Using Cross-Correlation Function to Assess Dynamic Cerebral Autoregulation in Response to Posture Changes for Stroke Patients

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Abstract

In this study, time-domain cross-correlation function was applied to evaluate the relationship between blood pressure and cerebral blood flow velocity signals acquiring from healthy subjects and stroke patients both in supine and head-up tilt positions to evaluate the effect of posture change. 10 stroke patients and 11 healthy subjects were included in this study. Results revealed that the mean arterial blood pressure (MABP) values of stroke patients in response to posture changes were reduced. However, MABP values in healthy subjects were become higher in head-up tilt position. Both of MABP values of healthy subjects in supine and head-up tilt were significantly lower than those in stroke patients ($p<0.05$). On the other hand, mean cerebral blood flow velocity (MCBFV) in healthy subjects remain constant. However, the values in stroke patients reduced in response to head-up tilt. In the results of cross-correlation function (CCF) analysis, max CCF values in healthy subjects were significantly higher than those in stroke patients ($p<0.05$) in both supine and head-up tile positions. It might indicate correlation of MABP and MCBFV was higher in healthy subjects. The max CCF index in stroke patients were close to 0 second in both positions (supine: -0.35±3.36 sec; head-up tilt: -0.29±3.20 sec). In healthy subjects, max CCF values should be around 2 seconds. Hence, it indicated the phase difference almost did not exist between MABP and MCBFV. This reveals the buffer function of CA were lower in stroke patients. Therefore, CA in stroke patients might be impaired by the results in response to posture changes.

Keywords: Stroke, Cerebral autoregulation (CA), Cross-correlation function (CCF), Blood pressure, Cerebral blood flow velocity

1. Introduction

Stroke has been the leading causes of mortality in Taiwan, even in the world for decades. Previous researches indicate the causes of cardiovascular diseases are highly related to the change of physiological parameters. Stroke can be resulted from rapid change or unstable cerebral blood flow due to the ineffective cerebral autoregulation (CA). The cerebral autoregulation mechanism refers to the cerebral blood flow (CBF) tendency to maintain relatively constant in the brain. Stroke is one of the cardiovascular diseases which has been the leading causes of mortality in the world for decades. Stroke can be resulted from unstable cerebral blood flow due to the cerebral autoregulation mechanisms being unable to work in effect. The balance between both sympathetic and parasympathetic nervous systems mainly controls blood pressure. Cerebral autoregulation is a feedback mechanism, which maintains cerebral blood flow constant despite change of blood pressure [1]. Cross-correlation functions analysis has been applied to evaluate dynamic cerebral autoregulation in previous studies. It can characterize and quantify CA between healthy subjects and patients [2-3]. Cross-correlation function (CCF) has been applied by previous investigators as a means to assess cerebral autoregulation [4-8]. Moreover, cross-correlation analysis of blood pressure and heart rate variability has been applied to investigate the relationship between pulse interval and systolic arterial blood pressure [6]. Previous studies showed that CCF would be a useful tool to assess cerebral autoregulation.

In this study, mean arterial blood pressure (MABP) and mean cerebral blood flow velocity (MCBFV) signals were acquired during both supine and head tilt-up (HUT) positions for applying cross-correlation functions analysis. The main purpose of this study is to investigate the effects of poster change on CA by using CCF analysis for providing a noninvasive, simple, quantitative assessment of stroke for physicians.

2. Materials and methods

2.1. Subjects and measurements

10 stroke outpatients (56±10.16 years) from the

Section of Neurology of Cheng-Ching General Hospital were enrolled in this study. These patients have to qualify (1)Blood pressure level was defined as a clinic blood pressure $\geq$ 140/90 mmHg (WHO/ISH Guidelines 2000). (2) National Institutes of Health Stroke Scale, NIHSS <15. (3) Stroke more than 7 days. On the other hand, 10 healthy subjects (57.40±8.41 years) were included only if they had no history of cardiovascular disease, heart problems, hypertension, migraine, epilepsy, cerebral aneurysm, intracerebral bleeding or other pre-existing neurological conditions. None of the subjects were receiving any medication during the period of the study. Continuous arterial blood pressure signals were acquired via using the Finapres (Ohemda 2300). Cerebral blood flow velocity signals were obtained through TCD (Transcranial Doppler ultrasound, EME TC2020). Subjects were examined on a tilt-table that enabled a motor-driven change from a supine to an upright position within 10 seconds. Data acquisition was started after a 10-min relaxation period in the supine position.

