The intermedius nucleus of the medulla: A potential site for the integration of cervical information and the generation of autonomic responses

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FROM ABSTRACT:

The intermedius nucleus of the medulla (InM) is a small perihypoglossal brainstem nucleus, which receives afferent information from the neck musculature and also descending inputs from the vestibular nuclei, the gustatory portion of the nucleus of the solitary tract (NTS) and cortical areas involved in movements of the tongue.

The InM sends monosynaptic projections to both the NTS and the hypoglossal nucleus.

It is likely that the InM acts to integrate information from the head and neck and relays this information on to the NTS where suitable autonomic responses can be generated, and also to the hypoglossal nucleus to influence movements of the tongue and upper airways.

Central to the integratory role of the InM is its neurochemical diversity. Neurones within the InM utilise the amino acid transmitters glutamate, GABA and glycine. A proportion of these excitatory and inhibitory neurones also use nitric oxide as a neurotransmitter.

Neurones in the InM receive inputs from glutamatergic sensory afferents. This glutamatergic transmission is conducted through both NMDA and AMPA ionotropic glutamate receptors.

In summary the InM contains a mixed pool of neurones including glutamatergic and GABAergic in addition to peptidergic neurones. Neurones within the InM receive inputs from the upper cervical region, descending inputs from brain regions involved in tongue movements and those involved in the coordination of the autonomic nervous system. Outputs from the InM to the NTS and hypoglossal nucleus suggest a possible role in the co-ordination of tongue movements and autonomic responses to changes in posture.

THESE AUTHORS ALSO NOTE:

The intermedius nucleus of the medulla (InM) is a small nucleus located lateral to the hypoglossal nucleus and ventral to the dorsal vagal nucleus.
Although the InM was first identified as a dense band of fibers coursing from the region of the cuneate nucleus, very little is understood about its function.

The InM is a rostral continuation of a cervical spinal cord nucleus which is located lateral to the central canal at the border of the dorsal and ventral horns. This spinal component of the nucleus has been named the central cervical nucleus, or the “medullary portion of the central cervical nucleus,” or the intercalated nucleus, or the nucleus intercalatus of Staderini.

Sensory fibers from the upper cervical dorsal root ganglion (DRG) directly enter the InM.

Sensory nerves from the suboccipital muscles, the sternocleidomastoid muscle and the longus capitis muscle also project to the InM via the same path.

“These projections from the cervical DRG to the InM have been proposed to be proprioceptive, which suggests that activity within the InM is heavily influenced by the position of the head relative to the trunk.”

“Chemical or electrical stimulation of the InM causes monosynaptic excitatory and inhibitory postsynaptic potentials in the nucleus of the solitary tract (NTS).”

There are also “monosynaptic projections from neurones in the InM directly onto hypoglossal motor neurones,” which co-ordinate movements of the tongue.

Neurons from the gustatory portion of the NTS project to the InM.

Muscle spindle afferents from the tongue travel to the InM via the upper cervical DRG.

“A subpopulation of baroreceptive neurones in the medial NTS send their axons through the InM, further implicating the InM in autonomic circuits relating to the cardiovascular system.

“Given that InM neurones are under the influence of information arising from the neck region, in particular the dorsal neck muscles and it sends projections to the NTS and the hypoglossal nucleus, it is possible that one of the functions of the InM may be to elicit autonomic responses to movements of the head to complement those triggered by the vestibular system.”

Stimulation of the otolith organs via head down neck flexion can increase muscle sympathetic nerve activity “showing a role for the vestibular system in the regulation of cardiovascular autonomic responses to head movements.”

Innocuous mechanical stimulation of the neck of humans that does not activate the vestibular system evokes changes in heart rate and blood pressure, perhaps through the InM.
Low threshold stimulation of the nerves entering the C1 and C2 DRG can elicit changes in the activity of both sympathetic and respiratory nerves.

Proprioceptive information can play a role in modulating the autonomic nervous system.

“Many of the autonomic responses to postural alterations involving movements of the head have been attributed to activation of the vestibular system. However, neck flexion in brain dead patients, in whom the vestibular system is not functional, has been shown to evoke sympathetic haemodynamic responses.” [Suggesting this is also secondary to upper cervical afferent influence of the InM]

The InM has surprising neurochemical diversity, generating both excitatory and inhibitory postsynaptic potentials through the amino acid neurotransmitters glutamate, GABA and glycine.

The neurochemical nitric oxide synthase is found in the InM. This “may be involved in the co-ordination of autonomic responses to activation of sensory structures within the neck.

Another peptide transmitter found within InM neurones is corticotropin releasing factor which has a role in regulating the cardiovascular system.

