Title: Congenital Insensitivity to Pain with Anhidrosis *GeneReview* - NGF-Dependent Neurons and the Role of TrkA
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NGF-Dependent Neurons and the Role of TrkA

Nerve growth factor (NGF), a prototype neurotrophin and the first growth factor to be identified [Levi-Montalcini 1987], plays pivotal roles in controlling the survival and differentiation of the nervous system during embryonic and early postnatal stages [Reichardt 2006]. NGF is a neurotrophic factor essential for the survival and maintenance of NGF-dependent neurons.

NGF-dependent neurons include NGF-dependent primary afferents and sympathetic postganglionic neurons in the peripheral nervous system (PNS).

NGF-dependent primary afferents are defined as primary afferent neurons with small-diameter, thinly myelinated Aδ–fibers, or unmyelinated C-fibers that depend on the NGF-TrkA system during development [Indo 2012].

NGF-dependent primary afferents not only detect noxious (painful) stimuli but also transmit sensation from the body's interior; this is known as interoceptive sense [Craig 2002]. NGF-dependent primary afferents are also referred to as 'interoceptive polymodal receptors' [Indo 2009]. The interoceptive system is considered to be a homeostatic afferent pathway representing the physiological status of all tissues of the body, including the mechanical, thermal, chemical, metabolic and hormonal status of the skin, muscles, joints, teeth, and viscera [Craig 2002]. NGF-dependent primary afferents are thus responsible for both nociceptive and homeostatic afferent pathways.

Sympathetic postganglionic neurons innervate blood vessels, piloerector muscles, and sweat glands as well as other target organs or tissues in the body. These neurons contribute to homeostasis in the body, together with NGF-dependent primary afferents [Indo 2012]. In response to the interoceptive polymodal inputs through NGF-dependent primary afferents, the brain regulates various functions of target organs and tissues through autonomic sympathetic postganglionic neurons.

NGF-dependent neurons in the PNS form an interface between the nervous system and the body-proper (the organism minus the neural tissues) and play critical roles in the neuronal networks responsible for interoception and homeostasis [Indo 2012]. Most information from the body is conducted to the brain unconsciously and the brain maintains homeostasis in the body via feedback mechanisms for which autonomic sympathetic neurons are indispensable. This is well illustrated by (unconscious) homeostatic control of body temperature. NGF-dependent primary afferents and sympathetic postganglionic neurons are also considered to be thermal receptors and thermal effectors, respectively. Evaporative heat loss for the control of body temperature is a species-dependent mechanism. Sweating is essential for body temperature control in humans. Therefore, recurrent febrile episodes in hot environmental conditions are characteristic features observed in individuals with CIPA.

Individuals with CIPA cannot maintain appropriate homeostatic control of the body, including body temperature, due to lack of NGF-dependent neurons. They are always at a disadvantage because of this, with threatened survival.

Intellectual disability and characteristic behaviors are probably neuron-deficient within the brain [Indo 2009; Indo 2012].

References

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