

Jugular Venous Reflux Could Influence Cerebral Blood Flow: A Transcranial Doppler Study

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Abstract-

Purpose: Studies have found significant associations between jugular venous reflux (JVR) and neurological disorders. However, there still lacks evidences that JVR could influence cerebral circulation. The aim of the present study is trying to provide evidences that the retrogradely-transmitted venous pressure of JVR could reach cerebral venous system and has an influence on cerebral blood flow (CBF).

Methods: We recruited 50 volunteers. Only 42 subjects' data (55.81 ± 19.96 , 23 - 85 years; 9 women) were analyzed due to poor temporal windows in eight subjects. JVR was determined by color-coded Duplex sonography. Transcranial Doppler study was used to examine the CBF changes during Valsalva maneuver (VM) in each subject.

Results: All JVRs were detected during VM. We divided subjects into people with right JVR (n=12), left JVR (n=13) and no JVR (n=21) and four had bilateral JVR. There was a more decrease in CBF during and immediately after VM in right-JVR group than no-JVR group, though the baseline characteristics and arterial blood pressure changes were similar. There were no demographic and hemodynamic differences between left-JVR group and no-JVR group.

Conclusion: We are the first to provide evidences that right JVR during VM could influence CBF. However, whether left JVR with or without right JVR may have similar effect on CBF deserves further study. The definite mechanism underlying this finding needs further studies.

Key Words: jugular venous reflux, transcranial Doppler, cerebral blood flow, Valsalva maneuver

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INTRODUCTION

Cerebral venous disease, such as venous sinus thrombosis or arteriovenous malformation (AVM), causes brain tissue ischemic via cerebral venous hypertension⁽¹⁻⁴⁾. Increased cerebral venular pressure would

decrease cerebral perfusion pressure (CPP) and then cerebral blood flow (CBF) to brain tissue⁽¹⁻⁴⁾. Jugular venous reflux (JVR), which could be detected at rest or during Valsalva maneuver (VM), is resulted from an abnormally reversed venous pressure gradient in internal jugular vein (IJV), which pressure is beyond the

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competence of IJV valves⁽⁵⁻⁷⁾. Since internal jugular vein (IJV) is a main extracranial tract for cerebral venous drainage, JVR might retrogradely transmit venous pressure into cerebral venous system⁽⁸⁻¹⁰⁾. More and more studies have found significant associations between JVR and neurological disorders^(5,6,11-14). However, there still lacks evidences that JVR could influence cerebral circulation. In the present study, we tried to test if JVR, which has a relative remote location of venous reflux compared with cerebral venous sinus thrombosis and lower retrograde-transmitted venous pressure than cerebral AVM, has similar influences on cerebral circulation, e.g. CBF decrement.

The cardiovascular effects of VM have been extensively studied. There are four distinct well-described phases of arterial blood pressure (ABP) changes⁽¹⁵⁻¹⁸⁾. With the beginning of the strain (phase I), there is a transient increase in ABP that is resulted from transmission of the intrathoracic pressure to the arterial system. At phase II, continuously increased intrathoracic pressure will impede venous return from vena cava to the heart. There will be a fall in ABP due to impaired atrial filling of the heart at early phase II (phase IIa). Then at late phase II (phase IIb), a sympathetic response (mediated mainly by baroreceptors) to the fall in ABP will produce a rise in ABP and heart rate. When the strain is relieved (phase III), more venous blood volume pools in the expanded intrathoracic capacitance veins because of sudden decrease of intrathoracic pressure, which in turn, decreases left atrial filling and ABP. This is followed immediately by an overshoot in ABP (phase IV) when the atrial filling is normalized accompanied by remain-elevated sympathetic tone (e.g. increased systemic vascular resistance). CBF will change in response to the changes in CPP, which approximately equals to ABP minus CVP when CVP is elevated⁽¹⁸⁻²³⁾. Thus, there is a similar four-phase CBF changes during VM. Besides decreased ABP, VM will cause elevated central venous pressure (CVP) at phase II, which has effects on CPP and CBF during VM as well⁽²⁴⁾.