Mean arterial blood pressure and mean cerebral blood flow velocity signals were acquired during both supine and head tilt-up positions. The personal computer combined with a general purpose data acquisition board and LabVIEW environment for acquiring signals correctly was developed in our pervious study [6,7].

2.2. Cross-correlation function

Assume MABP and MCBFV signals are f(n) and g(n), respectively. In order to assess autonomic nerve system in specific frequency bands, f(n) and g(n) signals were bandpass filtered in LF frequency ranges while applying the CCF. Where the range of LF is 0.04 through 0.15 Hz.. Assume that bandpass filtered f(n) and g(n) signals are $\hat{f}(n)$ and $\hat{g}(n)$, respectively. The CCF between $\hat{f}(n)$ and $\hat{g}(n)$ can be calculated as fallows:

$$CCF_i(k) = \frac{R_{\hat{f}\hat{g}}^i(k)}{\sqrt{R_{\hat{f}\hat{f}}^i(0)R_{\hat{g}\hat{g}}^i(0)}}, \qquad (1)$$

k=0,±1, ±2,… and i=1 to N−W+1

where $R_{\hat{f}\hat{g}}^i(k)$ is an estimate of cross-covariance in ith time window and it's defined as fallows:

$$R_{\hat{f}\hat{g}}^i(k) = \begin{cases} \frac{1}{W}\sum_{j=i}^{i+W}\hat{f}(i)\hat{g}(j+k), & k = 0,1,2,....... \\ \frac{1}{W}\sum_{j=i}^{i+W}\hat{f}(j-k)\hat{g}(j), & k = 0,-1,-2,.. \end{cases} \quad (2)$$

And

$$R_{\hat{f}\hat{f}}^i(0) = \frac{1}{W}\sum_{j=i}^{i+W}[\hat{f}(j)]^2 \qquad R_{\hat{g}\hat{g}}^i(0) = \frac{1}{W}\sum_{j=i}^{i+W}[\hat{g}(j)]^2$$

N is the total number of cardiac cycles, W is the window width and k is the time lag. CCFi(·) is the result of the CCF between $\hat{f}(n)$ and $\hat{g}(n)$ in the ith time window.

3. Results and discussion

3.1. BP and CBFV levels

Tables 1 and 2 indicate the results of blood pressure and cerebral blood flow velocity. It reveals that both blood pressures and cerebral blood flow velocities in stroke patients are higher than those in healthy subjects (p<0.05). In healthy subjects, blood pressure and cerebral blood flow velocity increase in response to HUT. However, blood pressure and cerebral blood flow velocity trend to decrease in response to HUT. There, cerebral autoregulation in stroke patients might be different from that in healthy subjects.

Table 1. Results of blood pressure.

		SABP(mmHg)	MABP(mmHg)	DABP(mmHg)
Healthy	supine	120.42±8.24*	88.34±8.20**	69.52±9.35***
	tilt	127.76±18.75#	95.32±11.69##	76.57±11.34###
Stroke	supine	168.17±20.31	117.99±17.50	92.89±18.85
	tilt	156.09±22.71	112.25±17.68	90.33±17.30

(*p<0.05, SABP in supine Healthy vs. Stroke; **p<0.05, MABP in supine Healthy vs. Stroke; ***p<0.05, DABP in supine Healthy vs. Stroke; #p<0.05, SABP in tile Healthy vs. Stroke; ##p<0.05, MABP in tilt Healthy vs. Stroke; ###p<0.05, DABP in tilt Healthy vs. Stroke)

Table 2. Results of cerebral blood flow velocity.

		SCBFV(cm/s)	MCBFV(cm/s)	DCBFV(cm/s)
Healthy	supine	58.51±9.77*	38.85±7.94**	23.58±6.88***
	tilt	60.31±14.50#	39.44±11.62##	23.64±10.16
Stroke	supine	139.78±72.25	79.07±43.79	48.72±31.92
	tilt	132.05±73.34	73.57±43.49	44.33±31.99

(*p<0.05, SCBFV in supine Healthy vs. Stroke; **p<0.05, MCBFV in supine Healthy vs. Stroke; ***p<0.05, DCBFV in supine Healthy vs. Stroke; #p<0.05, SCBFV in tile Healthy vs. Stroke; ##p<0.05, MCBFV in tilt Healthy vs. Stroke)

3.2. CCF analysis

Table 3 shows the CCF analysis results. It reveals the

results of max CCF values in healthy subjects are significantly higher than those in stroke patients (p<0.05). It may indicate max CCF value become lower with stroke in both supine and head-up tilt positions. That means the correlation between MABP and MCBFV are low in stroke patients. In general, the time lag in healthy subjects is around 2 seconds. In this study, time lag in stroke patients is around zero second. Therefore, CA function in stroke patients is lower in both supine and HUT positions.

