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ORIGINAL ARTICLE

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Effects of postoperative cognitive training on neurocognitive decline after heart surgery: a randomized clinical trial

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Key question

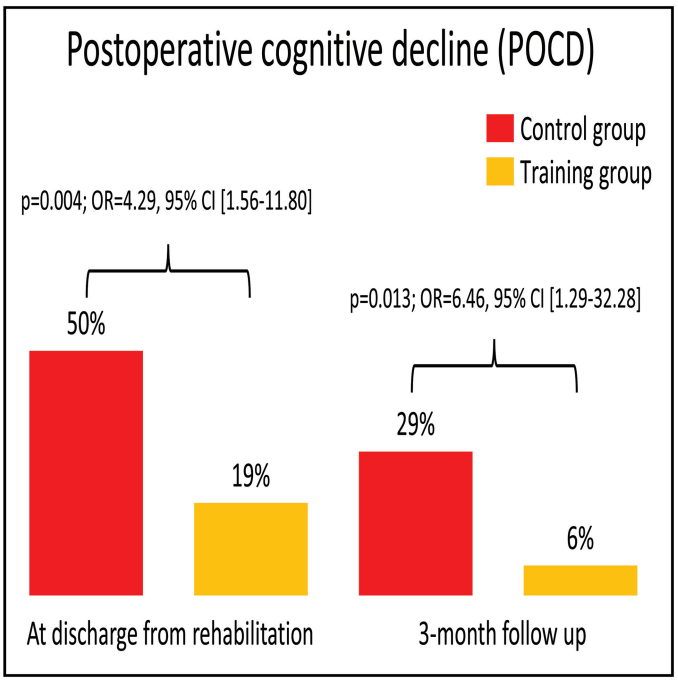
What is the effect of postoperative cognitive training on postoperative cognitive decline (POCD) after cardiac surgery?

Key finding(s)

POCD differed between groups at end of (control=50%, training=19%) and 3 months after the intervention (control=29%, training=6%).

Take-home message

A three-week randomized controlled cognitive training after cardiac surgery could be useful for the prevention of POCD.



Abstract

OBJECTIVES: Following cardiac surgery, postoperative cognitive decline (POCD) is a common complication that can impair the quality of life and increase mortality. The aim of this study was to investigate whether early postoperative cognitive training can decrease POCD after cardiac surgery.

METHODS: The study was a multi-centred, two-arm, randomized (1:1 ratio), controlled trial involving older patients undergoing elective heart valve surgery with extracorporeal circulation. Recruitment took place at the Department of Cardiac Surgery of the Kerckhoff-Clinic in Bad Nauheim (Germany) and the University-Hospital in Giessen (Germany). The patients were randomized to either a paper-and-pencil-based cognitive training group or a standard rehabilitation care control group. The cognitive training started 1 week after surgery and lasted about 3 weeks until discharge from rehabilitation. To detect POCD, neuropsychological functions were assessed prior to surgery, upon discharge from rehabilitation (primary outcome), and 3 months after discharge (secondary outcome). Data were primarily analysed in a per-protocol fashion.

RESULTS: The frequency of POCD at discharge from rehabilitation (training group, $n = 37$; control group, $n = 44$) was 50% in the control group and 19% in the training group ($\chi^2[1] = 8.45$, $P = 0.004$; odds ratio = 4.29, 95% confidence interval [1.56–11.80]). Three months after the cognitive training (training group, $n = 33$; control group, $n = 34$), POCD frequency was 29% in the control group and 6% in the training group ($\chi^2[1] = 6.21$, $P = 0.013$; odds ratio = 6.46, 95% confidence interval [1.29–32.28]).

CONCLUSIONS: Since our cognitive training showed beneficial effects, it could be a promising method to prevent POCD.

