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AGE-RELATED CHANGE IN P3 AMPLITUDE AS A FUNCTION OF PREDICTABLE AND UNPREDICTABLE RARE EVENTS

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The auditory event-related potentials (ERP's) of young, middle-aged and elderly subjects were measured over Fz, Pz, C3 and C4 in two different rare tone conditions. In the fixed condition, the rare tone occurred predictably, every fourth stimulus. In the random condition, the rare tone was presented unpredictably, with 1:4 probability. Large amplitude late positive waves (P3's) of middle aged subjects (N = 22) were present in the random condition at all placements, but absent in the fixed condition. Elderly subjects (N = 23) responded identically to both rare tone conditions at all placements. Young subjects (N = 7) had large amplitude P3 responses to both random and fixed conditions at all placements except Pz. Over Pz, young subjects had patterns similar to middle-aged subjects, with large P3's to the random rare tone but not the fixed rare tone. Elderly subjects may not differentiate the two conditions, either because they have less efficient memory, or because they primarily attend to the global probability of rare tone occurrence. The results with young subjects suggest that recent memory processes involved in discriminating rare tone conditions initially develop over the posterior (Pz) areas.

Keywords: Event-related potential, aging, memory development, P300

Among cognitive changes associated with advancing age, decline in episodic (short-term) memory is especially vulnerable. Squires, Wickens, Squires, and Donchin (1976) indicated that the amplitude of the late positive wave (termed P3) of the event-related potential (ERP) may be a sensitive index of memory. They demonstrated that global and local probabilities of common-rare tone sequences cooperated in determining P3 amplitude. Response to local events was dependent upon immediately preceding common-rare tone sequences. Single rare tones preceded by a large string of common tones yielded the largest P3 response. In addition to the influence of local or immediate sequences on P3, the global, or overall, probability of a rare event also contributed to P3 amplitude. Infrequent (unexpected) events reliably elicit larger P3's than expected events (Donchin, 1979; 1981; Rosler, Sutton, Johnson, Mulder, Fabini, Plooi-j-van Gorsel, & Roth, 1986).

Previous research has indicated that delayed latency (reflecting response or decision speed) and reduced amplitude of P3, accompanies advancing age (Pfefferbaum, & Ford, 1988; Pfefferbaum, Ford, Wenegrat, Roth, & Kopell, 1984; Ford, Hink, Hopkins, Roth, Pfefferbaum, & Kopell, 1979a; Ford, Roth, Mohs, Hopkins, & Kopell, 1979b; Ford, Duncan-Johnson, Pfefferbaum, & Kopell, 1982a; Ford, Pfeffer-

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baum, Tinklenberg, & Kopell, 1982b; Porjesz, Bergleiter, & Samuelli, 1979; Goodin, Squires, Henderson, & Starr, 1978; Syndulko, Hansch, Cohen, Pearce, Goldberg, Montana, Tourtellotte, & Potvin, 1981; Podlensky & Dustman, 1982). With sequential tree analysis, Ford *et al.*, (1982a) found increased P3 amplitude to unexpected common-rare tone patterns. However, elderly subjects appeared more sensitive than younger subjects to certain patterns (e.g.: repetition). These findings were interpreted to suggest that elderly subjects do use, and then remember, short-term sequences of information.

A reasonable alternative to the conclusion of Ford *et al.*, (1982a) may be that elderly subjects are more reliant on global probabilities than younger subjects. For instance Perlmutter, Adams, Berry, Kaplan, Person, & Verdonik, (1987), suggests that new information is organized by schemas developed from a lifetime accumulation of knowledge. The schema may grow and strengthen with age (Baltes & Brim, 1984; Horn, 1982). Global models of the environment may dominate behavior with advancing age and sensitivity to local events may decrease. In the Ford *et al.*, (1982a) study, elderly persons could develop the "model" that the target tone was very rare (1:10 ratio). Rare tones failing to support the global model may produce surprise and large P3's rather than the structure of immediate events themselves. The present study examined the influence of the structure of immediate events and global probabilities on P3 across the lifespan in a novel paradigm.

METHODS

Subjects

Fifty-two subjects were recruited from the hospital staff, their children, and from a group of elderly (over 65) volunteers. The number of Ss, mean age, and standard deviation for each group were; young group ($N = 7$, age = 11.57 ± 2.37); middle-age group ($N = 22$, age = 37.52 ± 11.58); elderly group ($N = 23$, age = 71.0 ± 6.04).

Procedures

Subjects were tested in an electrically shielded, sound attenuating chamber. Subjects reclined in a comfortable chair and electrodes were applied to the scalp. Binaural headphones were placed over the ears and white noise, supplied by floor speakers, saturated the cubicle to mask extraneous noise. Low level illumination (provided by a d.c. source) permitted the subjects to be viewed via a closed circuit television system from the control room. A communication system maintained continuous audio monitoring of the subjects.

The subjects were tested in two different conditions, one with a fixed or predictable distribution of common-to-rare (i.e.: AAABAAABAAAB. . .) stimuli, and a second condition in which the occurrence of the stimuli was random (i.e.: ABAAAAA-BAAAAABAB. . .). In both conditions, a 1:4 rare-to-common stimulus ratio was generated. Subjects were exposed to both the fixed and random conditions in the same test session with the order balanced across subjects.