Table 3. Results of CCF analysis both in supine and HUT positions.

		Max CCF index (beat)	Max CCF index (sec)	Max CCF value
Healthy	supine	-1.9±0.88	-1.68±0.84	0.57±0.13*
	tilt	-1.73±1.61	-1.35±1.32	0.55±0.19**
Stroke	supine	-0.3±3.95	-0.35±3.36	0.25±0.07
	tilt	-0.4±3.63	-0.29±3.20	0.28±0.11

(*p<0.05, Max CCF value in supine Healthy vs. Stroke; **p<0.05, Max CCF value in tilt Healthy vs. Stroke)

The CCF result of one sample in the healthy group during supine position was drawn in Fig.1. Fig.1(a) shows the correlation among CCF(k), CCF index and time index. 3D representative figures showed the results of CCF(k) in each beat and all of the 2D representative figures give the mean and standard deviation of the CCF for the representative subjects. Fig. 1(b) shows the max CCF value, max CCF time index and corresponding time lag. Similarly, Fig.2 presents the result of one healthy sample during HUT position. According to previous research, the CCF peak in negative time index is a result of the phase-lead property. The time lag could stands for the buffer function of cerebral autoregulation. As we can observed in Fig. 1(b) and Fig. 2(b), the mean CCF(k) curve (with the symbols ×) in the healthy subject is more smooth than that in stroke patients (Figures 3 and 4). The standard deviation curve (with the symbol ■) is also smooth in the healthy subjects. It may reveal that correlation between blood pressure and blood flow is more stable in healthy subjects. On the other hand, cerebral autoregulation might be affected in stroke patients make the correlation between blood pressure and blood flow unstable. That also indicates cerebral autoregulation in healthy subjects is more sensitive than that in stroke. According to the representative of Fig. 1 and Fig. 3, Fig. 2 and Fig. 4. It may show the difference of cerebral autoregulation between healthy subjects and stroke patients.
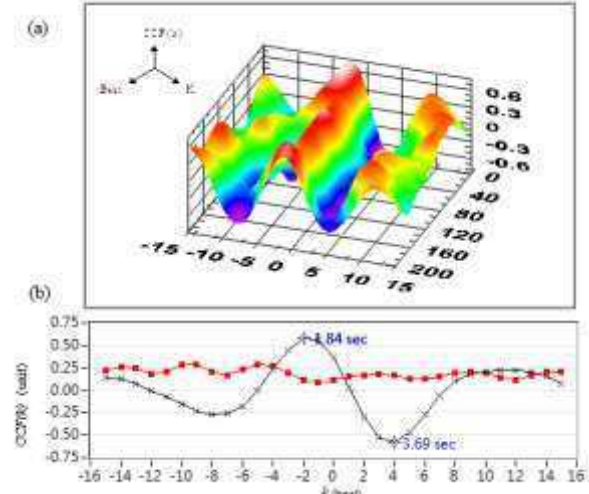

Fig. 2 CCF results of a typical sample subject in healthy group during supine position. (a) 3D representative figures of CCF (b) 2D representative figures of CCF with mean (x) and SD (■) in LF in supine position for a healthy subject. k is thetime index. CCF (k) is the mean value of CCF in time indices. The line with symbols (x) is the mean value of CCF in each time index. The line with symbols (■) is the standard deviation of CCF in each time index
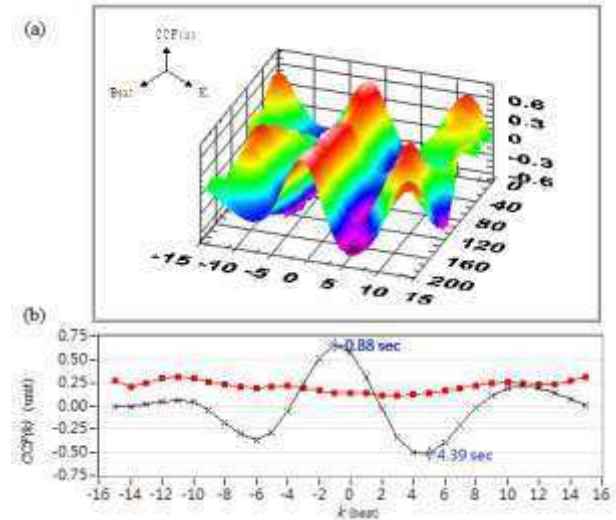