Keywords: Postoperative cognitive decline • Cardiac surgery • Cognitive training

ABBREVIATIONS

ANCOVA	Analysis of covariance
CABG	Coronary artery bypass grafting
CI	Confidence interval
HADS-D	Hospital Anxiety and Depression Scale
OR	Odds ratio
POCD	Postoperative cognitive decline
POCI	Postoperative cognitive improvement
SD	Standard deviation
ITT	Intention to treat

INTRODUCTION

Several neurocognitive complications have been described after cardiac surgery, including delirium [1], postoperative cognitive decline (POCD) [2] and dementia [3]. POCD can be defined as a decline of 1 standard deviation (SD) between a participant's pre-operative and postoperative cognitive performance, in at least 20% of all objectively measured cognitive domains (e.g. verbal memory, selective attention, word fluency or executive functions) [4]. A meta-analysis of coronary artery bypass grafting (CABG) patients that applied this definition showed a POCD prevalence of 28% between the first and fourth postoperative months and 22% between the sixth and 12th postoperative months [4]. POCD has further consequences such as reduced quality of life [5], increased mortality [6], increased economic costs [6] and long-term cognitive decline [2]. Although POCD often occurs subclinically and therefore often remains undetected, both patients and their relatives report a subjective decrease in the patients' cognitive abilities in daily life up to at least 3 months after cardiac surgery [7]. Besides POCD, postoperative cognitive improvement (POCI) can also be found after major surgery, with a frequency of 3–6 times lower than that of POCD [8]. Taken together, POCD seems to be a clinically relevant intervention target. Several studies have shown that healthy older individuals [9], cardiac surgery patients [10] or patients with mild cognitive impairment [11] can improve their cognitive functions through cognitive training. The aim of this prospective, randomized controlled trial was to investigate the effects of an early postoperative paper-and-pencil-based cognitive training programme in patients undergoing cardiac surgery with extracorporeal circulation.

PATIENTS AND METHODS

Ethical statement

The study, including obtaining informed consent, has been approved by the Ethics Committee of the Justus-Liebig University, Giessen (27 February 2014, Ref.: 28/14), and complies with the Declaration of Helsinki. Written informed consent of the patient was obtained prior to the enrolment.

Study design

This study was designed as a multi-centred, parallel group, 1:1 randomized and controlled trial, and it was conducted at the following locations: the Department of Cardiac Surgery of the Kerckhoff Heart and Thorax Center in Bad Nauheim, Germany; the Department of Cardiovascular Surgery at the University Hospital in Giessen, Germany; and the Department of Rehabilitation at the Kerckhoff Clinic in Bad Nauheim, Germany. Full details of the study protocol have been published elsewhere in advance [12]. With regard to the study protocol, no changes occurred in terms of eligibility criteria, interventions, examinations, data collection, methods of analysis and outcomes.

Patients

Patients scheduled for elective aortic or mitral valve replacement/reconstruction with or without CABG were included in this study. Cardiac surgery was performed with standard extracorporeal circulation. A sufficiently good knowledge of the German language was necessary as cognitive training and neuropsychological tests are language dependent. Exclusion criteria were history of stroke and pre-existing psychiatric or neurological disorders (e.g., dementia) that may impair the neuropsychological evaluation. Furthermore, patients were excluded when their health insurance did not cover postoperative rehabilitation at the Kerckhoff Clinic. The 2 participating study centres provided information on scheduled elective cardiac procedures to the study coordinators, who screened them according to eligibility criteria. Potential participants were contacted and informed in detail about the purpose and procedure of the study project.

Randomization and blinding

After recruitment and the first preoperative neuropsychological examination, the study coordinators allocated patients to the cognitive training group or the control group. The randomization was implemented using a computer-generated randomization list with a 1:1 blocked allocation ratio. The block sizes varied randomly. The randomization list was generated, sequentially numbered and concealed by a study coordinator prior to starting the study. The study coordinators informed the psychological training supervisor on which patients should be trained. The surgeons, neurologists and neuropsychologists involved in the assessment of outcome variables were blinded with respect to the randomization status.

Study procedures

At baseline, the documented data included age, sex, school and occupational education, body mass index, pre-existing conditions and the severity partition for left ventricular ejection fraction [13]. Duration of surgery, extracorporeal circulation, cross-clamp time and invasive ventilation time were recorded perioperatively. After surgery, postoperative complications and postoperative delirium were documented. Following the acute hospitalization, patients were directly transferred to the Department of Rehabilitation at the Kerckhoff Clinic in Bad Nauheim, Germany.

