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Review Article

The Sympathoexcitatory Pathway from the CVL to the RVL for Controlling Brain Vessels

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Abstract

We reported a regional differentiation of blood flow responses during the activation of the nucleus tractus solitarius (NTS) and caudal ventrolateral medullary depressor area (CVL). The neurons in the NTS and CVL have a vasoconstrictor effect on brain circulation and a vasodilator effect on systemic circulation. On the other hand, the neurons in the rostral ventrolateral medullary pressor area (RVL) have a vasoconstrictor effect on both brain and systemic circulation. We therefore hypothesized that there is a sympathoexcitatory pathway from the CVL to the RVL for controlling cerebral vessels and a sympathoinhibitory pathway from the CVL to the RVL for controlling systemic vessels, and that these different roles of the pathways from the CVL to the RVL for the different organs can explain the regional difference in sympathetic nerve activities. Here, we propose a sympathoexcitatory pathway from the CVL to the RVL for controlling brain vessels. (*Tzu Chi Med J* 2008;20(4):243–247)

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1. Introduction

The concept of regional differentiation of sympathetic efferents was proposed by Walther et al (1). They recorded nerve activities simultaneously from different sympathetic fiber bundles during central cooling and heating and found that differentiation of regional sympathetic efferent activity is the primary cause of the antagonistic vascular response pattern in thermoregulation (1). The concept of quantitative and qualitative non-uniformity of sympathetic nerve activity was proposed by Ninomiya et al (2,3). It remains to be determined what mechanisms in the brain operate to explain the concept of regional differentiation of sympathetic nerve activities or non-uniformity of sympathetic nerve activities.

We reported a regional differentiation of blood flow responses during the activation of the nucleus tractus solitarius (NTS) and caudal ventrolateral medullary depressor area (CVL) (4–7). The neurons in the NTS have a vasoconstrictor effect on brain and spinal cord circulation and a vasodilator effect on splenic and renal circulation (6). The neurons in the CVL also have a vasoconstrictor effect on brain circulation and a vasodilator effect on systemic circulation (5). On the other hand, neurons in the rostral ventrolateral medullary

pressor area (RVL) have a vasoconstrictor effect on both brain and systemic circulation (8).

We therefore hypothesized that there is a sympathoexcitatory pathway from the CVL to the RVL for controlling cerebral vessels and a sympathoinhibitory pathway from the CVL to the RVL for controlling systemic vessels, and that these different roles of the pathways from the CVL to the RVL for the different organs can explain the regional difference of sympathetic nerve activities. Here, we propose a sympathoexcitatory pathway from the CVL to the RVL for controlling brain vessels (9,10).

2. Role of NTS, CVL and RVL on cerebral and systemic circulation

2.1. *Role of NTS on blood flows of spleen, kidney, brain and spinal cord (4–7) (Fig. 1)*

Unilateral chemical stimulation of the NTS decreased brain blood flow and spinal cord blood flow and increased brain vascular resistance and spinal cord vascular resistance, whereas chemical stimulation of the NTS increased splenic blood flow and renal blood flow and decreased splenic vascular resistance and renal vascular resistance. These results suggest that the neurons in the NTS have a vasoconstrictor effect on brain and spinal cord circulation and a vasodilator effect on splenic and renal circulation. There is a regional qualitative differentiation of blood flow responses between these organs during activation of the neurons in the NTS.

