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Personality and Vulnerability to Depression in Stroke Patients

A 1-Year Prospective Follow-Up Study

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Background and Purpose—Depression is a frequent sequela of stroke that negatively interferes with rehabilitation outcome. Personality traits have been neglected as potential vulnerability factors for poststroke depression (PSD). In a 1-year prospective study, the influence of the 5 main personality traits (ie, neuroticism, extraversion, openness, agreeableness, and conscientiousness) on the development of PSD was studied.

Methods—One month after stroke, 190 consecutive patients with a first-ever supratentorial infarct were asked to complete a personality inventory, the NEO-Five Factor Inventory, which is based on the Five Factor Model of personality. Depressive symptoms were assessed 1, 3, 6, 9, and 12 months after stroke with 3 self-rating questionnaires as screening instruments for depression. PSD was diagnosed as major or minor depression through the use of the Structured Clinical Interview from the *Diagnostic and Statistical Manual of Mental Disorders*.

Results—The 1-year cumulative incidence of depression was 38.7%. Cox regression analysis showed that patients with high neuroticism scores had a 4.6-times-higher risk of developing PSD than patients with low neuroticism scores ($P=0.001$) regardless of lesion location. Level of handicap was the only other factor that showed an independent effect on the occurrence of PSD.

Conclusions—Neuroticism is an important predictor of PSD, a finding that emphasizes the need to take personality into account as a potential vulnerability factor for depression in stroke patients. Research on PSD should aim at delineating the interplay between neurological and psychological factors in the development of PSD. (*Stroke*. 2002;33:2391-2395.)

Key Words: depression ■ personality ■ risk factors ■ stroke, ischemic

Research into the determinants of poststroke depression (PSD) has to a large extent focused on specific biological stroke-related factors, in particular lesion location.¹ Although recent systematic reviews did not support the hypothesis that left hemisphere strokes increase the risk for PSD,^{2,3} Vataja et al⁴ reported new evidence from a large MRI-based study ($n=275$) showing that lesions affecting the prefrontal subcortical circuits, especially on the left side, are associated with PSD.

Recent evidence also suggests that in addition to (neuro)biological factors, psychological factors deserve further exploration. With reference to a recent publication on the effect of psychological distress on the risk of suffering a fatal stroke,⁵ Carney and Freedland⁶ discussed several mechanisms through which psychological distress and stroke are related. They suggested that psychological distress, a collective noun for a number of negative mood states, might interact with cerebrovascular disease in determining the course and prognosis of stroke rather than be the primary causal factor in the pathogenesis of (fatal) stroke. Analogous to this, the tendency to experience negative mood states, in psychological terms called neuroti-

cism⁷ or negative affectivity,⁸ may interact with stroke, thereby facilitating PSD. In a cross-sectional study including 90 patients, Morris et al^{9,10} linked neuroticism to PSD using a shortened version of the Neuroticism Inventory of Eysenck. However, personality traits as risk factors for PSD should preferably be studied prospectively in a large cohort and with a general assessment of personality traits.

In the present prospective study, a cohort of 190 patients was followed up for 1 year after a first-ever ischemic stroke. Personality was assessed 1 month after stroke with the NEO-Five Factor Inventory (NEO-FFI).⁷ The purpose of the study was to examine whether specific personality traits are a risk factor for PSD.

Patients and Methods

Patients

Between September 1, 1997, and September 1, 1999, 444 consecutive patients were diagnosed with a first-ever supratentorial infarct at the Emergency Department and the Ambulatory Neurology Clinic of the University Hospital of Maastricht (the Netherlands). This university hospital, the only hospital in the region, serves ≈200 000