Using transcranial Doppler (TCD), we can simultaneously record systemic ABP and flow velocities in middle cerebral arteries (MCA) during VM. Since MCA

diameter is found unchanged under several circumstances⁽²⁵⁻²⁷⁾, changes in MCA flow velocities are usually used to represent CBF changes^(19-21,23,28-37). In the present study, we used TCD to compare the patterns of MCA flow velocities changes during VM between people with JVR (JVR group) and people without JVR (non-JVR group). We hypothesized that JVR has an influence on CBF, e.g. VM-induced JVR would result in a more elevated CVP during VM by its retrograde-transmitted venous pressure, and the elevated venous pressure is sufficiently to influence CPP and CBF. A more MCA flow velocity decrement during VM in JVR group than non-JVR group would favor our hypothesis.

METHODS

Study population

We recruited 50 volunteered individuals. The presences of vascular risk factors, such as HTN, DM, and hyperlipidemia, heart diseases, cerebrovascular diseases, or respiratory diseases would be recorded.

JVR determination

Color-Doppler imaging was performed in a head straight, flat supine position with a 7-MHz linear transducer (Acuson; Sequoia, Mountain View, CA) after a 10-min quiet rest in all study individuals. Luxury amount of ultrasound gel was used and great care was taken to avoid compression of neck veins during examination. Bilateral IJVs were examined in all subjects at baseline and during VM. At baseline, the IJV was insonated initially with a longitudinal and then a cross-sectional view from the proximal part at neck base rostrally to the distal part at submandibular level to evaluate the IJV flow-pattern by color duplex. Then we put the distal margin of the window of the color signal at the tip of the flow divider of the internal carotid artery for Doppler spectrum study during VM. The VM was performed lasting for 15 seconds with intrathoracic pressure 40 mmHg maintained and was monitored by a pressure gauge connected to a flexible tube. JVR was defined as duplex ultrasound or/and Doppler spectrum indicating retrograde flow lasting more than 0.5 seconds spontaneously

(at baseline) or during VM.

TCD

CBF changes were represented as middle cerebral artery flow velocity (MCAV) changes. Bilateral MCAV was acquired by TCD (Multidop-X, DWL; Sippligen, Germany). The transducers were fixed in place by a probe holder, and MCAV was continuously recorded at the depth of the best signal (44-55 mm). Instantaneous ABP was recorded noninvasively by servocontrolled infrared finger plethysmography (Finapres, model 2300, Ohmeda Monitoring Systems, Englewood, CT, U.S. A.). Heart rate was monitored by ECG during TCD recording. All experiments were performed in the morning at least 2 hours after a light breakfast. After at least 10 minutes of supine rest, two VM were performed with a 5-minute interval between the two tests. The second VM was used for data analysis. The VM was performed lasting for 15 seconds with intrathoracic pressure 40 mmHg maintained and was monitored by a pressure gauge connected to a flexible tube.

Beat-to-beat ABP and MCAV measured for 15 seconds before the VM were averaged as baseline. Phasic changes in ABP and MCAV were defined previously. Relative changes in ABP and MCAV at each phases of VM are calculated as the ratio of the magnitude of the phasic changes at each phase divided by the baseline measurements.

Statistical analysis

Continuous data were expressed as mean (SD). The comparisons between the JVR group and the non-JVR group were analyzed by nonparametric Mann-Whitney U test. A *P* value < 0.05 was considered statistically significant. Analyses were performed with SAS software, version 9.1 (SAS Institute Inc, Cary, NC).

RESULTS

Fifty volunteered subjects were enrolled. Eight subjects were excluded due to poor temporal windows. There were 42 subjects' data being analyzed. Table 1 demonstrates the characteristics and the frequencies of

Table 1. The characteristics of study subjects and the results of Valsalva maneuver Transcranial Doppler (n=42)

Age, y	55.81 (19.96); 23-85
Gender, M/F	33/9
Vascular risk factors, n	
Hypertension	12 (28.6%)
Diabetes	5 (11.9%)
Hyperlipidemia	2 (2.4%)
Heart failure, n	0
Chronic obstruction pulmonary disease, n	14 (33.3%)
Jugular venous reflux, n	
Left	12 (28.6%)
Right	13 (31%)
Both-sided	4 (9.5%)
Nonea	21 (50%)
ABP, mmHg	
Baseline	80.00 (16.20)
Phase I	102.67 (18.91)
Phase IIa	75.94 (16.78)
Phase IIb	93.04 (23.86)
Phase III	65.96 (21.46)
Phase IV	95.59 (19.25)
MCAV, cm/s	
Baseline	52.50 (17.75)
Phase I	59.20 (19.85)
Phase IIa	38.01 (14.11)
Phase IIb	50.48 (20.34)
Phase III	48.61 (19.92)
Phase IV	69.04 (28.33)

Presented as means (SD), range, or numbers (percentages).

aMeans that neither side has jugular venous reflux.

