Cognitive aftermath of ischemic stroke
Gerritsen, Marleen Juliana Josephina

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The impact of asymptomatic brain lesions on cognitive functioning

Despite growing interest in cognitive functioning after stroke, little is known about the impact of silent brain infarcts and white matter lesions on objective and subjective cognitive changes after clinically first-ever ischemic stroke. In the present study a community-based group of 89 patients was examined with a structured interview and extensive neuropsychological test battery at three months post stroke. One year later 71 patients were assessed again. Patients with and without asymptomatic brain lesions were compared. The data demonstrated that the asymptomatic lesions were not related to cognitive functioning at T1. At T2 on the other hand, the patients with asymptomatic brain lesions appeared to have slower visuomotor decision times than patients without. Moreover, course of reasoning performance differed at the disadvantage of the patients with asymptomatic lesions. Subjectively experienced cognitive changes showed a trend toward more cognitive complaints in the patient group with asymptomatic lesions, but this just failed to reach significance. It is concluded that asymptomatic brain lesions are indeed asymptomatic with respect to both objective and subjective cognitive functioning, but long-term outcome may to some extend be compromised by asymptomatic brain lesions preceding stroke. Further research with larger patient groups and longitudinal MRI data is needed.


Submitted for publication
Introduction

Cognitive functioning after stroke has been studied rather intensively, especially in the last decade (Bowler, Hadar, & Wade, 1994; Hochstenbach, Mulder, van Limbeek, Donders, & Schoonderwald, 1998; Srikanth, et al., 2003; Tatemichi, et al., 1994). Relatively little, however, is known about the impact of asymptomatic ischemic cerebral events that may have preceded the clinically overt stroke on cognitive functioning and recovery of cognitive functioning.

In the present community based stroke study the relation between asymptomatic cerebral lesions and cognitive functioning in the subacute and chronic stage after first-ever ischemic stroke is studied. Asymptomatic cerebral lesions are radiological findings, and in this study we included both white matter lesions and silent infarcts, since both are considered to be of ischemic nature, occur without symptoms and are frequently seen in patients with a clinically first-ever stroke as well as in the stroke free elderly population (Chodosh, et al., 1988; Herderschee et al., 1992; Jorgenson, Nakayama, Raaschou, Gam, & Olsen, 1994; Kase, et al., 1989; Pantoni & Garcia, 1997; Price, et al., 1997; Vermeer, Koudstaal, Oudkerk, Hofman, & Breteler, 2002; Vermeer, et al., 2003).

White matter lesions and silent brain infarcts have been associated with cognitive decline in healthy elderly, at least to some degree, effecting mental speed and attentional abilities (Breteler et al., 1994; Vermeer et al., 2003, Ylikoski et al., 1993, O’Brien et al., 2002), global cognitive functioning as measured with the Mini-mental State Examination (de Groot et al., 2002), and subjective cognitive complaints (de Groot et al., 2001). Moreover, white matter lesions seem to be related to typical pathology in Alzheimer’s disease (De Leeuw et al., 2004). Vermeer and co-workers (2003) showed that, periventricular white matter lesions, and silent as well as clinically evident stroke increase the odds to develop dementia. Price et al. (2003) on the other hand, performed a post mortem study, and found clinical but not subclinical infarcts to be related to dementia.

In stroke patients white matter lesions or silent brain infarcts have been associated with cognitive decline or post stroke dementia in some (Burton et al., 2004; Pohjasvaara et al., 2000; Vataja et al., 2003), but not all studies (Bornstein et al., 1996; Censori et al., 1996). Pohjasvaara and colleagues (2000) suggested that post stroke dementia is not the result of one single stroke, but reflects more than one underlying pathology, among which the extent of white matter lesions. Censori and co-workers (1996) on the other hand found a trend, that just failed to reach significance, suggesting that asymptomatic CT-lesions were less frequent in demented stroke patients than in the non-demented stroke group. Possibly this was due to the large infarct volumes in the demented group masking the silent infarctions.

