Cognitive aftermath of ischemic stroke
Gerritsen, Marleen Juliana Josephina

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2004

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

Copyright
Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

Take-down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): http://www.rug.nl/research/portal. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.
There is little consensus about the relation between depressive mood and cognitive functioning after first-ever ischemic stroke. In the present community-based follow-up study 99 patients were examined at three and 80 of them at 15 months after stroke. An observer-rated (PSDRS) and a self-rated (HADS) depression scale, cognitive tests and a questionnaire for subjective cognitive changes were administered. Although patients with depressive mood had increasingly more cognitive complaints than those without, the patients did not differ in cognitive test scores when mood was self-rated. Moreover, change in mood was not related to change in cognitive performance. When the PSDRS criteria were applied, patients with depressive mood appeared to be mentally slower than those without.

The frequently suggested relation between post stroke depression and cognitive impairments was confirmed for the subjectively experienced cognitive changes, but only few significant relations between objectively measured cognitive impairment and depressive mood were found in this study. Moreover, the data demonstrated the decisive role of the instruments that are used to assess depressive mood and cognitive performance after stroke.

Cognitive functioning in ischemic stroke patients with and without depressive mood: a follow-up study.


Submitted for publication.
Introduction

Both cognitive disorders and depressive symptoms are common sequelae of stroke. Their relation, however, is still unclear (Gainotti & Marra, 2002). Several studies have found depression and cognitive disorders after stroke to be related (Andersen, Vestergaard, Riis, & Ingeman-Nielsen, 1996; Bolla-Wilson, Robinson, Starkstein, Boston, & Price, 1989; Desmond et al. 2003; Kauhanen, Korpelainen, & Hiltunen, 1999; Robinson, Bolla-Wilson, & Kaplan, 1986; Murata, Kimura, & Robinson, 2000; Spalletta, Guida, De Angelis, & Caltagirone, 2002), while others did not (Dam, 2001; Kase, et al., 1998; Madureira, Guerreiro, & Ferro, 2001).

It has been suggested that a relation between post stroke depression and cognitive disorders would exist only in a selection of patients, like in stroke patients with a major depression (Robinson et al., 1986), or in left hemisphere patients (Bolla-Wilson et al., 1989; Spalletta et al., 2002). According to Kauhanen and co-workers (2000), especially stroke patients with aphasia are at risk for post-stroke depression, but within their group of aphasic patients no differences between patients with and without depression were found in neuropsychological test scores.

Several hypotheses about the nature of the relation between post-stroke depression and cognition have been postulated. Robinson and colleagues (1986) suggested a theory that relates to ‘dementia of depression’, in which major depression is thought to cause cognitive disorders. In subsequent longitudinal and depression treatment studies they reported an association between the improvement in mood of depressed stroke patients and an improvement in cognitive functioning as measured with the Mini-Mental State Examination (MMSE) (Kimura, Robinson, & Kosier, 2000; Murata, et al., 2000; Narushima, Chan, Kosier, & Robinson, 2003). The authors argue that if ‘dementia’ was primarily due to structural brain damage it would remain unchanged irrespective of improvement in mood. House and co-workers (1990) on the other hand did not confirm this hypothesis; they did not find major depression to be associated with a different intellectual outcome after stroke. Moreover, Andersen and colleagues (1996) did not find an improvement in intellectual function in depressive stroke patient, despite improvement in mood. Based on their results they even suggested the opposite hypothesis: “depression of dementia”. Finally, depression and cognitive disorders might be concomitant but independent consequences of stroke as one might conclude from the fact that several studies do not find post stroke depression and cognition to be related.

In the stroke studies that investigated the relation between post stroke depression and cognitive functioning rather different measures were applied. Often a dementia screening instrument, like the MMSE, was used as the only tool to assess cognitive functioning, or even dementia (Anderson et al., 1996; House, Dennis, Warlow, Hawton, & Molyneux, 1990; Kase et al., 1998; Kimura et al., 2000; Murata et al., 2000; Narushima et al., 2003; Robinson et al., 1986; Spalletta et al., 2002), while some others used a more extensive neuropsychological test battery.
Using a neuropsychological test battery Bolla-Wilson and co-workers (1989) found that the left hemisphere patients, without language disorders, who were depressed performed worse on tasks for language and fluency, orientation, and Luria motor sequences, than left and right hemisphere patients without depression or right hemisphere depressive patients. No significant correlation was found between depression and memory performance and visuoconstructive functions. Kauhanen and colleagues (1999) on the other hand showed that memory, psychomotor speed, problem solving, and attention were the cognitive domains that were most likely to be decreased in depressed stroke patients.

