Resting Heart Rate Predicts Depression and Cognition Early after Ischemic Stroke: A Pilot Study

Arnaud Tessier, MS,*,† Igor Sibon, MD, PhD,†,‡ Mathilde Poli, MD,‡
Michel Audiffren, PhD,§ Michèle Allard, MD, PhD,†,‖,¶ and Micha Pfeuty, PhD†

Background: Early detection of poststroke depression (PSD) and cognitive impairment (PSCI) remains challenging. It is well documented that the function of autonomic nervous system is associated with depression and cognition. However, their relationship has never been investigated in the early poststroke phase. This pilot study aimed at determining whether resting heart rate (HR) parameters measured in early poststroke phase (1) are associated with early-phase measures of depression and cognition and (2) could be used as new tools for early objective prediction of PSD or PSCI, which could be applicable to patients unable to answer usual questionnaires. *Methods:* Fifty-four patients with first-ever ischemic stroke, without cardiac arrhythmia, were assessed for resting HR and heart rate variability (HRV) within the first week after stroke and for depression and cognition during the first week and at 3 months after stroke. *Results:* Multiple regression analyses controlled for age, gender, and stroke severity revealed that higher HR, lower HRV, and higher sympathovagal balance (low-frequency/high-frequency ratio of HRV) were associated with higher severity of depressive symptoms within the first week after stroke. Furthermore, higher sympathovagal balance in early phase predicted higher severity of depressive symptoms at the 3-month follow-up, whereas higher HR and lower HRV in early phase predicted lower global cognitive functioning at the 3-month follow-up. *Conclusions:* Resting HR measurements obtained in early poststroke phase could serve as an objective tool, applicable to patients unable to complete questionnaires, to help in the early prediction of PSD and PSCI. **Key Words:** Stroke—depression—cognition—autonomic nervous system—heart rate variability.

Introduction

Depression and cognitive impairments are common consequences of stroke whose early detection, however, remains difficult.[1] Current tools, mostly questionnaires, appear ill-suited in early phase, especially for aphasic patients.[2] It is therefore necessary to find other tools (observer-rated scales) and other channels (physiological) to help in the detection of patients at risk of poststroke depression (PSD) or cognitive impairment (PSCI).

Disruption of the autonomic nervous system has been reported in poststroke patients, with reduced heart rate variability (HRV) reflecting poor parasympathetic modulation.[3] Yet, low HRV has also been associated with depressive disorders[4] and with poor cognitive, especially executive, functioning.[5] Interestingly, 1 study revealed

that 5 months after stroke, HRV was reduced in depressed versus nondepressed patients, providing the first evidence that PSD is linked to lower parasympathetic activation.[6] This study, however, was limited to chronic phase and did not investigate the possible relationship with cognition.

The objective of this pilot study was to investigate whether resting HR measured in early poststroke phase could serve as a new tool for objective detection of patients at risk of PSD or PSCI, which could be applicable to patients unable to answer usual questionnaires. To this aim, we tested whether measures of resting HR and HRV performed during early poststroke phase (1) were associated with early-phase measures of depression and cognition and (2) predicted severity of depressive symptoms and global cognitive functioning 3 months later.

Methods

Study Population

The study included 54 consecutive patients who were admitted to our local comprehensive stroke center (from December 2012 to December 2013). The main inclusion criteria were as follows: 18 years or older and a first acute ischemic stroke confirmed by magnetic resonance imaging (MRI). The noninclusion criteria were as follows: history of psychiatric disorder or dementia and current prescription of antiarrhythmic medications. All patients (or the family) provided informed written consent for participation in this study. Early-phase evaluations (resting HR, depression, and cognition) were performed during hospitalization (2-7 days after stroke). Patients were reevaluated 3 months later for depression and cognition (see Fig 1 for study design). Stroke severity at admission was assessed with the National Institutes of Health Stroke Scale (NIHSS) and handicap at the 3-month follow-up was assessed with the modified Rankin scale. Ischemic stroke volume, extent of leukoencephalopathy (Fazekas scale), and

number of microbleeds (Brain Observer MicroBleed Scale) were evaluated on MRI. The study was approved by the local research ethics committee (DC2011/26 CHU Bordeaux).