Executive dysfunction has been associated with the degree of white matter lesions in stroke patients (Vataja et al., 2003). In another study involving older stroke patients (> 74 years), however, not executive functioning, but mental speed,
attention and memory functioning were related to white matter lesions, dependent on lesion location (Burton et al., 2004). To assess executive functioning Vataja and colleagues (2003) used a composite score of four neuropsychological tests, of which three relied on speed of information processing. This might, in part, explain these apparently contrasting results.

With respect to the prognostic value of asymptomatic brain lesions, periventricular white matter lesions as well as silent brain infarcts have been associated with steeper cognitive decline in the elderly population (De Groot et al., 2002, Vermeer et al., 2003). Moreover, Vermeer and co-workers (2003), demonstrated that this decline was confined to those people who had recurrent silent brain infarct at follow-up, 3.4 years after baseline MRI. Little is known about the impact of asymptomatic brain lesions on recovery of cognitive function after stroke. One study demonstrated the development of dementia after stroke, over a period of five years, was independent of the presence of silent brain infarcts (Bornstein, 1996). Ballard and colleagues (2003) examined cognitive functioning at three and 15 months post stroke, and based on their own results and earlier findings by Desmond et al. (1996), postulated the following hypothesis: “cognitive function after stroke improves unless individuals have concurrent cerebrovascular neurodegenerative disease or develop further cerebral insults”.

In sum cognitive decline has been associated with asymptomatic cerebral lesions that are common in stroke patients as well as in healthy elderly. Little, however, is known about the difference in cognitive functioning, objectively as well as subjectively, between stroke patients with and without these lesions preceding the overt stroke. In the literature cognitive dysfunction is often studied in terms of post-stroke dementia. This is a complex and somewhat controversial concept, and in our opinion using the DSM IV criteria might overrate the presence of dementia after stroke. Moreover, it lacks the, in our view essential, criterion of progressiveness of the disease. The present study is therefore concerned with cognitive functioning rather than dementia after stroke, in addressing the following questions:

What is the impact of previous asymptomatic ischemic brain lesions in stroke patients on objective and subjective cognitive functioning at three months post-stroke?

What is the impact of previous asymptomatic ischemic brain lesions in stroke patients on the course of objective and subjective cognitive functioning between three and 15 months post-stroke?

**methods**

**Patients**

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. Neurological and GPs’ reports were checked. In figure 1 the inclusion of the patients is summarised. For eleven patients too little information about the lesion variables was available for this study, due to lack of corporation from some of the hospitals that were involved. Moreover, other neurological disorders, psychiatric diseases, or alcohol abuse were criteria to exclude patients from the study. Finally, patients had to be able to keep up the testing procedures for at least half an hour. Aphasic patients were included in this study, unless they were unable to understand even the simplest test-instructions. Eventually, a group of 132 patients met all criteria, and 89 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 70 patients again participated in the study (T2).

The data are presented in table 1.

Table 1:  
patient inclusion.

<table>
<thead>
<tr>
<th>Admitted by GP, Stroke Unit</th>
<th>235</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exclusion criteria</td>
<td></td>
</tr>
<tr>
<td>▪ no clinically first, ischemic, unilateral stroke &lt; 3 months</td>
<td>47</td>
</tr>
<tr>
<td>▪ history of psychiatric or neurological disturbance or substance abuse</td>
<td>13</td>
</tr>
<tr>
<td>Insufficient lesion data available</td>
<td>11</td>
</tr>
<tr>
<td>Died before neuropsychological assessment (NPA)</td>
<td>9</td>
</tr>
<tr>
<td>Not able for NPA T1</td>
<td>16</td>
</tr>
<tr>
<td>Too severe receptive language disorder</td>
<td>7</td>
</tr>
<tr>
<td>Could not be reached or did not want to participate</td>
<td>43</td>
</tr>
</tbody>
</table>

| Neuropsychological assessesment (NPA) T1 | 89 |
| Died before NPA T2 | 3 |
| Not able for NPA T2 | 3 |
| Second stroke | 2 |
| Could not be reached or did not want to be tested T2 | 11 |

