Chronic memory impairment after cardiac arrest outside hospital

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Neil R Grubb, Ronan O'Carroll, Stuart M Cobbe, Jane Sirel, Keith A A Fox

Abstract

***Objectives*—To evaluate the nature, prevalence, and severity of chronic memory deficit in patients resuscitated after cardiac arrest outside hospital and to determine whether such deficits are related to duration of cardiac arrest.**

***Design*—Case-control study.**

***Subjects*—35 survivors of cardiac arrest outside hospital and 35 controls matched for age and sex who had had acute myocardial infarction without cardiac arrest.**

***Main outcome measures*—Subjects assessed at least two months after index event for affective state (hospital anxiety and depression scale), premorbid intelligence (national adult reading test), short term recall (digit recall test), and episodic long term memory (Rivermead behavioural memory test).**

***Results*—Cases and controls showed no difference in short term recall. Cases scored lower on Rivermead test than controls (mean (SD) score out of 24 points: 17.4 (5.4) v 21.8 (2.0), P<0.001), particularly in subtests relating to verbal and spatial memory. Moderate or severe impairment was found in 37% of cases and in no controls. Severity of impairment of memory correlated significantly with measures of duration of cardiac arrest. This deficit was not significantly associated with subjects' age, interval from index event to assessment, occupation, measures of comorbidity, social deprivation, anxiety or depression scores, or estimated premorbid intelligence.**

***Conclusions*—Clinically important impairment of memory was common after cardiac arrest outside hospital. Improvement in response times of emergency services could reduce the severity of such deficits. With an increasing numbers of people expected to survive cardiac arrest outside hospital, rehabilitation of those with memory deficit merits specific attention.**

Introduction

In 1989 the Heartstart Scotland initiative resulted in an automated external defibrillator being provided for each emergency ambulance of the Scottish Ambulance Service.[1] In addition paramedics have been trained to perform procedures such as endotracheal intubation before reaching hospital. Performing defibrillation outside hospital has been shown to improve survival rates in Britain[2] and in other countries.[3-5] The effect of paramedic interventions is less clear, and care should be taken in interpreting survival rates because of possible differences in the types of cases attended.[6] In Edinburgh, since the introduction of these measures, there has been a fourfold increase in the number of victims of cardiac arrest surviving to discharge from hospital.[7]

Most studies of outcome after cardiac arrest outside hospital have focused on mortality rather than morbidity, and there are few accounts of cognitive deficits among survivors. Existing studies provide variable accounts of the prevalence of memory deficit and often fail to compare the memory function of survivors of cardiac arrest with that of patients surviving other acute cardiac events.[8-10] This comparison is important to control for underlying disease and for the psychological consequences of admission to an acute cardiac care unit.[11]

Characterisation of chronic memory deficit after cardiac arrest outside hospital is needed to determine whether the rehabilitation requirements of such patients differ from those of patients surviving other acute cardiac events. It is known that memory deficit impedes rehabilitation in patients with other forms of brain injury.[12] With the provision of defibrillators to all British ambulance services by the end of 1991, and the launch in 1994 of Heartstart UK (an initiative promoting basic life support training),[13] we can expect to care for more of these patients in future.

This study was designed to identify the nature, prevalence, and severity of memory deficits in survivors of cardiac arrest outside hospital, compared with survivors of myocardial infarction not complicated by cardiac arrest. We also sought to identify whether any memory impairment occurring after cardiac arrest was related to the duration of circulatory arrest.

Subjects and methods

STUDY POPULATION

The Royal Infirmary of Edinburgh serves a principally urban catchment population of 604 070 in an area of 1291 km^2 and admits about 85 patients with cardiac arrest outside hospital annually, of whom about 40 patients are discharged alive.[14] We attempted to trace 54 consecutive patients discharged between May 1993 and July 1994 after cardiac arrest outside hospital. Five of the patients had died, and we could not contact 12 patients who lived outside Lothian Region. Of the 37 patients who were still alive and resident in the region, 35 (28 men and seven women) agreed to an assessment. We assessed them at least two months after their index event to eliminate any effects of transient memory impairment that can complicate cardiac arrest.[15] None of the cases had previously had a diagnosis of organic brain disease or stroke unrelated to the cardiac arrest.

The control group consisted of subjects who had survived acute myocardial infarction and who had never experienced cardiac arrest. These subjects had been admitted during the same period as the cases, and their hospital discharge records were used to match them with cases for age (within four years) and sex.