Measures of Depression and Cognition

To assess severity of depressive symptoms, different measures were used in each phase. In chronic phase, the Beck Depression Inventory (BDI-II, 21 items)[7] was used to measure the symptom severity over the previous 2 weeks. However, this scale seems inappropriate within the first few days after stroke and was replaced by the Hospital Anxiety and Depression Scale (HADS, 14 items) in early phase. Furthermore, to evaluate patients with aphasia or severe cognitive deficits, 2 nonverbal measures of depression were added: the Stroke Aphasic Depression Questionnaire (SADQ-10, 10 items),[8] which is an observer-rated scale, and a Visual Analog Scale for depression (VAS$_{Depression}$, 1 item). The scores obtained in these 3 depression scales (HADS, SADQ-10, and VAS$_{Depression}$) were correlated (r > .41, P < .002 for all correlations). For patients who were evaluated with the 3 scales, we calculated a *global z-score of depression* in early phase corresponding to the mean of the 3 standard z-scores. Global cognitive functioning was evaluated using the Montreal Cognitive Assessment (MoCA) scale[9] in early and chronic poststroke phases. Missing HADS and MoCA scores were due to lack of feasibility in patients with aphasia and/or hemiplegia.

Resting Heart Rate Measurements

During early poststroke phase, resting HR was measured in the morning (8:00-8:30) with HR monitor Polar-RS 800, while patients on an empty stomach were lying on their bed in their hospital room. Analyses were performed on 30-minute intervals, with the Kubios HRV Analysis Software 1.1 (Department of Applied Physics, University of Eastern Finland, Kuopio, Finland). Because of these strict methodological conditions, resting HR was measured only in the early phase. We collected time-domain indices with mean heart rate (mHR) in beats per minute (bpm) and RMSSD (root mean square of successive differences in RR intervals) in milliseconds, as well as power spectral density (in ms²) in different frequency bands: high-frequency (HF: 0.15-0.4 Hz) reflecting parasympathetic activation, low-frequency (LF: 0.04-0.15 Hz) reflecting parasympathetic and sympathetic activation, and the LF-to-HF ratio reflecting the sympathovagal balance. All indices (except mHR) were transformed in natural logarithm (Ln) to obtain normal distributions.

Statistical Analyses

Age and gender are known to affect HR and HRV,[10] and stroke severity is a well-identified predictor of PSD.[11] Pearson correlations were first used to assess potential associations between early-phase HR parameters and
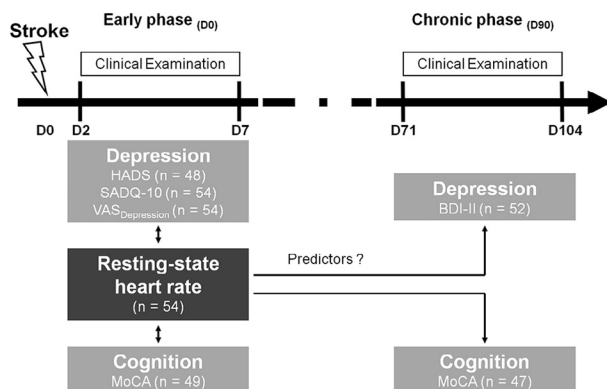