| Neuropsychological assessesment (NPA) T2 | 70 |

Lesion data

Data concerning the asymptomatic brain lesions were collected from the patients’ medical reports. All patients underwent CT or MRI (8%) scanning. Asymptomatic brain lesions were classified as such when infarct-like lesions or white matter lesions were visible on CT or MRI, without known history of stroke according to both the patient and the GP. Stroke was defined as an acute focal neurological deficit due to brain ischemia, with the symptoms lasting more than 24 hours, as shown by CT scan or of presumed ischemic nature after appropriate clinical and neuroradiological diagnosis (WHO, 1989). Like in the study of Johansson, Norrving, and Lindgren (2000) the Oxfordshire Community Stroke Project (OCSP) classification for the overt stroke was made retrospectively on the
basis of neurological reports, when possible (Bamford, Sandercock, Dennis, Burn, & Warlow, 1991). This was done by a senior medical student who was trained and supervised by a neurologist. Both were blind to any of the other data from this study.

**Functional measures**

The Barthel Index (BI) was used to measure the patient’s performance on ten basic functions of daily living (Mahoney & Barthel, 1965). The scores range from 0 to 20 with higher scores indicating greater independence in functional ability. The BI was scored by the interviewer based on observations and information provided by the patient and partner.

**Aphasia and neglect**

Aphasia was assessed using two subtests from a Dutch aphasia test battery: Word comprehension [1] and Sentence comprehension [2] (SAN; Deelman, Koning-Haanstra, Liebrand, & van de Burg, 1981), and a 40-item object naming task [3] (Butter, Berg, Deelman, & Maring, 1988). Cut-off scores were applied. Moreover aphasia, both expressive [4] and receptive [5], was rated by a neuropsychologist, who was blind for the neuropsychological test data, as absent (score 0), mild (score 1), or severe (score 2). Combining these five scores led to a sum score with a minimum of zero and a maximum of seven points. Every patient with a sum score of two or higher was classified as aphasic. According to this classification 17 patients suffered from aphasia.

Neglect was tested using the Star-cancellation test (Wilson, Cockburn, & Halligan, 1987) and the Line bisection task (Schenkenberg, Bradford, & Ajax, 1980). The number of omissions on each tests [1, 2], and a deviation of more than 10 percent from the true centres of the lines [3] were used as cut off criteria (Schenkenberg et al., 1980; Van Deusen, 1984; Soukup, Harrell, & Clarck, 1994). The presence of neglect was also rated as absent (score 0), mild (score 1) or severe (score 2) by the neuropsychologist [4]. Combining the four scores led to a sum score with a minimum of zero and a maximum of five points. Every patient with a sum score of two or higher was classified as having neglect. Eight patients had neglect according to our definition.

**Global cognitive screening**

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 reliability and validity, moreover 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.
Cognitive performance

To assess memory a paired-associate learning task (Couples Test) and the Rey Auditory Verbal Learning Test (AVLT) were used. The Couples Test contained 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, that is 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 memory score is expressed as the mean percentage correct in the three (sub) tests, hence higher scores indicate better performance.

Speed of information processing was measured using a reaction time apparatus that separately registered movement and decision times (Van Zomeren & Deelman, 1976). In this study only the decision times, measured in milliseconds, were used. Because of intra-individual outliers in decision times, median scores were used. Visuomotor decision time was measured with a simple and an eight choice reaction time task. Cognitive decision time was assessed with two semantic categorisation tasks, one verbal (words) and one non-verbal (pictures). Previous analyses showed that visuomotor decision times and cognitive decision times actually measure two different aspects of speed of information processing (Gerritsen, Berg, Deelman, Visser-Keizer, & Meyboom-de Jong, 2003).

The Snijders Oomen Non-verbal Intelligence Test (SON-R 5 ½ -17) was used to measure reasoning capacities. Originally the SON-R 5 ½ -17 was constructed for deaf children, 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 is expressed as the mean of the percentages correct in each of the (completed) subtests, therefore higher scores indicate better reasoning abilities.

All neuropsychological tests started with extra simplified practice items to test for the basic conditions needed to meet the test demands (for example sufficient vision). One patient had to be excluded based on these examples.

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). Patients were asked to rate the amount of emotional and cognitive change they observed due to the stroke on a 4-point scale ranging from ‘not changed’ (0) to ‘very much changed’ (3). For this study the sum-score of the 5 questions concerning cognitive change was 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 by the medical ethics comity of the University Hospital Groningen. The same procedure was followed at T1 and T2.