Fig. 3 CCF results of a typical sample subject in healthy group during HUT position. (a) 3D representative figures of CCF (b) 2D representative figures of CCF with mean (x) and SD (■) in LF in supine position for a healthy subject. k is thetime index. CCF (k) is the mean value of CCF in time indices. The line with symbols (x) is the mean value of CCF in each time index. The line with symbols (■) is the standard deviation of CCF in each time index
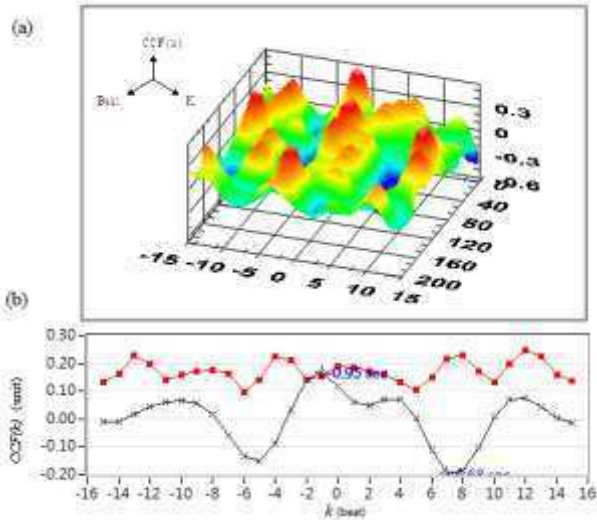
Fig. 3 CCF results of a typical sample subject in stroke group during supine position. (a) 3D representative figures of CCF (b) 2D representative figures of CCF with mean (×) and SD (■) in LF in supine position for a healthy subject. k is thetime index. CCF (k) is the mean value of CCF in time indices. The line with symbols (×) is the mean value of CCF in each time index. The line with symbols (■) is the standard deviation of CCF in each time index
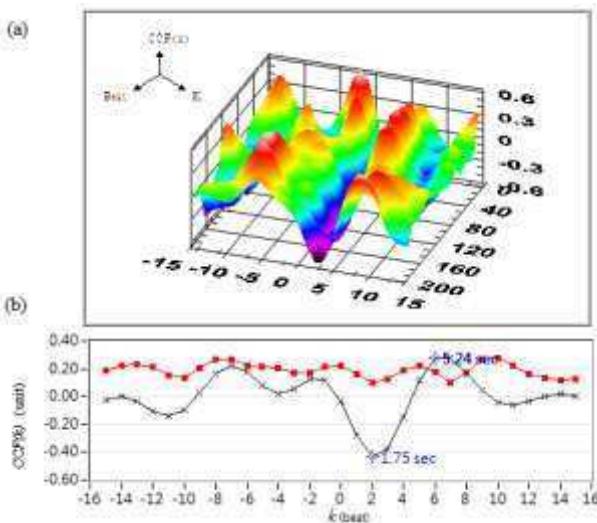

Fig. 4 CCF results of a typical sample subject in stroke group during HUT position. (a) 3D representative figures of CCF (b) 2D representative figures of CCF with mean (×) and SD (■) in LF in supine position for a healthy subject. k is thetime index. CCF (k) is the mean value of CCF in time indices. The line with symbols (×) is the mean value of CCF in each time index. The line with symbols (■) is the standard deviation of CCF in each time index

4. Conclusion

According to the results in this study that stroke would affect cerebral autoregulation mechanisms in both supine and HUT positions. Moreover, the correlation between blood pressure and cerebral blood flow velocity are high in healthy subjects. Therefore, if these physiological signals can be monitored and assessed by CCF , it would be helpful to diagnose primary stroke and prevent the second stroke in clinical practice.

Acknowledgements

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