JVR of our subjects. All JVR in our subjects were detected during VM. There were 12 subjects with right JVR, 13 subjects with left JVR (n=13), and 21 subjects with no JVR. There were 4 subjects with both-sided JVR. Table 1 also summarizes the results of VM TCD studies.

The characteristics between subjects with left JVR and none JVR, and between right JVR and none JVR were similar (Table 2). The baseline of ABP and MCAV among subjects with left JVR, right JVR, and none JVR

Table 2. The characteristics of subjects with left, right, and none JVR (None JVR versus left JVR and right JVR respectively)

	None JVR (n=21)	Left JVR (n=12)	<i>P</i>	Right JVR (n=13)	<i>P</i>
Age, y	55.24 (20.06)	60.92 (18.08)	0.5	58.85 (22.81)	0.696
Gender, M/F	16/5	8/4	0.561	13/0	0.061
Hypertension, n	6 (28.57%)	5 (41.67%)	0.450	4 (30.77)	0.893
Diabetes, n	2 (9.52%)	2 (16.67%)	0.551	3 (23.08%)	0.285
Hyperlipidemia, n	1 (4.76%)	0	0.450	0	0.431
Heart failure, n	0	0	-	0	-
COPD, n	6 (28.57%)	5 (41.67%)	0.450	6 (53.85%)	0.147

Presented as means (SD). JVR: Jugular Venous Reflux

Table 3. The comparisons of each phasic change in ABP and MCAV between subjects with none JVR versus left JVR and right JVR respectively

	None JVR (n=21)	Left JVR (n=12)	<i>P</i>	Right JVR (n=13)	<i>P</i>
ABP phasic changes, %					
Phase I	32.54 (14.65)	25.93 (19.97)	0.283	22.39 (10.98)	0.096
Phase IIa	- 5.85 (15.72)	-5.96 (20.49)	0.987	-5.06 (20.03)	0.834
Phase IIb	16.75 (18.99)	14.92 (32.26)	0.838	11.42 (22.47)	0.529
Phase III	-17.19 (19.38)	-18.44 (29.29)	0.884	-25.01 (20.36)	0.309
Phase IV	19.61 (14.42)	25.06 (33.11)	0.514	17.78 (10.00)	0.834
MCV phasic changes, %					
Phase I	15.06 (10.12)	16.51 (12.23)	0.715	6.7 (12.97)	0.076
Phase IIa	-20.27 (31.66)	-28.5 (13.51)	0.401	-30.09 (13.29)	0.529
Phase IIb	2.39 (20.16)	-2.69 (21.54)	0.501	-12.94 (15.35)	0.039
Phase III	- 3.98 (20.45)	-4.37 (18.43)	0.957	-16.47 (12.81)	0.036
Phase IV	34.51 (24.11)	32.86 (28.83)	0.861	25.46 (22.42)	0.600

Presented as means (SD).

were similar (ABP $P = 0.571$; MCAV $P = 0.929$). The comparisons of each phasic change in ABP and MCAV showed less increment of MCAV at phase IIb and more decrement of MCAV at phase III in subjects with right JVR than subjects with none JVR, though the phasic changes in ABP were similar (Table 3 & Figure 1). There were no differences in each phasic change in ABP and MCAV between subjects with left JVR and none JVR (Table 3). Since there were overlapping subjects between right-JVR group and left-JVR group ($n = 4$), we could not perform the comparisons between these two groups.

DISCUSSION

In VM TCD study, we have found that subjects with right JVR had a less increment of CBF at phase IIb and more decrement of CBF at phase III than subjects with none JVR. Since each phasic change in ABP was similar between these two groups, our results imply that the differences of CBF phasic changes were resulted from JVR.