Statistics

The differences between the stroke patients with and without asymptomatic brain lesions were assessed at both T1 and T2 for the subject characteristics: age, sex, and education, and for the stroke characteristics: side of stroke, aphasia, neglect, Barthel Index and Cognitive Screening Test. Dependent upon the distribution of the variables parametric T-tests, or non parametric Mann-Whitney U tests were used. The dichotomous variables were tested using Chi-square test statistics. Cognitive performance at both T1 and T2 was analysed using ANOVA considering capitalisation of chance. Moreover, MANOVA repeated measures were used to assess the course of cognitive functioning, with Time (T1 versus T2) as within group variables, and Group (patients with versus patients without asymptomatic lesions) as between group factor. Both ANOVA and MANOVA techniques were used instead of a single use of the multivariate analyses that would cause too much loss of information, due to dropout between T1 and T2, and occasional missing data. Subjective cognitive change was tested using both T-tests and MANOVA repeated measures. Differences in cognition between patients with one and more than one lesion were computed with Students’ t-tests. The alpha level was fixed at 0.05, and all tests were two-tailed (ns= non-significant).

Results

Prevalence of asymptomatic brain lesions

At T1, 23 stroke patients (26%) had asymptomatic brain lesions on CT or MRI. In this group 14 patients (61%) had one asymptomatic brain lesions, and 9 patients (39%) showed more than one asymptomatic brain lesions.
Drop out between T1 and T2

From the 18 patients who no longer participated at T2, five belonged to the group with previous lesions, and 13 to the group without ($\chi^2 = .04, p = .83$). In both groups one patient was excluded because of recurrent stroke. The other reasons for drop out were illness (stroke without asymptomatic brain lesion n = 2, stroke with asymptomatic brain lesion n = 1) or refusal to co-operate any longer (stroke without asymptomatic brain lesion n = 9, stroke with asymptomatic brain lesion n = 1). In both groups the patients who no longer participated at T2 did not significantly differ in age, sex or education from those who did participate.

Subject characteristics

Subject characteristics for both T1 and T2 are presented in table 2. The stroke patients with and without asymptomatic brain lesions did not differ in age, educational level or sex at either time of measurement. Moreover, there were no differences in the stroke-related factors: side, aphasia and neglect at T1. At T2 the number of aphasic and neglect patients was too small for statistical analyses. Table 2 clearly shows, though, that the absolute number of patients with neglect is larger in the patient group with asymptomatic brain lesions (n = 4), than in those without (n = 2). The level of daily activities (Barthel Index) was not different for the two groups either. None of the patients scored below cut-off on the dementia-screening test at both T1 or T2 (CST). The CST-score did not differ significantly between the two groups at T1, and just failed to reach significance at T2 ($p = .06$).

Objective cognitive performance

In table 1 and figure 1 the cognitive testscores are presented. At T1, ANOVA revealed no differences between the patients with and without asymptomatic brain lesions in reasoning capacities ($F(1,86) = 1.07, p = .30$), memory performance ($F(1,80) = 0.38, p = .54$), visuomotor decision time ($F(1,75) = 2.30, p = .13$) and cognitive decision time ($F(1,72) = 0.10, p = .75$). At T2, the same was true for reasoning ($F(1,70) = 2.71, p = .10$) and memory ($F(1,69) = 2.14, p = .15$), and the difference just failed to reach significance for the cognitive decision times ($F(1,64) = 3.14, p = .08$). Visuomotor decision times at T2, on the other hand, appeared to be significantly slower in the patients with asymptomatic brain lesions ($F(1,66) = 5.87, p = .02$).

After visual inspection of figure 1 there seems to be a difference in course of cognitive functioning between the two groups for all of the cognitive domains. Multivariate Repeated Measures, however, revealed no significant overall main effect of Time for the four cognitive domains ($F(4, 52) = 1.59, p = .19$), nor a significant interaction of Time x Group ($F(4, 52) = 1.79, p = .14$). However, univariately reasoning appeared to show a significant main effect of Time ($F(1, 55) = 4.81, p = .03$), and an interaction of Time x Group ($F(1, 55) = 4.54, p = .04$). As shown in figure 2, this indicates an improvement over time in reasoning performance for the patients without asymptomatic brain lesions, but not for those
with asymptomatic brain lesions. In the other cognitive domains no significant main effect of Time (df (1,55): memory F= 1.36, p= .25; visuomotor decision time F= 0.15, p= .70; cognitive decision time F= 2.45, p= .12), or interaction of Time x Group (df (1,55): memory F= 2.05, p= .16; visuomotor decision time F= 0.64, p= .43; cognitive decision time F= 3.35, p= .07) was found.

