Published in final edited form as:
Am J Geriatr Psychiatry. 2008 November ; 16(11): 867–873. doi:10.1097/JGP.0b013e318180057d.

Decreased heart rate variability is associated with poststroke depression

Robert G. Robinson, MD,
Department of Psychiatry, The University of Iowa Carver College of Medicine, Iowa City, IA

Gianfranco Spalletta, MD, PhD,
Laboratory of Clinical and Behavioural Neurology IRCCS Santa Lucia Foundation, Rome, and Department of Neuroscience, Tor Vergata University of Rome, Italy

Ricardo E. Jorge, MD,
Department of Psychiatry, The University of Iowa, Carver College of Medicine, Iowa City, IA

Andrea Bassi, MD,
Laboratory of Clinical and Behavioural Neurology, IRCCS Santa Lucia Foundation, Rome, Italy

Furio Colivicchi, MD,
Cardiovascular Department, San Filippo Neri Hospital, Rome, Italy

Alessandra Ripa, MA, and
Laboratory of Clinical and Behavioural Neurology, IRCCS Santa Lucia Foundation, Rome, Italy

Carlo Caltagirone, MD
Laboratory of Clinical and Behavioural Neurology, IRCCS Santa Lucia Foundation, Rome, and Department of Neuroscience, Tor Vergata University of Rome, Italy

Abstract

Objective—Although decreased heart rate variability (HRV) has been well documented in association with depression following myocardial infarction, this phenomenon has not been studied in patients with stroke. The present study was designed to prospectively assess HR in relationship to depression among patients with acute stroke.

Design—Using 24 hour Holter monitoring, assess HRV.

Setting—A large university rehabilitation hospital.

Participants—patients, with first ever stroke and no other severe physical illness, cigarette smoking or drug therapy that could affect HRV, were evaluated over 24 hours for heart rate variability.

Measurements—Patients were evaluated using the Structured Clinical Interview for depression diagnosis. Severity was assessed by Hamilton Depression Rating Scale. Stroke severity was assessed by the NIH Stroke Scale, the Barthel Index and the Mini Mental State Exam. The standard deviation of time in msec between normal heart beats (SDNN) was the primary measure of HRV.

Results—Among patients with poststroke major or minor depression (N=33), the SDNN was 109 ±32.6 SD compared with nondepressed patients (N=16) whose SDNN was 133.9±40.1 SD(Wilcoxon rank test S=492, p=0.048). The SDNN was significantly and independently related to the existence of depression, but no other intergroup differences.

Correspondence to: Robert G. Robinson.

Corresponding author: Robert G. Robinson, M.D. Department of Psychiatry The University of Iowa 200 Hawkins Dr. Iowa City IA 52242 319-356-1144 robert-robinson@uiowa.edu.

Conclusions—These findings, for the first time, have provided some evidence that both major and minor poststroke depression may lead to decreased HRV. Future research in larger groups of patients should determine whether other measures of HRV more specific to sympathetic-parasympathetic tone are decreased in patients with poststroke depression.

Keywords

heart; arrhythmia; depression; stroke; autonomic nervous system; heart rate variability

Objective

The association of poststroke depression in the elderly with increased mortality has been reported by several investigators during the past 15 years (1-3). These studies have consistently found that increased mortality is associated with mild as well as severe depression (1-4). Another consistent finding is that increased mortality associated with acute poststroke depression is detectable as early as 1 year (1), but lasts for at least 7 years post stroke. (2,3)

Although many explanations could be proposed for the association of poststroke depression with mortality, there is an extensive literature on the association of mortality with decreased heart rate variability (HRV) in patients with coronary heart disease and depression (5,6). Heart rate variability derives in part from interactions between sympathetic and parasympathetic actions on the cardiac pacemaker, as well as other factors such as circadian rhythms, cigarette smoking, medications, etc. Depression, however, may alter the sympathetic-parasympathetic balance in the sinus node leading to decreased heart rate variability (7). Although the majority of studies have reported decreased HRV among depressed patients following acute coronary heart disease, Gehi et al. 2005 (8) reported among patients with past history of heart disease which was now stable, that there were no differences in HRV between patients with current major depression (N=195) or no depression (N=678). This suggests that an acute cardiac event may augment the relationship of depression and HRV.

