A preliminary study of neck-stomach syndrome

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BACKGROUND:
c-Fos
c-fos is a gene which regulates and provides a reliable direct method to study the mechanism of functional gastrointestinal diseases. Previous studies have shown that the c-Fos expression in the gastric myenteric plexus is dramatically associated with c-Fos expression of the spinal cord in the rats with cervical spondylosis.

caspase-3
"Caspase-3 is a potential mediator of apoptosis after central nerve system (CNS) injury and its activation may be used as a marker of apoptotic cell death."
[Apoptosis is cell death by suicide] Cell death from spinal cord injury (SCI) involves caspase-3.

interleukin-1b (IL-1b)
IL-1b activates the caspase-3 apoptotic cell death pathway.

FROM ABSTRACT

AIM:
To determine the expression of c-Fos, caspase-3 and interleukin-1b (IL-1b) in the cervical cord and stomach of rats with cervical spondylosis, to analyze their relationship, and to offer an explanation of one possible cause for functional dyspepsia (FD) and irritable bowel syndrome (IBS) caused by cervical spondylosis.

METHODS:
The cervical spondylosis model in rats was established by destroying the stability of cervical posterior column.

The cord segments C4-6 and gastric antrum were collected 3 mo and 5 mo after the operation. Rats with the sham operation were used as controls.

The expressions of c-Fos, caspase-3 and IL-1b in the cervical cord and gastric antrum were determined by immunohistochemistry and/or Western blot.

RESULTS:
Immunohistochemical staining showed a few c-Fos, caspase-3 and IL-1b-positive cells in the cervical cord and antrum in the control.

There was a significant increase in c-Fos, caspase-3 and IL-1b expression in model groups [spondylosis] compared to the control groups at 3 months and 5 months after operation.

Western blot analysis showed time-dependent changes of caspase-3 and IL-1b protein in the cervical cord and gastric antrum of rats with cervical spondylosis.

There was no significant expression of caspase-3 and IL-1b protein in the control group at 3 months and 5 months after the sham operation, whereas there was a significant difference in caspase-3 and IL-1b protein levels between the model group rats followed up for 3 months and for 5 months.

CONCLUSION:
There is a significant association of c-Fos, caspase-3 and IL-1b expressions in the gastric antrum with that in the spinal cord in rats with cervical spondylosis, suggesting that the gastrointestinal function may be affected by cervical spondylosis. **[Important]**

THESE AUTHORS ALSO NOTE:

"Many patients with cervical spondylosis complain of gastrointestinal symptoms," including those who are not taking NSAIDs.

"There is a direct or indirect relationship between the neck and the stomach, called the neck-stomach syndrome."

"Cervical pathology, mediated through sympathetic nerves, has been associated with a number of disorders, which include about 20 kinds of diseases or symptom-groups, such as hypertension, cardiac arrhythmias, dizziness, eyesight malfunction and gastrointestinal dysfunction." **[Very Important]**

"Perhaps the clinical symptoms of cervical spondylosis include gastrointestinal disorders mediated through irritated sympathetic nerves."

In this study, expression of c-Fos, caspase-3 and IL-1b in the cervical cord and gastric antrum were examined in rats with cervical spondylosis.

c-fos is a gene which regulates and provides a reliable direct method to study the mechanism of functional gastrointestinal diseases. Previous studies have shown that the c-Fos expression in the gastric myenteric plexus is dramatically associated with c-Fos expression of the spinal cord in the rats with cervical spondylosis.

"It is the sympathetic nerve that results in the c-Fos expression both in the spinal cord and the gastric myenteric plexus in cervical spondylosis and this suggests that the gastrointestinal function may be affected by cervical spondylosis." **[Key Point]**

Neuronal apoptosis in the CNS is induced by increased IL-1b, which activates the caspase-3 apoptotic cell death pathway.

In this study, after establishing the cervical spondylosis model of rats, the cord and stomach were collected at 3 mo and 5 mo to determine the expression of c-Fos, caspase-3 and IL-1b in the cervical cord and gastric antrum by immunohistochemistry and/or Western blot. This study used 96 rats. X-ray films confirmed "disappeared or stiff nature cervical curve, stenosis of the vertebral space and osseous spur in the model groups compared with the control groups.

RESULTS

There was a significant increase in c-Fos in both the spinal cord and in the gastric antrum in the rats that had cervical spondylosis as compared to the control rats.

There was a significant increase in both caspase-3 and IL-1b in both the spinal cord and in the gastric antrum in the rats that had cervical spondylosis as compared to the control rats.

