Assessment of Coupling and Correlation between Cerebral Autoregulation and Baroreflex in Stroke Patients

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Abstract

Cardiovascular diseases are common nowadays. The main purpose of this research is to integrate the analysis of blood pressure, cerebral blood flow and heart rate to evaluate coupling effect in stroke patients. There are 10 stroke patients (56±10.6 years) included in this study. Results of blood pressure and cerebral blow velocity values in stroke are lower than those in healthy persons ($p<0.05$). Low frequency power of blood pressure and cerebral flow velocity are also decreased more than those in healthy subjects ($p<0.05$), it might be the effect of sympathetic nerve system. K2 means *"chaoticness". K2* values of cerebral flow velocity and mean heart rate in stroke subjects are higher than those in healthy subjects significantly ($p<0.05$), it might indicate cerebral flow and heart rate in stroke are more chaotic. The values of baroreflex sensitivity in healthy subjects are also higher significant ($p<0.05$). The values of independence of complexity and predictability of blood pressure, cerebral flow and heart rate between 0 and 1 indicate they are highly coupled. Therefore, if the correlation of blood pressure, cerebral flow and heart rate can be observed simultaneously, and the coupling degree of cerebral autoregulation and baroreflex can be investigated, the effect of diagnosis of cardiovascular diseases can be improved.

Keywords: Cardiovascular disease, Cerebral autoregulation, Baroreflex, Blood pressure, Cerebral blood flow velocity

1. Introduction

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 (CA) and baroreflex mechanisms being unable to work in effect. Both cerebral autoregulation and baroreflex are important mechanisms for protection in human body. Cerebral autoregulation is a feedback mechanism, which maintains cerebral blood flow constant despite change of blood pressure. Baroreflex refers to the system with rapid response for dealing with the change in blood pressure. Patients with baroreflex failure may present hypertension, pheochromocytoma and damage to the glossopharyngeal or vagal nerves [1-5].

However, the correlation between cerebral autoregulation and baroreflex is not clear. If the related physiological parameters about these mechanisms can be monitored as well to make the coupling between cerebral autoregulation and baroreflex clear, it would be helpful for diagnosing of stroke in clinical practice. Some studies have revealed that in the acute phase of an ischemic stroke blood, pressure is raised to help restoring cerebral perfusion which activates collateral arterial supply and enhances the treatment goal of minimizing infarct size so that antihypertensive drug should be taken when blood pressure is too high. Some other studies reported most patients with acute ischemic stroke do not need antihypertensive therapy because the rapid decrease of blood pressure may reduce cerebral blood flow owing to impaired cerebral autoregulation. In this study, blood pressure, cerebral flow velocity and heart rate signals are acquired simultaneously to analyze the relation between cerebral autoregulation and baroreflex by using linear and nonlinear approaches to assess independence of complexity and predictability for exploring the coupling effect between CA and baroreflex. The goal of this research is to provide a noninvasive, simple, quantitative assessment of stroke for physicians to achieve primary treatment and secondly prevention effectively for patients with cardiovascular disease in clinical practice.

2. Materials and methods

In this study, the MABP value was calculated for each heart beat as follows:

$$MABP_i = \frac{1}{N}\sum_{k=i}^{i+1} ABP_i(k) \quad (1)$$

where ABP(·) is the arterial blood pressure pulse signal continuously acquired from Finapres. ABP_i is the wave-through time index in the ith pulse beat, N is the total number between ith pulse beat and (i+1)th pulse beat. Therefore, $MABP_i$ is the calculated ABP value for the ith pulse beat. Representation of the ABP signal is drawn as Fig.1.

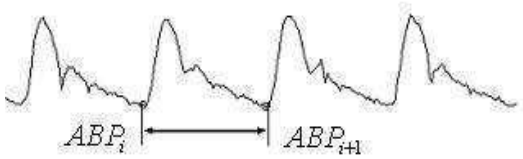

Fig.1 representation of the ABP signal

Similarly, the mean CBFV can be derived from Eqs. (2)

$$MCBFV_i = \frac{1}{N}\sum_{k=i}^{i+1} CBFV_i(k) \quad (2)$$

where CBFV(·) is the CBFV signal continuously acquired from the TCD. CBFVi is the time index of the wave-trough in the CBFV signal corresponding to the ith pulse beat and N is the total number between ith pulse beat and (i+1)th pulse beat. MCBFVi is the mean value of CBFV for the ith pulse beat.

