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Clinical Paper

Survivors of cardiac arrest with good neurological outcome show considerable impairments of memory functioning☆

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ABSTRACT

Background: Deficits in cognitive function are a well-known dysfunction in survivors of cardiac arrest. However, data concerning memory function in this neurological vulnerable patient collective remain scarce and inconclusive. Therefore, we aimed to assess multiple aspects of retrospective and prospective memory performance in patients after cardiac arrest.

Methods: We prospectively enrolled 33 survivors of cardiac arrest, with cerebral performance categories (CPC) 1 and 2 and a control-group ($n = 33$) matched in sex, age and educational-level. To assess retrospective and prospective memory performance we administrated 4 weeks after cardiac arrest the "Rey Adult Learning Test" (RAVLT), the "Digit-Span-Backwards Test", the "Logic-Memory Test" and the "Red-Pencil Test".

Results: Results indicate an impairment in immediate and delayed free recall, but not in recognition. However, the overall impairment in immediate recall was qualified by analyzing RAVLT performance, showing that patients were only impaired in trials 4 and 5 of the learning sequence. Moreover, working and prospective memory as well as prose recall were worse in cardiac arrest survivors. Cranial computed tomography was available in 61% of all patients ($n = 20$) but there was no specific neurological damage detectable that could be linked to this cognitive impairment.

Conclusion: Episodic long-term memory functioning appears to be particularly impaired after cardiac arrest. In contrast, short-term memory storage, even tested via free-call, seems not to be affected. Based on cranial computed tomography we suggest that global brain ischemia rather than focal brain lesions appear to underlie these effects.

1. Introduction

Global or regional cerebral hypoperfusion caused by stroke, traumatic brain injury and even coronary artery bypass (CABP) surgery, are well known as effectors for various types of dysfunction in cognitive performance including memory deficits.[1–3] In regard to these findings, the potential effects of cardiac arrest on cognitive performance have been targeted. The cerebral performance category (CPC) scale is a well established tool for evaluation of neurological damage after cardiac arrest and describes patients mental ability from CPC 1 (=return to normal cerebral performance) to CPC 5 (=brain death).[4] However, within animal-models both neuropathological and neuroimaging studies revealed specific vulnerability of hippocampal regions after global cerebral ischemia due to cardiac arrest.[5,6] Human data in this context remain scarce and not conclusive. In terms of neurobiological effects studies appear to converge in indicating that global cerebral hypoperfusion may lead to focal lesions especially in the hippocampal region.[7,8] The hippocampal region is essential for learning and the transfer of new information in the declarative memory. Site of long-term memory and short-term recall are the neo-cortex and numerous subcortical regions, with which the hippocampus has strong reciprocal connections (see Fig. 1).

In terms of psychological consequences, previous studies empirically testing the associated cognitive profile reported significant cognitive deficits in cardiac arrest survivors.[9–14] However, the exact pattern of impairment still appears to be underspecified.[15,16] While early reports have used rather crude methods of assessing cognitive functioning such as the Mini Mental State Examination,[17] recently,

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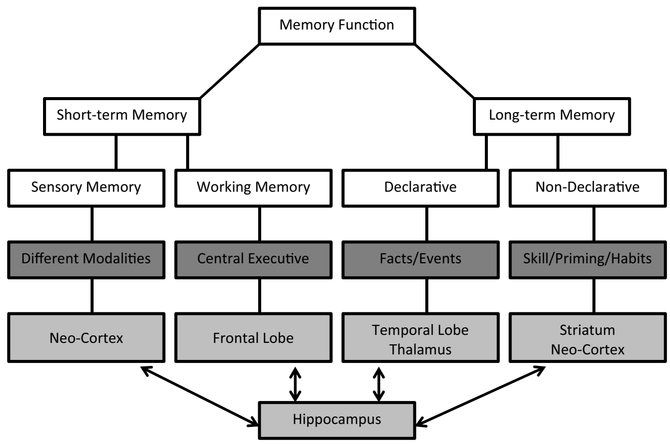

Fig. 1. Demonstrating the composition and the participate brain areas of human memory.

first studies have investigated cognitive functioning using a variety of established cognitive tests.[9,18]

Our study follows up on previous work exploring potential memory deficits in cardiac arrest survivors extending the existing literature in three aspects. First, we prospectively tested for potential memory deficits applying an age, sex and education matched control group. Second, we aimed at delineating potential memory deficits using a comprehensive battery of retrospective and prospective short and long-term memory measures. Third, we aimed at disentangling potentially different performance patterns in cardiac arrest patients according to their state of consciousness at time of admission to our department as well as according to their overall neurological status at time of testing.