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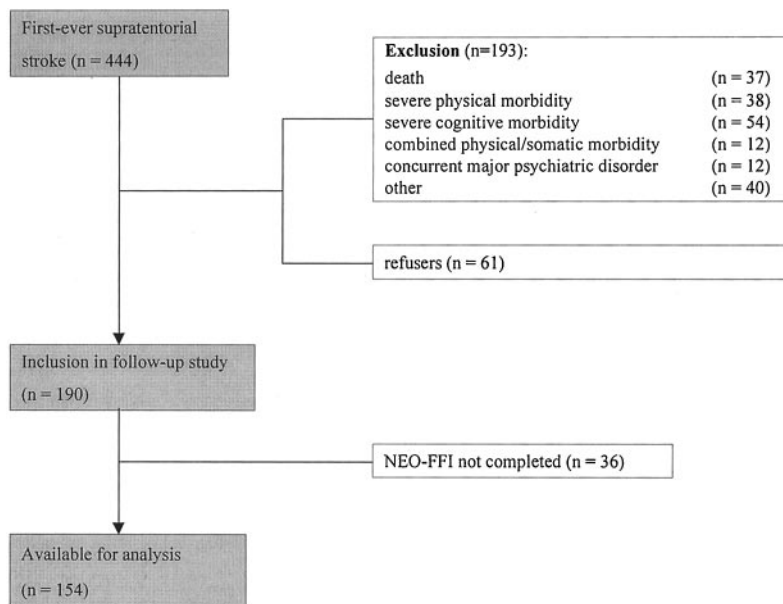


Figure 1. Patient selection and recruitment.

inhabitants. Stroke was diagnosed by a neurologist according to the World Health Organization criteria.¹¹ The ischemic nature of stroke was verified by CT. Differentiation between left- and right-sided stroke was based on CT data and/or clinical presentation.

One hundred ninety-three patients (43.5%) were excluded, mainly because of severe comorbidity. Exclusion of patients who were unable to communicate reliably (eg, because of severe aphasia or cognitive dysfunction) was based on combined clinical judgment and Mini Mental State Examination (MMSE) and Frenchay Aphasia Screening Test (FAST) results (see the Level of Disability section). Reasons for exclusion are shown in Figure 1.

Of the remaining 251 eligible stroke patients, 61 refused participation (24.3%). Refusers were somewhat older than participants (72.4 ± 9.7 versus 68.6 ± 11.7 years; $t=2.6$, $P=0.01$). No sex difference was found between these 2 groups. Moreover, 35 refusers (57.4%) who were willing to fill out 2 psychiatric self-rating scales (the 90-item Symptom Check List [SCL-90] and Hospital Anxiety and Depression Scale [HADS]; see below) did not report significantly more depressive symptoms than participants.

Thus, 190 stroke patients participated in the study. Major characteristics of this cohort are summarized in Table 1. All participants gave written, informed consent. The study was approved by the Medical Ethics Committee of the University Hospital Maastricht.

Initial Assessment of Depression

All patients were followed up during the first year after stroke. PSD was defined as an episode of major or minor depression according to *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV) criteria¹² on at least 1 assessment during the 1-year follow-up period. After 1 month, all patients were interviewed by use of both the depression section of the Structured Clinical Interview for DSM-IV (SCID-I-R)¹³ and the Hamilton Depression Rating Scale (HAM-D).¹⁴ The SCID is a structured psychiatric diagnostic interview allowing DSM-IV diagnosis of major or minor depression. The HAM-D is a clinical rating scale that measures the severity of depressive symptoms. All interviews were administered by the same clinician (I.A.), who was trained to use these instruments. No formal test of interrater reliability was performed.

Follow-Up Assessment of Depression

At 3, 6, 9, and 12 months after stroke, patients were asked to complete 3 psychiatric self-rating scales to screen for depression. These were the Beck Depression Inventory (BDI), HADS, and SCL-90. Cutoff levels were >9 for the BDI and >7 for both the depression and anxiety subscales of the HADS. For the depression

subscale of the SCL-90, the threshold was >22 for men and >27 for women. The predictive validity of these instruments in this cohort was analyzed previously.¹⁵ The sensitivity of this screening procedure was shown to be 93.8% at the 1-month assessment.