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 ≧ 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, 11 healthy subjects (58.40±8.0 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 (MABP) and mean cerebral blood flow velocity (MCBFV) 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. Independence of complexity and predictability

Independence factor I was from Hoyer et al, 1998. It is applied to evaluate coupling degree between sub-systems. In general, the relation between sub-systems is D(Q)=D(X)+D(Y). If the coupling degree is high, the equation is D(Q)=D(X)=D(Y). Therefore, the relation is independence, I =1. High coupling degree, I=0. Part coupling degree, $0<I<1$. The equation to estimate the independence I is Eq. (2). Then we can calculate independence of complexity (I_{CD}) and independence of predictability (I_{CE}) by Eq. (23) and (4).

$$I = \frac{\sum_{i=1}^{k}\left|D_q - D_i\right|}{(k-1)\sum_{i=1}^{k} D_i} \quad (2)$$

$$I_{CD} = \frac{\left|CD_q - CD_x\right| + \left|CD_q - CD_y\right|}{CD_x + CD_y} \quad (3)$$

$$I_{CE} = \frac{\left|CE_q - CE_x\right| + \left|CE_q - CE_y\right|}{CE_x + CE_y} \quad (4)$$

Where CD is correlation dimension and CE is K-entropy.

2.3. Baroreflex

Beat-to-beat index values were used to evaluate the baroreflex. In order to detect the changes in the heart rate and blood pressure in the meantime. This index is the beat-to-beat relationship between the heart rate sequence and blood pressure sequence with one beat lag in the heart rate sequence. In this study, we assumed the SBP sequence as the S(n), the RR interval as the R(n), and defined the new baroreflex index as T(n). Then T(n) can express as equation (5).

$$T(n) = \sum_{k=1}^{n}\frac{R(k)}{S(k)} \quad (5)$$

From the results of spectrum diagram, the high

frequency and low frequency power of heart rate are defined as P_{HF}^{HR} and P_{LF}^{HR}. The high frequency and low frequency power of blood pressure are also defined as P_{HF}^{BP} and P_{LF}^{BP}. Alpha index can be expressed as equation (6). Alpha index α is the square root of ratio between RRI and SBP power at LF (0.04-0.15 Hz) and HF (0.15-0.4 Hz). The alpha value is defined as a baroreflex index.

$$\alpha = \frac{1}{2}\left(\sqrt{\frac{P_{LF}^{HR}}{P_{LF}^{BP}}} + \sqrt{\frac{P_{HF}^{HR}}{P_{HF}^{BP}}}\right) \quad (6)$$

3. Results and discussion

3.1. BP, CBFV and HR 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). There, cerebral autoregulation might be different from that in healthy subjects.

Table 1. Results of blood pressure and heart rate.

		SABP(mmHg)	MABP(mmHg)	DABP(mmHg)	MHR(bpm)
Healthy	supine	120.42±8.24*	88.34±8.20**	69.52±9.35***	69.04±7.30
	tilt	127.76±18.75#	95.32±11.69##	76.57±11.34###	74.25±7.36
Stroke	supine	168.17±20.31	117.99±17.50	92.89±18.85	67.56±9.12
	tilt	156.09±22.71	112.25±17.68	90.33±17.30	73.28±9.99

(*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	72.95±10.21	41.26±7.74	25.42±7.93
	tilt	67.49±11.06	37.43±7.16	22.40±7.99

(*p<0.05, SCBFV in supine Healthy vs. Stroke)

3.2. PSD analysis

Tables 3 and 4 show the results of power spectral analysis of blood pressure and cerebral blood flow velocity. It indicates low frequency power (0.04-0.15 Hz) is lower than those in healthy subjects (p<0.05). The sympathetic nerve system is distinguish from that in healthy subjects.

Table 3. Results of power spectral density of MABP ($mmHg^2$/Hz).