After admission to the rehabilitation centre, the control group and the cognitive training group received inpatient cardiac rehabilitation therapies that were individualized and based on the International Classification of Functioning. Essential elements of the therapeutic treatments were endurance, strength training, respiratory gymnastics and educative lectures. On average, the patients received about 12–14 therapeutic units per week. In addition, patients of the training group underwent cognitive training. The detailed description of the development and concept of the cognitive training was previously published elsewhere [12]. In brief, our cognitive training included standardized paper-and-pencil-based exercises practicing multidomain cognitive functions, which are especially important for everyday life, social functions and earning capacity. These include word fluency, working memory, attention and the ability to plan. Daily training sessions last 36 min. These should be done 6 days a week for a period of 3 weeks. The control group did not receive a placebo intervention because placebos (e.g. reading a newspaper) could have effects on cognitive performance. Two trained neuropsychologists applied a battery of validated cognitive tests 1–2 days before surgery, upon discharge from rehabilitation, and 3 months after discharge from rehabilitation. When available, parallel test forms were used at follow-up assessments to minimize learning effects.

Outcomes

The primary outcome was the training effect on each neuropsychological function at discharge from rehabilitation. As another primary outcome, we used each neuropsychological function to hereby determine the diagnoses of POCD/POCI for the time of discharge from rehabilitation. The secondary outcomes were the training effect on POCD/POCI and on each neuropsychological function at 3 months after discharge and the training effect on depression and anxiety.

POCD was defined as a decline and POCI as an improvement from pre- to postassessment of at least 1 SD in at least 20% of all neuropsychological subdomains [4]. To measure the difference of 1 SD between pre- and postassessment, we used *Z*-scores, which were calculated by the difference of the individual raw values from the mean value of the total baseline data divided by the SD of the total baseline data. The neuropsychological subdomains were defined according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders* [14], as described in Supplementary Material, Table S1. As we have measured several neuropsychological parameters that can be contextually grouped into cognitive subdomains, we have summarized them by a mean value. A detailed description of the neuropsychological test battery was published elsewhere [12]. Patients assessed their recent (prior week) depressive and anxiety symptoms using the validated German version of the Hospital Anxiety and Depression Scale (HADS-D) [15].

Statistical analyses

Cognitive training for heart surgery patients conducted by de Tournay-Jetté *et al.* [10] showed training related medium to large effect sizes (η^2 = 0.10–0.23) in neuropsychological tests related to inhibition or verbal free recall (short delay). To avoid underestimating the needed sample size, we used the smaller effect size (η^2 = 0.10) for sample size calculation. Using this effect size, a total sample size of 73 patients were needed to obtain a statistical power of 80% at a significance level of $P = 0.05$ (two-tailed) in the context of an analyses of covariance (ANCOVA). We applied a dropout rate of 20% for each individual measurement time point. Accordingly, we expected a 20% dropout rate from baseline (114 patients) to discharge from rehabilitation (91.2 patients) and then a 20% dropout rate from discharge to 3-month follow-up (72.96 patients). Thus, the number of patients recruited at baseline assessment was fixed at 114 patients for the total sample size. For sample size and statistical power calculations, we used the analysis software G*Power (version 3.1.9.2).

To reveal the training effect on cognition, frequencies of dichotomous (yes/no) POCD and POCI variables were compared with Pearson's χ^2 test between the groups. The effect size of the difference in POCD/POCI frequencies between the groups is given by odds ratio (OR) with a 95% confidence interval (CI). To determine the effects of cognitive training on each neuropsychological parameter and on depression and anxiety, ANCOVAs were conducted with postoperative test value as the dependent variable, groups (control group or training group) as the fixed factor and preoperative test value as the covariate. Assumptions for ANCOVAs were tested using the Levene test for variance homogeneity of the dependent variable, QQ and distribution plots of the dependent variable for normality, and a statistically significant correlation between dependent variable and covariate (preoperative test value) calculated with Pearson's product-moment correlation. The effect sizes of the ANCOVA results are given in η^2. When assumptions for ANCOVA were violated, difference values between pre- and posttests were calculated, followed by the Mann–Whitney *U*-test for between-subject effects. To control for the possibility of confounder variables that could affect the results, we conducted the correlation analysis between demographic variables, perioperative details and neuropsychometrical changes between pre- and postoperative testing. In case of significant contributions of these variables, they were

