Neuropsychological findings in young-adult stroke patients

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Abstract

There are few data on neuropsychological deficits in young-adult stroke patients. This study investigates cognitive conditions in a young-adult stroke population, as well as tasks that detect their neuropsychological impairment.

Forty 18- to 47-year-old stroke patients, and a matched control group, completed a neuropsychological battery to evaluate deficits related to cognition, daily activities and mood.

Patients performed worse than controls; five patients were classified as demented, three had global cognitive impairment and eight partial cognitive impairment. Cognitive impairment was more closely associated with reduced performance of daily activities than with motor deficits.

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1. Introduction

Stroke is rare in young people: only 5–10\% of acute cerebrovascular events occur in people younger than 45 years of age. The annual incidence of stroke in people younger than 35 is 3.5/100,000, a figure which rises to 30–50/100,000 for 35- to 44-year-old patients and doubles every decade thereafter (Bogousslavsky \& Regli, 1987; Bogousslavsky \& Pierre, 1992).

Although the long-term outcome of cerebral infarction is better in young adults than in older patients, morbidity and mortality is still significant. A recent study shows a favourable functional outcome in 77.9\% of patients after a mean follow-up of 5.7 years; mortality in that study was 5, 11 and 12\% at 1, 5 and 10 years, respectively (Naess, Nyland, Thomassen, Aarseth, \& Myhr, 2004). Other hospital-based studies (15- to 44-year age group) have reported long-term mortality ranging from 5 to 16\% (Hindfelt \& Nilsson, 1992; Chancellor, Glasgow, Ockelford, Johns, \& Smith, 1989; Marini, Totano, \& Carolei, 1999; Snyder \& Ramirez-Lassepas, 1980).

Outcome data vary according to different authors. Hindfelt and Nilsson (1992) followed 74 young patients for 13–26 years: 12 died of severe underlying disease, while seven suffered a new cerebrovascular event. As regards resuming work, 63\% were able to keep their previous position, while 27\% resigned from their job. Only 8\% of the subjects who resigned were affected by a moderate or severe motor deficit. The authors of another study (Alfassa et
al., 1997) assessed a population composed of 199 patients aged 17–49 years by means of a structured questionnaire based on patient and/or family interviews. In a 3/6-month period, they found an average improvement in measures of functional outcome of 4%, in social activities of 15% and in working abilities of 8%; after a 6/12-month period these figures dropped to 3, 10 and 2% respectively. Moreover, 67% of the whole patient sample were able to resume work.

These results demonstrate that the relatively high recovery rate and functional improvement during follow-up do not match improvement rates in employment and social integration.

Two conclusions can be drawn: first, differences in outcomes reported in previous works may be due to the outcome criteria considered or the different types of patients enrolled; second, despite a good functional and motor outcome, young-adult patients usually encounter difficulties in social activities and work caused by a cognitive impairment as opposed to a severe motor deficit. Although there are few data on cognitive impairment in young-adult stroke patients, many authors have described neuropsychological deficits following stroke in the elderly (Pohjasvaara, Erkinjuntti, Vataja, & Kaste, 1997; Tatemichi et al., 1990, 1992; Srikanth et al., 2004); Tatemichi et al. (1992), after studying a cohort of 251 patients with acute cerebrovascular diseases over 60 years, found that 26.3% developed dementia, compared with 3.2% of controls.

Since few studies have been conducted on cognitive assessment in young post-stroke patients (Hindfelt & Nilsson, 1992; Saeki, Ogata, Okubo, Takahashi, & Hoshuyama, 1995), we decided to investigate the neuropsychological deficits in such patients to quantify the incidence of cognitive impairment and dementia, and identify the clinical characteristics, such as cerebrovascular risk factors, previous strokes, neurological conditions, neurosonology and neuroimaging patterns, of cognitively impaired patients.

2. Subjects and methods

Between January 1995 and June 1997, we admitted 46 consecutive patients younger than 49 years of age with a first-ever ischemic stroke.