For the assessment of depression too, a wide variety of measures has been used that may lead to different results (Schramke, Stowe, Ratcliff, Goldstein, & Condray, 1981). Pohjasvaara and colleagues (2002) for example found that a higher score on a self-rated depression scale (Beck) was related to executive dysfunction, but an observer-rated scale (MADRS) or clinical psychiatric evaluation were not.

Some authors favour the use of semi-structured interviews to diagnose depression based on DSM-IIIR or DSM-IV criteria (Robinson, & Starkstein, 1997). This method has been found to be valid by some authors (Federoff et al., 1991, Paradiso & Robinson, 1999; Starkstein & Lischinsky, 2002), while others recommend caution because of the physical symptoms included in the diagnosis of depression that could be due to the brain lesion and not the depression (Desmond et al., 2003; Gainotti, et al., 1997; Schramke et al., 1998). Gainotti and colleagues (1997) compared stroke patients with and without depression and non-brain damaged patients with functional depression, using the Post-Stroke Depression Rating Scale (PSDRS). They concluded that post stroke depression was mainly caused by exogenic factors related to the consequences of the stroke.

The goal of the present study is to investigate the relation between depressive mood and cognitive functioning after first-ever ischemic stroke in a community based population. Depressive mood was assessed with both an observer-rated and a self-rated depression scale. In this study 'depression' was always considered in terms of depressive mood, since the used scales are not designed to diagnose depressive disorder. Besides a dementia screening instrument, tests of memory, speed of information processing, and reasoning were administered, using at least three instruments for each domain. Moreover, subjective cognitive changes as experienced by the patients themselves and their partners, were registered as well.

To gain more insight into causal relations between cognition and depression, the course of cognitive functioning and depressive mood was assessed with a one-year time interval between three and 15 months post stroke onset. In sum, the main questions in this study are: first, is cognitive functioning in the three cognitive domains: speed of information processing, memory, and reasoning, related to depressive mood according to an observer-rated and / or a self-rated depression
scale? Second, is there a longitudinal relation between cognitive functioning and depressive mood after stroke? Third, is there a difference between left and right hemisphere patients with respect to the relation between cognitive functioning and depressive mood?

Methods

Participants

Patients who were clinically diagnosed as having a unilateral, first-ever, ischemic stroke were recruited from general practitioners (GPs) in the northern part of the Netherlands, and from the stroke unit of the University Hospital Groningen. The GPs and the stroke unit presented 235 stroke patients. Neurological and GPs’ reports were checked, and 47 patients did not meet the stroke-related inclusion criteria (unilateral, first-ever, and ischemic). Moreover, other neurological disorders, psychiatric diseases, or alcohol abuse were criteria to exclude patients from the study (n= 13). Finally, patients had to be able to keep up the testing procedures for at least half an hour, which appeared to be impossible for 17 patients. Aphasic patients were included in this study, unless they were unable to understand even the simplest test-instructions (n= 7). Nine patients died before the neuropsychological test-procedure. Eventually, a group of 142 patients met all criteria, and 99 of them were willing to participate in the interview and neuropsychological test-procedure at three months post stroke (T1). One year after the first assessment (T2) 80 of the 99 patients again participated in the study (3 had died, 3 were too ill, 2 had suffered a second stroke, and 11 did not want to co-operate any longer).

To compose a comparable control group, control subjects (n= 72) were also recruited by five of the GPs. The controls were matched with the patients for age and gender. They had no history of stroke, had no other neurological or psychiatric disorders, and no history of alcohol abuse. One year after the first assessment 64 control subjects were also examined again (4 were too ill to participate any longer, 3 didn’t feel like it, and 1 moved abroad).