Table 2: Characteristics of patients with and without asymptomatic brain lesions (ABL).

<table>
<thead>
<tr>
<th>T1</th>
<th>Stroke with ABL</th>
<th>Stroke without ABL</th>
<th>Group comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 23</td>
<td>n = 66</td>
<td></td>
</tr>
<tr>
<td>Age (mean, sd)</td>
<td>69 (11)</td>
<td>65 (12)</td>
<td>t = -1.43 ns</td>
</tr>
<tr>
<td>Education (mean, sd)</td>
<td>4.1 (1.3)</td>
<td>3.8 (1.4)</td>
<td>Z = -0.55 ns</td>
</tr>
<tr>
<td>Sex</td>
<td>65% male</td>
<td>62% male</td>
<td></td>
</tr>
<tr>
<td>Side</td>
<td>52% RH</td>
<td>50% RH</td>
<td></td>
</tr>
<tr>
<td>OCSP</td>
<td>lacs 48% pacs 22%</td>
<td>lacs 41% pacs 26%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>tacs 17% pocs 4%</td>
<td>tacs 9% pocs 3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>unknown 9%</td>
<td>unknown 21%</td>
<td></td>
</tr>
<tr>
<td>BI</td>
<td>18.4</td>
<td>18.5</td>
<td>t = 0.14 ns</td>
</tr>
<tr>
<td>Aphasia</td>
<td>26%</td>
<td>17%</td>
<td>(\chi^2 = 0.98) ns</td>
</tr>
<tr>
<td>Neglect</td>
<td>17%</td>
<td>6%</td>
<td>(\chi^2 = 2.68) ns</td>
</tr>
<tr>
<td>CST (mean, sd)</td>
<td>17.3 (3.44)</td>
<td>18.5 (1.73)</td>
<td>Z = -0.85 ns</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T2</th>
<th>Stroke with ABL</th>
<th>Stroke without ABL</th>
<th>Group comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 18</td>
<td>n = 53</td>
<td></td>
</tr>
<tr>
<td>Age (mean, sd)</td>
<td>67 (9)</td>
<td>64 (11)</td>
<td>t = -1.01 ns</td>
</tr>
<tr>
<td>Education (mean, sd)</td>
<td>4.3 (1.3)</td>
<td>3.9 (1.3)</td>
<td>Z = -0.76 ns</td>
</tr>
<tr>
<td>Sex</td>
<td>62% male</td>
<td>61% male</td>
<td>(\chi^2 = 0.01) ns</td>
</tr>
<tr>
<td>Side</td>
<td>56% RH</td>
<td>51% RH</td>
<td>(\chi^2 = 0.12) ns</td>
</tr>
<tr>
<td>OCSP</td>
<td>lacs 48% pacs 22%</td>
<td>lacs 51% pacs 26%</td>
<td></td>
</tr>
<tr>
<td>BI</td>
<td>19.1</td>
<td>19.3</td>
<td>t = 0.43 ns</td>
</tr>
<tr>
<td>Aphasia</td>
<td>28% (n = 5)</td>
<td>15% (n = 8)</td>
<td>*</td>
</tr>
<tr>
<td>Neglect</td>
<td>22% (n = 4)</td>
<td>4% (n = 2)</td>
<td>*</td>
</tr>
<tr>
<td>CST (mean, sd)</td>
<td>17.4 (2.80)</td>
<td>18.8 (1.47)</td>
<td>Z = -1.88, p = .06</td>
</tr>
</tbody>
</table>

* Groups too small for statistical analyses.
Subjective cognitive change 

Like objective cognitive performance, subjective cognitive change did not differ significantly between the patients with and without asymptomatic brain lesions (t = -0.54, p = .60) at T1. At T2 a near-significant difference between the two groups appeared (t = -1.91, p = .06), indicating a trend towards more subjectively experienced cognitive changes in the group with asymptomatic brain lesions at T2. The data are presented in figure 2.