“Neurones in the InM are under the influence of sensory afferent information arising from the neck region which would be glutamatergic.”

The InM receives afferent input from the vestibular nuclei.

The InM also receives descending inputs from the prefrontal cortex and the amygdala.

Upper cervical DRG afferent fibers project to the InM. These fibers appear to be the “thicker proprio- and mechano-ceptive afferents” and not nociceptors. Also, these afferents appear to be of muscle origin, “adding weight to the theory that the InM is under the influence of cervical muscles.”

DISCUSSION

“The InM is a surprisingly complex nucleus which receives sensory inputs from the neck region via the upper cervical DRG.”

“One of the functions of the InM would be to integrate information from many areas which influence the activity of the tongue and use this information to co-ordinate tongue movements, for example to prevent inspiratory tongue movements during the presence of a food bolus in the mouth.”
“Changes in the positioning of the head relative to the trunk, or sensory information arising from the neck musculature, have been clinically implicated in the control of heart rate and blood pressure.”

When the sternocleidomastoid muscle loses (denervation) its normal proprioceptive input into the vestibular nucleus and/or NTS, there is an exaggerated vagal response subsequent to stimulation of the carotid sinus.

“The InM acts to integrate information from both the neck musculature and the vestibular system before relaying this information on to the NTS.”

This pathway from the neck musculature to the NTS might be behind the “changes in heart rate and blood pressure observed following upper cervical chiropractic manipulations and autonomic disturbances observed in whiplash patients.”

“Both excitatory and inhibitory neurones from the InM project to the NTS providing scope for the InM to evoke differential responses within NTS neurones according to the sensory information that it receives, rather than simply acting as a relay.”

“InM neurones are strongly targeted by afferent fibres projecting via the upper cervical DRG,” and this “information can manifest as changes in autonomic variables.”

“The InM is a little investigated nucleus in the brainstem which has surprisingly diverse neurochemistry. It is possible that this complex nucleus plays a role in the generation of autonomic responses to movements of the head, especially as it is monosynaptically connected with both the NTS and hypoglossal nuclei.”

**KEY POINTS FROM DAN MURPHY**

1) The intermedius nucleus of the medulla (InM) [nucleus intermedius] is in the medulla. It receives afferent information from:
   A) The neck musculature
   B) The vestibular nuclei
   C) The gustatory portion of the nucleus of the solitary tract (NTS)
   D) Cortical areas involved in movements of the tongue

2) The nucleus intermedius sends monosynaptic projections to:
   A) The nucleus of the solitary tract (NTS)
   B) The hypoglossal nucleus

3) The nucleus intermedius integrates information from the head and neck and relays this information on to the nucleus of the solitary tract where suitable autonomic responses are generated.
4) The nucleus intermedius also communicates with the hypoglossal nucleus to influence movements of the tongue and upper airways.

5) Nucleus intermedius neurones receive inputs from sensory afferents that use glutamate as a neurotransmitter. [Some excitotoxin experts insist that dietary glutamate {MSG, hydrolyzed protein, etc.} will adversely influence the function of glutamatergic neurons]

6) Outputs from the nucleus intermedius to the nucleus tractus solitarius and hypoglossal nucleus suggest a role in the co-ordination of tongue movements and autonomic responses to changes in posture. [Very Important: the nucleus intermedius co-ordinates autonomic responses to postural changes]

7) The nucleus intermedius has a spinal cord component called the “central cervical nucleus” or the “medullary portion of the central cervical nucleus” or the “intercalated nucleus” or the “nucleus intercalatus of Staderini.”

8) The spinal cord component of the nucleus intermedius (central cervical nucleus) is “located lateral to the central canal at the border of the dorsal and ventral horns.”

9) Sensory fibers from the upper cervical dorsal root ganglion (DRG) directly enter the nucleus intermedius. [Very Important]

10) Sensory nerves from the suboccipital muscles, the sternocleidomastoid muscle and the longus capitis muscle project to the nucleus intermedius via the upper cervical spine dorsal root ganglion. [Very Important: the sensory projections from these muscles are mechanoreceptors and proprioceptors; alterations of mechanical afferent input from these muscles alters the input to the nucleus intermedius, then to the nucleus tractus solitarius and to subsequent autonomic responses]

11) “These projections from the cervical DRG to the nucleus intermedius have been proposed to be proprioceptive, which suggests that activity within the nucleus intermedius is heavily influenced by the position of the head relative to the trunk.” [Very Important]

12) “Chemical or electrical stimulation of the nucleus intermedius causes monosynaptic excitatory and inhibitory postsynaptic potentials in the nucleus of the solitary tract (NTS).”

13) The authors suggest that the greatest influence of the nucleus intermedius is to the “autonomic circuits relating to the cardiovascular system.”

