

## Opening the Cardiac Chambers Does Not Make Any Difference in P300 Measurement

Ihsan Iskesen,<sup>1</sup> Hikmet Yilmaz,<sup>2</sup> Funda Yildirim,<sup>1</sup> Deniz Selcuki,<sup>2</sup>

Departments of <sup>1</sup>Cardiovascular Surgery and <sup>2</sup>Neurology, Celal Bayar University School of Medicine, Manisa, Turkey

### ABSTRACT

**Objective.** Cognitive brain dysfunction after open heart surgery is a serious complication caused by cardiopulmonary bypass (CPB). The presence of gaseous and/or particulate emboli in the CPB circuit and cerebral hypoperfusion may be the causes of neurologic problems after cardiac operations.

**Methods.** In this prospective study we examined 42 consecutive cardiac surgery patients (24 mitral valve replacement [MVR] and 18 coronary artery bypass grafting [CABG] patients). In addition to determination of clinical measurements, cognitive brain function was measured objectively by P300 auditory-evoked potentials before operation, at day 7, and at 4-month follow-up. Electroencephalographic evaluations were also performed.

**Results.** In preoperative measures there was no difference between the groups (peak latencies in the MVR group were  $324 \pm 8$  milliseconds; CABG group,  $318 \pm 6$  milliseconds;  $P > .05$ ). At day 7, cognitive P300 auditory-evoked potentials were significantly impaired (prolonged) in both groups compared to preoperative values (MVR group,  $347 \pm 7$  milliseconds; CABG group,  $342 \pm 7$  milliseconds;  $P < .05$ ). P300 measurements almost returned to normal at 4-month follow-up (MVR group,  $331 \pm 6$  milliseconds; CABG group,  $319 \pm 8$  milliseconds;  $P > .05$  compared to preoperative values). One week and 4 months after surgery no difference between the 2 groups could be found ( $P > .05$ ).

**Conclusion.** Postoperative patients had prolonged P300 values according to the preoperative measurements and we have not found any difference between the groups whether cardiac chambers were opened or not.

### INTRODUCTION

Cognitive brain dysfunction is a serious complication after open heart surgery and it is associated with the use of cardiopulmonary bypass (CPB) and many other factors. The incidence of cognitive impairment is related to the interval

between cardiac surgery and the assessment of cognitive function. It has profound implications because neurocognitive impairment prolongs the duration of hospitalization and affects the quality of life of the patient [Newman 2001]. The incidence of cognitive brain dysfunction after open heart surgery with CPB may range from 20% to 80%. This wide variability may be related to different sensitivities of the test batteries used to assess cognitive brain function [Newman 2001; Kilo 2001]. Objective cognitive P300 auditory-evoked potential measurements have demonstrated their usefulness to determine cognitive brain dysfunction after coronary artery bypass graft (CABG) operations [Zimpfer 2003].

The aim of this prospective study was to objectively measure neurocognitive deficit after CABG and mitral valve replacement (MVR) operations and to investigate whether the type of operation has any impact on P300 measurement and neurocognitive function 7 days and 4 months after surgery.

### METHODS

We performed this prospective study to determine the measurement of P300 in the patients who underwent cardiac valve or coronary artery surgery. After institutional ethics committee approval was obtained, 18 patients undergoing elective CABG and 24 patients undergoing MVR operations gave their written informed consent and were enrolled in the study. Patients who had a history of symptomatic cerebrovascular disease or psychiatric illness, patients with a significant carotid artery stenosis (of more than 70%), or patients with a history of previous transient ischemic attacks or stroke were excluded from the study. Characteristics of our 42 patients are listed in Table 1.

### *Evaluation of Neurocognitive Function, P300 Measurement*

The investigator performing the preoperative and postoperative assessments was blinded to the group classification of each patient. All patients were informed about the measurement methods. To exclude some conditions, such as mental state or encephalopathy, an electroencephalographic evaluation was performed for each patient. Patients who had normal electroencephalographic evaluation results were included in the study. All electroencephalographic evaluations were performed in the same daily period, in the afternoon under

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Address correspondence and reprint requests to: Dr. Ihsan Iskesen, Celal Bayar Universitesi Tip Fakultesi Kalp Damar Cerrahisi ABD, Manisa, Turkey; fax: 90-236-237-02-13 (e-mail: [iskesen@yahoo.com](mailto:iskesen@yahoo.com)).