Table 1: Baseline demographics and characteristics

	Training ($n = 47$)	Control ($n = 47$)
Demographics		
Age (years)	71.2 (4.7)	73.0 (4.9)
Sex		
Women	8 (17%)	13 (28%)
Men	39 (83%)	34 (72%)
Education (years)	13.5 (3.0)	13.4 (3.0)
Medical history		
Body mass index (kg/m^2)	27.7 (3.8)	26.6 (3.8)
Arterial hypertension	31 (66%)	31 (66%)
Diabetes mellitus	10 (21%)	5 (11%)
Renal insufficiency	4 (9%)	7 (15%)
Dyslipidaemia	39 (83%)	37 (79%)
LV EF (mildly abnormal)	5 (11%)	6 (13%)
LV EF (moderately abnormal)	3 (6%)	1 (2%)
Heart failure	10 (21%)	9 (19%)
Type of surgery		
AVR	23 (50%)	22 (47%)
AVR + CABG	18 (38%)	19 (40%)
MVR	4 (9%)	1 (2%)
MVR + CABG	0 (0%)	3 (6%)
AVR + MVR	2 (4%)	2 (4%)
Perioperative details		
Duration of surgery (min)	190.3 (38.1)	200.6 (58.9)
Duration of extracorporeal circulation (min)	96.5 (26.5)	105.2 (37.5)
Cross-clamp time (min)	69.1 (19.9)	74.7 (26.7)
Ventilation time invasive (min)	616.2 (331.3)	588.1 (213.6)
Postoperative complications		
Delirium	2 (4%)	4 (9%)
Arrhythmia	18 (38%)	21 (45%)
Atrial fibrillation	18 (38%)	17 (36%)
Renal insufficiency	6 (13%)	6 (13%)
Acute blood loss anemia	10 (21%)	12 (26%)
Transient ischaemic attack	1 (2%)	0 (0%)
Dysathria/aphasia	0 (0%)	1 (2%)
Medical details at admission to rehabilitation		
Blood pressure (systolic; mmHg)	128.1 (12.7)	127.7 (18.4)
Blood pressure (diastolic; mmHg)	74.5 (11.1)	71.4 (10.6)

Data are mean (SD) or number of subjects (%). Renal insufficiency was defined by a creatinine value above the in-house norms (men: >1.2 mg/dl, women: >0.9 mg/dl).

AVR: aortic valve replacement; CABG: coronary artery bypass grafting; LF EV: left ventricular ejection fraction; MVR: mitral valve replacement/reconstruction; SD: standard deviation.

implemented in addition to the preoperative cognitive values as further covariates to the ANCOVA. The criterion for statistical significance was set at $P < 0.05$ (two-sided). Our data set was evaluated using a per-protocol analysis. In a secondary approach, we used an intention-to-treat (ITT) analysis with the following specifications. For each single neuropsychological parameter with missing data at follow-up assessments, due to patient dropout (see reasons in the flowchart), we used a multiple imputation process in SPSS (version 22). The method of imputation was the fully conditional specification method, which is an iterative Markov chain Monte Carlo method. We set the number of iterations to 10. Within a linear regression model, we used group, age, education and the neuropsychological values from baseline, discharge from rehabilitation and 3-month follow-up as predictors. We set the number of imputations to 29 because about 29% of the data were missing at 3-month follow-up. We used the average of the 29 imputations for each neuropsychological parameter to replace the missing data. All analyses were performed using the statistical software SPSS (version 22) and JASP (version 0.12.2). The implementation of a data monitoring committee was not considered.