Figure 1. *Design of the protocol. Abbreviations: BDI-II, Beck Depression Inventory II; HADS, Hospital Anxiety and Depression Scale; MoCA, Montreal Cognitive Assessment; SADQ, Stroke Aphasic Depression Questionnaire; VAS$_{Depression}$, Visual Analog Scale for depression.*

demographic characteristics (age, gender), stroke severity (NIHSS at admission and lesion volume), as well as early and chronic phase measures of depression and cognition. Furthermore, differences in HR parameters according to stroke laterality (left versus right) were examined with *t*-tests, and the potential association in chronic phase between depression and cognition was assessed with a Pearson correlation. Then, multiple regression analyses were performed to determine whether early-phase measures of HR and HRV were associated with, or predicted, early and chronic phase measures of depression and cognition after controlling for age, gender, NIHSS at admission, and lesion volume. Statistical analyses were performed using IBM SPSS 22.0 (IBM, Chicago, IL). Because of the exploratory nature of this study, the significance level was set at *P* less than .05 without correction for multiple testing. Correlations and regressions that remained significant after

Bonferroni correction for the multiple HR parameters tested ($P < .05/5 = .01$) were reported.

Results

The characteristics of the study population are presented in Table 1. Overall mean age was 51.7 years (±13.0), 32% were female, the mean NIHSS on admission was 5.2 (±5.0), and 54% of the patients had a stroke located in the middle cerebral artery territory. Of the 52 patients evaluated at the 3-month follow-up, 15 (29%) had mild to severe depression (BDI-II ≥ 12).

Associations between early-phase HR parameters and demographic characteristics (age, gender), stroke severity (NIHSS at admission and lesion volume), as well as early and chronic phase measures of depression and cognition are summarized in Table 2. Age and gender were

Table 1. *Characteristics of the study population*

	n	%	Mean (SD)	Min	Max
Sample characteristics (n = 56)					
Gender, female	17	32			
Age	54		51.7 (13.0)	24	83
Hypertension, yes	23	43			
Diabetes, yes	2	4			
Dyslipidemia, yes	20	37			
Lesion volume, >15 mm	31	57			
Infarct side: left/right/both	21/28/5	39/52/9			
Vascular territory: MCA/ACA/PCA/Cerebellum/Other	29/2/7/13/3	54/4/13/24/6			
Aphasia, yes	13	24			
Microbleeds, yes	5	9			
Leukoencephalopathy (Fazekas, 1-3)	21	39			
Admission NIHSS score (early phase)	54		5.2 (5.0)	0	19
Modified Rankin Scale (chronic phase)	47		1.2 (1.3)	0	4
Early phase (D_0) depression					
HADS	48		9.8 (6.3)	1	29
SADQ-10	54		3.0 (3.7)	0	14
VAS$_{Depression}$	54		2.0 (2.6)	0	10
Early phase (D_0) cognition					
MoCA	49		25.7 (4.2)	11	30
Chronic phase (D_{90}) depression					
BDI-II	52		7.7 (7.4)	0	36
BDI-II, ≥12 (mild to severe depression)	15	29			
Chronic phase (D_{90}) cognition					
MoCA	47		26.8 (4.2)	8	30
Early phase (D_0) heart rate parameters					
mHR	54		70.47 (10.80)	48.10	93.07
Ln(RMSSD)	54		3.07 (.66)	1.70	4.53
Ln(LF)	54		6.16 (1.12)	3.53	8.69
Ln(HF)	54		4.85 (1.33)	2.26	7.65
Ln(LF/HF)	54		1.31 (.68)	-.21	3.44

Abbreviations: ACA, Anterior Cerebral Artery; BDI-II, Beck Depression Inventory II; HADS, Hospital Anxiety and Depression Scale; HF, high-frequency; LF, low-frequency; MCA, Middle Cerebral Artery; MoCA, Montreal Cognitive Assessment; mHR, mean heart rate; NIHSS, National Institutes of Health Stroke Scale; PCA, Posterior Cerebral Artery; RMSSD, root mean square of successive differences in RR intervals; SADQ, Stroke Aphasic Depression Questionnaire; SD, standard deviation; VAS$_{Depression}$, Visual Analog Scale for depression.

