Short Communication


Effect of Topical Administration of Glucose on Neurons Innervating Abdominal Viscera in Dorsal Motor Nucleus of Vagus in Rats

Motoi Kobashi and Akira Adachi

Department of Physiology, Okayama University Dental School, Okayama, 700 Japan

Summary Neural responses in the dorsal motor nucleus of the vagus (DMV) to topical administration of glucose were investigated electrophysiologically using multibarrel electrodes in anesthetized rats. Of 52 neurons that showed the antidromic response to the ventral gastric vagus, 4 neurons increased and 14 neurons decreased their discharge rates in response to topical administration of glucose from the multibarrel pipette. Thirty-four neurons did not respond to this administration. Of 4 neurons that showed the antidromic response to the accessory celiac vagus, 1 neuron increased and 1 neuron decreased their discharge rates in response to topical administration of glucose. Two neurons did not respond to this administration. These results suggest that some DMV neurons innervating the abdominal viscera may have an enteroceptor function detecting the change in glucose concentration of their environment.

Key words: glucose, vagus, dorsal motor nucleus of the vagus.

It is well known that glucose sensors exist in the hepatoporal area [1], and these signals invade the nucleus tractus solitarius (NTS) [2] and the dorsal motor nucleus of the vagus (DMV) [3]. The DMV involves the preganglionic cell bodies of the vagus that innervate the abdominal viscera and are postsynaptically influenced by the hepatoporal glucose sensors [4]. Very likely, such autonomic reflexes involved in the brainstem regulate insulin release [5], gastric acid secretion [6], and gastric motility [7]. It is certain that the vagal efferents control the visceral functions. Another report that glucose injection into the NTS and the DMV inhibited gastric acid secretion [8] suggests the existence of the glucose sensor in the medulla. Virtually, the glucose responsive neurons have been identified in the NTS, area postrema [9–12] and the hypothalamus [13]. However, the response of the DMV neurons to glucose is not clear. The aim of the present

Received on September 12, 1994; Accepted on October 20, 1994

729
study is to confirm whether the DMV neurons innervating the abdominal viscera have an ability to sense glucose using electrophysiological methods.

Forty-nine male 260–350 g Sprague-Dawley rats were used. Each rat was anesthetized with an intraperitoneal injection of urethane-chloralose (urethane, 0.8 g/kg; chloralose, 65 mg/kg body wt.). After an abdominal incision, a bipolar stimulating electrode (Unique Medical, Japan) was attached to the ventral (anterior) gastric branch of the vagus and the accessory celiac branch of the vagus without section to identify the DMV neurons that innervate the abdominal viscera by antidromic stimulation. A recording electrode, filled with 2% pontamine sky blue, was glued to a multibarrel pipette, with its tip extending 30–50 μm beyond the multibarrel pipette tip. Each barrel was filled with one of the following chemicals: 0.16 M sodium chloride; 2.0 M monosodium glutamate (pH 8); 0.5 M glucose (in 0.16 M NaCl). Neural activity was recorded from the left DMV. To minimize movements of the medulla caused by respiration and blood pulsation, the recording site was pressed by small metal ring. Stimulation for antidromic activation was delivered through the stimulating electrode attached to the ventral gastric or accessory celiac branch. After identification of the antidromic response, current less than 100 nA was injected through the pipette containing glucose or NaCl. Because glucose was dissolved in NaCl solutions for electro-osmotic injections [13], neurons which responded similarly to pure NaCl solution and to a mixture of glucose and NaCl were not counted as glucose responsive neurons, whereas those neurons which responded differentially to the mixture were classified as glucose-responsive. The effect of topical administration of NaCl will be reported in another paper. Results were analyzed by one-sided paired t-test. Data are presented as mean ± SEM. Recording sites were marked by pontamine sky blue to confirm that neural activities were recorded in the DMV. Histological examination revealed no staining outside of the DMV.

The antidromic responses to electrical stimulation of the ventral gastric vagus of 84 neurons and those to electrical stimulation of the accessory celiac vagus of 9 neurons in the DMV were recorded. The antidromic responses were ascertained by a cancellation of the elicited response by collision with a spontaneous discharge, a constant latency and an ability to follow double-pulse stimulation with an interval shorter than 10 ms (Fig. 1). Latencies of the antidromic responses varied from 105 to 205 ms (mean ± SE; 148.7 ± 2.3 ms). Because the distance from the stimulating site to the recording site was approximately estimated at 0.1 m, conduction velocities ranged from 0.5 to 1.0 m/s. The mean spontaneous discharge rate of neurons that projected to the ventral gastric vagus is 1.95 ± 0.19 impulses/s and that of neurons that projected to the accessory celiac vagus is 1.22 ± 0.32 impulses/s.