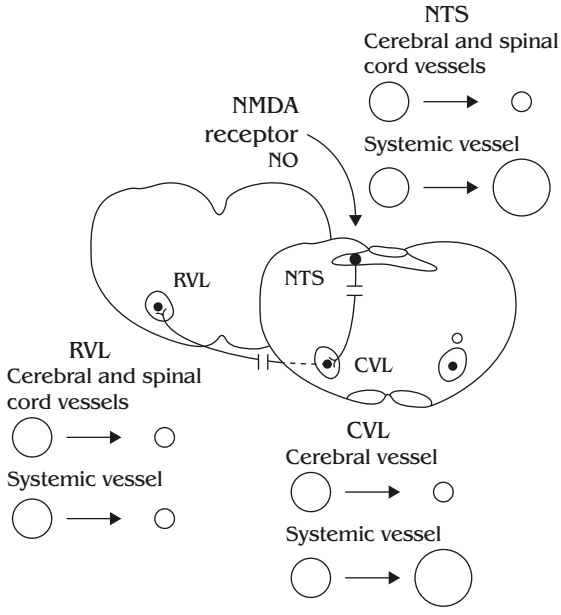

Fig. 1 — Schematic representation of the role of the neuronal cell bodies within the nucleus tractus solitarius (NTS), the caudal ventrolateral medullary depressor area (CVL), and the rostral ventrolateral medullary pressor area (RVL) in regulating cerebral and spinal cord circulation and the receptor type in the NTS to control cerebral circulation. (Reproduced with permission from Reference 13.)

2.2. *Role of CVL on cerebral circulation (5) (Fig. 1)*

Moderate hypertension was induced by blood transfusion. Unilateral chemical stimulation of the CVL in these rats decreased arterial blood pressure (ABP) but it remained within normotensive range. A significant decrease in cerebral blood flow (CBF) and a significant increase in cerebrovascular resistance (CVR) were observed in the ipsilateral cerebral cortex of these rats. These results suggest that the neurons within the CVL have a vasoconstrictor effect on cerebral circulation and a vasodilatory effect on systemic circulation.

2.3. *Role of RVL on cerebral circulation (8) (Fig. 1)*

Unilateral chemical stimulation of the RVL produced a significant increase in ABP, a significant decrease in CBF, and a significant increase in CVR in the ipsilateral cerebral cortex. In another group of rats, cervical sympathetic trunks were sectioned bilaterally and CBF was measured during chemical stimulation of the RVL. CBF and CVR did not change significantly in these rats. This observation indicates that the pathway mediating cerebral vasoconstriction induced by RVL stimulation includes the cervical sympathetic nerves. These results suggest that the neurons within the RVL have vasoconstrictor effects on the systemic circulation and cerebral circulation via the cervical sympathetic nerves.

3. Physiological role of NTS and CVL in cerebral autoregulation

The physiological role of the NTS and CVL in the regional differentiation of the blood flows of various organs may be speculated to be as shown in Fig. 2 (4–6,11–13). During acute development of hypertension (e.g., during extensive transfusion of blood), the neurons in the NTS and CVL are activated via the baroreflex. When ABP remains increased, the vessels of the brain and spinal cord are constricted so as to keep the brain and spinal cord blood flows constant (cerebral and spinal cord autoregulation). In fact, lesions of the NTS (14) impair such cerebrovascular