Table 2. *Pearson correlations between heart rate parameters measured in early poststroke phase (D_0) and demographic characteristics (age, gender), stroke severity (NIHSS at admission and lesion volume), as well as cognitive and depression scores obtained in early (D_0) and chronic (D_{90}) poststroke phases*

		Early phase (D_0) heart rate parameters									
		mHR		Ln(RMSSD)		Ln(LF)		Ln(HF)		Ln(LF/HF)	
	n	r	P	r	P	r	P	r	P	r	P
Demography											
Age	54	.063	.653	−.440	**.001***	−.584	**<.001***	−.473	**<.001***	−.035	.800
Gender (1 = male, 2 = female)	54	.353	**.009***	−.247	.072	−.290	**.033**	−.189	.170	−.107	.442
Stroke severity											
NIHSS at admission	54	−.059	.670	.105	.452	.005	.969	.117	.399	−.219	.111
Lesion volume	54	.053	.706	−.109	.433	−.102	.463	−.096	.491	.019	.891
Early phase (D_0)											
Depression											
HADS	48	.477	**.001***	−.276	.057	−.286	**.049**	−.233	.111	−.027	.857
SADQ-10	54	.220	.110	−.325	**.016**	−.365	**.007***	−.342	**.011**	.068	.626
VAS$_{Depression}$	54	.338	**.012**	−.323	**.017**	−.221	.108	−.381	**.004***	.380	**.005***
Global z-score	48	.482	**.001***	−.380	**.008***	−.367	**.010**	−.378	**.008***	.127	.390
Cognition											
MoCA	49	−.038	.797	.066	.651	.215	.138	.093	.523	.166	.255
Chronic phase (D_{90})											
Depression											
BDI-II	52	.318	**.022**	−.229	.102	−.102	.473	−.234	.095	.279	**.046**
Cognition											
MoCA	47	−.266	.071	.325	**.026**	.410	**.004***	.325	**.026**	.002	.991

Abbreviations: BDI-II, Beck Depression Inventory II; HADS, Hospital Anxiety and Depression Scale; HF, high-frequency; LF, low-frequency; MoCA, Montreal Cognitive Assessment; mHR, mean heart rate; NIHSS, National Institutes of Health Stroke Scale; RMSSD, root mean square of successive differences in RR intervals; SADQ, Stroke Aphasic Depression Questionnaire; VAS$_{Depression}$, Visual Analog Scale for depression.

Bold indicates *P* values < .05.

*Correlations that remained significant after Bonferroni correction for the multiple heart rate parameters tested (*P* < .05/5 = .01).

shown to correlate with early-phase HR parameters, whereas NIHSS at admission and lesion volume were not. Furthermore, HR parameters did not differ according to stroke laterality (*P* > .30 for all parameters), and no correlation was observed between MoCA and BDI-II scores at 3 months after stroke (r = −.17, *P* = .256).

In early phase, after controlling for age, gender, NIHSS at admission, and lesion volume, the HADS score was associated with mHR, Ln(RMSSD), and Ln(LF); the SADQ-10 score was associated with Ln(RMSSD) and Ln(HF); the VAS$_{Depression}$ score was associated with mHR, Ln(RMSSD), Ln(HF), and Ln(LF/HF); and the global z-score of depression was associated with mHR, Ln(RMSSD), Ln(LF), Ln (HF), and Ln(LF/HF). The MoCA score was not significantly associated with any HR parameter. The associations between the HADS score and mHR, between the VAS$_{Depression}$ score and Ln(HF) and Ln(LF/HF), and between the global z-score of depression and mHR, Ln(RMSSD) and Ln(HF) remained significant after Bonferroni correction (Table 3).

At the 3-month follow-up, the BDI-II score was predicted by Ln(LF/HF), and the MoCA score was predicted by mHR, Ln(RMSSD), Ln(LF), and Ln(HF). The predictions of the BDI-II score by Ln(LF/HF) and of the MoCA score by Ln(LF) remained significant after Bonferroni correction (Table 3).

Discussion

The present study investigated the relationship between resting HR, depression, and cognition following stroke. It revealed that resting HR measurements performed in early poststroke phase (1) correlate with early-phase measures of depression and (2) predict severity of depressive symptoms and global cognitive functioning 3 months later.