Out of 84 neurons that showed the antidromic response to the ventral gastric vagus, 4 neurons increased and 14 neurons decreased their discharge rates in response to topical administration of glucose. Thirty-four neurons did not respond to this administration. Because the other 32 neurons responded similarly to both topical administration of glucose dissolved in saline or NaCl solution, these neurons

*Japanese Journal of Physiology*
RESPONSE OF DMV NEURONS TO GLUCOSE

Fig. 1. The antidromic response of a DMV neuron elicited by electrical stimulation of the ventral gastric branch. A: The response to double-pulse stimulation (interval; 10 ms) of the ventral gastric branch. B: The response to double-pulse stimulation triggered by spontaneous impulses. First impulses are canceled by collision (indicated by an arrow). Ten sweeps were superimposed. Each pulse was delivered at an initiation of sweep.

<table>
<thead>
<tr>
<th>Antidromic responses to</th>
<th>Gastric branch</th>
<th>Celiac branch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Decrease</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>No response</td>
<td>34</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>4</td>
</tr>
</tbody>
</table>

Table 1. Response of DMV neurons to topical administration of glucose.

were not counted as glucose-responsive. Figure 2 shows a typical response to topical administration of glucose. Nine neurons showed the antidromic response to electrical stimulation of the accessory celiac branch. Out of 9 neurons, 1 neuron increased and 1 neuron decreased their discharge rates in response to topical administration of glucose. Two neurons did not respond to topical administration. Because the other 5 neurons responded similarly to NaCl as well as glucose dissolved in saline, these neurons were not counted as glucose-responsive. The effect of topical administration was analyzed by one-sided paired t-test. The discharges for 10 s just before the administrations were compared to those for 10 s after the initiation of the administrations. On neurons that showed an increase in the discharge rate, the mean discharge rate during the topical administration (4.683 ± 1.419 impulses/s) is larger than that before the topical administration (2.517 ± 0.618 impulses/s), showing a significant increase ($t = 2.480, p < 0.05, n = 5$). On neurons that showed a decrease in discharge rate, the mean discharge rate during the topical administration (0.736 ± 0.131 impulses/s) is smaller than that.
Fig. 2. Two different response types of DMV neurons to topical administration of glucose. A: One example of a DMV neuron that decreased its discharge rate in response to topical administration of glucose. This neuron showed the antidromic response to electrical stimulation of the accessory celiac branch. Right panels show the discharges recorded from the time indicated by an asterisk in the left panel. B: The other example of DMV neuron that increased its discharge rate in response to topical administration of glucose. This neuron showed the antidromic response to the ventral gastric branch. Right panels show the discharges recorded from the time indicated by an asterisk in the left panel.

before the topical administration (1.879±0.289 impulses/s), showing a significant decrease ($t = 4.967, p < 0.001, n = 14$).

A brief survey of the findings of earlier workers is as follows: Infusion of glucose into the carotid artery affects the activity of pancreatic vagal efferent [4]. Electrical stimulation of the hypothalamus affects activities of DMV neurons [14] and injection of glucose to the hypothalamus affects vagal efferent activities [15]. The present study revealed that the glucose-responsive neurons are involved within
the DMV. Therefore, it is likely that the glucose-responsive DMV neurons (glucose sensors) may regulate the vagal efferent activities. Hierarchical control of the vagal efferent neurons should be present. However, the role of the glucose-responsive neurons in the DMV has not yet been elucidated. Because injection of glucose into the DMV suppressed gastric acid secretion induced by gastrin [8], the possible role may be the inhibition of gastric acid secretion. This observation corresponds to our present investigations because most DMV neurons decreased their discharge rates in response to topical administration of glucose. It is emphasized that the glucose responsive neurons in the medulla modify the vago-vagal reflex.

This work was supported by a Grant-in-Aid for Encouragement of Young Scientists (No. 06771627) from the Ministry of Education, Science and Culture of Japan, and Grant-in-Aid for General Scientific Research (No. 05454502) from the Ministry of Education, Science and Culture of Japan.

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Vol. 44, No. 6, 1994

Japanese Journal of Physiology