All of right JVRs detected in our study subjects were during VM. In the four phases of CBF during a VM, the intrathoracic pressure was increased by straining during

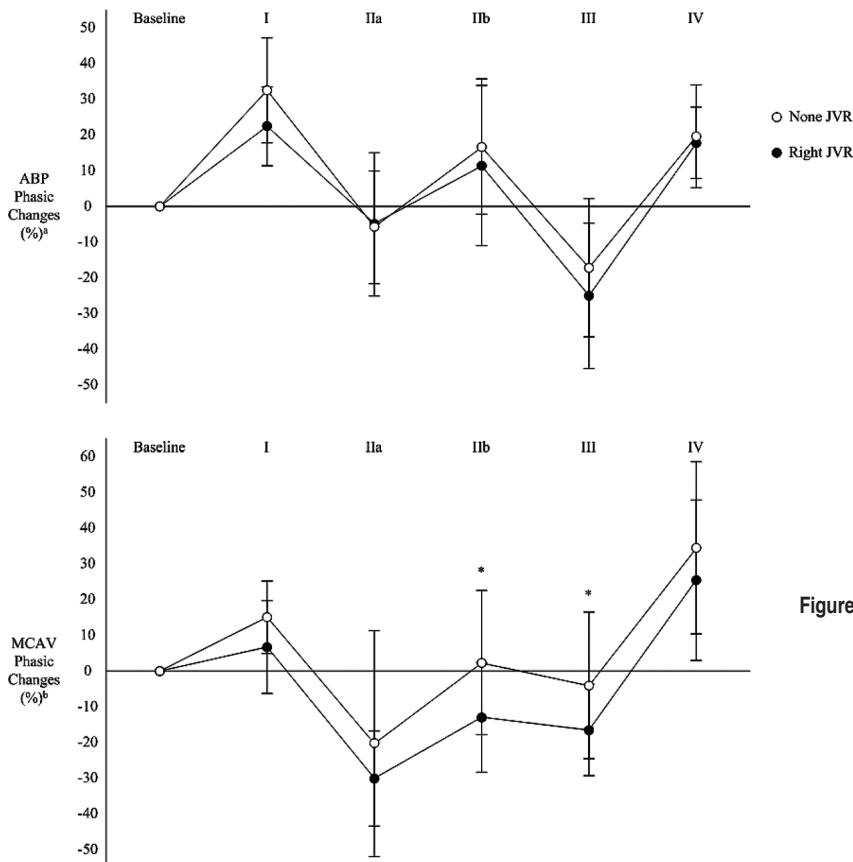


Figure 1. There was a less increment of MCAV at phase IIb and more decrement of MCAV at phase III in subjects with right JVR than subjects with none JVR, though the phasic changes in ABP were similar. Presented as mean (dots) \pm SD (lines).
^a $(BP_{\text{each phase}} - BP_{\text{baseline}}) / BP_{\text{baseline}}$.
^b $(MCAV_{\text{each phase}} - MCAV_{\text{baseline}}) / MCAV_{\text{baseline}}$. * <0.05 .

phase I to phase IIb. We suggest that JVR during VM could retrogradely transmit venous pressure into cerebral venous system, decrease CPP, and consequently decrease CBF at phase IIb. A delayed influence of CBF after VM (phase III) related to JVR might be due to a venoarterial reflex, which is a delayed arterial vasoconstriction in response to elevated downstream venous pressure⁽³⁹⁻⁴¹⁾. An alternative hypothesis to explain the CBF changes by JVR at phase IIb and phase III is the activation of hematological cells (e.g. leukocyte, platelet, etc.) or cerebral endothelium by sudden hemodynamic changes (e.g. increased venous pressure, slow or stagnant flow in venous circulation). Activation of hematological cells and endothelium might lead to transient vasospasm or vascular obstruction by hyper-aggregated cells⁽¹²⁾. We need further studies to elucidate the definite mechanism between JVR and CBF changes during VM.

Blood flow volume is greater in right IJV than left

IJV in most people⁽⁴²⁻⁴⁴⁾. Therefore, right JVR during VM would bring a higher retrograde-transmitted venous pressure than left JVR⁽⁴⁵⁾. This could explain why only subjects with right JVR had an effect on CBF during VM. One may concern that neurological diseases associated with JVR are not confined to right JVR only, and how about the effect of left JVR on CBF? Due to our study design, we could only evaluate the impact of JVR during VM on CBF changes. In our previous studies, most left JVR associated with neurological diseases were at baseline and accompanied right JVR^(6,7,46). Does left continuous JVR (JVR at baseline) with or without right JVR have a greater or/and exacerbated effect on CBF demands other studies.

We are the first to provide evidences that right JVR during VM could influence CBF. However, whether left JVR with or without right JVR may have similar effect on CBF deserves further study. This finding is contribu-

tive to elucidating the pathophysiology of JVR and other neurological diseases that are related to JVR.

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