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Anesthesiology
78:209-210, 1993
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J. B. Lippincott Company, Philadelphia

Quantitative Electroencephalographic Monitoring during Cardiopulmonary Bypass

To the Editor:—In a recent editorial Levy¹ states that there is no role for intraoperative electroencephalography (EEG) monitoring during cardiopulmonary bypass (CPB) surgery. This editorial precedes the paper "Electroencephalography during Surgery with Cardiopulmonary Bypass and Hypothermia," by Bashein *et al.*,² and uses the data presented within to support this negative viewpoint. We found many of Levy's arguments flawed, especially since they rely heavily on the results of the Bashein *et al.* study, which itself has severe limitations.

We agree with Levy that any single EEG channel reflects local cortical activity and does not reflect activity from distant cortical regions or from subcortical regions in general. Thus, a major shortcoming of the Bashein *et al.* study is identified. Two EEG channels are not adequate for monitoring cortical function during CPB surgery. It is not surprising that only weak relationships were found between the EEG features measured and neuropsychologic test performance. Regional measures of parietal/occipital EEG should not be expected to predict neuropsychologic test performance for nonvisual/spatial type tasks. Note that Bashein *et al.*² found parietal/occipital EEG changes correlated with visual motor task performance and an increase in the EEG power drop index correlated with both verbal memory and overall neuropsychologic test performance. However, these findings appear to be all but ignored and written off as due to type I statistical errors. Ignored also are two recent studies reporting significant relationships between EEG changes and postoperative neurologic status as well as improvements in neurologic outcome due to quantitative electroencephalographic (QEEG) monitoring.^{3,4}

Levy argues that the failure of Bashein *et al.* to find any systematic relationship between EEG and temperature changes induced during hypothermia makes it impossible to identify EEG changes due to ischemic injury during hypothermia. We believe that their failure to identify systematic relationships between EEG features and hypothermia is due to the inadequacy of the study design as well as the EEG measure set used. Given the number of EEG measures used, the percentage of EEG artifact contamination described, the use of bolus injections of opioids during anesthesia, and the small number of subjects used, it is understandable why no systematic EEG/hypothermia relationships were found and why Bashein *et al.* were unable to replicate the findings of Russ *et al.*⁵ In fact, a temperature correction formula for EEG defined cerebrocortical dysfunction during hypothermic CPB procedures has been reported recently,⁴ and John and colleagues have published temperature correction formula for brainstem auditory evoked potential components.⁶

It has been our experience that raw QEEG measures can vary a great deal both within and across patients, making it difficult to identify systematic group QEEG changes.⁷ Like Edmonds *et al.*,⁴ we have found that the use of a baseline self-norm, with z-transformation against this norm, increases the reliability of EEG changes within and across individuals because it takes into account the inherent variability of each EEG measure and makes it easy to identify changes

outside the normal variability of the measure. In addition, we do not have the problems of pump and electrical artifact described by Bashein *et al.*, especially using a centrifugal type pump.

In all fairness to Bashein *et al.*, they clearly point out the shortcomings of their study and conclude only that two-channel EEG monitoring with current technology appears to have little utility in detecting harbingers of brain injury. We believe a multichannel system utilizing self-norm statistical comparisons and univariate and multivariate QEEG features⁷ could overcome the problems encountered by Bashein *et al.* Further research with these kinds of systems should be encouraged rather than discouraged. Then, and only then, will the key research issues described in the closing paragraph of the Bashein *et al.* paper be addressed adequately.

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CORRESPONDENCE

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Damage Before and After Cardiac Surgery. Edited by Willner A. Lancaster, MTP Press in press, 1992

(Accepted for publication October 16, 1992.)

Anesthesiology

78:210-211, 1993

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In Reply:—My coauthors and I appreciate Edmonds and colleagues' interest in our work. I would like to address their criticisms by pointing out the ways in which our approach differs from theirs and what I perceive to be significant weaknesses of their study.