We examined several potential confounding variables. We noted treatment with β adrenergic antagonists, which might affect memory function,[16] and whether subjects had undergone cardiopulmonary bypass, which can be complicated by cognitive impairment.[17] We also generated a comorbidity score by calculating the total number of the following comorbidities attributed to each patient: heart failure, hypertension, hyperlipidaemia, diabetes mellitus, chronic pulmonary disease, chronic renal disease, and malignancy. We noted subjects' current smoking habit at assessment.

ASSESSMENT OF PSYCHOSOCIAL FACTORS

We assessed affect with the hospital anxiety and depression questionnaire.[18] Clinically important anxiety or depression is likely with a score of 11 or more points (maximum 21) in the relevant component of the test. A score of 9 or 10 points is of borderline clinical significance. We used the national adult reading test to estimate premorbid intelligence.[19] In this test the subject reads aloud fifty irregular, non-phonetic words. The number of correctly pronounced words provides an approximate index of intelligence. We chose this test because performance is relatively unaffected in other forms of dementia.

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To determine whether socioeconomic factors influenced performance in the cognitive tests, we assigned each subject to one of seven Carstairs and Morris deprivation categories (updated for the 1991 census by McLoone and Carstairs) according to their postcode, based on four variables: unemployment, car ownership, overcrowding, and percentage of residents in socioeconomic groups IV and V.[20] We examined occupation as a separate variable by recording the type of occupation (manual or non-manual; former occupation if retired) of the principal wage earner in each subject's household.

ASSESSMENT OF MEMORY FUNCTION

We asked our subjects to attend hospital for assessment, and, to those who declined (five cases and two controls), we offered assessment at home. Assessments were conducted by a single, unblinded, trained examiner.

The Rivermead behavioural memory test was used as the principal measure of episodic long term memory.[21] This test is designed to identify memory difficulties which patients might encounter during everyday living. It provides a sensitive measure of memory functioning with several subtests—remembering a name (after a 20 minute delay), the location of a hidden personal item (20 minute delay), an appointment (20 minute delay), a news report (immediate and delayed), objects and faces from picture cards (3-4 minute delay), a short route (immediate and delayed), and orientation questions. Each subtest scores between 0 and 2 points, giving a maximum total score ("profile" score) of 24 points. This test divides performance into four categories of memory impairment according to the profile score—normal (22-24 points), mild (17-21 points), moderate (11-16 points), and severe (<11 points).[21]

We used the digits forward and digits backwards subtests from the revised Wechsler memory scale as measures of primary short term working memory.[22]

DURATION OF CARDIAC ARREST

We obtained the relevant times (time of emergency call for an ambulance and time of successful defibrillation) from the database of Heartstart Scotland. Times were recorded to the nearest minute. We selected the time of the emergency call as the first well defined index time of each cardiac arrest since bystanders' estimates of the time of collapse tend to be variable. The time of the emergency call was recorded by the ambulance dispatcher. The time of defibrillation was stored in the memory of the defibrillator, which had an internal clock synchronised with that of the ambulance dispatcher.

Table 1—*Characteristics of 35 cases who had had cardiac arrest outside hospital and 35 controls who had had myocardial infarction. Values are mean (SD) unless stated otherwise*

	Cases	Controls	Difference (95% confidence interval)	P value
Age	65.0 (10.8)	66.1 (10.2)	1.1 (−4.1 to 6.3)	0.675
Time from index event to assessment (months)	6.7 (4.4)	8.6 (3.8)	1.9 (−0.1 to 3.9)	0.055
Hospital anxiety and depression scale:				
Anxiety score	5.2 (4.6)	3.6 (3.0)	1.6 (−0.2 to 3.5)	0.080
Depression score	4.2 (3.9)	3.3 (2.4)	0.9 (−0.6 to 2.5)	0.226
National adult reading test (correct responses)	29.4 (10.7)	29.9 (11.8)	0.5 (−5.5 to 5.7)	0.957
Comorbidity index	1.3 (0.9)	1.4 (1.0)	0.1 (−0.3 to 0.9)	0.394
Social deprivation index	4.0 (1.4)	3.3 (1.8)	0.7 (−0.1 to 1.6)	0.071
Smoking status:				
No (%) of current smokers	10 (29)	12 (34)	5 (−17 to 27)	>0.50 (χ^2 = 0.07)
No (%) of non-smokers	25 (71)	23 (66)		
Occupation:				
Manual	16 (46)	20 (57)	4 (−20 to 28)	>0.10 (χ^2 = 0.51)
Non-manual	19 (54)	15 (43)		

STATISTICAL METHODS

We used unpaired, two tailed Student's t tests with separate variance analyses to compare the baseline characteristics (age, premorbid intelligence, and ratings of anxiety and depression) and memory test scores of the cases and controls. We also treated the anxiety and depression scores as categorical data (normal or borderline scores *v* high scores) to identify the number of cases with probable clinically important anxiety or depression. We treated subjects' smoking habit and occupation as categorical data. We used χ^2 tests (with Yates' correction for 2×2 tables) to compare the categorical data. To identify associations between baseline characteristics and memory scores within groups, we used Spearman correlations.