Inclusion criteria were: acute cerebrovascular disease either in the carotid or in the vertebrobasilar territory, literacy. Exclusion criteria were: psychiatric disorders, mental retardation, alcohol or drug abuse, neoplasms, metabolic disorders and any other central nervous system diseases. Patients with a score <3 on the Aphasia Severity Rating Scale from the Boston Diagnostic Aphasia Examination (Goodglass & Kaplan, 1972, 1983) were excluded. Informed consent was obtained from all the patients.

Six of the patients (four men and two women, mean age 34.25, S.D. 7.2, range 20–44) were excluded: one had severe mental retardation, three had aphasia, one a psychiatric illness, while the last did not wish to participate.

The final study sample was composed of 40 patients (16 men and 24 women) with a mean age of 38.8 years (range 18–47, S.D. 8.3) and a mean education level of 11.3 years (range 8–17).

While hospitalized, all the patients underwent a daily clinical examination comprising the Canadian Neurological Scale (CNS) (Côté, Hachinski, Shurvell, Norris, & Wolfson, 1986), brain CT and/or MRI, and examinations capable of detecting etiopathogenetic causes of stroke. After a 6–12-month period (mean 9.2 months) after stroke onset, all the patients completed a neuropsychological battery of tests designed to evaluate orientation, verbal memory, verbal functions and language skills, and concept formation and reasoning. A scale to evaluate the patients’ abilities in domestic conditions was also administered. The patients enrolled were matched with 40 healthy controls (mean age 37.8, S.D. 8.4; mean education level 11.7 years, S.D. 3.4), all of whom completed the same neuropsychological battery of tests.

2.1. Neuropsychological assessment

All the patients underwent the following tests:

2.1.1. Mini mental state examination (MMSE) (Folstein, Folstein, & McHugh, 1975)

A brief screening instrument for dementia. Correction for education level was performed. Scores below 24 are considered be indicative of dementia (Lezak, 1995).
2.2. Memory tests

2.2.1. Auditory-verbal learning test (AVLT) (Rey, 1964)

The learning and immediate and delayed recall of 15 high-frequency, semantically unrelated words administered five times. This test detects both short-term retention (given by the number of words recalled after each administration or, as we preferred, by summing up the five trial scores) (Lezak, 1995) and long-term memory, as assessed by the number of words recalled after 15 min of interpolated activity without a further presentation.

2.2.2. Digit span test (DST)

Composed of Digit Forward (DST-F) and Digit Backward (DST-B) (Wechsler, 1955, 1981); this is one of most common tests in the Wechsler batteries for measuring span of immediate verbal recall.

2.2.3. Babcock story recall test (BSRT) (Babcock & Levy, 1940)

In this test, a 21-unit story is used to measure both immediate and delayed recall.

2.3. Linguistic tasks

2.3.1. Token test (Boller & Vignolo, 1966)

The patient has to touch several tokens of different shapes and colors in the order chosen by the examiner. Although this test is simple to administer, score and perform for almost all non-aphasic people, it is sensitive to disrupted comprehension processes, which are central to aphasic disability even when communication behavior has remained intact. Performance of this test also involves immediate span for verbal sequences and capacity to use syntax (Lesser, 1976).

2.3.2. Semantic verbal fluency (SVF) (Lezak, 1995)

This is measured by the quantity of words produced, usually within a restricted category. Name categories are semantic (animals, cities, fruits and colors), and the patient is given 60 s to name as many words as possible in each category. The score is obtained by summing up all the words produced.

2.3.3. Boston naming test (BNT) (Kaplan, Goodglass, & Weintraub, 1983)

This consists of large ink drawings of items which decrease in familiarity, from the most common, such as “tree” or “pencil”, to less common ones, such as “sphinx” and “trellis”.