Assessment: mood

The Hospital Anxiety and Depression Scale (HADS) (Zigmond & Snaith, 1983) is a self-rating scale with a depression and an anxiety scale; in this study the depression scale was used. The scores range from zero to 21, higher scores indicating more depressive mood. According to Johnson an colleagues (1995) the cut-off score for the HADS-depression scale should be 5 when a community based stroke group is studied. Change from T1 to T2 had to be at least 3 points to be considered reliable (Vermeer, Koudstaal, Oudkerk, Hofman, & Breteler, 2002). This leads to four subgroups: subjects who did not show a depressive mood at either T1 or T2 (non-depressive cases: NONDEP), individuals who had a depressive mood at both T1 and T2 (depressive cases: DEP), people with a
Chapter 7 ______________________________________________________

114

depressive mood at T1 but no longer at T2 (recovered cases: REC), and finally those who had a depressive mood at T2 but not yet at T1 (new cases: NEW).

A neuropsychologist also rated mood for 99 patients and 71 control subjects after a structured interview. The neuropsychologist was blind for the cognitive data, but not for the HADS-questionnaire. The first section of the Post Stroke Depression Rating Scale (PSDRS) (Gainotti et al., 1997) was used to rate the level of depressive mood, ranging from ‘well balanced mood’ (0) to ‘gloomy black mood’ (5). The cut-off for depressive mood was set at 2: ‘mood clearly more oriented toward sadness and pessimism than before illness’. Change from T1 to T2 on the PSDRS led again to four subgroups (non-depressive, depressive, recovered and new cases).

Assessment: cognitive performance

A Dutch dementia screening test, the Cognitive Screening Test (CST-20) was administered in all subjects (De Graaf & Deelman, 1992). The CST-20 is comparable to the MMSE with respect to the reliability and validity, while the CST-20 is less sensitive to the influence of age, education, depression and premorbid intelligence (Schmand, Deelman, Hooijer, Jonker, & Lindeboom, 1996). The maximum score is 20 points, higher scores indicate better performance, and the cut-off that indicates possible dementia is 12 points.

To assess memory, a paired-associate learning task (the Couples Test) and the Rey Auditory Verbal Learning Test (AVLT) were used. The Couples Test is a paired-associate learning task with a verbal (Names) and non-verbal (Faces) subtest. Subjects had to memorise 10 couples of male and female first names or male and female faces, in five successive trials. In each trial all stimuli, the couples, are presented, and immediate recall is measured by asking the subjects to match the females with the males (forced guessing). To reduce the chance for guessing five distracters, not previously presented female names or faces, were added when the recall was tested. The Dutch version of the AVLT is a test in which subjects have to learn 15 one-syllable words in five successive trials (Saan & Deelman, 1986). The sum score of the free recalls on the 5 trials was used. The mean of the percentages correct in each completed memory tests renders a total memory score, higher scores indicating better performance.

Speed of information processing was measured using a reaction time apparatus that registered both movement and decision times. In this study only the decision times, measured in four tasks, were used. Decision times were measured in milliseconds. Visuomotor decision time is the mean of the median decision times on a simple and an eight choice reaction time task (Van Zomeren & Deelman, 1976). Cognitive decision time represents the mean of the median decision times on two semantic categorisation tasks, one verbal (words) and one non-verbal (pictures) (Gerritsen, Berg, Deelman, Visser-Keizer, & Meyboom-de Jong, 2003).
Reasoning was tested using the Snijders Oomen Non-verbal Intelligence Test (SON-R 5½ -17). Originally the SON-R 5½ -17 was constructed for deaf children (Snijders, Telegen, & Laros, 1989), but the test appeared to be reliable and valid to be used in older adults as well (Gerritsen, Berg, & Deelman, 2001; Lezak, 1995). Based on pilot studies three subtests were selected for the present study:

- Categories (abstract reasoning),
- Stories (concrete reasoning) and
- Mosaics (visuospatial abilities).

The reasoning score represents the mean of the percentages correct in each of the completed subtests, therefore higher scores indicate better reasoning abilities.

**Assessment: subjective cognitive change**

Subjective emotional and cognitive changes were assessed using a 20-items questionnaire. The questions are based upon clinical relevance according to both neuropsychological literature and interviews with partners of stroke patients (Schure, 1995). Both patients and their partners (n= 73 at T1, n= 69 at T2) were asked to rate the amount of emotional and cognitive change they attributed to the stroke on a 4-point scale ranging from ‘not changed’ (0) to ‘very much changed’ (3). For this study only the 5 questions concerning cognitive change were used: memory, slowness, orientation in time and place, planning, and concentration.

