irritants, even when there is no evidence of an allergic mechanism of response. Thus, while both Bascom et al. (5) and Cummings et al. (7) observed a higher prevalence of environmental tobacco smoke (ETS)-related upper airway symptoms among subjects with a history of atopy, neither assays for allergic mediators in nasal lavage fluid (5) nor skin test reactivity to tobacco leaf extracts or tobacco smoke condensates (8) suggests an allergic mechanism of response. These data are consistent with a role for neuropeptides in the genesis of ETS-related nasal symptoms, as well as a modulatory effect of atopy upon neuropeptide release (9). Thus, atopy may constitute one of the most important “disorders of regulation of neurogenic inflammation” referred to by Meggs (p. 236).

An understanding of respiratory tract responses to irritant chemicals requires familiarity with concepts in allergy/immunology, sensory science, and toxicology. Meggs has made an important and accessible contribution to the literature by discussing neurogenic inflammation as a component of the airway response.

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