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Auditory evoked potentials, clinical vs. research applications[1]

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Abstract

Evidence of abnormal auditory evoked potentials (EPs) in patients suffering from schizophrenia has been accumulating. In spite of the magnitude of the EPs in schizophrenia literature, EPs have not been found to be clinically useful thus far. In this study we attempted to replicate the findings in a large sample of schizophrenia patients, and describe how auditory EPs may be used as supplemental tests in the differential diagnostic process. Five subject groups were formed; paranoid (PAR) and disorganized/undifferentiated (disorg/undiff) schizophrenics, schizoaffective (SA), bipolar, and a normal control group. All patients were stable on medications. Subjects underwent one EP recording session. Classification and regression trees (CART) based on EP amplitudes were used to classify subjects into subgroups. The optimal Bayes classification rule that minimizes the expected misclassification cost was then constructed for various misclassification cost functions. In a standard 'Odd Ball' paradigm the N100 amplitudes were significantly decreased in the disorg/undiff group than in the bipolar or normal subjects. The P200 amplitude was smaller in the PAR, disorg/undiff and the SA groups than in the normal controls. Both the disorg/undiff and the PAR groups had significantly lower P300 amplitudes than the normal controls. Classification rules used to classify subjects into normal or ill were sensitive to the relative cost of misclassifying a subject, as well as the prior clinical probability that this subject was ill. Our data largely agree with the existing literature showing abnormally decreased N100, P200, and P300 amplitudes in schizophrenic patients, particularly the disorg/undiff patients. We conclude that whether EP measures are clinically useful depends on the clinical situation. In particular, the prior probability of the diagnosis in question being present and the cost of misclassifying the patient are critical.

Keywords: Evoked potentials; Bipolar; Classification; Schizophrenia; Differential diagnosis

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1. Introduction

Electrophysiological recordings from the scalp, whether electroencephalography (EEG) or evoked potentials (EPs), are completely non-invasive, and without risks to human subjects (Tueting, 1991). The techniques are also relatively inexpensive compared with other procedures such as magnetic resonance imaging (MRI) and positron emission tomography (PET). The above two attributes are essential if a test modality is to become clinically useful. Essential, also, is evidence that the objective test data can significantly and meaningfully improve the clinical care of a particular patient.

Evoked potential (EP) techniques have been utilized to study the auditory, visual, and somatosensory systems. In this article, we review the currently available evidence, as well as providing new data to support the usefulness of auditory evoked potentials as a clinical tool. The brain's response to auditory stimuli can generally be classified into three stages based on post-stimulus latency. The earliest response is the brain-stem evoked auditory response (BEAR), which occurs within 10 ms from stimulation. A number of evoked response components follow between 10 and 250 ms. Buchsbaum (1977) reported that, for a subject sitting quietly without a specific task, the largest vertex (C_z) EP components are a positive, negative, positive sequence occurring at 50–100, 110–140, 160–200 ms. These components are commonly referred to as the P50 (or P_1), N100, and P200 mid-latency auditory evoked responses (MLAERs). Lastly, the event-related potentials (ERPs) are those evoked responses that appear as a result of the subject's performing a cognitive task. A number of ERPs have been described with the P300 being the most studied in clinical populations. The P300 ERP is a large positive response appearing between 250–450 ms most commonly elicited by an odd stimulus imbedded among common or frequent stimuli. Evidence for an abnormally small P300 in schizophrenia is substantial (Ford et al., 1992; for a recent review).

Evidence for abnormal MLAERs in schizophrenia has also been accumulating for the last three decades (Buchsbaum, 1977). Iwanami et al. (1994) studied 27 medicated individuals with schizophrenia. They found the amplitude of the MLAER N100 to be decreased at C_z as compared to normal controls ($P < 0.01$). Roth et al. (1980) using long interstimulus intervals also showed the N100 to be decreased in amplitude in schizophrenia. Other researchers have also found similar decreases in N100 amplitudes in schizophrenia (Pfefferbaum et al., 1980, 1989; Roemer and Shagass, 1990; Roth et al., 1991). In contrast, the P200 was found to be decreased in amplitude in schizophrenia patients by some investigators (Faux et al., 1987), but not by others (Roth et al., 1980). Shagass et al. (1978) studied somatosensory, auditory, and visual EPs in 102 patients, 50 of whom were diagnosed with schizophrenia. They found that the EPs of overtly psychotic patients (schizophrenics, depressives or manics) differed markedly from the EPs of normal control subjects. Psychotic patients had significantly decreased amplitudes of events occurring 100 ms or later after stimulation. In a subsequent study, the same group studied the EPs of 253 unmedicated patients, including 76 with schizophrenia (Shagass et al., 1985). Through the use of combinations of EP amplitude measurements, non-patients were differentiated from patients with schizophrenia with a significance level of $P = 10^{-5}$.

In a discussion of the usefulness of the P300 in diagnosing schizophrenia, itwas shown that a criterion P300 amplitude can be established, above which one can rule out the diagnosis of schizophrenia (+1.6 S.D.), but no criterion amplitude can reasonably establish a positive diagnosis of schizophrenia (Ford et al., 1992).

Only a few EP studies have divided patients with schizophrenia into clinical subtypes in order to decrease the effect of heterogeneity. Baribeau (1993) found that small N100 was correlated with severe tardive dyskinesia and that both the decreased N100 and N200 amplitudes were correlated with the presence of formal thought disorder (Laurent and Baribeau, 1992). John et al. (1994), in addition to reaffirming the powerful ability of EP and EEG measures to differentiate between normal subjects and patients with schizophrenia, provided evidence that EEG/EP measures can be used to develop a number of