2.4. Visual spatial analysis

2.4.1. Corsi’s block-tapping board (Milner, 1971)

This consists of nine, black 1 1/2-inch cubes fastened in random order to a blackboard; each time the examiner taps the blocks in a prearranged sequence, the patient must copy the tapping pattern.

2.5. Concept formation and deductive reasoning


In this test of verbal concept formation, the subject is asked to explain what pairs of words have in common.

2.5.2. Raven’s progressive matrices (RPM) (Raven, 1960, 1976; Burke, 1997)

This is a well-known test of visual spatial intelligence which entails picking, from a set of distractors, the items logically missing in a given visual spatial pattern.

In order to compare the results of tests obtained from the two populations, we selected a cut-off for each test using the following formula: \( Av_{co} - 2SD \), where \( Av_{co} \) is the average score obtained by controls.
2.6. Daily activity abilities:

The Barthel Index (Mahoney & Barthel, 1965) was used; this index contains 10 items that measure daily functioning, particularly activities of daily living and mobility. The items include feeding, transferring from a wheelchair to bed and back, grooming, transferring to and from a toilet, bathing, walking on an even surface, going up and down stairs, dressing, and bowel and bladder continence. The overall score ranged from 0 to 100.

2.7. Neurological conditions:

The Canadian Neurological Scale was administered both during hospitalization and when the patients were assessed subsequently. This scale assesses the level of consciousness, orientation, language and motor strength. Each domain is assigned a score. The overall score ranges from 0 to 11.5.

2.8. Depression scale

The Self-Rating Depression Scale (SDS) (Zung Scale) (Zung, 1967) was administered to evaluate depressed mood; this is a 20-item scale, used above all for persons between the ages of 19 and 65, as the scores of older and younger subjects tend to be excessively high.

We defined patients as mildly, moderately or severely depressed according to the Zung Self-Rating Depression Scale Software by N. Bertuccio.

2.9. Diagnostic criteria

Subtypes of stroke were defined according to the TOAST criteria (Adams et al., 1993): large and small vessel atherosclerosis, cardioembolism, other determined causes, unknown cause. As regards other causes, we identified the following as possible causes of stroke:

(1) Autoimmune stroke: characterized by antiphospholipid antibody syndrome and autoimmune diseases (Fieschi, Rasura, Anzini, & Beccia, 1998).
(2) Cervical artery dissection: extravasation of blood into the arterial wall with partial or complete obstruction of the lumen (Fieschi et al., 1996).
(3) Migraine stroke: persisting focal neurological deficit accompanied by migraine, with the exclusion of all other etiologies (Fieschi et al., 1996).

A diagnosis of dementia was made when the MMSE score was lower than 24/30.

In addition, we considered the scores obtained in the following tests designed to assess language, memory and reasoning: SVF, AVLT for delayed recall, RPM, Token test, Similarities. When the results of all 5 tests were below the established cut-off, the patients were considered “globally impaired”, whereas patients who failed three or four tasks were considered “partially impaired”.

2.10. Neuroimaging assessment pattern

All the patients underwent a brain CT or MRI to determine which hemisphere was impaired as well as both the number and distribution of the lesions divided according to the following areas: anterior cerebral artery (ACA), middle cerebral artery (MCA), posterior cerebral artery (PCA) and vertebrobasilar (VB). The size of the lesions was classified according to the TOAST stroke subtypes, i.e. infarct or lacuna.

2.11. Statistical analysis

The statistical analysis was performed using the $\chi^2$-test. Fisher’s Exact Test was used when the minimum estimated value was less than 5. Student’s $t$-test was used to compare group means. To study the influence of several factors on a
single parameter, we used an ANOVA model. The results were corrected using Bonferroni’s formula (0.05/number of variables). All the analyses were performed using the statistical software package by BMDP.

3. Results

The age, sex and education level of the stroke patients and controls are shown in Table 1; the cerebrovascular risk factors, territory involved and etiological diagnosis of the patients are shown in Table 2.