Patients whose scores exceeded the cutoff value for at least 1 of the self-rating scales were reinterviewed with the SCID and HAM-D to diagnose major or minor depression. In 50% of these patients, the interview was administered within 2 weeks; in 75%, within 3 to 3.5 weeks.

In 18 patients, the follow-up assessment of depression was incomplete, while the event of interest (depression) had not yet occurred. Of these, 7 withdrew their consent, 4 died, 4 had comorbidity that was too severe, and 3 did not respond at the final assessment (12 months).

Personality

Personality was assessed 1 month after stroke with the NEO-FFI,⁷ which has been translated into Dutch.¹⁶ This self-report questionnaire consists of 60 statements covering the 5 main dimensions of personality: neuroticism, extraversion, openness to new experiences, agreeableness, and conscientiousness. Neuroticism has been related to depression most frequently¹⁷ and is defined as a stable disposition to experience psychological distress across time and situations consisting of negative emotions such as fear, anger, and frustration.⁷ Each statement is rated on a 5-point scale ranging from "strongly disagree" to "strongly agree," resulting in total dimension scores between 12 and 60.

Nonresponse concerning the assessment of personality occurred for 36 patients (18.9%) because of either study withdrawal or difficulty completing the NEO-FFI.

Level of Disability

The MMSE¹⁸ and FAST¹⁹ were administered 1 month after stroke to measure global cognitive functioning. At the same time, level of disability and handicap were rated with the Barthel Index²⁰ and Rankin score,²¹ respectively. Data concerning demographics, level of education, living situation, and family history of psychiatric disorders were also collected. Personal history of depression was measured with the SCID-I-R.

Statistical Analysis

Cox regression was used to analyze the relative hazard of increasing scores for the 5 dimensions of personality (as measured with the NEO-FFI) on the incidence of PSD (major and minor depression combined). Personality traits were entered into the analysis as

TABLE 1. Demographic and Outcome-Related Characteristics of Stroke Patients Included in the Study

| | |
|--|-----------|
| Female sex, % | 46.8% |
| Age, y | |
| Mean±SD | 68.6±11.7 |
| Range | 36–89 |
| Level of education, % | |
| Primary school | 42.2 |
| Junior secondary vocational education | 25.8 |
| Senior secondary vocational education | 19.0 |
| (Pre)university education | 13.0 |
| Living alone, % | 35.7 |
| Stroke lesion location, % | |
| Left | 46.8 |
| Right | 53.2 |
| MMSE | |
| Median | 26 |
| Minimum | 16 |
| Maximum | 30 |
| ≤23, % | 21.5 |
| FAST | |
| Median | 27 |
| Minimum | 9 |
| Maximum | 30 |
| Barthel | |
| Mean | 17.4 |
| SD | 4.7 |
| Median | 20 |
| Rankin | |
| Mean | 2.4 |
| SD | 1.2 |
| Median | 2 |
| Personal history of depression, % | 21.8 |
| Family history of depression, % | 20.1 |
| Family history of other psychiatric disorders, % | 43.3 |

MMSE minimum score=0, maximum score=30; FAST minimum score=0, maximum score=30; Barthel Index (completely dependent in activities of daily living=20; no disabilities=0); Rankin (no handicaps=0, bedridden=5). n=190.

independent variables, and sex, age, history of depressive disorder, and level of handicap (Rankin score) were added as potential confounders. Both forward and backward stepwise modeling procedures were applied to optimize the model. The likelihood ratio statistic based on the maximum partial likelihood estimate was used for variable entry and

removal. The criterion for entry or removal was set at $P<0.05$. The output of the Cox analyses was checked for instability by influential cases and for violation of both the proportional-hazards assumption and the assumption of linearity of effects.