Figure 1: Course of cognitive performance for patient with and without asymptomatic brain lesions (ABL). DT = decision time.

Figure 2: Course of subjective cognitive change for patients with and without asymptomatic brain lesions (ABL).
GLM Repeated Measures showed a main effect of Time for the cognitive change that was experienced by the patients ($F(1,69) = 19.22, p < .01$), but no significant interaction Time x Group ($F(1,69) = 1.71, p = .20$). As can be seen in figure 2, this means that at T2 both patient groups experienced more cognitive changes, but this increase was not different for the groups with and without asymptomatic lesions.

**Number of asymptomatic lesions**

There were no differences between patients with one and patients with more than one asymptomatic brain lesion in cognitive test performance at T1 (*memory* $F(1,18) = 0.31, p = .59$; *reasoning* $F(1,21) = 0.46, p = .51$; *visuomotor decision time* $F(1,19) = 0.40, p = .56$; *cognitive decision time* $F(1,18) = 0.62, p = .44$). The same was true for T2 (*reasoning* $F(1,17) = 0.23, p = .64$; *memory* $F(1,16) = 0.10, p = .76$; *visuomotor decision time* $F(1,16) = 0.003, p = .96$; *cognitive decision time* $F(1,16) = 0.50, p = .49$).

Subjective cognitive change in patients with one and patients with more than one asymptomatic brain lesion did not differ at both T1 ($t = -0.42, p = .68$) and T2 ($t = 0.63, p = .54$) either.

**Conclusions & discussion**

In the present study the relation between asymptomatic brain lesions preceding stroke and post stroke objective and subjective cognitive functioning was examined. We focused on a community-based patient group, a group that has been relatively neglected in research as well as in clinical care.

Asymptomatic brain lesions were present in 26% of our patient group. There was no difference in age between the patients with and without asymptomatic brain lesions. Population-based studies consistently reported increasing age to be related to higher prevalence of silent brain infarcts and white matter lesions (for a review see Van Dijk, Prins, Koudstaal, & Breteler, 2002). Like in the present study, however, Price et al. (1997) found no relation between age and presence of silent infarcts in stroke patients, even though they did find this relation to be significant in their non-stroke group. Moreover, we found no difference in gender between the patients with and without asymptomatic brain lesions. The relation between white matter lesions or silent brain infarcts and sex in population-based studies is inconsistent, but if any difference was found women were more likely to have silent brain infarcts or white matter lesions than men (Van Dijk et al., 2002). In stroke patients male sex was found to be a predictor of silent brain infarcts in one study (Jorgensen et al., 1994), no relation between sex and white matter lesions was found in another (Wiszniewska, Deuyst, Bogousslavsky, Ghika, & Van Melle, 2000).

Stroke outcome with respect to basic self-care abilities, and both objective and subjective cognitive functioning appeared to be statistically the same for the
stroke patients with and without asymptomatic brain lesions at three months post-stroke. Moreover, no differences in cognition appeared between patients with one and patients with more than one asymptomatic lesion. So, the asymptomatic brain lesions were indeed asymptomatic. At 15 months post-stroke, on the other hand, the patients with asymptomatic brain lesions were significantly slower in visuomotor speed of information processing than the patients without asymptomatic lesions. Moreover, the patients with asymptomatic lesions showed less improvement in reasoning performance than those without. Improvement in cognitive decision time, reflecting a higher order level of speed of information processing, just failed to reach significance (p = .07), but showed the same trend that patients without asymptomatic lesions had become faster at T2, while the patients with asymptomatic lesions even got slower. No differences in memory performance at T2, or course of memory functioning were found.