Although reduced HRV is associated with depression[4] and is reported in poststroke patients,[3] only 1 study[6] investigated the relationship between depression and HRV after stroke. This study revealed that the standard deviation of time between normal heart beats (SDNN), a measure of HRV derived from 24-hour Electrocardiography-Holter monitoring, was reduced in depressed versus nondepressed patients 5 months after stroke. Using time-domain (mHR, RMSSD) and frequency-domain (HF, LF,

Table 3. *Prediction of the severity of depressive symptoms and of cognitive functioning in early (D_0) and chronic (D_{90}) poststroke phases by resting heart rate parameters measured in early phase (D_0) using hierarchical regression analyses controlling for age, gender, NIHSS at admission, and lesion volume*

Depressive and cognitive variables predicted by early phase (D_0) heart rate parameters	β	Standard error	Partial correlation	*P* value
Early phase (D_0) depression: HADS				
mHR	0.261	0.076	.469	**.001***
Ln(RMSSD)	−3.123	1.446	−.316	**.037**
Ln(LF)	−2.067	0.974	−.311	**.040**
Ln(HF)	−1.395	0.732	−.282	.063
Ln(LF/HF)	0.596	1.285	.071	.645
Early phase (D_0) depression: SADQ-10				
mHR	0.045	0.042	.155	.281
Ln(RMSSD)	−1.527	0.717	−.294	**.038**
Ln(LF)	−0.884	0.488	−.253	.076
Ln(HF)	−0.903	0.352	−.347	**.014**
Ln(LF/HF)	1.177	0.611	.268	.060
Early phase (D_0) depression: VAS$_{Depression}$				
mHR	0.074	0.031	.323	**.022**
Ln(RMSSD)	−1.458	0.546	−.359	**.010**
Ln(LF)	−0.507	0.387	−.186	.196
Ln(HF)	−0.917	0.262	−.452	**.001***
Ln(LF/HF)	1.815	0.420	.529	**<.001***
Early phase (D_0) depression: Global z-score				
mHR	0.031	0.009	.476	**.001***
Ln(RMSSD)	−0.466	0.166	−.398	**.008***
Ln(LF)	−0.253	0.115	−.321	**.034**
Ln(HF)	−0.247	0.082	−.421	**.004***
Ln(LF/HF)	0.297	0.146	.299	**.048**
Early phase (D_0) cognition: MoCA				
mHR	−0.052	0.056	−.140	.358
Ln(RMSSD)	0.513	1.008	.077	.614
Ln(LF)	0.967	0.664	.217	.153
Ln(HF)	0.324	0.504	.098	.524
Ln(LF/HF)	0.573	0.851	.102	.504
Chronic phase (D_{90}) depression: BDI-II				
mHR	0.167	0.096	.248	.089
Ln(RMSSD)	−2.246	1.729	−.188	.200
Ln(LF)	.317	1.183	.040	.790
Ln(HF)	−1.287	0.861	−.215	.142
Ln(LF/HF)	4.054	1.363	.402	**.005***
Chronic phase (D_{90}) cognition: MoCA				
mHR	−.133	0.052	−.374	**.013**
Ln(RMSSD)	2.193	0.927	.347	**.023**
Ln(LF)	1.683	0.611	.395	**.009***
Ln(HF)	1.047	0.467	.330	**.030**
Ln(LF/HF)	−.566	0.831	−.106	.500

Abbreviations: BDI, Beck Depression Inventory; HADS, Hospital Anxiety and Depression Scale; HF, high-frequency; LF, low-frequency; MoCA, Montreal Cognitive Assessment; mHR, mean heart rate; NIHSS, National Institutes of Health Stroke Scale; RMSSD, root mean square of successive differences in RR intervals; SADQ, Stroke Aphasic Depression Questionnaire; VAS$_{Depression}$, Visual Analog Scale for depression.

*Regressions that remained significant after Bonferroni correction for the multiple heart rate parameters tested ($P < .05/5 = .01$).

