Aging Decreases Auditory Event-Related Potentials to Unexpected Stimuli in Humans

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Received 14 August 1984

KNIGHT, R. T. Aging decreases auditory event-related potentials to unexpected stimuli in humans. NEUROBIOLOGICAL AGING 8(2) 109-113, 1987.—A P300 event-related potential (P3a) was recorded to unexpected, deviant auditory stimuli requiring no behavioral response. This brain potential underwent systematic latency prolongation and amplitude decrease with advancing age. The age-related changes paralleled those of the P300 (P3b) recorded in target detection tasks. These results provide physiological evidence of a decremented CNS response to unexpected stimuli with aging.

Two subtypes of P300 event-related brain potentials (ERP's) have been described. Tasks which require subjects to detect the occurrence of infrequently occurring stimuli (targets) generate a parietally distributed P300 (P3b) in all sensory modalities. This is often preceded by an N200 potential which has a modality specific scalp distribution [21,22]. Numerous laboratories have reported that the P3b undergoes either latency prolongation or a combined latency prolongation and amplitude diminution with advancing age [3, 7, 8, 13, 17, 18].

Whereas P3b generation requires active subject participation in the behavioral task, delivery of deviant, unexpected stimuli (novels) requiring no overt behavioral response also generates a P300 wave (P3a). In contrast to the P3b, the P3a is equipotential in amplitude at midline scalp sites, occurs approximately 50 msec earlier than the P3b in both the visual and auditory modalities and undergoes rapid habituation over repeated trials. Based on these characteristics the P3a to deviant, unexpected stimuli has been proposed to represent a CNS component of the orienting response [5, 11, 20, 23, 26].

The novelty P3a has not received as much clinical attention as the target P3b, although its independence from behavioral response makes it a potentially valuable tool for analysis of orientation ability in clinical syndromes, particularly those in which behavioral output or cooperation might be impaired. Although the orienting response is reportedly reduced with advancing age, only a few studies in the visual modality have investigated the effects of age on the P3a. Both latency prolongation and latency prolongation coupled with amplitude decrements of the P3a have been reported [2,24]. In order to examine whether a decrease in the P3a is a generalizable effect across stimulus modalities, we investigated the effects of age on the P3a generated to deviant, unexpected auditory stimuli.

METHOD

Subjects

An initial group of 27 subjects ranging in age from 21 to 71 was recruited after exclusion of subjects with history of audiological or neurological disease. All subjects had normal neurological exams and were naive to the experimental procedures.

Procedure

The experiments were conducted with the subjects comfortably seated in a reclining chair in a sound attenuated room. In each ear, audiometric thresholds at 500 and 1500 Hz were determined by the method of ascending and descending limits. Briefly, stimuli were decremented in 2dB steps until the subject behaviorally reported disappearance of the tones. The tones were then incremented in 2dB steps until the tones reappeared. The entire procedure was repeated three times and the mean obtained was defined as the subject's threshold (SL). Five subjects with greater than 15 dB interaural threshold difference were excluded from further analysis leaving a group of 22 subjects. This group was divided into 10 subjects below 45 and 12 above. At 500

1This research was supported by the Medical Research Service of the Veterans Administration and by grants from the NIH (NS 21135) (R. T. Knight).
TABLE 1
AMPLITUDE IN MICROVOLTS (±SEM) AND LATENCIES IN MILLISECONDS (±SEM) FOR THE N200, SLOW NEGATIVITY AND P300 RECORDED TO EITHER TARGET OR NOVEL AUDITORY STIMULI

<table>
<thead>
<tr>
<th>Targets Alone</th>
<th>Novels</th>
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<tbody>
<tr>
<td>Fz</td>
<td>Cz</td>
</tr>
<tr>
<td>N200</td>
<td>4.8±1.0</td>
</tr>
<tr>
<td>Slow</td>
<td>7.4±1.5</td>
</tr>
<tr>
<td>P300</td>
<td>6.5±1.5</td>
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</tbody>
</table>

FIG. 1. Event-related potentials to a deviant, unexpected auditory stimulus (novel) in three young and three aged subjects. Note the decreased novelty P300 (P3a) in the aged group (hatched area) accompanied by a decrease in the following negativity. Each tracing is the average of 20 trials from the Pz electrode.