Our work was an observational study. We sought first to characterize the influence of varying temperature on the electroencephalogram (EEG) during cardiopulmonary bypass in the "normal" situation and then to find associations between changes in EEG descriptors and postoperative neuropsychologic dysfunction. We found no consistent pattern of EEG changes with temperature, weak associations between changes in two of eight EEG descriptors and early postoperative neuropsychologic impairment, and no association at 7-month follow-up. Realizing the difficulty of proving what turned out to be an essentially negative result, we invested a great deal of human and computer time in diligently searching for underlying relationships that may not have been evident from simpler analysis of our data. We were also careful to point out what we believe to be the major limitations of our work: two-channel monitoring, frequent roller pump interference, and our particular anesthetic technique.

Edmonds *et al.*¹ tried to go a step further than we did. They made therapeutic interventions (increasing arterial pressure or perfusion pump flow) in response to prolonged focal increases in δ -band power as indicated by a commercial instrument that indexes the EEG descriptors to adaptively derived baseline values. According to their published article, these interventions resulted in a large reduction in the incidence of postoperative disorientation among their patients.¹ Their letter also alludes to unpublished data supporting an additional claim of a reduction in major neurologic injury due to these interventions, which, taken at face value, suggests that they have made a major therapeutic breakthrough in the intraoperative management of cardiac surgical patients. Scrutiny of this portion of their work must await peer review and publication of the full details. I wish, however, to point out some of the major design flaws present in their already published work. (Similar flaws also may be found in the work of Arom *et al.*,² mentioned in Edmonds *et al.*'s letter.)

First, the Edmonds study was susceptible to bias because it was nonblinded, the assessors of outcome were supported by the manufacturer of the equipment tested, and the study used nonparallel controls. It is entirely possible that other differences in total perioperative care between their sequential patient groups may account for the observed differences in outcome. Second, their outcome measure (disorientation) was severely limited in scope and was assessed only on the fifth postoperative day, when residual effects of drugs, sleep deprivation, pain, etc. could have influenced the results. Third, few details were provided about their routine management of blood pressure and perfusion flow during bypass and the type, magnitude, and frequency of the interventions actually made. (In our study we

employed high-flow perfusion and carefully tried to keep mean arterial pressure in the range of 60–80 mmHg, and thus we may have avoided episodes that would have prompted interventions in Edmonds *et al.*'s patients.) Fourth, fluctuations in anesthetic depth caused by their technique of "repeated bolus doses of fentanyl or sufentanil" could have produced some of the EEG and blood pressure changes that they observed.

The lack of long-term follow-up is another major limitation of their work. Numerous studies have found one-third or more of patients to exhibit some form of neuropsychologic impairment during the first week or so after cardiac surgery. However, a large majority of impaired patients in most series make a complete recovery within weeks or months. Without follow-up, it is not clear that the interventions advocated by Edmonds *et al.* confer any long-term benefit.

Our quoted statement about a "prohibitively large sample size" was based upon a simple statistical fact: given the approximately 5% severe neurologic injury rate in recent studies (references 31 and 32 in our paper), it would require approximately 500 patients each in treatment and control groups to have 80% confidence of detecting a 50% or greater reduction in the rate of impairment.³ Edmonds and his colleagues may have been lucky and acquired a set of data that happened to achieve statistical significance with a smaller sample size, but this occurrence could not have been lucky and acquired a set of data that happened to achieve statistical significance with a smaller sample size, but this occurrence could not have been expected a priori and was likely due to the large false positive rate (68%) that was accepted in choosing their criteria for intervention.

In summary, although our work essentially failed to find EEG correlates of postoperative neuropsychologic impairment, the possibility remains that others may yet succeed in this endeavor. However, on the basis of their work published to date, I do not believe that Edmonds *et al.* have made a convincing case for making therapeutic interventions based upon readings from their instrument (other than gross signal dropout). EEG monitoring is expensive, technically demanding, subject to confounding factors (e.g., of anesthetic type and depth, body temperature), and diverts the anesthesiologist's attention from other aspects of patient care. Thus, before routine monitoring can be advocated, the benefit of interventions based upon monitoring should be demonstrated in a properly designed clinical trial utilizing a randomized, prospective, double-blinded study design and including neurologic and neuropsychologic assessment and follow-up.

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