2. Methods

2.1. Study population

We prospectively enrolled 33 patients (23 [70%] male, age 50 [±15] years) after cardiac arrest admitted to the Department of Emergency Medicine at Vienna General Hospital, a university affiliated tertiary care center. To be included in our study, patients had to be at least 18 years old and had to show CPC 1 or 2. Patients were excluded if they had insufficient knowledge of the German language, were unable to speak and if they had suffered any cerebrovascular incident or disease of the central nervous system prior to the cardiac arrest.

2.2. Data acquisition

Patient data were collected by instructed personnel and inserted into a predefined data record abstraction form. Data about the patient's medical history, home drug treatment, neurological (CPC) and general physical status before the arrest, cardiac risk factors, first-aid and emergency medical service response intervals, extent and amount of emergency cardiac care and CPC on arrival and over a follow-up period of 4 weeks when the tests were collected. Memory tests were scheduled 4 weeks after cardiac arrest. Participants had to sign a written informed consent for inclusion in our study. After patient interviews were completed, a sex, age and education matched control group was tested for comparison. Recruitment of healthy controls was done by public postings and amounted to 33 healthy patients (23 [70%] male, age 51 [±14] years). The two interviewers were – especially by an experienced neuro-psychologist trained – medical doctors. The study was approved by the local ethics committee at Medical University of Vienna and was in accordance with the Declaration of Helsinki.

2.3. Testing procedures

Rey Adult Verbal Learning Test (RAVLT)[19] was used to assess immediate, delayed free recall and recognition in several ways. The interviewer read aloud 15 words to the participant in 5 subsequent trials and participants had to recall as many words as possible after each trial. Each trial's performance was noted separately. After the 5th trial an interference list of 15 different words (Interference Trial) was read to the participants and they had to recall those words. Performance in trials 1–5 and the interference list was taken as indicators for immediate free recall – as measured in single trial performance as well as a combined overall score.[9] The relative increase in performance from trial 1–5 was used as a measure for the participant's learning ability. For assessment of delayed recall participants had to recall the 15 words from trial 1–5 right after the interference list had been tested (trial 6) and about 30 min thereafter (trial 7). To examine participants recognition performance, in trial 8, they had to recognize the 15 words from trial 1–5 from an orally presented word list also containing 35 words from the interference list and phonetic or semantic similar distractor words.

Digit-span-backwards from Wechsler Adult Intelligence Scale-Revised (WAIS-R)[20] was used for assessment of working memory. Here, the participant had to repeat increasing sequences of numbers in backward direction.

The Red-Pencil-Test[21] was used for assessment of prospective memory. At the beginning of the interview the participant was instructed to remember to say aloud "red pencil" whenever the interviewer uses the expression "red pencil". The cue appeared 4 times across the test session.

The logical memory subscale from Wechsler Memory Scale-Revised (WMS-R)[22] was performed to test performance in prose recall. A standardized story was read to the participant by the experimenter. Participants were asked to listen and, when the story was finished, to recall as many details as possible. The number of propositions correctly recalled was the prose recall score.

2.4. Statistical analysis

Continuous data are shown as median and interquartile range (IQR) if non-parametric distribution, discrete data as counts and percentages. Discrete data were analyzed using Chi-Square test and Mann–Whitney-*U*-test for continuous variables. Data were tested for normal distribution using the Kolmogorov–Smirnov test. For normally distributed variables group differences in cognitive functioning were assessed by single factors analyses of variance (ANOVA) or mixed repeated-measures ANOVA, respectively. As within-subjects factor we used the respective RAVLT trials and as between-subjects factor patients versus controls or different patient subgroups were used in the respective ANOVAs. Where appropriate, the Tukey Honestly Significant Difference post hoc tests (Tukey HSD post hoc test) or planned comparisons using *t*-tests were performed and *P*-values were adjusted according to Bonferroni, or Greenhouse–Geisser (in the repeated measures data). We chose two-sided *P*-values <0.05 as statistical significant. Effect size is given in η^2 indicating proportion of explained variance. Statistical analyses were performed using SPSS 11.5 (IBM USA).

3. Results

Between May 1st, 2004 and April 30th, 2005 all patients admitted after cardiac arrest ($n = 174$) were screened and finally