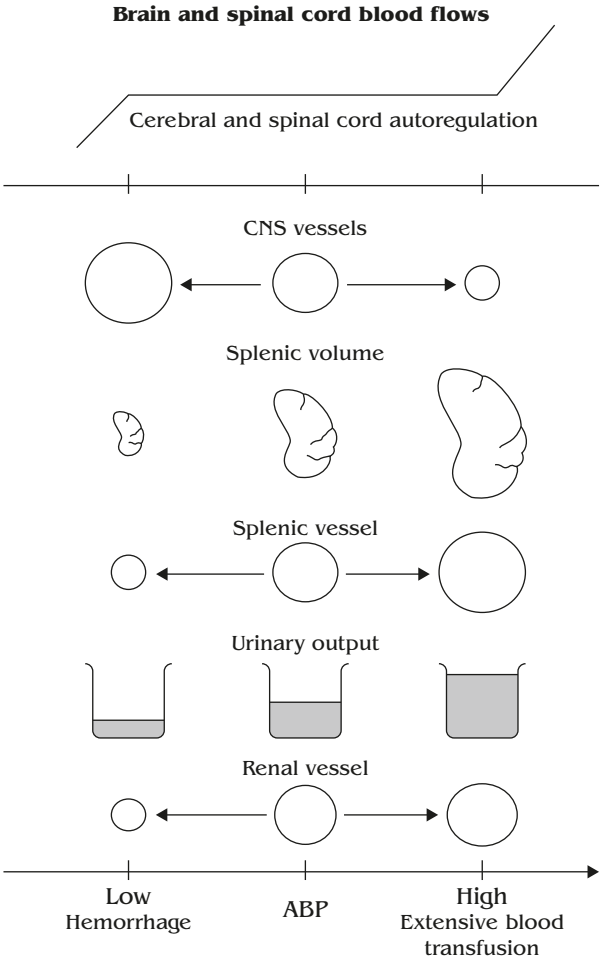

Fig. 2 — Schematic representation of the postulated role of the nucleus tractus solitarius (NTS) and caudal ventrolateral medullary depressor area (CVL) in the circulation of the brain, spinal cord, spleen and kidney. During acute development of hypertension (e.g., during extensive transfusion of blood), the neurons in the NTS are activated via the baroreflex. The vessels of the brain and spinal cord are constricted so as to keep the brain and spinal cord blood flows constant. Splenic vasodilatation causes the spleen to store blood. The rate of urinary output increases due to pressure-diuresis. During acute development of hypotension (e.g., during hemorrhagic hypotension), the neurons in the NTS are inhibited. The vessels of the brain and spinal cord are dilated so as to keep the brain and spinal cord blood flows constant. Splenic vasoconstriction expels much of the blood within the spleen into the general circulation. Increased renal sympathetic nerve activity constricts the renal vessels associated with the renin-angiotensin system, resulting in decreases of renal blood flow and glomerular filtration rate. The rate of urinary output decreases in order to prevent a decrease in arterial blood pressure (ABP). These controls may be provided by the NTS and CVL. (Reproduced with permission from Reference 13.)

autoregulation. The spleen has the role of a reservoir of blood. During hypertension, dilatation of vessels within the spleen causes the spleen to store blood [15]. Inhibition of the splenic sympathetic nerves results in considerable splenic expansion with consequent storage of blood [15]. During hypertension, the rate of urinary output increases due to pressure-diuresis or -natriuresis. Such natriuresis is affected by baroreflex reduction in renal sympathetic nervous activity (RSNA) [16,17] and renal denervation increases basal renal blood flow [16]. On the other hand, during acute development of hypotension (e.g., during hemorrhagic hypotension), the neurons in the NTS are inhibited via the baroreflex. The vessels of the brain and spinal cord are dilated so as to keep the brain and spinal cord blood flows constant. Constriction of the splenic vessels expels much of the blood within the spleen into the general circulation [15]. During hypotension, increased RSNA constrict the renal vessels associated with the renin-angiotensin system, resulting in decreases of renal blood flow and glomerular filtration rate [18]. The rate of urinary output decreases in order to prevent a decrease in ABP. Sodium excretion is modified by the baroreflex [16]. The vascular resistances of the brain and spinal cord change in the opposite direction to those of the spleen and kidney under such conditions. These controls are provided by the NTS which is the termination site from the baroreceptors and by the CVL.

4. Pathway to control cerebral circulation from CVL [9,10]

Chemical stimulation of the CVL produced a significant decrease in CBF and a significant increase in CVR in the cerebral cortex ipsilateral to the stimulated CVL side [5]. Cervical sympathectomy blocked the decrease in CBF and increase in CVR elicited by chemical stimulation of the CVL. Depression of the RVL neurons induced by microinjection of muscimol, a GABA agonist, into the RVL blocked the CBF decrease and CVR increase following chemical stimulation of the CVL [9,10]. These results suggest that the vasoconstrictive pathway to control cerebral vessels from the CVL is mediated via the cervical sympathetic nerves and the RVL.