**Procedure**

The interview, in which several (neuro)psychological and health questionnaires were administered, and the neuropsychological assessment took place in three sessions of about two hours each. The first two sessions took place at the participant’s home; the third at the University Hospital Groningen. Participants who were not able to come to the hospital were again visited at home. The patients and the control subjects signed informed consent preceding the interview, and the study was approved of by the medical ethics comity of the University Hospital Groningen. The same procedure was followed at both T1 and T2.

**Statistics**

The alpha level was fixed at 0.05, and all tests were two-tailed. First, the left and right hemisphere patients and control subjects were compared for age, gender and educational level with respectively: Student’s t-test, Mann-Whitney-U and Chi-square test. Moreover the relation between these demographic variables and the mood scales were assessed with Spearman’s rho correlation coefficient and chi-square tests.

Second, the number of patients with depressive mood according to both scales are presented and compared to the number of control subjects with depressive mood using chi-square tests. The numbers of patients who had
depressive mood at both times (DEP), T1 only (REC), T2 only (NEW) and neither T1 or T2 (NONDEP) are presented for the patients only, considering the very small numbers of control subjects with depressive mood.

Third, the differences between the patients and the control subjects with respect to the neuropsychological test performances are analysed at both T1 and T2 using student’s t-tests. This could not be done for the subjectively experienced cognitive change, as cognitive change due to stroke cannot be experienced by control subjects. Moreover, both groups were checked for presence of dementia according to the CST.

Fourth, the relation between depressive mood and cognitive function was analysed comparing cognition of patients with and without depressive mood according to the HADS and according to the PSDRS at both T1 and T2. ANOVA was used for the objective neuropsychological test scores, Mann Whitney-U for the subjective data. To analyse the relation over time, GLM-repeated measures were used to analyse the interaction between Time, T1 versus T2, and Group: DEP, REC, NEW and NONDEP. This was done for the test scores, the subjective data according to the patients, and the subjective data according to the partners.

Finally, the effect of side of stroke was analysed. The numbers of left and right hemisphere patients with and without depressive mood were compared using Chi-square. Within the patient groups with depressive mood left and right hemisphere patients were compared using ANOVA for the test scores, and Mann Whitney-U tests for the subjective data. The course of mood between the subgroups with respect to course of mood (DEP, REC, NEW, NONDEP) could not be analysed due to the small sample sizes.

Results

Sample and depression scale characteristics

The subject characteristics are presented in table 1. There were no differences in age, gender and education between the left and right hemisphere patients and the control subjects.

At T1, neither the HADS nor the PSDRS depression scores were significantly correlated with age or education in either patients or control subjects (rho max= .21). Female control subjects had higher PSDRS-scores than male control subjects (Z= -2.21, p= .01), no other gender differences were found (control- HADS: Z= -.24, p= .81; patient-HADS: Z= -0.74, p= .46; patient-PSDRS: Z= -0.80, p= .43).
Table 1:  Subject characteristics

<table>
<thead>
<tr>
<th>Group</th>
<th>T1</th>
<th>T2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Age M (sd)</td>
</tr>
<tr>
<td>RH-patients</td>
<td>47</td>
<td>66.5 (11.0)</td>
</tr>
<tr>
<td>LH-patients</td>
<td>53</td>
<td>66.6 (12.7)</td>
</tr>
<tr>
<td>Controls</td>
<td>72</td>
<td>66.0 (11.9)</td>
</tr>
<tr>
<td>Group</td>
<td>Anova</td>
<td>Chi-square</td>
</tr>
<tr>
<td>comparison</td>
<td>F = 0.03</td>
<td>χ² = 1.88</td>
</tr>
<tr>
<td></td>
<td>P = .97</td>
<td>p = .39</td>
</tr>
</tbody>
</table>

Depressive mood

At both T1 and T2 there were more stroke patients than control subjects with depressive mood, according to the HADS (T1: χ² = 21.13, p< .001; T2: χ² = 8.00, p< .01) as well as the PSDRS (T1: χ² = 5.56, p= .02; T2: χ² = 8.33, p< .01). The numbers of persons with depressive mood according to both measurements are presented in table 2.

Table 2:  Number of patients and control subjects with (DEP) and without (NON-DEP) depressive mood according to the HADS and the PSDRS.