Hz the mean db difference between these two groups showed an elevation of 6.2±3.1 dB at 500 Hz and 9.4±4.3 dB at 1500 Hz in the elderly group. In order to account for the threshold increase with age, all stimuli were presented binaurally at 45 dB above each individual threshold at 1500 Hz (45 dBSL). Tones were delivered through stereo headphones which produced a subjective midline sound localization.

Two different tone sequences were used. The first sequence was designed to elicit only a target P3b. It consisted of 3 blocks of tones each lasting 3 minutes with each block containing 150 tones occurring every second. In this sequence 91.4% of the tones were at 500 Hz and 200 msec duration (designated standards) and 8.6% occurred randomly at 375 Hz and 200 msec duration (designated targets). The subjects were instructed to press a button when they detected a target tone. Accuracy and not speed was stressed.

The second sequence was designed to elicit both a target P3b and a novelty P3a. It consisted of 500 Hz standards (82.8%), 375 Hz randomly occurring target tones (8.6%) and, in addition, a randomly occurring simulated dog bark (160 msec duration, 8.6%) designated as the "novel" stimulus. The dog bark was matched in loudness to the target 375 Hz tone by normal listeners and had a peak to peak voltage slightly less than either of the pure tones. There were no large transients in the novel stimulus and its spectral energy centered at 1600 Hz. Subjects were not warned of the occurrence of the dog bark and were instructed to continue pressing a button only when they detected the target 375 Hz stimulus. The simulated dog bark was chosen as the novel stimulus since in prior studies it had been shown to elicit large evoked responses which did not habituate in amplitude after the first two or three stimuli [11]. This permitted us to obtain clear averages with a small number of stimuli and also allowed us to examine single trial responses in some subjects.

Brain electrical activity was recorded with Ag/AgCl electrodes placed at Fz, Cz, Pz and under the right eye, all referenced to linked mastoids. The EEG was amplified (bandpass 0.1-70 c/sec) and stored on FM tape for off-line analysis by a computer. The averaging epoch was 1024 msec, including 100 msec of pre-stimulus baseline. Individual trials with excessive muscle activity or eye blinks were excluded.
The P300 components to both the target and novel stimuli were defined as the most positive peak occurring in a post-stimulus window of 250–450 msec. Latency was measured at the peak positivity in this window and amplitude at this latency point was measured relative to the pre-stimulus baseline. In 5 subjects (3 under 40, 2 above 60) a clear bipeaked P300 was observed and latency was taken at the intersection of the descending and ascending slopes of the positivity in the 250–450 msec window. Amplitude was measured in microvolts at the most positive point in the 250–450 msec epoch in all cases. The N200 was defined as the most negative peak occurring in a post-stimulus window of 150–250 msec and the negative slow wave was defined as the most negative peak occurring 400–700 msec post stimulus. Latency and amplitude measures were obtained at these points and the data were subjected to linear regression with calculation of Pearson coefficients (r).

RESULTS

Behavior

During both conditions (target alone, target plus unexpected novels) all subjects performed at near ceiling levels with rare misses of targets. Overall target detection was 99.2% for the targets alone condition and 98.4% for the targets plus novel condition. False alarms were rare to the novel stimulus. Three subjects were eliminated from electrophysiological analysis due to excessive eye blink artifact contamination of the EEG.

Event-Related Potentials

Target ERPs. In the remaining 19 subjects a well delineated parietal maximal P3b was observed (see Table 1) with a mean latency of 406 msec in the targets alone condition and 411 msec in the targets plus novel condition. This difference was not significant. Both the latency and the amplitude of the P3b underwent comparable systematic changes with increasing age in both the targets alone and the targets plus novels conditions. Latency progressively increased (1.29 msec/year, r = .62, p < 0.005) and amplitude diminished (at Pz = 0.21 µV/year, r = −.7, p < 0.001) in the targets alone condition. Similarly for the P3b during the targets plus novel condition, latency increased (1.35 msec/year, r = .57, p < 0.025) and amplitude diminished (at Pz = 0.23 µV/year, r = −.66, p < 0.025).

A centrally distributed N200 (231 msec) was generated to target stimuli. No systematic changes in N200 amplitude or latency with age were observed in either condition (target alone, at Cz r = .35, p = n.s. for amplitude vs. age). A frontocentral negative slow wave (586 msec for targets alone, 601 msec for targets plus novels) similarly did not show clear evidence of age-related changes in amplitude or latency (targets alone, Cz, r = .34, p = n.s. for amplitude vs. age).

