

## Evoked potentials in subjects at risk for Alzheimer's Disease

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### Abstract

Evoked potential (EP) changes accompanying dementing processes have been documented in a number of studies. However, EPs have not been studied in subjects who are at heightened risk for the development of Alzheimer's Disease (AD). Nineteen volunteers with no immediate family members with a history of AD and 33 healthy subjects with at least one first-degree relative with AD were studied. Of the 33 subjects with a positive family history of AD, the illness of the sick relative was classified as possible AD in 10 subjects, probable AD in 17 subjects, and definite (autopsy-proven) AD in 6 subjects. Mid-latency evoked potentials (P50, N100, and P200) and P300 event-related potentials were recorded in an oddball paradigm. The amplitudes of the P50 responses to the frequent stimuli and of the P300 responses were significantly higher in the subjects whose relatives had definite AD as compared with the other three groups. The amplitude of the N100 component was also larger in the same group, but the difference was only statistically significant from the group of healthy volunteers without a family history of AD. A process of increased sensitivity to incoming stimuli may be reflected in the increased P50, N100, and P300 amplitudes in the subjects at increased risk for developing AD.

*Keywords:* Electrophysiology; Genetics; Geriatric psychiatry; Dementia

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### 1. Introduction

Evidence that changes in brain evoked potentials (EPs) accompany dementing processes has been accumulating. In several studies, these changes reflect impairment in brain inhibitory processes (McGreer et al., 1978). It has been suggested that during aging the excitatory/inhibitory balance

is shifted in the direction of relatively less inhibition and consequently relatively more excitation (Frolkis and Bezrukov, 1979). An electrochemical bias toward greater excitation would be expected to affect behavior in various ways depending upon the magnitude of inhibitory deficit.

Enhanced neuronal excitation consequent to reduced inhibitory activity should also be reflected in the brain's more gross electrical manifestations, i.e., in the electroencephalogram (EEG) and in

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EPs. Straumanis et al. (1965) compared healthy young subjects (mean age = 24 years) with healthy older subjects (mean age = 72 years). They found that some early visual EP components from occipital scalp (latencies < 100 ms) were of larger amplitude (Straumanis et al., 1965; Shagass, 1972). Other investigators replicated this finding and suggested that these larger amplitudes might indicate a reduction of central inhibition in old age (Dustman and Beck, 1969). This possibility has recently been supported by the finding of more positive visual EP amplitude-intensity slopes in older individuals (Dustman et al., 1990). Somatosensory EP components occurring before 100 ms poststimulus are also larger for older than for younger adults. Shagass and Schwartz (1965) stimulated the median nerve of 89 healthy subjects (aged 15–80 years) and observed that amplitudes of four components of the somatosensory EP significantly increased with advancing age. Differences in responsiveness with aging were also found with auditory stimulation. In a recovery cycle study, a group of older healthy individuals had decreased ability to attenuate their auditory EPs with slow repetition as compared with a group of younger individuals (Papanicolaou et al., 1989).

In clinical populations, a group of adult Down's syndrome patients without detectable cognitive decline had larger and prolonged N100 waves as compared with normal subjects (Vieregge et al., 1992). The cognitive decline in patients with Alzheimer's Disease (AD) is also mirrored by a decline in the amplitude of the P300 component of the auditory EP (Goodin and Aminoff, 1986; Kraiuhin et al., 1986). Such changes can be detected in the early stages of AD. Polich et al. (1990) found significantly lower P300 amplitudes and prolonged latencies in 16 early-stage AD patients. These data suggest that EP measures in a variety of sensory modalities may be able to detect changes in information processing before or very early after the onset of clinically detectable dementing symptoms.

Early identification of dementing processes is important because implementation of treatment at this stage may have a beneficial effect. We conducted the current study in normal individuals who are deemed on the basis of family history to

have a heightened risk for the development of AD. We attempted to identify EP changes that could serve as a marker for such risk. We hypothesized that a subset of those subjects may evidence an enhanced neuronal sensitivity to sensory stimulation, as compared with subjects who are at a lesser risk for developing AD (negative family history).

## 2. Methods

### 2.1. Subjects

Thirty-three "high-risk" subjects were recruited for the study. They were selected from the families of AD patients screened in the Ohio State University cognitive disorders clinic. Subjects were also recruited through Alzheimer's Disease support groups in Columbus and Central Ohio. Subjects had to have a parent or a sibling meeting criteria for possible, probable, or definite (autopsy-proven) AD (McKhann et al., 1984; American Psychiatric Association, 1987). Three at-risk groups were formed: possible at-risk (SAR), probable at-risk (PAR), and definite at-risk (DAR). The SAR group included 10 subjects (2 men and 8 women) with a mean age of 53.8 years (range = 50–61 years). The PAR group comprised 17 subjects (3 men and 14 women) with a mean age of 52.5 years (range = 49–59 years). The DAR group included six subjects (1 man and 5 women) with a mean age of 52.3 years (range = 49–60 years). Subjects were not taking central nervous system active drugs at the time of recording. Subjects with a history of psychiatric, neurological, or substance abuse disorders were excluded. After a preliminary telephone screening, subjects were invited to the laboratory. Subjects underwent a clinical interview and a detailed neurological examination. Nineteen age-matched normal subjects without a history of AD in their first-degree relatives (6 men and 13 women; mean age = 53.6 years; range = 47–60). The parents of the comparison subjects were either still alive or had died at comparable ages as had parents of subjects in the at-risk groups.

### 2.2. Recording procedures

Subjects were asked to sit on a recliner in a comfortable position with their heads supported.

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