<table>
<thead>
<tr>
<th></th>
<th>Patient</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PSDRS-DEP</td>
<td>NON-DEP</td>
</tr>
<tr>
<td></td>
<td>PSDRS-DEP</td>
<td>NON-DEP</td>
</tr>
<tr>
<td>T1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HADS-DEP</td>
<td>7</td>
<td>22</td>
</tr>
<tr>
<td>NON-DEP</td>
<td>7</td>
<td>63</td>
</tr>
<tr>
<td>Total</td>
<td>14</td>
<td>85</td>
</tr>
<tr>
<td>T2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HADS-DEP</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>NON-DEP</td>
<td>7</td>
<td>59</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>70</td>
</tr>
</tbody>
</table>

As is shown in table 2, there is some, but certainly no complete overlap between the two ratings of depressive mood.

From the patients who participated at both times of measurement, 13 (16%) recovered from depressive mood (REC), 10 (12%) had depressive mood at both times (DEP), 5 (6%) patients became depressive (NEW), and finally 53 (65%) patients had no depressive mood at both times (NONDEP) according to the
HADS. Following the PSDRS criteria this were respectively, 5 (6%), 5 (6%), 6 (8%), and 64 (80%) patients.

**Cognitive test performance**

At T1, the stroke patients had significantly lower memory scores ($t= 3.64, p< .001$), reasoning abilities ($t= 4.90, p< .001$), and were slower on both visuomotor ($t= -3.48, p< .01$) and cognitive ($t= -2.42 p= .02$) decision times than the control subjects. All subjects scored above cut off on the dementia-screening test (CST). At T2, the patients still performed worse than the controls with respect to memory ($t= 3.31, p< .01$), reasoning ($t= 3.33, p< .01$), and cognitive decision times ($t= - 2.08, p= .10$), but they did not differ on visuomotor decision times ($t= - 1.68, p= .10$). At T2, still none of the participants scored below cut-off on the CST.

**Depressive mood and cognition: objective cognitive test performance**

In table 3 the objective cognitive test scores and ANOVA statistics for the patients with and without depressive mood are presented. At both T1 and T2 there were no differences in cognitive functioning between patients with and without depressive mood according to the HADS. The patients with depressive mood as measured with the PSDRS, on the other hand, had slower visuomotor decision times than the non-depressive patients at both T1 and T2. Moreover, at T2 the patients with PSDRS depressive mood showed worse reasoning performance than the patients without PSDRS depressive mood.

GLM-repeated measures for the cognitive test performance from the four patient subgroups according to the change in depressive mood (NONDEP, DEP, REC, NEW) revealed no significant Time x Group interactions when the patient groups were compared according to the HADS (**memory** $F(3,72)= 1.83, p= .15$; **reasoning** $F(3,74)= 1.19, p= .32$; **visuomotor decision time** $F(3,67)= 0.18, p = .91$; **cognitive decision time** $F(3,62)= 0.84, p = .48$). The same was true for the four subgroups according to the PSDRS (**memory** $F(3,71)= 1.12, p= .35$; **reasoning** $F(3,73)= 2.19, p= .10$; **visuomotor decision time** $F(3,66)= 0.68, p= .57$; **cognitive decision time** $F(3,61)= 0.52, p= .67$). So, course of cognitive performance and course of depressive mood were not related significantly.

**Depressive mood and cognition: subjective cognitive change in patients**

With respect to the subjective cognitive data, the patients with HADS-depressive mood experienced significantly more cognitive changes than patients without depressive mood at both T1 ($Z= -3.04, p< .01$), and T2 ($Z= -2.55, p= .01$). Analyses of the 5 cognitive items separately revealed significant differences at T1 and T2 in the experienced mental slowness (T1: $Z= -2.46, p= .01$; T2: $Z= -2.59, p< .01$) and concentration (T1: $Z= -2.48, p= .01$; T2: $Z= -2.73, p= .01$), and only at T1 in orientation in time and place ($Z= -2.67, p= .01$).
The difference in experienced cognitive change between patients with and without PSDRS-depressive mood, on the other hand, failed to reach significance at T1 ($Z = -1.76$, $p = .08$). At the level of the separate items the patients with depressive mood according to the PSDRS complained more about changes in concentration ($Z = -2.03$, $p = .04$) and orientation ($Z = -3.15$, $p < .01$). Moreover at T2, the difference was significant for the sum-score ($Z = -4.60$, $p < .001$), and all five items separately ($p < .01$).