The association of heart rate variability with poststroke depression has never been examined. In this preliminary prospective study, we hypothesized that patients with poststroke major or minor depression would demonstrate decreased HRV compared with similar nondepressed patients. We selected the standard deviation of normal to normal beats (SDNN) as our primary measure of HRV because it reflects all factors influencing HRV, not just sympathetic-parasympathetic function, and with a relatively small sample, would be the most likely measure to show significant group differences. We hypothesized that patients with poststroke depression would have significantly lower SDNN than nondepressed patients and there would be no other factor in demographics, stroke characteristics or impairment severity that would be associated with lower HRV.

Methods

Subjects

Consecutive inpatients admitted to Santa Lucia Rehabilitation Hospital in Rome, Italy, following acute stroke over a 12-month period were evaluated using the following inclusion/exclusion criteria.

Inclusion:

- Greater than age 50 years and admitted after a first-ever acute stroke without significant impairment of verbal comprehension

Exclusion:

- Clinically significant arrhythmia or heart disease on admission, including atrial fibrillation, congestive heart failure, moderate to severe valvular dysfunction, any form of cardiomyopathy, previous acute myocardial infarction, left ventricular hypertrophy or use of a cardiac pacemaker.
- Use of any pharmacological treatment, including beta-blockers, that could affect the autonomic nervous system, or smoking tobacco (hospital prohibition) within 15 days prior to assessing HRV.
- Major concurrent illness.

The study protocol was approved by the Ethics Committee of Santa Lucia Foundation and written informed consent was obtained. A total of 84 consecutive patients met the inclusion/exclusion criteria, but 35 patients declined because they did not want to undergo a psychiatric interview. Thus, a total of 49 patients (24 men and 25 women; mean age 63.0±13.3 years) provided informed consent and were enrolled in the study. This rate of refusal to participate in a detailed psychiatric interview is typical based on the culture and is consistent with prior studies at this site (9). The patients were about 4 to 5 months post stroke because this is the traditional time in Italy to move from acute to rehabilitation care following stroke.

Neurological and Psychiatric evaluation

Overall stroke severity was assessed using the total score on the National Institutes of Health (NIH) stroke scale (10). Impairments in activities of daily living (ADL) were quantified using the Barthel Index (BI) (11). All patients accepted to Santa Lucia are required to be mobile (walk or use a wheelchair) so they could participate in rehabilitation therapy. Severity of cognitive impairment was assessed using the Mini-Mental State Examination (MMSE) (12).

Patients were examined using the Structured Clinical Interview for DSM-IV diagnoses (SCID) (13). Depression diagnoses included “mood disorder due to stroke with major depressive like episode” or “minor depression” (research criteria). Anxiety diagnoses included “anxiety disorder due to stroke with generalized anxiety.” Patients were also administered the Hamilton Depression Rating Scale (HAM-D-17) (14) as well as the Hamilton Anxiety Rating Scale (HAM-A) (15) which are both reliable and valid measures of severity of depression and anxiety in the poststroke population (16). Family history of psychiatric disorder, previous personal history of psychiatric disorder and history of other physical illnesses was obtained by interviewing the patient and available family members.

HRV evaluation

All patients underwent 24-hour Holter monitoring (HM). Recordings were performed using a 3-channel bipolar recorder and were evaluated after digitization using commercially available software (ELA Medical Synescope version 1.0 analysis system). The beat classification was verified and corrected appropriately by an experienced cardiologist, blinded to clinical details. The following time-domain measures of HRV were obtained by using the continuous data for 24 hours (17):

1. standard deviation of all normal-to-normal RR intervals (SDNN),
2. standard deviation of the averages of all normal-to-normal RR intervals in all 5-minute segments of the entire recording (SDANN),
3. root-mean-square of differences of adjacent normal-to-normal RR intervals (RMSSD),
4. number of normal-to-normal RR intervals differing by more than 50 ms from adjacent interval divided by the total number of all normal-to-normal RR intervals (pNN50).