At stroke onset, the mean Canadian Neurological Scale score was 9.8 (range 3.5–11.5, S.D. 1.96). Twenty patients (50%) (five men and 15 women) had a mildly to moderately depressed mood on the SDS Scale. No controls were depressed. The mean Canadian Neurological Scale score at the time of neuropsychological evaluation was 10.6. The mean Barthel Scale score was 87.

Patients performed worse than controls in the neuropsychological tests; this finding emerges from both the mean score obtained in each test by the patients (Table 3) and the number of failed tests. The following tests were those failed significantly more often by patients than by controls: Token test, RPM, AVLT Delay and Similarities (Table 4).

Table 1
Age, sex and education of patients and controls

<table>
<thead>
<tr>
<th></th>
<th>Sex (M/F)</th>
<th>Age ± S.D. (range)</th>
<th>Education level (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>15/25</td>
<td>37.8 ± 8.5 (18–47)</td>
<td>11.7</td>
</tr>
<tr>
<td>Stroke patients</td>
<td>16/24</td>
<td>38.8 ± 8.3 (18–47)</td>
<td>11.3</td>
</tr>
</tbody>
</table>

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Table 2
Characteristics of patients

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>9</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>18</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>0</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>6</td>
</tr>
<tr>
<td>Peripheral vasculopathy</td>
<td>6</td>
</tr>
<tr>
<td>Obesity</td>
<td>4</td>
</tr>
<tr>
<td>Oral contraceptives</td>
<td>10</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>1</td>
</tr>
<tr>
<td>Migraine</td>
<td>7</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>2</td>
</tr>
<tr>
<td>Etiopathology</td>
<td></td>
</tr>
<tr>
<td>Cardioembolic</td>
<td>18</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>10</td>
</tr>
<tr>
<td>Coagulation/immunologic pathologies</td>
<td>3</td>
</tr>
<tr>
<td>Arterial dissection</td>
<td>4</td>
</tr>
<tr>
<td>Undetermined/Unknown</td>
<td>5</td>
</tr>
<tr>
<td>Arterial Territory</td>
<td></td>
</tr>
<tr>
<td>ACA</td>
<td>3</td>
</tr>
<tr>
<td>MCA</td>
<td>14</td>
</tr>
<tr>
<td>PCA</td>
<td>1</td>
</tr>
<tr>
<td>Verteobasilar</td>
<td>7</td>
</tr>
<tr>
<td>Multiple lesions</td>
<td>15</td>
</tr>
<tr>
<td>Side of lesion</td>
<td></td>
</tr>
<tr>
<td>Left hemisphere</td>
<td>15</td>
</tr>
<tr>
<td>Right hemisphere</td>
<td>18</td>
</tr>
</tbody>
</table>

ACA indicates anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery.
By contrast, no correlation emerged between these tests and the number and site of lesions, ultrasound pattern and neurological conditions.

Five patients (two men and three women, mean age 43.4, S.D. 1.3) had a MMSE score lower than 24/30; no controls had a MMSE score lower than 24. Three of these five patients had been employed before the stroke. None of the demented patients differed from the other patients as regards cerebrovascular risk factors, CNS score or SDS score. Two patients had multiple lacunas in the white matter, one had a stroke in the posterior limb of the left internal capsule, one in the right thalamus and one in the right parietal temporal area. There were no significant differences in the neuroradiological findings between demented and non-demented patients.

In order to correctly define “cognitively impaired” patients, we used the previous definition of global and partial impairment on the basis of the patient’s performance in different neuropsychological tasks. We found three patients with “global” and eight with “partial impairment”. These patients did not differ from others as regards age, cerebrovascular risk factors, etiological diagnosis, ultrasound pattern or SDS score. A correlation was instead found in these patients between education level and cognitive performance (Table 5).