Table 3: The differences in cognitive performance at T1 between patients with (HADS-D and PSDRS-D) and without (HADS-ND and PSDRS-ND) depressive mood.

<table>
<thead>
<tr>
<th></th>
<th>HADS-ND M (SD)</th>
<th>HADS-D M (SD)</th>
<th>(df) F</th>
<th>p</th>
<th>PSDRS-ND M (SD)</th>
<th>PSDRS-D M (SD)</th>
<th>(df) F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visuo-DT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>455 (180)</td>
<td>417 (93)</td>
<td>(1, 82) 1.61</td>
<td>.55</td>
<td>557 (229)</td>
<td>408 (86)</td>
<td>(1, 81) 16.42</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>T2</td>
<td>407 (85)</td>
<td>422 (103)</td>
<td>(1, 75) 0.27</td>
<td>.60</td>
<td>500 (152)</td>
<td>405 (81)</td>
<td>(1, 75) 9.60</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Cogn-DT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>1069 (321)</td>
<td>1019 (321)</td>
<td>(1, 78) 0.36</td>
<td>.22</td>
<td>1154 (383)</td>
<td>1014 (375)</td>
<td>(1, 77) 1.65</td>
<td>.203</td>
</tr>
<tr>
<td>T2</td>
<td>969 (280)</td>
<td>1057 (522)</td>
<td>(1, 72) 0.49</td>
<td>.49</td>
<td>1290 (561)</td>
<td>1001 (462)</td>
<td>(1, 72) 3.04</td>
<td>.09</td>
</tr>
<tr>
<td>Memory</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>38.3 (17.4)</td>
<td>32.7 (12.0)</td>
<td>(1, 90) 2.95</td>
<td>.09</td>
<td>29.3 (11.1)</td>
<td>35.0 (14.8)</td>
<td>(1, 89) 1.73</td>
<td>.192</td>
</tr>
<tr>
<td>T2</td>
<td>38.8 (17.0)</td>
<td>36.8 (16.4)</td>
<td>(1, 79) 0.17</td>
<td>.68</td>
<td>30.0 (20.1)</td>
<td>38.3 (15.6)</td>
<td>(1, 79) 2.46</td>
<td>.11</td>
</tr>
<tr>
<td>Reasoning</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>40.2 (18.9)</td>
<td>44.8 (19.5)</td>
<td>(1, 95) 1.12</td>
<td>.29</td>
<td>37.5 (21.0)</td>
<td>44.4 (20.7)</td>
<td>(1, 94) 1.41</td>
<td>.237</td>
</tr>
<tr>
<td>T2</td>
<td>55.4 (18.9)</td>
<td>46.8 (21.9)</td>
<td>(1, 80) 2.00</td>
<td>.16</td>
<td>36.0 (18.4)</td>
<td>51.2 (20.7)</td>
<td>(1, 80) 9.61</td>
<td>&lt; .01</td>
</tr>
</tbody>
</table>

Cogn-DT = cognitive decision time, Visuo-DT = visuomotor decision time.

Figure 1: Course of subjective cognitive functioning according to the patients. Patients are classified according to the PSDRS: NDEP = not depressive at both T1 and T2, REC = depressive at T1 but not at T2, NEW = depressive at T2 but not at T1, DEP = depressive at both T1 and T2.
GLM repeated measures for the four groups according to change in mood (NONDEP, DEP, REC, NEW) showed no significant interactions Time x Group for the HADS depressive patients, but it did for the PSDRS-depressive patients (F(3, 76)= 4.75, p < .01), as is illustrated in figure 1.

Figure 1 shows that the reported cognitive complaints increase disproportionately in the depressive stable (change = 2.4 points) and new cases (change = 2.2 points) as compared to the recovered (change is zero points) and non-depressive stable (change = 0.5 points) cases.