Post hoc, SCL-90 total scores for the 1-month assessment were entered into the optimized model as a measure of distress. Although neuroticism refers to a stable disposition to experience psychological distress across time and situations, distress refers to the momentary level of distress and is more dependent on situational characteristics. In additional post hoc analyses, incident cases of depression 1 month after stroke were excluded from the analysis to ensure that the effects were not due to depression affecting the personality assessment. Potential effects of side of stroke lesion (left versus right hemisphere) and sex on associations between personality dimensions and depression were also tested.

For group comparisons of descriptive sample characteristics, Student's *t* test was used in the case of continuous, normally distributed variables. The χ^2 test was used for all dichotomous variables. Level of significance was set at $P<0.05$ (2 tailed) for all analyses. When appropriate, results are given as mean±SD.

Results

Personality Traits and Depression

The 1-year cumulative incidence of depression was 38.7% (adjusted for patients with incomplete follow-up). Cross-sectionally, the incidence rates were 21.6% (41 of 190) at 1 month, 5.1% (7 of 137.5) at 3 months, 6.0% (7 of 117) at 6 months, 5.6% (6 of 107) at 9 months, and 7.1% (7 of 98) at 12 months. Of these, 41 patients (23.3%) met DSM-IV criteria for major depressive disorder, and 27 (15.4%) met criteria for minor depressive disorder. The mean HAM-D score was 19.2±4.1 for patients with major depression, 13.2±4.3 for patients with minor depression, and 7.3±4.1 for nondepressed patients. These differences were statistically significant ($F=198.2, P<0.001$).

Mean personality domain scores measured 1 month after stroke, as well as the concordant hazard ratios (HRs) from bivariate Cox regression analyses, indicating the relative risk to develop depression at any time during the 1-year follow-up, are shown in Table 2. Neuroticism scores ranged from 12 to 46 (mean±SD, 30.1±7.3). On average, depressed patients (both major and minor) scored 5 points higher on the neuroticism scale than nondepressed patients or patients with incomplete follow-up (censored cases). On bivariate Cox regression analysis, each 1-point increase in neuroticism score increased the relative hazard (HR) for PSD (major and minor depression combined) by 8% ($P=0.0001$). This means that a patient who scored 1 SD above the mean had a relative risk of 1.75 of developing PSD compared with someone with an average neuroticism score.

TABLE 2. Mean Personality Domain Scores (NEO-FFI) and HRs From Bivariate Cox Regression

| | Neuroticism | Extraversion | Openness | Altruism | Conscientiousness |
|------------------|-------------|--------------|----------|----------|-------------------|
| Major depression | 33.5±7.3 | 37.6±6.5 | 31.2±6.3 | 44.5±5.7 | 44.8±5.9 |
| Minor depression | 33.3±6.7 | 37.3±7.6 | 33.5±6.0 | 45.0±3.4 | 45.1±4.7 |
| No depression | 28.3±6.4 | 40.1±4.8 | 33.6±6.1 | 43.5±5.0 | 45.5±5.3 |
| Censored | 28.2±8.6 | 38.1±5.3 | 30.3±6.8 | 46.5±5.8 | 45.7±5.6 |
| HR | 1.08 | 0.94 | 0.98 | 1.02 | 0.98 |
| <i>P</i> | 0.0001 | 0.01 | 0.36 | 0.41 | 0.50 |

n=154. Censored indicates cases with incomplete follow-up.

TABLE 3. Multivariate Cox Regression Analysis of the 5 Personality Traits of the NEO-FFI as a Risk Factor for PSD at Any Time Point During the First Year After Stroke, Controlling for Age, Sex, Personal History of Depression, and Level of Handicap