Neuroimaging studies

Brain MRI scans were obtained more than a month following stroke as part of the patient's poststroke care using a 1.5 Tesla GE scanner. The scans were assessed by a neuroradiologist for lesion location, and any other anomalies. Scans were performed on 30 of the 49 patients. The patients who were not scanned either refused the examination (n=13) or had a contraindication because of metal devices (n=6).

Data analysis

Statistical analyses were performed using the student's t test or Fisher exact test depending upon the sample size. Heart rate variability measures were compared between depressed and nondepressed groups using the Exact Mann-Whitney test. Logistic regression was used to assess the independent effects of relevant variables on heart rate measurements. Correlations were analyzed using Spearman's r.

Results

Among the 49 enrolled patients, 11 met criteria for major depression, 22 for minor depression and 16 were nondepressed. Since our primary outcome variable was the standard deviation of the R to R interval (SDNN), the patients with minor depression (n=22) (SDNN minor dep=109.5±34.1 SD) were compared to patients with major depression (n=11) (SDNN major dep=108.6±30.7 SD). Since these measures were virtually identical, the major depressed and minor depressed groups were combined into a single depression group (n=33).

The background characteristics are shown in Table 1. There was a significantly greater frequency of women in the depressed compared with the nondepressed group. There were no other significant differences. Patients in the depressed group (major depression ± minor depression) had significantly more impaired Barthel Index scores (Table 2). Because the Barthel scores were significantly different between groups, we examined the relationship between Barthel score and severity of depression. Barthel scores did not correlate significantly with Hamilton depression scores (Spearman $r = -0.25$, $n = 49$, $p = 0.087$). We did not have measures of lesion volume, but the depressed patients appeared to have more severe ischemic injury than the nondepressed patients. The Mini-Mental State Examination, however, was not significantly different between groups.

Of the depressed group 36.4% met criteria for GAD while none did in the nondepressed group (Fisher exact, p=.0046).

There were no significant differences between the nondepressed and the depressed patients in the frequency of diabetes, hypertension, right versus left hemisphere stroke, frequency of motor symptoms, sensory symptoms or visual field defects, or ischemic versus hemorrhagic strokes (Table 3). Brain MRI scans, obtained in 30 of the 49 patients, showed no statistically significant differences between groups for any lesion locations (i.e. cortical, insular, basal ganglia, thalamus or brainstem) (Table 4).

The measurements of heart rate variability in the depressed and nondepressed groups are shown in Table 5. Because the distribution of individual measures deviated slightly from normality (the data, however, were not skewed), we analyzed our findings using non-parametric statistics. Using the Exact Mann-Whitney test, we found a significant difference between the depressed and nondepressed on SDNN (Table 5). Although we also found significant intergroup differences in SDNN-cut comparing the frequency of scores in the depressed and nondepressed groups below a cutoff measure, the other measures of heart rate variability did not show statistically significant group differences. All measures, however, were lower in the depressed than the nondepressed patients. Although the HRV measures were highly correlated with each

other using Spearman's r correlation analysis (e.g. n=49, SDANN-SDNN, r=0.84, p=0.001, RMSSD-SDNN, r=0.45, p=0.001), SDNN did not significantly correlate with impairment scores Ham-A, r=-0.069, p=0.64; (Ham-D, r= -0.17, p=0.25; Barthel r=0.19, p=0.19; or Mini Mental r=-0.012, p=0.94).

There were 3 patients in each group with prior personal history of psychiatric disorder (i.e., 4 depressions, 2 unknown type). We, therefore, reanalyzed our findings excluding these 6 patients. Thus, all patients in the depressed group had their first ever depression following the stroke. The Exact Mann-Whitney test continued to show significant intergroup difference (s=362.5, p=0.004).