Table 1. Characteristics of the Groups\*

Characteristics	MVR Group, n = 24 with 7 AVR	CABG Group, n = 18
Age, y	47.5 ± 13	55.1 ± 9
Male/Female	9/15	11/7
Cardiopulmonary bypass time, min	50.5 ± 2	41.5 ± 3
Cross-clamp time, min	87.1 ± 5	70.2 ± 6

\*MVR indicates mitral valve replacement; AVR, aortic valve replacement; CABG, coronary artery bypass graft.

comparable conditions, with the patients awake in a dark and silent room. All recordings were made with an 18-channel monitored Medelec-Vickers Medical device (Modul USA, Danbury, CT, USA). Electrodes were placed according to the 10-20 system. Deep hyperventilation was required for at least 4 minutes, and intermittent visual stimulations were presented periodically at 5, 10, and 20 stimuli per second. Electroencephalographic examinations were made preoperatively (T1), on the seventh postoperative day (T2), and in the fourth postoperative month (T3). All recordings were inspected thoroughly for ground activity, alpha frequency, amplitude, paroxysmal activity, and lateralized or localized abnormalities. Latencies in P300 peak were assessed in patients who had normal electroencephalography. The recordings for the cognitive P300 auditory-evoked potentials were made with a Medelec Sapphire 2E (Medelec, Surrey, UK) in the standard oddball paradigm while the patient was lying supine in a dark and silent room. Binaural target tone and nontarget tone stimuli of 85 dBL intensity were applied, and both target and nontarget tones were recorded. Auditory frequency of the target tone was applied as 8 KHz and auditory frequency of the nontarget tone was determined as 1 KHz. Target stimuli were given in random 15% frequencies, and 32 target stimuli were applied during the whole period; the frequency of stimuli was settled as 0.5/sec 0.1 to 50 Hz band-pass filter and a 1-second analyzing time was applied. Evoked potential measurements were detected by cortical leads. Electrodes were placed according to the international 10-20 system. The active electrode at the recording site was Cz (vertex), the reference electrode was A2 (earlobe), and the ground electrode was Fpz (frontal). Electrode impedance was maintained at less than 5 ohm. Amplitudes were measured as a total value of peak-positive plus peak-negative values. Latencies were assessed in the interval between positive peaks and negative peaks as milliseconds. Patients were also evaluated by echocardiography, electrocardiography, blood tests, and clinical investigation at all points of follow-up. Cardiac chambers were explored to find thrombus, and the functional state of the heart valves was assessed echocardiographically.

### Operative Management

Nonpulsatile perfusion of 2.4 L/min per m<sup>2</sup> was maintained during CPB with an ascending aorta cannula and a single 2-stage right atrial cannula. Aortic cannulation was performed in areas free of atherosclerotic plaque as assessed by digital palpation. Intraoperative epi-aortic ultrasonography

Table 2. Preoperative and Postoperative P300 Values\*

	P300 latencies, ms, Mean ± SEM		P300 Amplitude, Mean ± SEM	
	MVR Group	CABG Group	MVR Group	CABG Group
T1	324 ± 8	318 ± 6	16.6 ± 2.0	16.2 ± 1.6
T2	347 ± 7	342 ± 7	14.6 ± 1.6	15.5 ± 1.2
T3	331 ± 6	319 ± 8	15.8 ± 2.3	17.3 ± 1.4

\*SEM indicates standard error mean; MVR, mitral valve replacement; CABG, coronary artery bypass graft; T1, preoperative; T2, early period (seventh postoperative day); T3, late period (fourth postoperative month).

was not employed. The pump was primed with crystalloid solution. Arterial carbon dioxide tension was maintained at 35 to 40 mmHg (uncorrected for temperature) throughout the CPB procedure, and the partial pressure of oxygen was maintained at 150 to 250 mmHg. During CPB, hematocrit was maintained between 20 and 25 and mean arterial pressures were between 50 and 70 mmHg. Myocardial protection was provided by cold antegrade blood cardioplegia. No hemodynamic comparison was made because of the differences of the diseases of the groups.

### Statistical Analysis

Data are reported as mean ± standard error mean. P300 values for the evaluation of cognitive brain function were analyzed by means of the paired Student *t* test between preoperative and postoperative values and unpaired Student *t* test for both groups.

## RESULTS

In preoperative measures there was no difference between patients undergoing MVR and patients undergoing CABG (MVR group, 324 ± 8 milliseconds; CABG group, 318 ± 6 milliseconds; *P* > .05). P300 peak latencies were prolonged (impaired) in both groups compared with preoperative values (MVR group, 347 ± 7 milliseconds, *P* < .05; CABG group, 342 ± 7 milliseconds, *P* < .05) at 7 days after surgery. There was no difference between the groups (*P* > .05). All operations resulted in a significant prolongation (impairment) of cognitive P300 peak latencies at 7-day follow-up compared to those before operation (MVR group, 324 ± 8 milliseconds versus 347 ± 7 milliseconds [*P* < .05]; CABG group, 318 ± 6 milliseconds versus 342 ± 7 milliseconds [*P* < .05], respectively). Four months after surgery, P300 auditory-evoked potentials returned to normal in both groups. At 4-month follow-up, P300 peak latencies were almost normalized as compared with preoperative values (MVR group, 324 ± 8 milliseconds versus 331 ± 6 milliseconds [*P* > .05]; CABG group, 318 ± 6 milliseconds versus 319 ± 8 milliseconds [*P* < .05]) (Table 2).