**Depressive mood and cognition: subjective cognitive change according to partners**

At T1, the partners of the patients with depressive mood did not report more cognitive changes in the patients than the partners of the patients without depressive mood. This was true for both depression scales (HADS: Z= -1.08, p= .28, PSDRS: Z= -1.39, p=.17). No differences were found at item level either. The same was true at T2 (HADS: Z= -0.90, p= .37, PSDRS: Z= -1.37, p= .17). Moreover, GLM-repeated measures revealed no significant interaction of Time by Group for either depression scale (HADS F(3,53)= 0.02, p= .99; PSDRS F(3,53)= 0.54, p= .66).

**Side of stroke**

Mood. Side of stroke was not significantly related to mood at both T1 and T2: there were no significant differences in the number of left and right hemisphere patients with depressive mood according to the HADS (T1: $\chi^2 = 0.31$, p=.58; T2: $\chi^2 = 0.07$, p=.80), and the PSDRS (T1: $\chi^2 = 2.57$, p= .11; T2: $\chi^2 = 0.09$, p=.76). According to the HADS-criteria at T1 13 (28%) right hemisphere and 16 (30%) left hemisphere patients had depressive mood, at T2 these were respectively 7 (18%) and 8 (19%) patients. According to the PSDRS 10 (22%) right hemisphere patients, and 4 (7.5%) left hemisphere patients had depressive mood at T1. At T2 respectively 6 (16%) and 5 (12%) patients had depressive mood according to the PSDRS.

Mood and cognition. Within the patient group with depressive mood according to the HADS, there were no differences in cognitive functioning between left and right hemisphere patients at T1 (reasoning p=.57, memory p= .79, visuomotor DT p= .12, cognitive DT p= .81, subjective cognition according to the patient p= .91, subjective cognitive change according to the partner p= .23). The same was true for the PSDRS depressive patients (reasoning p= .42, memory p= .06, visuomotor DT p= .68, cognitive DT p= .07, subjective cognition according to the patient p= .54, subjective cognitive change according to the partner p= .71). At T2 too, there were no differences with respect to lateralisation in any of the cognitive measures for both the HADS and the PSDRS-depressive patients (data not presented).
Conclusions & discussion

The objective of the present study was to examine the relation between depressive mood and cognitive functioning at three and fifteen months post stroke in a community-based patient group with first-ever unilateral ischemic stroke. Three cognitive domains: memory, speed of information processing and reasoning, were studied with at least three measurements each. Moreover, depressive mood was examined with both a self-rated (HADS) and an observer-rated (PSDRS) scale. In addition a dementia screening test (CST) was applied. Remarkably, the results were, to some extent, contradictory.

Patients with depressive mood according to the HADS did not perform worse on any of the cognitive measures than patients without depressive mood at three and 15 months post stroke. Moreover, course of depressive mood was not related to course of cognitive performance. Patients with depressive mood according to the observer-rated scale (PSDRS), on the other hand, showed slower visuomotor decision times than patients without depressive mood at three months post stroke. One year later, the patients with PSDRS depressive mood still had slower visuomotor decision times than patients without depressive mood. Moreover, they showed worse reasoning performance than the non-depressive patients. However, there were no interactions between course of cognitive performance and course of depressive mood according to he PSDRS criteria either. Cognitive decision times and memory performance were not related to either of the depressive mood measurements.

The finding that different measures of depressive mood reveal differences with respect to the relation with cognitive functioning is in line with a study recently presented by Pohjasvaraa and colleagues (2002). In contrast to the present data, however, they found that a relation was present only when a self-rated depression scale was used and not with the observer-rated methods. We cannot rule out the possibility that in the present study the self-rated scale overrated the presence of depressive mood compared to the observer-rated method, thus including more patients with relatively mild depressive mood. The HADS has been shown to have a misdiagnosis rate of 20%, which even was the lowest percentage of three self-rating scales (Aben, Verhey, Lousberg, Lodder, & Honig, 2002). In fact our results do show nearly twice as many patients with depressive mood according to the HADS (29%) than patients with depressive mood according to the PSDRS (14%). The latter amount is comparable to a cohort study by Desmond and colleagues (2003) who found a comparable observer-rated (Structured Interview Guide for the Hamilton Depression Rating Scale) percentage of depressive stroke patients, and like our study, excluded patients with a history of depression.