In order to determine whether depression diagnosis was an independent correlate of HRV, significant intergroup differences were controlled in a multiple linear regression including gender, Barthel Index, time since stroke and depression or anxiety diagnosis. The only significant factor independently associated with SDNN was depression (F=5.24, df=1,47, p=0.027). This finding supports our primary hypothesis proposed at the beginning of the study that SDNN would be lower in depressed patients and that no other background or impairment measure would be related to this measure of HRV.

Conclusion

This study has demonstrated for the first time that patients with poststroke major or minor depression, examined at approximately 4-5 months following first-ever acute stroke, had significantly reduced 24 hour heart rate variability, as measured by the standard deviation of normal to normal heart beat intervals (SDNN), compared with nondepressed patients.

Before discussing these findings, the methodological limitations of the study need to be acknowledged. First, patients included in the study were examined cross-sectionally. We therefore do not know the onset, duration or outcome of decreased heart rate variability. Second, the patients in the depressed group were predominantly women while the nondepressed group was predominantly men. Gender, however, was not independently associated with decreased heart rate variability. Third, the only measure of HRV which was significant was SDNN. Fourth, 35 of 84 consecutive patients meeting inclusion criteria refused a psychiatric interview and 24 hour Holter monitor and 67% of this sample was depressed. Thus, the patients who refused to participate may have produced a bias in our sample and our findings may not be applicable to all stroke patients. Although the refusal rate and depression rate were high, they were within the ranges previously reported in this population (9). Finally, this was a relatively small study lacking power to show other changes in HRV besides SDNN. Thus, larger studies of this interesting, potentially important, phenomenon need to be done.

Although we are unaware of anyone previously examining HRV in relationship to depression following stroke, there are a few studies of HRV following stroke (18,19). Korpelainen et al. (18), for example, examined HRV in 31 consecutive patients during the acute phase following hemispheric stroke and at 1 and 6 months follow-up. Using both time based (e.g. SDNN) and frequency domain (e.g. very low frequency power) measurements of HRV, patients with hemispheric infarction had abnormal HRV compared with 31 age and sex matched healthy controls. Furthermore, Makikallio et al. (19) examined 84 patients following acute stroke and measured their HRV. At 7 years follow-up, multivariate analysis showed that abnormalities in the spectral characteristics over ultra low and very low frequency bands was the best predictor of death (Hazard ratio=3.8; 95% CI=1.8-8.2, p<0.001). Neither of these studies, however, examined for effects of depression. Depression likely was present in a significant number of these patients (20).

Among patients with coronary heart disease, however, there is an extensive literature on depression, HRV, and mortality. Carney et al. (21) found that, among 311 patients with depression following acute myocardial infarction, 27% of all cause mortality during 30 months of follow-up was attributable to the effect of depression on the log of very low frequency power (95% CI, 0.23-0.31, p<.001). Thus, the effect of depression on mortality following myocardial infarction is partially mediated by HRV among patients with coronary heart disease.

Among patients with stroke, depression is a frequent clinical finding. An analysis of the pooled data from the world's literature found that the mean prevalence of major depression among patients who were hospitalized for acute stroke or rehabilitative care was 21.6% (n=2769 stroke patients examined) and 20.0% for minor depression (i.e. subsyndromal major depression). Although the cause of poststroke depression is not known, a number of factors have been significantly associated with this disorder including severity of impairment in activities of daily living and cognitive function, social support, personal history, family history and personality traits (20). In addition, however, acute poststroke depression has been associated with lesion location (22,23). During the first two months following stroke, major depression has been associated with lesions of the left frontal cortex or left basal ganglia (20,24) and severity of depression was significantly correlated with the proximity of the left hemisphere lesion to the frontal pole (25).

We have also previously reported that, among 104 acute poststroke patients treated for 12 weeks with fluoxetine or nortriptyline, the survival rate at 7 to 9 years follow-up was 59% (42 of 71) compared to 36% (12 of 33) for placebo treated patients (Kaplan Meyer survival analysis p=0.03) (26). Although fluoxetine was not an effective treatment for depression, the survival rate was identical whether the patients received nortriptyline or fluoxetine or whether they were depressed or nondepressed when they were treated (26).