Rivermead test scores showed some degree of negative skewness, and we therefore square root transformed the data to get an approximately normal distribution before performing statistical analyses. To identify potential confounding influences on differences in the groups' memory scores, we entered the following variables as covariates in an analysis of covariance: age, sex, comorbidity index, smoking habit, social deprivation category, occupational status, anxiety, depression and national adult reading test scores.

We also calculated Spearman correlation coefficients for two time intervals versus the Rivermead test profile score. These time intervals were from the emergency call to the first successful defibrillation (the first shock to result in an organised rhythm >25 beats/min determined from defibrillator printouts) and from the emergency call to the last shock (to account for the effects of refibrillation). Two tailed significance values were calculated.

Results

PATIENT CHARACTERISTICS

Table 1 shows that the baseline characteristics of the cases and controls were similar. More of the cases had borderline or high scores for anxiety than did the controls (8 *v* 2, χ^2 = 2.9, 1 df, P>0.05). At assessment, two of the cases had implanted cardioverter-defibrillators—one had experienced several defibrillator discharges (anxiety score 13 points), while the other had not experienced any (anxiety score 6 points). Cases lived in areas with slightly greater social deprivation (mean deprivation value 4.0 *v* 3.3, t = 1.83, P = 0.07), but no correlation existed between the deprivation score and Rivermead test score (Spearman correlation r^2 = 0.001). The two groups had similar occupational backgrounds.

Four of the cases and three of the controls had undergone surgery involving cardiopulmonary bypass after their index events, all at least two months before assessment. At assessment, 14 cases and 20 controls were receiving β blockers (χ^2 = 2.02, 1 df, P>0.05). The two groups were well matched in their comorbidity index and for current smoking habit (table 1).

MEMORY FUNCTION

The two groups showed no difference in either component of the digit recall test (table 2). However, cases attained lower profile scores in the Rivermead test (mean difference 4.4 points, P<0.001) (fig 1). This difference is clinically important—13 cases had moderate or severe memory impairment by predefined criteria,[21] while none of the controls had this level of impairment (table 3). This result was not significantly altered when the potential confounding variables were entered as covariates (analysis of covariance F = 26.82, P<0.001).

Of the four cases who had undergone cardiopulmonary bypass, one had moderate memory impairment and one had severe impairment. Cases scored significantly lower in eight of the Rivermead subtests (table 2)—in tests of spatial (route) and verbal memory (news report) and in subtests directed at delayed recall

Table 2—*Mean (SD) results of memory tests for 35 cases who had had cardiac arrest outside hospital and 35 controls who had had myocardial infarction*

	Cases	Controls	Difference (95% confidence interval)	P value
Digit recall test:				
Digits forward	6.74 (1.31)	6.97 (1.34)	0.23 (−0.41 to 0.87)	0.473
Digits backward	4.77 (1.54)	5.00 (1.26)	0.23 (−0.45 to 0.91)	0.498
Rivermead subtests:				
Appointment	1.46 (0.78)	1.86 (0.36)	0.40 (0.11 to 0.69)	0.008
Hidden belonging	1.06 (0.91)	1.66 (0.54)	0.60 (−0.18 to 1.34)	0.001
Current date	1.66 (0.68)	1.86 (0.36)	0.20 (−0.06 to 0.46)	0.131
Orientation	1.63 (0.69)	1.86 (0.43)	0.23 (−0.05 to 0.50)	0.102
Face recognition	1.60 (0.65)	1.63 (0.60)	0.03 (−0.19 to 0.23)	0.849
Picture recognition	1.80 (0.53)	2.00 (0.00)	0.20 (0.02 to 0.38)	0.033
Name recall	1.25 (0.91)	1.37 (0.84)	0.12 (−0.31 to 0.53)	0.589
Delivering message	1.54 (0.74)	2.00 (0.00)	0.46 (0.20 to 0.72)	0.001
Route (immediate)	1.34 (0.94)	1.89 (0.32)	0.55 (0.21 to 0.88)	0.002
Route (delayed)	1.29 (0.96)	1.89 (0.40)	0.60 (0.25 to 0.95)	0.001
Story (immediate)	1.34 (0.76)	1.89 (0.32)	0.55 (0.27 to 0.83)	<0.001
Story (delayed)	1.46 (0.74)	1.91 (0.28)	0.45 (0.19 to 0.71)	0.001
Rivermead profile score	17.4 (5.4)	21.8 (2.0)	4.4 (0.11 to 0.69)	<0.001