Study population

Between 13 July 2016 and 8 January 2020, a total of 130 patients were enrolled, randomized and tested preoperatively. The last patient was tested on 27 February 2020 for the 3-month follow-up. After randomization of the 130 patients, 36 patients (training group, $n = 18$; control group, $n = 18$) were lost to follow-up before the training or control intervention had started. Thus, 94 patients (training group, $n = 47$; control group, $n = 47$) were considered for the baseline sample, which has no between-group differences in baseline characteristics (see Table 1), or baseline neuropsychological tests. Furthermore, 13 patients (training group, $n = 10$; control group, $n = 3$) were lost to follow-up until discharge from rehabilitation, resulting in 81 patients (training group, $n = 37$; control group, $n = 44$), with another 15 patients (training group, $n = 5$; control group, $n = 10$) lost to follow-up at the 3-month follow-up, resulting in 67 patients (training group, $n = 33$; control group, $n = 34$). Reasons for losing patients to follow-up are shown in Fig. 1. The training intervention lasted 14.9 (SD 2.5) days and did not cause adverse events.

RESULTS

Per-protocol analysis

Primary outcome measures. At the time of discharge from rehabilitation, the training group ($n = 37$) showed an improvement compared to the control group ($n = 44$) in domains of selective attention measured with the Trail Making Test-A (TMT-A) ($F[2.78] = 5.66$, $P = 0.020$, $\eta^2 = 0.04$), and phonetic word fluency revealed with the Regensburger Word Fluency Test (RWT) ($F[2.78] = 6.18$, $P = 0.015$, $\eta^2 = 0.06$), whereas patients in the control group deteriorated in these domains. The significant interaction effects are shown in Supplementary Material, Fig. S1. A full description of the results of all neuropsychological test parameters is given in Supplementary Material, Table S2. Potentially confounding continuous demographic variables or intraoperative details made no significant contribution to the results, which were implemented as covariates in an adjusted ANCOVA.

Furthermore, at discharge from the rehabilitation clinic, POCD frequency was 50% ($n = 22$) in the control group and 19% ($n = 7$) in the training group, with a significant group difference ($\chi^2[1] = 8.45$, $P = 0.004$; OR = 4.29, 95% CI [1.56–11.80]). POCI frequency was 22% ($n = 8$) in the training group and 18% ($n = 8$) in the control group, with no significant group difference ($\chi^2[1] = 0.15$, $P = 0.699$; OR = 0.81, 95% CI [0.27–2.41]).

Secondary outcome measures. The specific effects on neuropsychological parameters are given as follows. Analysis of 67 patients (training group, $n = 33$; control group, $n = 34$) at 3 months after discharge from rehabilitation showed a statistically significant beneficial effect for the training group compared to the control group in domains of visual recognition memory revealed with the Short Performance Test ("Syndrom-Kurztest", SKT) ($U = -2.22$, $P = 0.027$, $\eta^2 = 0.07$), verbal free recall (short