The few studies that found a relation between depressive mood and cognitive functioning while using a neuropsychological test battery, showed a rather broad range of cognitive domains to be impaired in depressed patients (Bolla-Wilson et al., 1989; Kauhanen et al., 1999). In non-stroke studies focussing on
major depressive disorder speed of information processing has been suggested to be the central cognitive impairment (Den Hartog, 2002; Nebes, 2000). This is in line with the present findings that mainly speed of information processing is more impaired in patients with (observer-rated) depressive mood than in patients without depressive mood. Moreover, reasoning was more impaired in this group, but only at 15 months post stroke. A possibility that needs consideration is that for as far as the mental slowness can be observed, this might have been interpreted as a sign of depressive mood by the observer.

Kauhanen et al. (1999) too found more significant relations between depressive mood and cognitive functions at one year after stroke than at three months post onset. The opposite was shown by House et al. (1990), though: they found weak, but significant, correlations between the MMSE and depression at one and six months post stroke, but not at 12 months. For further longitudinal examination of the relation between change in mood and cognition, our patients were divided into four subgroups according to their change in mood. No relation between change in mood and change in cognitive function was found, however, for either of the mood measurements. Hence, these data cannot confirm either the theory of 'dementia of depression' (Kimura et al., 2000; Murata et al., 2000) or 'depression of dementia' (Anderson et al., 1996) after stroke.

Not only objective measures of cognitive functioning were used in this study, but the patients were also asked to what extent they experienced cognitive changes due to the stroke. Like Dam (2001) we found that patients with depressive mood reported more cognitive change due to their stroke than patients without depressive mood did. At T1, both PSDRS and HADS-depressive mood patients felt that they had more trouble concentrating and orientating than patients without depressive mood. In addition, the patients with depressive mood according to the HADS had more complaints about mental slowness. At T2, patients with depressive mood according to the HADS still had more complaints about decline in mental speed and concentration. The patients with depressive mood according to the PSDRS felt more decline in cognitive function than the patients without depressive mood in all five domains at T2.

So, the cognitive complaints increased with time, and according to the PSDRS classification of depressive mood this appeared to be related to change in mood; especially the patients with depressive mood at both T1 and T2 and the patients who’s mood became depressive between T1 and T2, experienced more cognitive changes at T2 compared to T1. So the present findings are, to some extent, in line with the conclusion by Gainotti et al. (1999) that depressive mood is related to the experienced impairments due to stroke even though this was not confirmed by the objective cognitive data. The patients who’s mood recovered on the other hand, did not show a decrease in cognitive complaints, but they had a very low level of complaints to begin with three months after stroke.

The partners of the patients with, versus the partners of the patients without depressive mood (according to both the self-rated and the observer-rated scale) did
not differ with respect to the cognitive changes they perceived in the patients. Nor was there a relation between course of mood and course of cognitive functioning as perceived by the partners.

Carson and colleagues (2000) systematically reviewed the literature and could not confirm the hypothesis that the occurrence of depression after stroke is related to the side of the stroke. Our findings are in line with this conclusion. With respect to the relation between cognitive dysfunction and depression it has been suggested that this relation is specific for left hemisphere patients (Bolla-Wilson et al., 1989; Spalletta et al. 2002). The present study did not confirm these findings though; there were no differences between left and right hemisphere patients with respect to the relation between cognitive functioning and mood.

Two major restrictions need to be considered when interpreting the presented data. First, though the size of the patient group (n = 99) can be considered adequate, the subgroups of patients with depressive mood were small. Second, we could not systematically control for the use of anti-depressants. Two patients with HADS-depressive mood and three with PSDRS-depressive mood used anti-depressive medication. However, in the groups without depressive mood there were also patients (respectively 7 and 6) who used anti-depressants. Therefore we assume that use of these drugs did not strongly contaminate our data.

In sum, the results show that a relation between depressive mood and cognitive functioning after stroke is clearly present when subjective cognitive changes according to the patients are considered. Objective cognitive test scores and partners' reports, on the other hand, could not confirm this relation. With one exception though: observer-rated depressive mood appeared to be related to speed of information processing at both times of measurement, and reasoning at 15 months post stroke.

Considering the lack of significant relations between (course of) cognitive test performance and (course of) depressive mood after stroke, this study suggests that these are two entities that can independently occur after stroke. Still, like suggested by Gainotti and co-workers, post stroke depression can be a reaction to the experienced changes, among which the perceived cognitive changes. Finally, the present results emphasise the decisive role of the choice of measures that are used to assess both depression and cognitive functioning.
References