Table 6 shows the correlation between MMSE and cognitive performance: patients who scored lower than 24 were characterized by more than three failed tests; most of the patients who scored higher than 24 did not present cognitive impairment. However, some “partially impaired” patients had a MMSE score that was lower than 24, while others had...
Table 5
Comparison of global/partial impairment and education level

<table>
<thead>
<tr>
<th>Cognitive impairment</th>
<th>Education level (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;8</td>
</tr>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Partial</td>
<td>2</td>
</tr>
<tr>
<td>Global</td>
<td>0</td>
</tr>
</tbody>
</table>

\( p = 0.03 \)

Table 6
Comparison of global/partial impairment and MMSE

<table>
<thead>
<tr>
<th>Cognitive impairment</th>
<th>MMSE</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;24</td>
<td>&gt;24</td>
</tr>
<tr>
<td>None</td>
<td>1</td>
<td>28</td>
</tr>
<tr>
<td>Partial</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Global</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

\( p = 0.01 \)

Table 7
Comparison of MMSE score < 24 and “failed” tests

<table>
<thead>
<tr>
<th>Test “failed”</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>RPM</td>
<td>0.0003*</td>
</tr>
<tr>
<td>AVLT delayed recall</td>
<td>0.16</td>
</tr>
<tr>
<td>AVLT immediate recall</td>
<td>0.01*</td>
</tr>
<tr>
<td>BSRT</td>
<td>0.01*</td>
</tr>
<tr>
<td>SVF</td>
<td>0.7</td>
</tr>
<tr>
<td>Token test</td>
<td>0.3</td>
</tr>
<tr>
<td>BNT</td>
<td>0.08</td>
</tr>
<tr>
<td>DST-F</td>
<td>0.09</td>
</tr>
<tr>
<td>DST-B</td>
<td>0.002*</td>
</tr>
<tr>
<td>Corsi</td>
<td>0.09</td>
</tr>
<tr>
<td>Similarities</td>
<td>0.03*</td>
</tr>
</tbody>
</table>

For abbreviations see text.

* Result is significant if \( p \) less than 0.05.

A score that was higher than 24. Furthermore, even some patients with a global impairment had an MMSE score higher than 24.

An MMSE score lower than 24 was linked with the following failed tests: RPM (\( p = 0.0003 \)), DST-B (\( p = 0.002 \)), Similarities (\( p = 0.03 \)), BSRT (\( p = 0.01 \)) and AVLT for immediate memory (\( p = 0.01 \)) (Table 7).

We did not find any correlation between the size, number and side of lesions with either demented, globally or partially impaired patients or with an etiological diagnosis of stroke.

Dementia and cognitive impairment were associated with a lower Barthel Scale score (Tables 8 and 9).

Table 8
Comparison of neurological conditions/daily activity abilities and dementia

<table>
<thead>
<tr>
<th></th>
<th>Mean Barthel Index Score</th>
<th>( p )</th>
<th>Mean CNS(^a) Score</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demented (MMSE &lt;24)</td>
<td>68</td>
<td>0.03</td>
<td>9.8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Non-demented (MMSE &gt;24)</td>
<td>90</td>
<td></td>
<td>10.8</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) CNS: Canadian Neurological Scale.
Table 9
Comparison of neurological conditions/daily activity abilities and cognitive impairment

<table>
<thead>
<tr>
<th>Cognitive impairment</th>
<th>Mean Barthel Index Score</th>
<th>$p$</th>
<th>Mean CNS(^a) Score</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>92</td>
<td></td>
<td>10.7</td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>88</td>
<td>0.05</td>
<td>10.7</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Global</td>
<td>71</td>
<td></td>
<td>10.1</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) CNS: Canadian Neurological Scale.

4. Discussion

Our study shows how young adults who have had a stroke may, despite a good motor outcome, develop cognitive impairment which causes difficulties in social activities.

The patients’ cognitive performances were worse than those of controls, both as regards the average scores and the number of failed tests. Some tests, such as AVLT, Similarities, Token test and RPM, were found to be particularly sensitive to cognitive impairment.