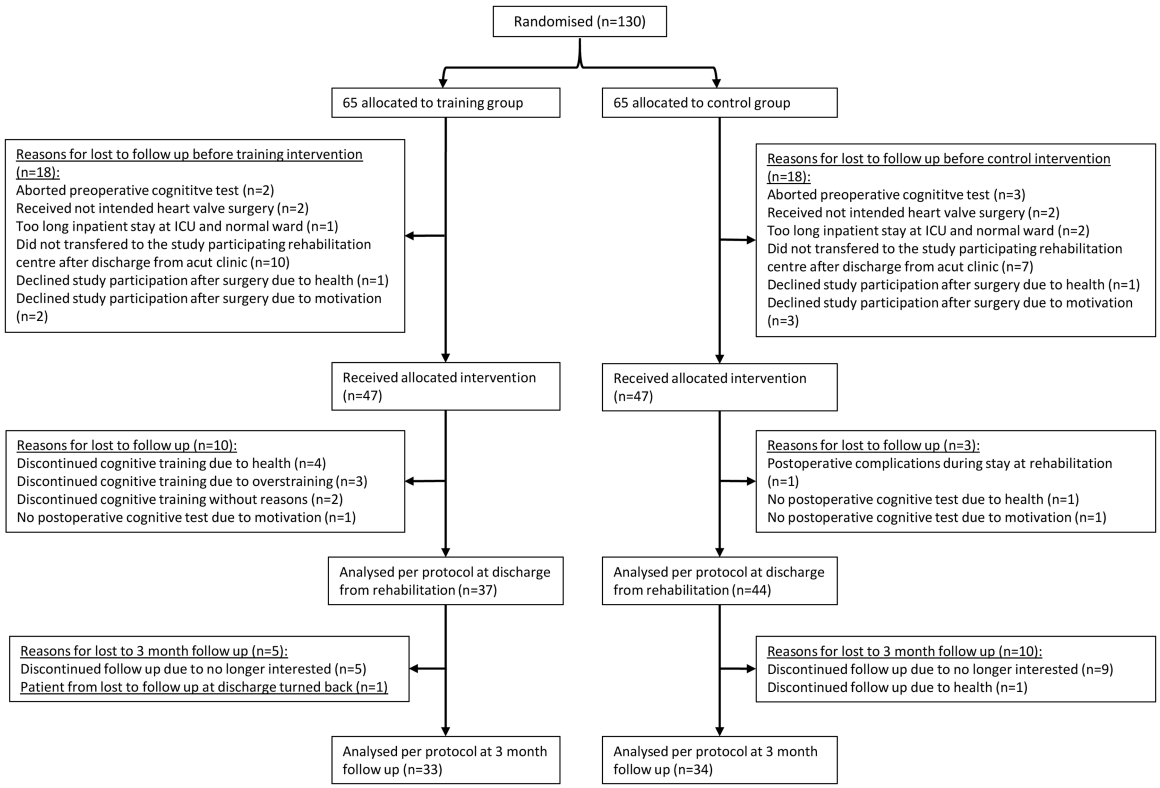


Figure 1: Consolidated Standards of Reporting Trials flowchart illustrating all steps in the study from randomisation to follow-up and analysis. ICU: intensive care unit.

delay) measured with the Auditory Verbal Learning and Memory Test ("Verbaler Lern- und Merkfähigkeitstest", VLMT) (F[2.64] = 4.21, P = 0.044, η^2 = 0.04), verbal working memory span tested with the Letter Number Span Test (LNS) (F[2.64] = 6.77, P = 0.011, η^2 = 0.07), cognitive inhibition speed measured with the SKT (F[2.64] = 4.02, P = 0.049, η^2 = 0.02) and phonetic word fluency tested with the RWT (F[2.64] = 6.99, P = 0.010, η^2 = 0.07). The significant interaction effects are shown in Supplementary Material, Fig. S2. A full description of the results of all neuropsychological test parameters is given in Supplementary Material, Table S3. In the adjusted ANCOVA with potentially confounding continuous demographic variables, only education as an additional covariate contributed significantly to cognitive inhibition speed revealed with the SKT (F[3.63] = 4.25, P = 0.043, η^2 = 0.02). In the adjusted ANCOVA with potentially confounding continuous demographic variables or intraoperative details, only education as an additional covariate contributed significantly to cognitive inhibition speed revealed with the SKT (F[3.63] = 4.25, P = 0.043, η^2 = 0.02).

At 3-month follow-up, POCD frequency was 29% (n = 10) in the control group and 6% (n = 2) in the training group, which differs significantly between the groups (χ^2[1] = 6.21, P = 0.013; OR = 6.46, 95% CI [1.29–32.28]). POCI frequency was 36% (n = 12) in the training group and 15% (n = 5) in the control group, with significant group difference (χ^2[1] = 4.15, P = 0.042; OR = 0.30, 95% CI [0.09–0.99]).

From baseline to discharge from rehabilitation, no group difference (training group, n = 36; control group, n = 40) in depression or anxiety was detected using the HADS-D. At 3-month follow-up, a marginal improvement in depression was shown in the training group (n = 33) compared with the control group (n = 33) measured with the HADS-D (U = -1.86, P = 0.063, η^2 = 0.05).