5. Mechanisms for regional differentiation of sympathetic nerve activities (Fig. 3)

The pathway in the brainstem through which the neurons in the NTS have a regional differentiation of the blood flow changes remains to be determined. The following pathway is thought to mediate the baroreflex: an excitatory projection from the NTS to the CVL and an inhibitory GABAergic projection from the CVL to the RVL [19–21] (Fig. 3). In this way, chemical stimulation of the NTS inhibits the neurons in the RVL, an origin of the sympathetic nerve activities in the brain

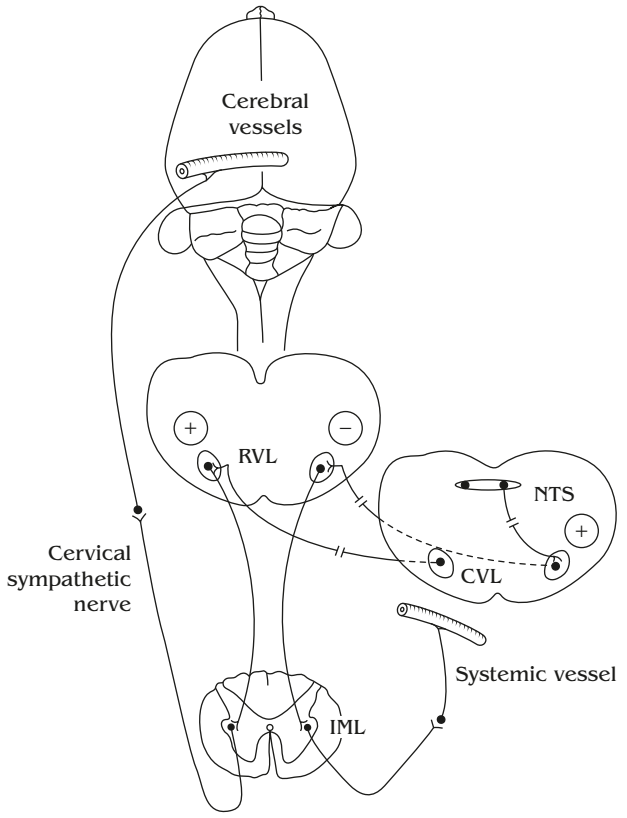

Fig. 3 — Schematic representation of the proposed cerebral vasoconstrictive pathway from the caudal ventrolateral medullary depressor area (CVL) and the mechanisms in the brainstem for regional differentiation of the sympathetic efferents. Cervical sympathectomy blocks the cerebral blood flow (CBF) decrease response and cerebrovascular resistance (CVR) increase response elicited by chemical stimulation of the CVL. Depression of the rostral ventrolateral medullary pressor area (RVL) neurons blocks the CBF decrease and CVR increase responses. These results suggest that the vasoconstrictive pathway to control cerebral vessels from the CVL is mediated via the RVL and the cervical sympathetic nerves. These results also suggest that there is a sympathoexcitatory pathway from the CVL to the RVL for controlling cerebral vessels and a sympathoinhibitory pathway from the CVL to the RVL for controlling systemic vessels. These different roles of the pathways from the CVL to the RVL for the different organs can explain the regional difference in sympathetic nerve activities. (Reproduced with permission from Reference 10.)

and results in a decrease in ABP. The dilatation of the splenic and renal vessels is mediated via this pathway. On the other hand, the details of a vasoconstrictor pathway from the NTS to the brain and spinal cord vessels are not completely known. However, the vasoconstrictor pathway from the CVL to the brain vessels is reported (9,10). Cervical sympathectomy blocked the cerebral vasoconstrictor responses elicited by chemical stimulation of the CVL. Depression of the RVL neurons induced by microinjection of muscimol, a GABA agonist, into the RVL also blocked the same responses from the CVL. The neurons within the RVL have a role of cerebral vasoconstriction which is mediated via the cervical sympathetic nerves, as reported (8). It is suggested that the cerebral vasoconstrictor effect from the CVL is mediated via the RVL and the cervical sympathetic nerves, and that there is a sympathoexcitatory pathway to control cerebral circulation from the CVL to the RVL. Because the projection from the NTS to the CVL is excitatory, the changes in brain and spinal cord blood flows may be mediated via excitatory projections from the NTS to the CVL and from the CVL to the RVL and the sympathetic nerves.

Our results suggest that there is a sympathoexcitatory pathway from the CVL to the RVL for controlling cerebral vessels and a sympathoinhibitory pathway from the CVL to the RVL for controlling systemic vessels. These different roles of the pathways from the CVL to the RVL for the different organs can explain the regional difference in sympathetic nerve activities.

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