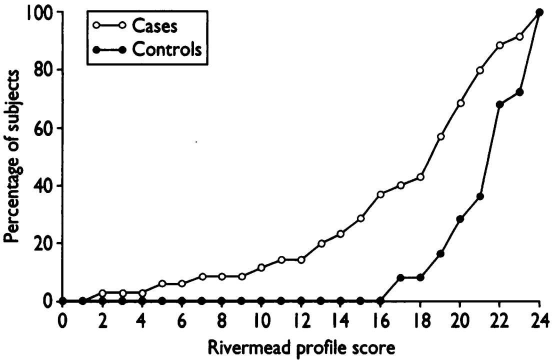

Fig 1—*Cumulative frequency curve of Rivermead behavioural memory test profile scores for 35 cases who had had cardiac arrest outside hospital and 35 controls who had had myocardial infarction*

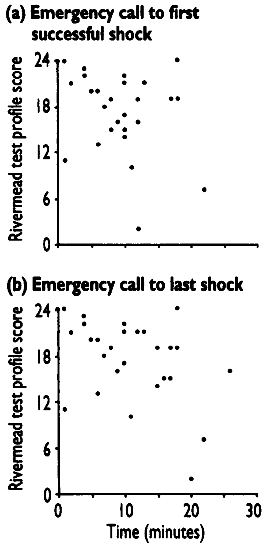

Fig 2—*Correlation between Rivermead behavioural memory test scores of subjects who had had cardiac arrest outside hospital and (a) time from emergency call to first successful defibrillation (r = −0.29, P = 0.13), and (b) time from emergency call to last shock (r = −0.47, P = 0.01)*

of specific instructions (appointment, belonging, and message). Table 4 shows the degree of impairment in the two groups compared with other groups of subjects examined with the Rivermead test.

TEMPORAL EFFECTS ON MEMORY

The times of the emergency call and of defibrillation were available for 28 of the cases. Figure 2 shows the Rivermead test scores for the time from emergency call to first successful shock (Spearman correlation $r = -0.29$, $P = 0.13$) and for the time from call to last shock ($r = -0.47$, $P = 0.01$). Information about resuscitation by bystanders was available for 33 of the cases, and 24 of these had received immediate cardiopulmonary resuscitation. There was no significant difference between the memory scores of those receiving cardiopulmonary resuscitation and the scores of those not receiving resuscitation.

Discussion

This study shows that chronic impairment of episodic long term memory was a clinically important problem among 35 people who had had a cardiac arrest outside hospital. Their performance in the Rivermead behavioural memory test, a test of episodic long term memory, was substantially impaired compared with matched patients who had survived acute myocardial infarction without cardiac arrest. Thirteen of the cases showed a level of memory impairment that was likely to impair their daily functioning. They performed poorly in tests of spatial and verbal memory and recall of instructions. These deficits were independent of age, sex, time from index event to assessment, comorbidity, and measures of affect, premorbid intelligence, social class, and social deprivation. Performance in tests of orientation and short term memory (often used by doctors as bedside measures of cognitive function) was unimpaired, suggesting that important deficit in long term memory may not be noticed unless it is actively sought. This cognitive profile is suggestive of hippocampal damage, which has been previously described in the classic amnesic syndrome following hypoxia.[23]

Memory scores were inversely correlated with the duration of the cardiac arrest, suggesting that improvement of the emergency services' response times might result in better cognitive outcomes. Studies of the effects of duration of cardiac arrest on mortality showed that death rates rose considerably if defibrillation was delayed beyond seven minutes.[24] However, up to 14% of patients survive to discharge even after delays greater than 10 minutes if bystanders had given immediate cardiopulmonary resuscitation.[25] Encouragingly, this study shows that after similarly long delays, survival with relatively minor cognitive impairment is possible. We did not find that cardiopulmonary resuscitation before defibrillation affected memory performance, but only a small proportion of our cases had not received resuscitation from bystanders.