Subgroup analyses. Our sample showed an unequal distribution of delirious patients between the groups at discharge from the rehabilitation and at 3-month follow-up (control group n = 4; training group n = 0). As delirium is considered as a risk factor for the development of POCD [16] and we do not want to overestimate our described training's effect on POCD, we calculated a *post hoc* explorative analysis in which we excluded all delirious patients. In this adjusted analysis, excluding all delirious patients, the training effect on POCD/POCI at the time of discharge from the rehabilitation clinic was nearly the same as that with delirious patients (POCD: 50% [n = 20] in the control group, 19% [n = 7] in the training group; χ^2[1] = 8.16, P = 0.004; OR = 4.29, 95% CI [1.53–12.01]/POCI: 22% [n = 8] in the training group, 18% [n = 7] in the control; χ^2(1) = 0.21, P = 0.648; OR = 0.77, 95% CI [0.25–2.38]). Even 3 months after the cognitive intervention, the training effect on POCD/POCI seemed to remain, independent of delirium (POCD: 30% [n = 9] in the control group, 6% [n = 2] in the training group; χ^2[1] = 6.25, P = 0.012; OR = 6.64, 95% CI [1.30–33.88]/POCI: 36% [n = 12] in the training group, 13% [n = 4] in the control; χ^2[1] = 4.40, P = 0.036; OR = 0.27, 95% CI [0.08–0.96]).

Intention-to-treat analysis

A full description of the ITT analysis is given in Supplementary Material, File 1S.

DISCUSSION

The cognitive training demonstrated a statistically significant difference between the groups in POCD frequency at discharge. The frequency in the control group was 50% (23% in ITT analysis),

whereas it was 19% (6% in ITT analysis) in the training group. As a long-term effect, at 3 months after discharge, the control group's POCD frequency remained significantly higher, at 29% (30% in ITT analysis), than that of the training group, which was 6% (13% in ITT analysis). Besides the lower incidence of cognitive decline in the training group, a significantly higher POCI was observed 3 months after discharge from rehabilitation for the training group with 36%, compared to 15% in the control group. Furthermore, our training programme could be performed well in the early rehabilitation phase in ∼80% of the patients randomized to the training group. About 20% of the patients were not able to start or continue the training due to health reasons or overstraining from the exercises.

For the per-protocol approach, a *post hoc* power analysis of the difference in POCD incidence between the groups showed a sufficiently high power of 0.83 at the time of discharge from rehabilitation and a power of 0.7 at the 3-month follow-up, which is slightly underpowered but in our opinion clinically relevant. Within the ITT analysis, the *post hoc* power of the training's effect on POCD was 0.64 at the time of discharge and 0.53 at the 3-month follow-up, which is clearly underpowered. However, it should be noted that the powers of some single neuropsychological parameters were sufficiently high [at discharge: phonetic word fluency = 0.85; at 3-month follow-up: phonetic word fluency = 0.92, verbal free recall (short delay) = 0.83, verbal working memory = 0.81].

At this time, 2 studies have investigated the effect of computer-based cognitive training on postoperative cognition after cardiac surgery. In the study conducted by O'Gara *et al.* [17] the training was performed at least 10 days before surgery up to 4 weeks postoperatively, which had no significant effect on the frequency of POCD. However, this study cannot be compared with our study design, because we used a paper-and-pencil procedure, which started 1 week after surgery. A paper-and-pencil procedure might be more feasible and effective than computer-based training for older patients. However, this question cannot be answered because O'Gara *et al.* did not investigate the training effect between the preoperative and postoperative training phases separately. The training carried out by de Tournay-Jetté *et al.* [10] in 2012 began in the sixth to tenth weeks postoperatively and showed a positive effect on cognition. Again, comparison with our data is difficult because, contrary to our study, the baseline neuropsychological data used for their training effect were collected 1 month postoperatively. Furthermore, their training started relatively late (sixth to tenth weeks postoperatively) compared with the training in our study (1 week postoperatively). The optimal time for postoperative cognitive training to begin is still not clear. For example, animal studies suggest a time-dependent increase in neuroplasticity (plastic window) after ischaemic injury, with a peak at 7–14 days and near completion at 30 days [18]. With this dynamic of neuroplasticity, which is important for cognitive recovery, early neuropsychological rehabilitation seems to be more beneficial than later rehabilitation.