LF/HF) measures of resting HR and HRV, our study confirms this association, showing that higher mHR, lower HRV (lower RMSSD, LF, and HF), and higher sympathovagal balance (higher LF/HF) are related to higher severity of depressive symptoms assessed from verbal (HADS) and nonverbal scales (SADQ-10, VAS$_{Depression}$), as early as within the first week after stroke. In particular, the RMSSD, which predominantly reflects parasympathetic activation, is negatively associated with each of the depression scales. Furthermore, higher sympathovagal balance (higher LF/HF) in early phase predicts higher severity of depressive symptoms at the 3-month follow-up.

These findings suggest that resting HR measurements obtained in the early phase could be useful to assess severity of depressive symptoms, especially in patients with aphasia and/or severe cognitive deficits who cannot complete questionnaires, and to detect those with increased risk to develop depression during the chronic phase.

However, it is not clear whether the HR parameters measured within the first week after stroke are related to the stroke or reflect prestroke state of the patients. First, they could be a direct consequence of stroke. Indeed, on the one hand, a more important HRV reduction after right-sided than left-sided stroke has been previously reported[3] and, on the other hand, a cortico-limbic network has been strongly associated with autonomic regulation.[12] Unfortunately, no association between HRV and stroke laterality was observed in our study, and the heterogeneity of stroke location in our small sample size did not allow examining associations between specific locations and HRV. Moreover, no correlation was found between HR parameters and stroke severity (NIHSS at admission and lesion volume), therefore suggesting that stroke itself is not the major cause of HRV.

A second hypothesis could be that HR measurements obtained within the first week after stroke mainly reflect prestroke state of the patients and represent an underlying risk factor for PSD. According to the neurovisceral integration model,[5,12] individual differences in vagal function, as indexed by resting HRV, would reflect capacity of self-regulation and low HRV would be associated with unsuccessful adaptation to stressful events. In line with this hypothesis, several studies showed that low resting HRV increases an individual's vulnerability to develop posttraumatic stress disorder.[13,14] Therefore, we can assume that, in the present study, patients with higher sympathovagal balance before stroke would have more difficulty to overcome stroke consequences, contributing to higher severity of depressive symptoms.

Interestingly, we also found that higher mHR and lower HRV in early poststroke phase predicts lower global cognitive functioning at the 3-month follow-up, supporting the relationship between low vagal tone and poor cognitive functioning reported in the literature.[5] This is also in line with a recent study showing that mHR was a baseline factor predicting poststroke cognition.[15] This association was not observed with the MoCA score measured in early phase, suggesting that cognitive functioning assessed few days after stroke is related to other factors such as handicap or fatigue. The prediction of cognitive functioning in chronic phase by the HR parameters measured in early phase could be explained by the well-known influence of depression on cognitive functioning after stroke.[16] However, no correlation was observed between depression and cognition during chronic phase. We thus cannot rule out the hypothesis that high mHR and low HRV in early phase would have a causal effect on cognitive functioning in chronic phase, possibly mediated by cerebral hypoperfusion. Indeed, it has been recently reported that low resting HRV is associated with reduced whole-brain perfusion,[17] which itself has been related to an increased risk of poststroke dementia.[18]

Altogether, the results of this study suggest that higher mHR, lower HRV, and higher sympathovagal balance in early poststroke phase could be markers of higher vulnerability to develop PSD but also PSCI. However, these results have to be interpreted cautiously and cannot be generalized to all stroke patients due to several limitations. First, the sample size is small, precluding any firm conclusions, but this was a pilot study, first designed to evaluate the feasibility of such approach in stroke patients. Second, heterogeneous scales of depression were used between early and chronic phases, which limits the direct comparison between scales. However, the BDI-II scale that we used to assess depression in chronic phase is not appropriate within the first few days after stroke and was replaced in early phase by the HADS as well as 2 nonverbal scales (SADQ-10, VAS$_{Depression}$) to include patients unable to answer self-administered questionnaires. Third, the resting HR measurement was not performed at the 3-month follow-up, therefore preventing from disentangling causal relationship between cardiac autonomic functioning, depression, and cognitive impairment following stroke. Furthermore, larger multicenter longitudinal studies using neuroimaging techniques are needed to confirm our results and to allow a better understanding of the pathophysiological mechanisms which relate autonomic functioning, mood disorders, and cognitive impairment after stroke.