MABP		LF_{MABP}	HF_{MABP}	LF%	HF%
Healthy	supine	6.54±2.17*	1.30±0.44	81.90±8.97**	18.10±8.97****
	tilt	7.60±5.14	1.20±0.83	85.51±4.13##	14.49±4.13###
Stroke	supine	3.66±2.20	1.40±0.55	70.08±9.75	29.92±9.75
	tilt	5.06±3.84	1.92±1.29	70.63±14.61	29.37±14.61

(*p<0.05, LF_{MABP} in supine Healthy vs. Stroke; **p<0.05, LF % in supine Healthy vs. Stroke; ***p<0.05, HF% in supine Healthy vs. Stroke; ##p<0.05, LF % in tilt Healthy vs. Stroke; ###p<0.05, HF% in supine Healthy vs. Stroke)

Table 4. Results of power spectral density of MCBFV ($(cm/s)^2$/Hz).

MCBFV		LF_{MCBFV}	HF_{MCBFV}	LF%	HF%
Healthy	supine	4.79±6.04	1.71±0.98	63.37±8.57*	31.63±8.57**
	tilt	9.69±8.89	3.27±2.58	69.80±13.51#	30.20±13.51##
Stroke	supine	15.00±20.18	17.82±31.85	51.21±16.12	48.79±16.12
	tilt	8.57±10.65	8.21±8.78	46.88±12.82	53.12±12.82

(*p<0.05, LF % in supine Healthy vs. Stroke; **p<0.05, HF %in supine Healthy vs. Stroke; ##p<0.05, LF % in tilt Healthy vs. Stroke; ###p<0.05, HF% in supine Healthy vs. Stroke)

3.3. Kolmogorov entropy (K2) analysis

K2 metric evaluates the degree of "chaoticness" of the system, or the average rate at which information is generated by the system, or equivalently, the rate at which current information about system is lost. When K2=0, the system is regular; K2=∞, the system is random; K2>0 and finite, the system has chaotic behavior. Table 5 shows

the results of K-entropy analysis. It indicates K2 results of MCBFV and heart rate are higher in stroke patients ($p<0.05$). That reveals MCBFV and heart rate are more chaos in stroke patients.

Table 5. Results of K-entropy analysis.

		$K2_{MABP}$	$K2_{MCBFV}$	$K2_{HR}$
Healthy	supine	2.59±0.40	3.14±0.59*	2.59±0.66
	tilt	2.56±0.38	2.84±0.46**	2.20±0.43***
Stroke	supine	2.60±0.55	4.07±0.54	2.97±0.76
	tilt	2.36±0.44	3.84±0.73	2.93±0.54

(*$p<0.05$, K2 in supine Healthy vs. Stroke; **$p<0.05$, K2 in tilt Healthy vs. Stroke, ***$p<0.05$, K2 in tilt Healthy vs. Stroke)

3.4. Coupling analysis

Table 6 show the results of coupling analysis. Due to the relation is independence, I =1. High coupling degree, I=0. The results indicate BP, CBFV and HR are highly coupled.

Table 6. Results of coupling analysis

		I_{CD}	I_{CE}
Healthy	supine	0.34±0.25	0.14±0.11
	tilt	0.37±0.20	0.14±0.10
Stroke	supine	0.33±0.20	0.11±0.08
	tilt	0.41±0.27	0.17±0.10

3.5. Baroreflex analysis

Table7 shows the results of baroreflex analysis. BRS results in healthy subjects are higher than those in stroke patients ($p<0.05$). α index in stroke patients is significantly different between supine and tilt positions ($p<0.05$). However, it does not change significantly in healthy subjects. It might indicate stroke affect baroreflex function.

Table 7. Results of baroreflex analysis

		BRS	**α index**
Healthy	supine	7.29±0.88*#	12.76±9.03
	tilt	6.43±0.98##	10.06±6.61
Stroke	supine	5.50±1.25	10.21±3.61**
	tilt	5.37±0.95	7.14±2.72

(*$p<0.05$, BRS in healthy supine vs. tilt; **$p<0.05$, α index in stroke supine vs. tilt; #$p<0.05$, BRS in supine Healthy vs. Stroke; ##$p<0.05$, BRS in tilt Healthy vs. Stroke)

4. Conclusion

According to the results in this study that stroke would affect physiological mechanisms in human body. Moreover, blood pressure, cerebral blood flow velocity and heart rate are highly coupled. Therefore, the correlation between cerebral autoregulation and baroreflex is high. If these physiological signals can be monitored, it would be helpful in diagnosis.

Acknowledgements

The authors would like to thank the National Science Council, Taiwan, ROC, for supporting this research under Contract No. NSC 98-2221-E-241 -008 -MY2.

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