Previous studies provide limited information about the prevalence of chronic memory impairment in people who survived a cardiac arrest outside hospital. Hillis reported minor deficits in 14 subjects,[8] while Dougherty found important memory deficits after one year in 15 subjects, associated with high levels of anxiety.[9] All patients in that series had an internal cardioverter-defibrillator implanted, and such devices are associated with substantial psychological morbidity.[26] Beuret reported moderate disturbance of free recall in five out of 10 long term survivors.[10] These studies are confined to small numbers of subjects, and two of these lacked a control group.

STUDY LIMITATIONS

Our psychological assessments were unblinded and could have been biased by the observer's knowledge of the patient's history. The assessments of memory, however, were presented at a fixed rate with a predefined mode of verbal delivery and were scored using a marking key. Observer bias is therefore unlikely to substantially alter the results. We did not attempt to identify perceptual deficits, which can accompany memory deficit in brain injured

Table 3—*Results of Rivermead behavioural memory tests for 35 cases who had had cardiac arrest outside hospital and for 35 controls who had had myocardial infarction*

	Memory impairment (profile scores)			
	Normal memory (22-24)	Mild (17-21)	Moderate (10-16)	Severe (0-9)
No (%) of cases	7 (20)	15 (43)	10 (29)	3 (9)
No (%) of controls	22 (63)	13 (37)	0	0

Table 4—*Comparison of Rivermead test profile scores of cases (cardiac arrest outside hospital) and controls (myocardial infarction) with those of patients with other pathologies (from Wilson et al[21])*

Pathology	Mean (SD) score
Cases	17.4 (5.4)
Controls	21.8 (2.0)
Healthy population	22.2 (1.9)
Severe closed head injury	12.9 (7.3)
Left hemisphere stroke	16.3 (6.3)
Right hemisphere stroke	17.2 (5.1)

Key messages

- Surviving cardiac arrest outside hospital is becoming increasingly common
- In this study of 35 such patients we found that over a third had important chronic deficits in long term memory, though orientation and short term memory were unimpaired
- Memory scores were inversely correlated with the duration of the cardiac arrest, suggesting that improvement of emergency services' response times might result in better cognitive outcomes
- Targeted rehabilitation strategies could train patients to make the best use of their remaining memory function
- Assessment of cognitive function is an important component of patients' management after discharge from hospital

patients,[27] and which might affect memory. Such deficits may be present in survivors of cardiac arrest and merit separate investigation. Perceptual assessment is time consuming, and, for accurate assessment of memory function, it was important that we limited the duration of psychological assessment to preserve the subjects' attention and concentration.

FUTURE CONSIDERATIONS

With widespread use of ambulance defibrillators, and with initiatives which promote public knowledge of basic life support, more patients are likely to be discharged into the community after cardiac arrest. Although psychological interventions cannot restore these patients' memory functions to premorbid levels,[28] problems with memory may be partially ameliorated by targeted rehabilitation strategies to train patients to make the best use of existing function—such as by using external aids (a daily diary) and adapting the home environment.[29] Furthermore, it may be possible to counsel relatives about handicaps that might be encountered after discharge.

We propose that assessment of memory function is included as a part of postdischarge management after cardiac arrest outside hospital. Further investigations are required to examine other areas of cognitive impairment, such as deficits in perception and executive function, and to determine whether psychological interventions can assist rehabilitation.

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ONE HUNDRED YEARS AGO

FRENCH VIEWS ON MEDICAL PROTECTION.

The proposal to banish foreign practitioners from France under pretext of placing them on an equality with native doctors naturally provokes a good deal of interest on both sides of the Channel. The possibility of their successful foreign rivals being ousted has caused a certain not unnatural feeling of satisfaction to many French doctors, especially those practising in watering places and health resorts frequented by sufferers of other than French nationality. The French Government has an incontestable right to exact an adequate standard of proficiency on the part of those who aspire to practise on French territory, but this has been rigorously enforced for some years past, and the advocates of further protection are fain to base their arguments, first, on the ground that foreigners are not required to pass the preliminary *baccalauréat* which corresponds to our matriculation examination, and, secondly, that foreigners, not having to submit to military service, have an advantage over their French rivals.

Now it has always been the custom to require from foreign candidates for the degree of doctor of medicine proofs of their having passed an examination in general knowledge equivalent to that expected of French students, so that this argument falls to the ground. Although Englishmen and Americans certainly rejoice in an immunity from compulsory military service, this is not the case with candidates from other European countries, and the advantage is compensated by the obligation to become familiar with a foreign language.