| | HR | 95% CI | P |
|-------------------------|------|-----------|--------|
| Full model | | | |
| Neuroticism | 1.08 | 1.03–1.13 | 0.003 |
| Extraversion | 0.98 | 0.93–1.04 | 0.56 |
| Openness | 0.99 | 0.95–1.04 | 0.79 |
| Altruism | 1.04 | 0.98–1.10 | 0.24 |
| Conscientiousness | 1.02 | 0.97–1.08 | 0.51 |
| Age | 1.00 | 0.97–1.02 | 0.80 |
| Sex | 1.23 | 0.69–2.22 | 0.48 |
| History of depression | 1.50 | 0.76–2.93 | 0.24 |
| Level of handicap | 1.36 | 1.03–1.79 | 0.03 |
| Stepwise-obtained model | | | |
| Neuroticism | 1.08 | 1.04–1.12 | 0.0001 |
| Level of handicap | 1.36 | 1.08–1.72 | 0.01 |

HR indicates the relative risk-increasing effect for each 1-point increase in the value of the covariate. n=154.

Depressed patients had scores for extraversion about 3 points lower than those of nondepressed patients. Overall, scores on this scale ranged from 20 to 54 (mean±SD, 38.9±5.8). For each 1-point-lower score for extraversion, the HR for PSD increased by 6% ($P=0.005$). The other domains of the NEO-FFI did not show significant bivariate effects on the risk of PSD.

Multivariate Cox Regression Analysis

If all domains of the NEO-FFI were entered into the analysis, together with the controlling variables sex, age, history of depression, and level of handicap (Rankin), the effect of a high level of neuroticism remained statistically significant ($P=0.006$), whereas the effect of a low level of extraversion disappeared (Table 3). Level of handicap was the only covariate that showed an independent significant effect ($P=0.03$). Both forward and backward stepwise modeling resulted in the same model involving only neuroticism and level of handicap (Table 3).

In addition, the above-described model was reanalyzed using 3 categories for both neuroticism and Rankin Scale scores. To create categories of similar size, the tertiles of the observed values were used as cutoff points. For neuroticism, this resulted in low (≤ 26), intermediate (27 to 33), and high (≥ 34) categories. In the case of Rankin, this resulted in categories of 0 to 1, 2 to 3, and 4 to 5. For convenience, this model was used to show the effect of neuroticism in Figure 2.

Entry of the total SCL-90 score as a measure of distress into the analysis did not diminish the effect of neuroticism as measured with the NEO-FFI ($P=0.02$), nor did removal of those patients who already suffered from depression at 1 month after stroke when the NEO-FFI was administered ($P=0.007$).

Post Hoc Analysis: Effect of Lesion Location, Sex, and MMSE

Eighty-nine patients (46.8%) had a left-sided stroke, and 101 patients (53.2%) had a right-sided stroke. PSD was not more frequent in left-sided strokes (45.7%) than in right-sided strokes (41.4%; $\chi^2=0.3$; $P=0.59$), and lesion location was not related to personality domain scores ($P>0.6$ for each of the 5 NEO-FFI domains). Most importantly, the side of the stroke lesion (left versus right hemisphere) did not change the risk-increasing effect of neuroticism on PSD.

Further post-hoc analysis to see whether patient sex influenced the relationship between high level of neuroticism and depression revealed an interaction effect after removal of 3 outliers (HR, 0.90; $P=0.03$) and showed that the effect of neuroticism was stronger in men than in women.

Finally, no significant relation was found between MMSE scores and PSD ($t(134)=1.1$, $P=0.29$). Higher MMSE scores were associated with more extraversion and openness to experience and with less neuroticism, agreeableness, and conscientiousness ($r^2=0.15$ to 0.23, $P=0.06$ to 0.004).

Discussion

This study showed that neuroticism is a vulnerability factor for depression in the first year after a first-ever cerebral infarct. For each 1-point increase in neuroticism, the risk of depression increased by a factor of 1.08. Moreover, our data indicated that this effect was stronger in men than women.