Among patients with coronary artery disease, treatment of depression has sometimes reversed this change in HRV but other times it has not. Carney et al. (27), for example, showed that daytime RMSSD, but not other indices, improved to control levels among the severely depressed heart disease patients given cognitive behavioral therapy. Both Roose et al. (28) and Davidson et al. (29), however, showed that antidepressant drugs which inhibit norepinephrine as well as serotonin reuptake led to further decreases in heart rate variability compared with selective serotonin reuptake inhibitors which had no demonstrable effect. Glassman et al. (30) recently reported that HRV showed a partial non-significant improvement after 16 weeks of sertraline or mood improvement, but patients given placebo showed a further decrease in HRV compared to pretreatment levels over 16 weeks of treatment. Thus, the duration of continued depression after acute myocardial infarction may worsen HRV.

These findings, along with those reported in patients with acute stroke, raise the issue of whether this protective effect of antidepressants is related to their effect on depression, which seems unlikely, or to changes in HRV or some other mechanism.

In summary, this preliminary study has demonstrated for the first time that decreased heart rate variability was associated with poststroke depression. Larger longitudinal studies are needed to confirm this finding using both time based and frequency domain measures of HRV. The ultimate question, however, is whether poststroke depression leads to increased long term mortality through changes in HRV.

Acknowledgements

All sources of support: This work was supported in part by a grant from Santa Lucia Hospital and NIH grant R01-MH-65134.

References

1. House A, Knapp P, Bamford J, Vail A. Mortality at 12 and 24 months after stroke may be associated with depressive symptoms at 1 month. Stroke 2001;32(3):696–701. [PubMed: 11239189]
2. Williams LS, Ghose SS, Swindle RW. Depression and other mental health diagnoses increase mortality risk after ischemic stroke. Am J Psychiatry 2004;161(6):1090–5. [PubMed: 15169698]
3. Morris PLP, Robinson RG, Andrezejewski P, Samuels J, Price TR. Association of depression with 10-year post-stroke mortality. Am J Psychiatry 1993;150:124–129. [PubMed: 8417554]
4. Morris PLP, Robinson RG, Samuels J. Depression, introversion and mortality following stroke. Aust N Z J Psychiatry 1993;27(3):443–449. [PubMed: 8250788]
5. Carney RM, Rich M, TeVelde A, Saini J, Clark K, Freedland KE. The relationship between heart rate, heart rate variability and depression in patients with coronary artery disease. J Psychosom Res 1988;32:159–164. [PubMed: 3404497]
6. Carney RM, Blumenthal JA, Stein PK, Watkins L, Catellier D, Berkman LF, Czajkowski SM, O'Connor C, Stone PH, Freedland KE. Depression, heart rate variability, and acute myocardial infarction. Circulation 2001;104(17):2024–2028. [PubMed: 11673340]
7. Dalack GW, Roose SP. Perspectives on the relationship between cardiovascular disease and affective disorder. J Clin Psychiatry 1990;51(suppl):4–9. [PubMed: 2195012]
8. Gehi A, Mangano D, Pipkin S, Browner WS, Whooley MA. Depression and heart rate variability in patients with stable coronary heart disease: findings from the Heart and Soul Study. Arch Gen Psychiatry 2005;62(6):661–6. [PubMed: 15939843]
9. Spalletta G, Guida G, De Angelis D, Caltagirone C. Predictors of cognitive level and depression severity are different in patients with left and right hemispheric stroke within the first year of illness. J Neurol 2002;249(11):1541–1551. [PubMed: 12420095]
10. Kunitz SC, Gross CR, Heyman A, Kase CS, Mohr JP, Price TR, Wolf PA. The pilot stroke data bank: Definition, design and data. Stroke 1984;15(4):740–746. [PubMed: 6464070]
11. Mahoney FI, Barthel DW. Functional evaluation: Barthel index. Md Med J 1965;14:61–65.
12. Folstein MF, Folstein SE, McHugh PR. Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. J. Psychiatr. Res 1975;12:189–198. [PubMed: 1202204]
13. Spitzer, RL.; Williams, JBW.; Gibbon, M. Structured Clinical Interview for DSM-IV (SCID). Biometric Research, New York State Psychiatric Institute; New York: 1995.
14. Hamilton MA. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960;23:56–62. [PubMed: 14399272]
15. Hamilton M. The assessment of anxiety state of rating. Br. J. Med. Psychol 1959;32(1):50–55. [PubMed: 13638508]
16. Castillo CS, Starkstein SE, Fedoroff JP, Price TR, Robinson RG. Generalized anxiety disorder following stroke. J Nerv Ment Dis 1993;181:100–106. [PubMed: 8426166]
17. van der Kooy KG, van Hout HP, van Marwijk HW, de Haan M, Stehouwer CD, Beekman AT. Differences in heart rate variability between depressed and non-depressed elderly. Int J Geriatr Psychiatry 2006;21(2):147–50. [PubMed: 16416460]
18. Korpelainen JT, Sotaniemi KA, Huikuri HV, Myllya VV. Abnormal heart rate variability as a manifestation of autonomic dysfunction in hemispheric brain infarction. Stroke 1996;27(11):2059–63. [PubMed: 8898816]
19. Makikallio AM, Makikallio TH, Korpelainen JT, Sotaniemi KA, Huikuri HV, Myllyla VV. Heart rate dynamics predict poststroke mortality. Neurology 2004;62(10):1822–6. [PubMed: 15159485]
20. Robinson, RG. The Clinical Neuropsychiatry of Stroke. Cambridge University Press; Cambridge: 2006.
21. Carney RM, Blumenthal JA, Freedland KE, Stein PK, Howells WB, Berkman LF, Watkins LL, Czajkowski SM, Hayano J, Domitrovich PP, Jaffe AS. Low heart rate variability and the effect of depression on post-myocardial infarction mortality. Arch Intern Med 2005;165(13):1486–1491. [PubMed: 16009863]
22. Robinson RG, Kubos KL, Starr LB, Rao K, Price TR. Mood disorders in stroke patients: importance of location of lesion. Brain 1984;107(Pt 1):81–93. [PubMed: 6697163]