## DISCUSSION

The aim of this prospective study was to objectively measure neurocognitive deficit after CABG and MVR operations and to evaluate the operations impact if any on neurocogni-

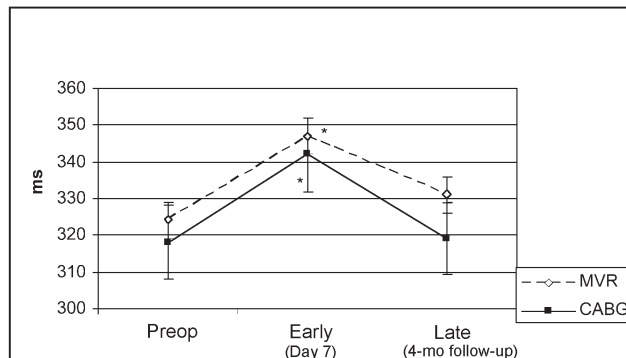
tive function for the short and long term after surgery. Neurologic complications are the primary causes of morbidity and mortality after cardiac operations. Patients whose cognitive functions decline immediately after heart surgery are at increased risk for long-term cognitive decline and a reduced level of overall cognitive functioning. The early cognitive impairment is clinically significant and is a harbinger of later cognitive impairment [Newman 2001].

The use of CPB may be the only predictor of impaired cognitive brain function after open heart surgery. The role of CPB as a cause of cognitive impairment is not clear. Cognitive decline frequently occurs following cardiac surgery. The use of CPB has been shown to be associated with cognitive decline [Ho 2004]. This adverse event affects length of hospital stay and quality of the patient's life.

P300 auditory-evoked potentials are a highly sensitive method for evaluation of cognitive function [Kilo 2001]. Evoked potentials are stable sequences of negative and positive electroencephalographic peaks after a stimulus within a period of several hundred milliseconds. P300 event-related potentials are late positive cortical deflections occurring after certain cognitive tasks. These objectively reflect important aspects of neurocognitive function. They are highly sensitive and reproducible tools for evaluation of impaired cognitive brain function of various disorders. P300 peak latencies also increase with age [Zimpfer 2003].

The negative effect of CPB on cognitive dysfunction is demonstrated by the measurement of P300 and some standard psychometric test batteries [Grimm 2000; Kilo 2001]. The determination of cognitive P300 auditory-evoked potentials is an objective and valid measure of neurocognitive function and it allows a quantification of cognitive brain function [Zimpfer 2003]. We did not perform any standard psychometric test because these tests have been shown to fail to detect any subclinical cognitive impairment after CABG operations [Kilo 2001]. P300 auditory-evoked potentials were shown to be much more sensitive than psychometric tests for detecting impairment of neurocognitive function [Grimm 2000, 2003; Korpelainen 2000; Zimpfer 2003].

We have shown that cognitive brain function was significantly impaired at 7 days after cardiac operations according to the measurements of P300. We have seen that both patient groups had a similar degree of impaired cognitive functions at the first 7-day period postoperatively. Postoperative cognitive decline may be caused by impaired cerebral perfusion during CPB and postoperative systemic inflammatory response as well as microembolism and macroembolism [Zimpfer 2003]. Activation of systemic inflammatory response mediators, operative trauma, the presence of gaseous and/or particulate emboli in the CPB circuit, the operative procedure, and cerebral hypoperfusion have been implicated in neurologic dysfunction and some perioperative cognitive decline after cardiac operations [Zimpfer 2002; Hedayati 2004]. Possible sources of cerebral emboli during cardiac surgery may be the ascending aorta, carotid arteries, or intracardiac cavities [Puskas 2000]. The major source site of emboli during operations is the ascending aorta, which is the place where many surgical manipulations are performed. Embolization of atherosclerotic debris is most likely to occur during aortic



Serial recordings of P300 peak latencies before operation, at day 7, and at 4-month follow-up. MVR indicates mitral valve replacement; CABG, coronary artery bypass grafting.  
\* $P < .05$ .

cannulation/decannulation, cross-clamp application/removal, and the construction of proximal anastomoses [Harringer 2000; Borger 2001; Likosky 2003]. But in our study there was not any difference between the groups whether cardiac chambers were opened or not.

Some mechanisms were proposed to explain the possible high microembolization after mechanical heart valve operations. This embolization may be related to blood/mechanical valve surface interaction, as mechanical heart valves have been shown to produce microemboli entering the cerebral blood circuit and these microembolic events may result in neurocognitive damage [Grimm 2003]. But in our study there was not any difference between the groups in relation to neurocognitive events.

The use of intra-aortic filters [Reichenspurner 2000], alternative aortic cannulation techniques [Borger 1999; Hedayati 2004], and the minimizing of aortic manipulation are some useful methods for decreasing cerebral embolization. In some studies it was shown that valve surgery patients had prolonged P300 values compared to CABG patients [Zimpfer 2002]. But in contrast to these studies we have not found any differences between the groups in which cardiac chambers were opened or not opened (Figure).

## CONCLUSION

After open heart surgery patients had prolonged P300 values according to the preoperative measurements, and we have not found any difference between the groups whether cardiac chambers were opened or not opened.

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