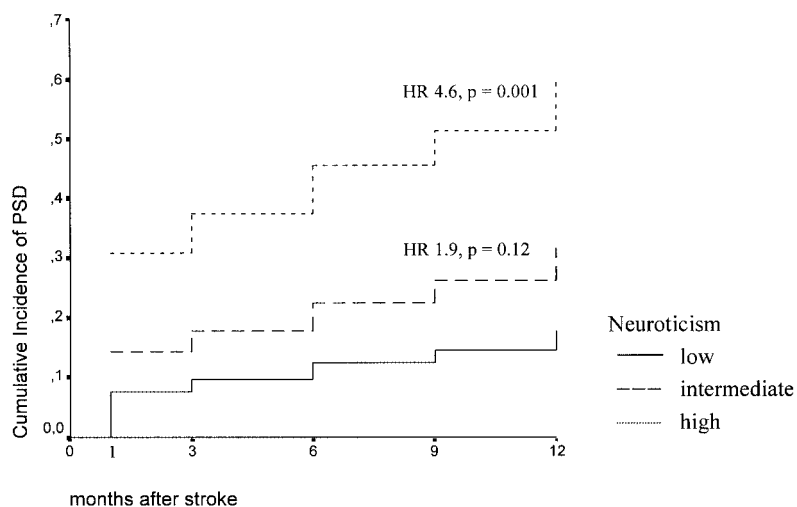


Figure 2. Cumulative 1-year incidence of PSD in patients with low, intermediate, and high neuroticism scores (categories based on tertiles). For the HR, low neuroticism was the reference group.

Apart from neuroticism, no other dimension of the Five Factor Model of personality showed an independent significant effect on the development of PSD.

The findings of our study are important from both a clinical and a theoretical perspective. Personality assessment may help to detect patients at risk of PSD early after stroke. Moreover, our findings support the notion that in addition to anatomical factors, PSD involves psychological factors. On the one hand, the study by Vataja et al⁴ revealed new evidence for lesions affecting the prefrontal subcortical circuits to increase the risk of PSD.⁴ On the other hand, stroke should also be considered a negative life event to which patients may respond with depression, depending on the interaction between personality factors and the severity of the negative physical, psychological, and social consequences of stroke.²² To determine which factors are independent predictors of PSD, further studies are needed in which neuroticism is taken into account as an important potential interactor or confounder.

A first limitation of our study is that we assessed personality 1 month after stroke. Because stroke is known to potentially cause personality changes, our results may not exclusively reflect premorbid personality traits. However, after controlling for distress as measured with the total score on the SCL-90, the trait neuroticism effect of the NEO-FFI remained statistically significant. Moreover, the finding that the neuroticism effect found in our study proved to be linear contradicts the suggestion that the effect is caused by a subset of patients with stroke-related personality changes based on the location of the stroke lesion. In this case, a more logistic distribution (*J*-form curve) would probably have appeared. As a consequence, we believe that our findings reflect the effects of premorbid personality traits on the development of PSD.

A second limitation is that a substantial percentage of PSD patients were diagnosed with depression at the time of personality assessment. It has been reported that depression affects self-rated personality scores toward more pathology,²³ although this has been contradicted by Bagby et al.²⁴ The effect of neuroticism in our study, however, remained significant after the exclusion of patients who were already depressed 1 month after stroke.

Third, a large percentage of patients were excluded from this study, mainly because of severe handicap and/or comorbidity. This limits the generalizability of our findings to stroke patients with a first-ever hemispheric infarct who survive stroke without such severe physical or cognitive disabilities that cognitive, psychological, and psychiatric evaluations are seriously hampered. In general, diagnosing depression in stroke patients is complicated by several different factors, including specific consequences of stroke (eg, aphasia, anosognosia, denial, and emotional lability) and the high incidence of aspecific symptoms that might or might not be caused by depression (eg, fatigue, motor slowness, and difficulty concentrating).²²

The findings of the present study emphasize the need to take personality into account as a potential determinant of depression in patients recovering from stroke. Hence, future research should aim at delineating the interplay between neurological and psychological factors in the development of PSD.

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