Novelty ERPs. In contrast to the parietal maximal P3b, the novel stimulus elicited an equipotential amplitude P3a at Fz, Cz and Pz (see Table 1) with a mean latency of 361 msec. Similar to the target P3b systematic decreases in the novelty P3a were observed with increasing age (see Fig. 1). P3a amplitude underwent a progressive diminution at all electrode sites with a decrease of 0.38 µV/year at the Pz electrode (r = −.84, p < 0.001, see Fig. 2). Latency also systematically lengthened at a rate of 1.13 msec/year (r = .6, p < 0.01, see Fig. 3).

An enhanced centrally distributed N200 (222 msec) was generated by the novel stimulus. As for the target stimulus, systematic age-related changes were not observed in amplitude or latency. The novel stimulus generated a frontocentral slow wave (526 msec). The novelty slow wave did undergo an age-related decrease in amplitude at all electrode sites (at Cz = 0.19 µV/year, r = −.64, p = 0.005), although no systematic changes in latency were observed.

DISCUSSION

These results provide evidence of parallel age-related changes in the P3b generated in active target detection tasks and in the P3a generated to an unexpected stimulus requiring no overt behavioral response. Both these potentials undergo
a comparable progressive amplitude diminution and latency prolongation with increasing age. The P3b results of latency prolongation coupled with amplitude diminution are similar to those reported in the visual and auditory modalities by others [3, 7, 8, 13, 18, 27]. The auditory novelty P3a findings of age-related amplitude diminution and latency prolongation are comparable to the changes reported in the visual novelty P3a [2, 24]. It is unlikely that the decrease in the P3a is due to peripheral age-related hearing loss since the stimuli were delivered at a fixed dB above each subject's threshold which was near the peak threshold of the deviant auditory stimulus. Furthermore only the P300 and not the N200 to the deviant stimulus was decremented with age. The parallel findings in the visual and auditory modalities of an age related decrease in the novelty P3a provide evidence of a generalized decrease in response to unexpected stimuli with advancing age.

A more general question arises in separating late positive potentials into a P3a and P3b classification. For instance, in the current paradigm our P3a to the deviant stimulus might be considered simply a No-GO P3b response. Several lines of evidence, however, indicate that the P3a to deviant stimuli is a separate brain potential from the P3b. The P3a to deviant auditory and visual stimuli has a more frontal distribution and occurs approximately 50 msec earlier than the P3b generated in NO-GO tasks [5, 10, 11, 30]. In addition recent intracerebral recordings in pre-surgical epileptics report an earlier, frontal P300 response which may be a depth analogue of the surface P3a [29].

Both the target and novelty P300 may represent neural elements of a common cerebral mismatch detector underlying the orienting response [25] with the target P3b generated by active and the novelty P3a generated by passive engagement of the circuitry activated during orientation. The prolonged latency of the target P3b relative to the novelty P3a may be related to the interpolated decision processes required in identifying the stimulus as a target and subsequently orienting to it, whereas highly deviant unexpected stimuli would generate a novelty P3a without the need of an intervening decision process.

We did not find evidence of an age-related decrease in the N200 generated to either target or novel stimulus. This may in part be due to the large P300 responses recorded in the young subjects which partially obscured the N200 response. The slow negative wave to the novel stimulus occurring after the P300 did undergo a systematic decrease in amplitude with age. This is not surprising since this potential is routinely found to accompany the novelty P3a in orienting experiments [12].

The neural substrate underlying the age related changes in P3a and P3b is uncertain, although the fact that amplitude and latency for both the P3a and P3b undergo parallel changes with aging suggests that these brain potentials may share elements of a common neural system. Various generator sites of the P300 potential have been proposed including sources in neocortical, limbic, thalamic and corpus callosum regions [6, 9, 16, 19, 31]. The recent attempts to develop an animal model of P300 may help to resolve these critical anatomical questions [1, 4, 14, 15, 28].

ACKNOWLEDGEMENTS
I would like to thank Neal Cohen for use of stimulus tapes developed by him and David Woods for helpful discussions of the data.

REFERENCES