23. Finset A, Goffeng L, Landro NI, Haakonsen M. Depressed mood and intrahemispheric location of lesion in right hemisphere stroke patients. Scand J Rehabil Med 1989;21:1–6. [PubMed: 2711134]

24. Starkstein SE, Robinson RG, Price TR. Comparison of cortical and subcortical lesions in the production of post-stroke mood disorders. Brain 1987;110:1045–1059. [PubMed: 3651794]

25. Narushima K, Kosier JT, Robinson RG. A reappraisal of post-stroke depression, intra and inter-hemispheric lesion location using meta-analysis. J Neuropsychiatry Clin Neurosci 2003;15(4):422–430. [PubMed: 14627768]

26. Jorge RE, Robinson RG, Arndt S, Starkstein SE. Mortality and post-stroke depression: A placebo controlled trial of antidepressants. Am J Psychiatry 2003;160(10):1823–1829. [PubMed: 14514497]

27. Carney RM, Freedland KE, Stein PK, Skala JA, Hoffman P, Jaffe AS. Change in heart rate and heart rate variability during treatment for depression in patients with coronary heart disease. Psychosom Med 2000;62(5):639–47. [PubMed: 11020093]

28. Roose SP, Glassman AH, Attia E, Woodring S, Giardina EG, Bigger JT Jr. Cardiovascular effects of fluoxetine in depressed patients with heart disease. Am J Psychiatry 1998;155:660–665. [PubMed: 9585718]

29. Davidson J, Watkins L, Owens M, Krulewicz S, Connor K, Carpenter D, Krishnan R, Nemeroff C. Effects of paroxetine and venlafaxine XR on heart rate variability in depression. J Clin Psychopharmacol 2005;25(5):480–4. [PubMed: 16160626]