Another borderline significant trend between the two patient groups was seen for the test performance on the cognitive screening test (CST, p = .06) and subjective cognitive functioning (p = .06) at T2: patients with asymptomatic lesions had lower CST-scores, and experienced more cognitive changes than the patients without asymptomatic brain lesions. Moreover, at 15 months post stroke the number of neglect patients was larger in the patient group with asymptomatic brain lesions, but the number of patients was too small for statistical analyses. This finding merely states that there was a little more drop-out of neglect patients in the group without than in the group with asymptomatic lesions. The fact that some of the effects that were found just failed to reach significance might be explained by the small number of patients in the group with asymptomatic brain lesions, that was even smaller at T2. Further research with larger groups would be needed.

So, the first main finding was that although there were no differences in cognitive functioning at three months post stroke between patients with and without asymptomatic lesions, course of cognitive functioning and performance at T2 differed between the two patient groups at the disadvantage of the patients with asymptomatic lesions. The present results seem to be in line with the hypothesis formulated by Ballard et al. (2003), suggesting that cognitive function in stroke patients improves unless concurrent cerebrovascular or neurodegenerative diseases are present, or new cerebral insults occur. Hence, the capacity to compensate for or adapt to the effects of the clinical stroke might be diminished by the presence of the asymptomatic brain lesions. In future research it would be interesting to examine the MRI correlates of cognitive functioning in stroke patients at follow-up in order to study whether the presence of asymptomatic lesions at time of first-ever stroke, or the development of new silent strokes or expansion of white matter lesions contributes to the diminished improvement of cognitive functioning. The only study we know of that studied cognitive functioning as well as MRI correlates longitudinally was performed in stroke free elderly and showed that cognitive decline was stronger in patients with recurrent asymptomatic brain lesions (Vermeer, 2003). In the present study the number of asymptomatic lesions
preceding clinical stroke did not influence stroke outcome with respect to the used outcome measures, but no neuroradiological follow-up data were available.

Second, the cognitive domains that appeared to be most sensitive to the effects of asymptomatic brain lesions were visuomotor decision speed, categorisation decision speed and reasoning. Speed of information processing has been related to white matter lesions in stroke patients (Burton et al., 2004) and in healthy elderly to silent infarcts or white matter lesions (O’Brien, et al., 2002; Vermeer et al., 2003; Ylikoski, et al., 1993). In contrast to Burton and co-workers (2004) we found no relation between asymptomatic lesions and memory functioning in the stroke patients. Burton and colleagues examined an older group (80 years mean) of patients and only looked at white matter lesions, not silent brain infarcts. White matter lesions may have been more extensive in their patient group considering the strong relation between extension of white matter lesions and increasing age (Van Dijk, et al., 2002). Executive functioning was found to be related to white matter lesions in stroke patients in one study (Vataja, et al., 2003), but not in another (Burton, et al., 2004). Executive functioning can be considered a complex of various cognitive capacities, among which reasoning, and can be operationalised and thus measured in many different ways. Reasoning may be considered an essential skill in solving many of the new problems that one has to cope with after stroke. The relation between reasoning and asymptomatic brain lesions has not explicitly been studied before.

Finally, both patient groups subjectively experienced more cognitive change in time, but the difference between the groups at T2 just failed to reach significance. This is in line with the findings demonstrated by De Groot and co-workers (2001) in a population study, but we know of no studies investigating the relation between subjective cognitive decline and asymptomatic lesions in stroke patients.

The major limitation of this study was the lack of uniform MRI data concerning the asymptomatic lesion variables. Since this was a community-based study most patients only had a CT-scan within a few days after stroke. First of all, this might cause an underestimation of the number of patients with asymptomatic lesions, especially white matter lesions being better detected and defined by MRI (Wahlund et al., 2001). Second, since the data were derived from the patient’s medical reports, the lesions were not described consistently enough to reliably compare the differences between patients with silent brain infarcts, periventricular or subcortical white matter lesions, or a combination of asymptomatic lesions. Still, if these data could be interpreted the subgroups would be too small, lacking too much statistical power. Hence, the present study did not pretend to relate specific lesions to specific cognitive functions.
In conclusion, the presented data demonstrated that in a community-based patient group with clinically first-ever ischemic stroke, preceding asymptomatic brain lesions had no significant impact on objective or subjective cognitive functioning at three months post stroke. However, improvement of speed of information processing and reasoning between three and 15 months post-stroke were to some extent compromised by the presence of asymptomatic brain lesions.
References