A possible explanation for the effectiveness of our training could be the intervention-related alteration in neuroplasticity. For example, various studies have shown that cognitive training can increase patterns in the brain structure in healthy subjects [19] and in patients with memory impairments [20].

There are a few limitations to consider. First, we only examined patients who had been operated on with the use of extracorporeal circulation. Therefore, comparison with patients without extracorporeal circulation or a healthy control cohort is not possible. A second major limitation of this study is that we do not know whether the patients performed cognitively enhancing activities (playing games, reading books, social engagement) [21] between the end of cognitive training and the 3-month follow-up. Third, the training was designed for older patients, so it might be too easy for younger patients and therefore not achieve any cognitive effect. As we studied a mixed cohort of single surgeries such as AVR or MVR and combination surgeries such as CABG + AVR, transmissibility of the effects on single patient populations, such as AVR without CABG or CABG without AVR, cannot be adequately performed. The training results regarding POCD incidence display relatively wide confidence intervals, probably due to the small sample size. To better quantify the confidence intervals, the data would need to be replicated in a larger sample. An unexpectedly high number of patients (36%) were excluded between the time of recruitment and preoperative testing and the time of admission to the rehabilitation clinic; thus, our anticipated dropout rate of 20% was an underestimation. For organizational reasons, we were unable to reach the expected 91.2 patients at discharge and had to end the study with 81 patients.

As our cognitive training in the early rehabilitation phase has shown to be feasible and effective at maintaining or improving cognition, this intervention could be a promising method to protect against cognitive decline after cardiac surgery. Although the beneficial effect at the short-term follow-up seems promising, the results at a 1-year follow-up would also be of great interest.

Economically and organizationally, the integration of the training into the treatment programmes of rehabilitation centres is possible without much effort, because the cognitive exercises are independently workable and need no elaborate supervision, and rehabilitative centres usually have psychologists or occupational therapists who can be involved in the organization of the exercises, distribution of tasks or clarification of questions. Furthermore, the paper-and-pencil-based process is inexpensive, so we assume that the benefit outweighs the cost. As it is unclear during the early rehabilitation who will be affected by long-term POCD, our training could be useful for patients at particularly increased risk.

Furthermore, it could be integrated in preoperative as well as peri- and postrehabilitative treatment settings or in the context of cognitive impairment after stroke and in the progression of dementia. Postoperative care of patients in rehabilitative clinics generally has a positive effect on the overall outcome. With cognitive training, in addition to standardized rehabilitation, a further benefit can be achieved with regard to cognition. Comparison to cognitive training that can be performed independently by the patients in a postoperative in-home rehabilitation setting would be interesting and should be considered in further research. Preoperative cognitive training (prehabilitation) in particular could build up cognitive reserves [22], which could potentially protect the brain against postoperative neurocognitive dysfunctions such as delirium or POCD.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Conflict of interest: none declared.

Data Availability Statement

De-identified participants' data analysed during the current study are available from the corresponding author on reasonable request.

Author contributions

Marius Butz: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing. **Tibo Gerriets:** Conceptualization; Funding acquisition; Project administration; Writing—review & editing. **Gebhard Sammer:** Conceptualization; Methodology; Supervision; Validation; Writing—review & editing. **Jasmin El-Shazly:** Conceptualization; Funding acquisition; Investigation; Methodology; Project administration; Writing—review & editing. **Marlene Tschernatsch:** Writing—review & editing. **Hagen B. Huttner:** Writing—review & editing. **Tobias Braun:** Writing—review & editing. **Andreas Boening:** Resources; Writing—review & editing. **Thomas Mengden:** Conceptualization; Resources; Writing—review & editing. **Yeong-Hoon Choi:** Writing—review & editing. **Markus Schoenburg:** Conceptualization; Funding acquisition; Project administration; Writing—review & editing. **Martin Juenemann:** Conceptualization; Funding acquisition; Project administration; Supervision; Writing—review & editing.

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