To conclude, this proof-of-concept pilot study revealed that HR parameters measured at rest in early poststroke phase could be helpful in the prediction of PSD and PSCI, especially when questionnaires cannot be applied due to severe aphasia or cognitive disturbance.

References

1. Ayerbe L, Ayis S, Crichton S, et al. The long-term outcomes of depression up to 10 years after stroke; the South London Stroke Register. J Neurol Neurosurg Psychiatry 2014;85:514-521.
2. Townend E, Brady M, McLaughlan KA. Systematic evaluation of the adaptation of depression diagnostic methods for stroke survivors who have aphasia. Stroke 2007;38:3076-3083.
3. Dütsch M, Burger M, Dörfler C, et al. Cardiovascular autonomic function in poststroke patients. Neurology 2007;69:2249-2255.
4. Kemp AH, Quintana DS, Gray MA, et al. Impact of depression and antidepressant treatment on heart rate variability: a review and meta-analysis. Biol Psychiatry 2010;67:1067-1074.
5. Thayer JF, Hansen AL, Saus-Rose E, et al. Heart rate variability, prefrontal neural function, and cognitive performance: the neurovisceral integration perspective on self-regulation, adaptation, and health. Ann Behav Med 2009;37:141-153.

6. Robinson RG, Spalletta G, Jorge RE, et al. Decreased heart rate variability is associated with poststroke depression. Am J Geriatr Psychiatry 2008;16:867-873.

7. Beck AT, Steer RA, Brown GK. BDI-II, Inventaire de Dépression de Beck, 2ème édition. ECPA 1997;1-51.

8. Bennett HE, Thomas SA, Austen R, et al. Validation of screening measures for assessing mood in stroke patients. Br J Clin Psychol 2006;45:367-376.

9. Nasreddine ZS, Phillips NA, Bedirian V, et al. The Montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc 2005;53:695-699.

10. Antelmi I, De Paula RS, Shinzato AR, et al. Influence of age, gender, body mass index, and functional capacity on heart rate variability in a cohort of subjects without heart disease. Am J Cardiol 2004;93:381-385.

11. Kutlubaev MA, Hackett ML, Part II. predictors of depression after stroke and impact of depression on stroke outcome: an updated systematic review of observational studies. Int J Stroke 2014;9:1026-1036.

12. Thayer JF, Åhs F, Fredrikson M, et al. A meta-analysis of heart rate variability and neuroimaging studies: implications for heart rate variability as a marker of stress and health. Neurosci Biobehav Rev 2012;36: 747-756.

13. Gillie BL, Thayer JF. Individual differences in resting heart rate variability and cognitive control in posttraumatic stress disorder. Front Psychol 2014;5:758.

14. Minassian A, Maihofer AX, Baker DG, et al. Association of predeployment heart rate variability with risk of postdeployment posttraumatic stress disorder in active-duty marines. JAMA Psychiatry 2015;72:979-986.

15. Ankolekar S, Renton C, Sare G, et al. Relationship between poststroke cognition, baseline factors, and functional outcome: data from "efficacy of nitric oxide in stroke" trial. J Stroke Cerebrovasc Dis 2014;23:1821-1829.

16. Hommel M, Carey L, Jaillard A. Depression: cognition relations after stroke. Int J Stroke 2015;10:893-896.

17. Allen B, Jennings JR, Gianaros PJ, et al. Resting high-frequency heart rate variability is related to resting brain perfusion. Psychophysiology 2015;52:277-287.

18. Desmond DW, Moroney JT, Sano M, et al. Incidence of dementia after ischemic stroke results of a longitudinal study. Stroke 2002;33:2254-2262.