30. Glassman AH, Bigger JT, Gaffney M, Van Zyl LT. Heart rate variability in acute coronary syndrome patients with major depression: influence of sertraline and mood improvement. Arch Gen Psychiatry 2007;64(9):1025–31. [PubMed: 17768267]

Table 1

Demographics

	Not-depressed (n=16)	Depressed (n=33)	Test used	P value
Female N(%)	4 (25.0)	21 (63.6)	Fisher's exact	0.016
Mean (SD)				
Age (years)	62.2 (10.8)	63.8 (13.3)	t=0.41	0.689
Education (years)	9.2 (5.7)	12.4 (5.1)	t=1.98	0.053
Time since stroke (days)	139.3 (164.5)	157.9 (235.7)	t=0.28	0.779
Personal history of psychiatric disorder N (%)	3 (18.8)	3 (9.1)	Fisher's exact	0.377
Family history of psychiatric disorder N (%)	1 (6.3)	4 (12.1)	Fisher's exact	1.0

Table 2

Psychiatric variables

	Not-depressed (n=16)	Depressed (n=33)	Test used	P value
Diagnosis N (%)				
General Anxiety Disorder	0 (0.0)	12 (36.4)	Fisher's Exact	0.005
Minor Depression	0	22 (66.7)	Fisher's Exact	0.001
Major Depression	0	11 (33.3)	Fisher's Exact	0.001
Severity measures-Mean (SD)				
HAM-A	6.3 (2.5)	11.8 (3.9)	t=5.12	0.001
HAM-D-17	5.7 (2.4)	13.0 (3.9)	t=6.81	0.001
CGI	1.3 (0.7)	3.8 (0.9)	t=10.01	0.001
Barthel Index	65.3 (34.0)	44.2 (25.5)	t=2.43	0.019
MMSE	25.4 93.4)	24.4 (4.9)	t=0.77	0.446

CGI-Clinical global impression, MMSE-Mini Mental State Exam

Table 3

Neurological and medical history

N (%)	Not-depressed (n=16)	Depressed (n=33)	Test used	P value
Neurological findings				
Hemisphere of infarction: left	7 (43.8)	12 (36.4)	χ^2= 4.70	0.095
Any motor symptoms	16 (100.0)	32 (97.0)	Fisher's	1.0
Sensory symptoms	11 968.7)	19 (57.6)	Fisher's	0.541
Visual field deficits	1 (6.3)	8 (24.2)	Fisher's	0.238
Type of stroke				
Ischemic	12 (75.0)	27 (81.8)	Fisher's	0.708
Co-morbid medical history				
Diabetes	2 (12.5)	7 (21.2)	Fisher's	0.698
Hypertension	12 (75.0)	23 (69.7)	Fisher's	1.0

Table 4

Stroke lesion locations

	Not-depressed (n=8)	Depressed (n=22)	Test used	P value
Left hemisphere (%)	3 (37.5)	19 (40.9)	Fisher's	0.92
Cortical (%)	3 (37.5)	14 (63.6)	Fisher's	0.24
Insular (%)	2 (25)	9 (40.9)	Fisher's	0.67
Basal ganglia (%)	4 (50)	16 (72.7)	Fisher's	0.38
Thalamus (%)	3 (37.5)	14 (63.6)	Fisher's	0.30
Brainstem (%)	1 (12.5)	5 (22.7)	Fisher's	0.59

Table 5

Heart rate variability measures

N (%)	Not-depressed (n=16)	Depressed (n=33)	Exact Mann-Whitney Scores	p-value
SDNN-cut	3 (18.8)	16 (48.5)	χ^2=4.01	0.045
Mean (SD)				
SDNN	133.9 (40.1)	109 (32.6)	S=492	0.048
SDANN	106.5 (24.2)	95.1 (37.9)	S=469	0.141
RMSSD	63.0 (72.6)	38.3 (30.0)	S=457	0.228
SDNN index	60.7 (35.1)	48.0 (31.3)	S=486	0.066
Heart rate	68.9 (8.8)	72.6 (12.5)	S-385	0.765