14) Nucleus intermedius neurones are “under the influence of information arising from the neck region, in particular the dorsal neck muscles.”
15) One of the functions of the nucleus intermedius is to elicit autonomic responses to movements of the head to complement those triggered by the vestibular system.

16) The vestibular system regulates cardiovascular autonomic (sympathetic) responses to head movements.

17) Innocuous mechanical stimulation of the neck of humans that does not activate the vestibular system evokes changes in heart rate and blood pressure, perhaps through the nucleus intermedius. [This is like saying that altered mechanical afferent input from the neck {innocuous mechanical stimulation} subsequent to the chiropractic subluxation alters the neurological influence to the nucleus intermedius, in turn influencing the autonomic control of heart rate and blood pressure. Recall that the study in the *Journal of Human Hypertension*, March 2007, showed that specific upper cervical chiropractic adjustments (NUCCA) significantly reduced blood pressure, and the outcomes remained stable during an 8 week follow-up period]

18) Low threshold stimulation of the nerves entering the C1 and C2 DRG can elicits changes in the activity of both sympathetic and respiratory nerves. [Very Important: supports chiropractic adjustments influencing sympathetic neurology]

19) Proprioceptive information can play a role in modulating the autonomic nervous system. [Very Important: this is a central theme to chiropractic clinical approaches to many non-musculoskeletal syndromes]

20) “Neurones in the nucleus intermedius are under the influence of sensory afferent information arising from the neck region.” [Very Important]

21) The nucleus intermedius receives afferent input from the vestibular nuclei. [Important because the vestibular nucleus also receives monosynaptic inputs from upper cervical spine afferents]

22) The nucleus intermedius also receives descending inputs from the prefrontal cortex and the amygdala. [This explains some of the emotional influences on the autonomic neurological activity]

23) Upper cervical DRG afferent fibers project to the nucleus intermedius, and these fibers are “proprio- and mechanoceptive afferents” and not nociceptors. [This is very important because it implies that non-painful aberrant mechanical afferent input from the upper cervical spine can alter autonomic function. In the study from the *Journal of Human Hypertension*, March 2007, which showed a significant reduction of blood pressure with specific upper cervical chiropractic adjustments, the authors noted that none of the patients were suffering from neck or back pain]
24) The authors suggest the primary afferents influencing the nucleus intermedius are from the upper cervical muscles “adding weight to the theory that the nucleus intermedius is under the influence of cervical muscles.”

25) “The InM is a surprisingly complex nucleus which receives sensory inputs from the neck region via the upper cervical DRG.”

26) “Changes in the positioning of the head relative to the trunk, or sensory information arising from the neck musculature, have been clinically implicated in the control of heart rate and blood pressure.”

[Very Important: the upper cervical chiropractic subluxation is a change in the “positioning of the head relative to the trunk, or sensory information arising from the neck musculature”]

27) “The nucleus intermedius acts to integrate information from both the neck musculature and the vestibular system before relaying this information on to the nucleus tractus solitarius.”

28) This pathway from the neck musculature to the nucleus tractus solitarius might be behind the “changes in heart rate and blood pressure observed following upper cervical chiropractic manipulations and autonomic disturbances observed in whiplash patients.”

[Very Important: these authors acknowledge the ability of upper cervical chiropractic adjustments to influence heart rate and blood pressure, both autonomic functions]

29) “The nucleus intermedius neurones are strongly targeted by afferent fibres projecting via the upper cervical DRG,” and this “information can manifest as changes in autonomic variables.”

30) The nucleus intermedius “plays a role in the generation of autonomic responses to movements of the head,” especially as it is monosynaptically connected with the nucleus tractus solitarius.

COMMENTS FROM DAN MURPHY

This is a very important article for chiropractors. It explains the neuroanatomical relationship between upper cervical spine subluxation (a mechanical problem) and visceral autonomic neurology. The authors use chiropractic adjustments of the upper cervical spine influencing cardiac function as support for their neuroanatomical findings. This study supports the 115 years of clinical observations of chiropractors. It shows the “biological plausibility” of the influence of chiropractic adjustments on non-musculoskeletal syndromes.

I would be unable to share this information with so many were it not for the efforts of ICA Board Member Dr. George Curry, an excellent chiropractor and scholar.
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Proprioceptors / Mechanoreceptors from

Sternocleidomastoid Muscle
Suboccipital Muscle
Longus Capitus Muscle

Upper Cervical Dorsal Root Ganglion

Nucleus Intermedius (medulla)

Nucleus Tractus Solitarius (medulla)

Autonomic Cardiovascular Responses

Control / Co-ordination of Autonomic Responses to Head Movements and Changes in Posture