DISCUSSION

"The definition of neck-stomach symptoms is gastrointestinal disorders resulting from cervical spondylosis."

Sympathetic nerve fibers are distributed in the periphery of the dorsal root ganglion (DRG), in the joints of Luschka, articular capsule, cervical facet joints, cervical posterior longitudinal ligaments, posterior annulus fibrosus of the disc and vertebral artery.

Parts of the cervical nerve roots connect with the superior cervical sympathetic ganglion via postganglionic fibers.

"When the sympathetic fibers are irritated, the clinical syndromes result from the spinal and brain-spinal reflex pathways."

"The mechanism of neck-stomach syndrome is that when the sympathetic nerve is irritated by nerve roots, degenerated disc and facet joints disorders due to osteophytes, cervical muscle overexertion and/or injury, the irritation reaches to the brain cortex by nerve reflex and produces a higher or lower sympathetic irritability, and then results in multiple dysfunctions of the neck, upper limbs, cardiac and gastrointestinal reflexes, etc." **[Very Important]**

Increased c-Fos expression is related to functional gastrointestinal diseases, such as CNS in inflammatory bowel disease (IBD), irritable bowel syndrome (IBS) and Crohn's disease.

In this study there was an increased c-Fos, caspase-3 and IL-1b expression in rats given spondylosis at 3 and 5 months after injury in both their cervical cords and gastric antrums.

"Expression of c-Fos, caspase-3 and IL-1b in the gastric antrum were dramatically associated with that in the spinal cord of rats with cervical spondylosis, suggesting that the gastrointestinal function may be affected by cervical spondylosis."

"The conception of brain-intestine axis and neurogastroenterology has been put forward, which indicates that the alimentary canal is controlled by both motor and sensory nerves."

"When a nerve is injured, the lesion will impact on both the sense and motion realms. Even though the lesion is limited in only one realm, the change will result in the change of other region's function. Theoretically, only when the gastrointestinal tract and CNS are integratively investigated, can the multiple physical and pathophysiological diseases be further understood."

"The previous studies had proven mechanisms of functional dyspepsia and irritable bowel syndrome were associated with CNS. In the present study, we found the same results and believe that there are relationships between the neck and stomach."

KEY POINTS FROM DAN MURPHY

1) "Many patients with cervical spondylosis complain of gastrointestinal symptoms," including those who are not taking NSAIDs.

2) "There is a direct or indirect relationship between the neck and the stomach, called the neck-stomach syndrome."

3) "Cervical pathology, mediated through sympathetic nerves, has been associated with a number of disorders, which include about 20 kinds of diseases or symptom-groups, such as hypertension, cardiac arrhythmias, dizziness, eyesight malfunction and gastrointestinal dysfunction." **[Very Important]**

4) "The clinical symptoms of cervical spondylosis include gastrointestinal disorders mediated through irritated sympathetic nerves."

5) "It is the sympathetic nerve that results in the c-Fos expression both in the spinal cord and the gastric myenteric plexus in cervical spondylosis and this suggests that the gastrointestinal function may be affected by cervical spondylosis." **[Key Point]**

6) "The definition of neck-stomach symptoms is gastrointestinal disorders resulting from cervical spondylosis."

7) Sympathetic nerve fibers are distributed in the periphery of the dorsal root ganglion (DRG), in the joints of Luschka, articular capsule, cervical facet joints, cervical posterior longitudinal ligaments, posterior annulus fibrosus of the disc and vertebral artery.

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8) "When the sympathetic fibers are irritated, the clinical syndromes result from the spinal and brain-spinal reflex pathways."

9) "The mechanism of neck-stomach syndrome is that when the sympathetic nerve is irritated by nerve roots, degenerated disc and facet joints disorders due to osteophytes, cervical muscle overexertion and/or injury, the irritation reaches to the brain cortex by nerve reflex and produces a higher or lower sympathetic irritability, and then results in multiple dysfunctions of the neck, upper limbs, cardiac and gastrointestinal reflexes, etc." **[Very Important]**

10) The results of this study indicate that "gastrointestinal function may be affected by cervical spondylosis."

11) "The conception of brain-intestine axis and neurogastroenterology has been put forward, which indicates that the alimentary canal is controlled by both motor and sensory nerves."

12) "The previous studies had proven mechanisms of functional dyspepsia and irritable bowel syndrome were associated with CNS. In the present study, we found the same results and believe that there are relationships between the neck and stomach."