Our results show that the Token test, though apparently easy to perform, can induce mistakes due to defective auditory comprehension, difficulty in recognizing shapes and colors and, in non-aphasic patients, to difficulty in flexibility and execution of multiple commands. Thus, this test may effectively detect cognitive impairment (Swihart, Panisett, Becker, Beyer, & Boller, 1989). Thus, “failures” were due to general cognitive deficits rather than to specific auditory disturbances. There was no correlation between the type of patients who failed the Token test and the site of the ischemic lesion, which suggests that non-aphasic subjects are also sensitive to this test (De Renzi & Vignolo, 1962).

The BSRT, like other span tests, reveals both attentional and memory problems (Lezak, 1995). Our data reveal a correlation between the BSRT and other tests designed to assess memory functions, such as the AVLT, DST and SVF. Hence, since the BSRT is sensitive to immediate memory, it could be used to assess global memory impairment in young-adult stroke subjects.

Tests designed to assess reasoning and concept formation are easily failed by patients. As confirmed by data in the literature, the Similarities test tends to be more sensitive than other tests to the effects of brain injury, regardless of the site of the lesion (Hirschenfang, 1960).

Low scores in the Similarities test are observed in demented patients (Hart, Kwentus, Taylor, & Hamer, 1988; Whelihan & Lesher, 1985) and represent an early predictor of cognitive decline in middle-aged persons (La Rue & Jarvik, 1987). In our study, patients with a low MMSE score had difficulty in performing the Similarities test, which may therefore represent, together with the RPM, a marker of severe cognitive impairment in young-adult stroke patients.

Although the MMSE and cognitive impairment are correlated, some of the patients in our study defined as partially or globally impaired had an MMSE score higher than 24. This suggests that the MMSE alone cannot detect a neuropsychological deficit in young people. It is worth noting that even if a score below 24 is usually considered to be an indicator of dementia, some authors have recommended a cut-off of 27 and 25 respectively for multiple sclerosis (Beatty & Goodkin, 1990) and for well-educated Alzheimer patients (Galasko et al., 1990). However, we maintained a cut-off of 24 in accordance with previous studies conducted on dementia following stroke in the elderly.

We assessed the ability of tests to detect “partial” and “global” impairment in order to measure the patients’ functional abilities, since the definition of dementia based on a low MMSE score may be unsuitable for young patients.

Subjects with an MMSE score lower than 24 did not differ from other patients as regards cerebrovascular risk factors, age, CNS and SDS scores, neuroimaging and previous cerebrovascular diseases.

A low score on the daily activity scale was found in patients with dementia and cognitive impairment (Tables 8 and 9); these data suggest a difficulty in living activities related to a neuropsychological deficit rather than motor involvement, which confirms the findings in previous papers (Alfassa et al., 1997).

We found no correlation between failed tests, cognitive impairment, dementia and ultrasound examinations, cerebrovascular risk factors, previous stroke or neuroimaging pattern. The correlation between neuroimaging and the involvement of some functions, such as concept formation and deductive reasoning, was, as previously reported in the literature, not related to the site of the lesions, (Hart et al., 1988).
In conclusion, our data suggest that cognitive impairment may, even in a young-adult stroke population, occur 6–12-months after stroke onset. The characteristics of young ischaemic stroke patients defined as demented are different from those found in an elderly population (Bevan, Sharma, & Bradley, 1990), in whom diabetes and previous cerebrovascular events, associated with a characteristic pattern of brain lesions, have been found to be predictive of dementia. By contrast, we did not observe any correlation between cognitive impairment and neuroimaging, age, CNS or SDS scores.

Finally, a cognitive impairment classification designed to shed light on a patient’s performance in daily activities could be used to assess the state of post-stroke populations as well as the results achieved by means of rehabilitation or pharmacological therapy.

In conclusion, our findings confirm that severe cognitive impairment may explain the difficulties encountered in social activities by a high number of young stroke patients who have made an otherwise good motor recovery.

References