The subjects were informed of which condition was being tested. In both conditions, they were asked to close their eyes and count to themselves the number of target stimuli. At the end of each condition, they were asked to report the number of

target stimuli they heard. All subjects reported accurately within one or two tones the number of stimuli presented. A pretesting session determined the subject's ability to discriminate the common and rare stimuli. The stimuli were pure tones of 450 and 550 Hz. The tones were 94 db SPL against white noise background of 72 db SPL at the head phone cone (Bruel and Kjaer, Model 2203 sound level meter).

EEG Procedures

Physiological recordings were made with a Grass polygraph, Model 79, equipped with 7P511 amplifiers. Data collection and formatting were accomplished with a MINC 11/23 computer (Digital Equipment Corp). Stimuli were initiated by the same computer system, via a Grass Click-Tone Control Module (Model S10CTCMA).

Grass silver cup electrodes were placed according to the International 10-20 system at C3, C4, Fz and Pz and were referenced to linked mastoids in monopolar arrays. The electrodes were filled with Grass EC-2 creme and affixed to the scalp. Electrode placements were matched for impedance (no greater than 1000 ohm differences) and pairs of electrodes with impedance of greater than 10 k ohms were replaced. The EEG signals were amplified with 1/2-amplitude settings at 100 Hz (high) and 0.30 Hz (low), the latter being equivalent to a 1.1 stc.

Event-Related Potential Analysis

ERPs were collected by sampling the EEG at 200 Hz for 1280 ms. The computer initiated the stimulus and then sampled backward to zero the ERP array, resulting in 280 ms prestimulus and 1000 ms poststimulus epochs. For each data point, the average and the variance was collected for the forty target trials.

Forty ERP's to the targets in both conditions were averaged for each subject. In the data collection program the original sampling period was 200 Hz. Four sequential samples were added together to produce each data point for analysis. This technique of integration and decimation was utilized to ensure that each data point was representative of the resulting 50 Hz sampling rate and to eliminate phase error. An analog filter also was used to condition the signal prior to digitization (12 db/octave, 3 db at 100 Hz). This minimizes aliasing errors at 200 Hz and the phase error at 25 Hz. These data were preserved as *absolute values* and were used in the BMDP(7M) Stepwise Discriminant Function Analysis (SWDA) program.

The latencies and peak-to-peak amplitudes of the major components were identified and automatically formatted for use in the BMD P2V analysis of variance program. In this analysis, the *absolute peak-to-peak amplitude differences* (uv) between components were the dependent values. The entire ERP waveforms, including the pre-stimulus segments, were evaluated by a trained technician to identify the prominent peaks within specific latency windows (P1, 30-80 ms; N1, 70-150 ms; P2, 130-250 ms; N2, 180-320 ms; P3, 250-600 ms). A semi-automated scoring program displayed the ERP's on a CRT and placed cursors at the points of greatest positivity and negativity. In the data analysis program, a spectral interpolation technique was applied for measurement of the latency of waveform peaks. The waveform was approximated as a sum of sinusoids (the Fourier coefficients) resulting in unlimited temporal resolution and accurately describing components comprised of frequencies up to 25 Hz (the Nyquist frequency). Latencies in this study were rounded off to 5 ms.

Artifact Rejection

Trials associated with eyeblinks or muscle movement were rejected. EEG responses exceeding ± 50 uv at any electrode placement, within 1000 ms of the stimulus were automatically eliminated. This procedure reliably detected eyeblinks scalp muscle activity and postural adjustments. Common-rare tone sequences rejected because of artifact in the EEG, were repeated.

RESULTS

Three separate analyses were computed. First, the *absolute values* of the ERP for the three age groups were subjected to Stepwise Discriminant Analysis (SWDA) and a jackknifing validation procedure. In SWDA entire waveforms were compared across fixed and random conditions and age groups. Second, the *absolute peak-to-peak differences* between major scored components of the waveform were compared across conditions and age groups by analysis of variance. Third, the relationship of the components to age was determined by regression analysis.

Stepwise Discriminant Analysis

Three general features were observed in the grand average waveforms for rare tones in the fixed and random conditions at the four placements. First, only the "middle aged" subjects displayed significantly different ERPs in the fixed and random sequence at each placement. Further, at C3, C4, and Pz, variables within the P3 latency range were the first (most significant) to enter the discriminant equation. At Fz, a late negative component (N480) entered first, followed by a P3 component. The second observation was that ERPs in the fixed/random sequences of elderly subjects were not significantly different at any of the placements. Classification percentages were below those of the other two groups (Table 1 shows results for Fz and Pz). A third observation was that amplitude in the P3 region in the "young" group was larger than in the other groups, in both conditions, and at all placements except at Pz for the fixed sequence. Only at Pz was the discrimination significant between the fixed and random sequences for the young subjects. As illustrated in Figure 1, the P3 region contributed the first variable to enter the discriminant equation at Pz.

TABLE I
Comparison of Jackknifed Percent Correct Classification Scores for Fixed and Random Conditions at Fz and Pz for All Three Age Groups Using 2-Way SWDA

Groups	Condition	Placements	
		Fz	Pz
Elderly	Fixed	58	65
	Random	54	54
Middle	Fixed	82	81
	Random	73	86
Young	Fixed	78	78
	Random	89	89

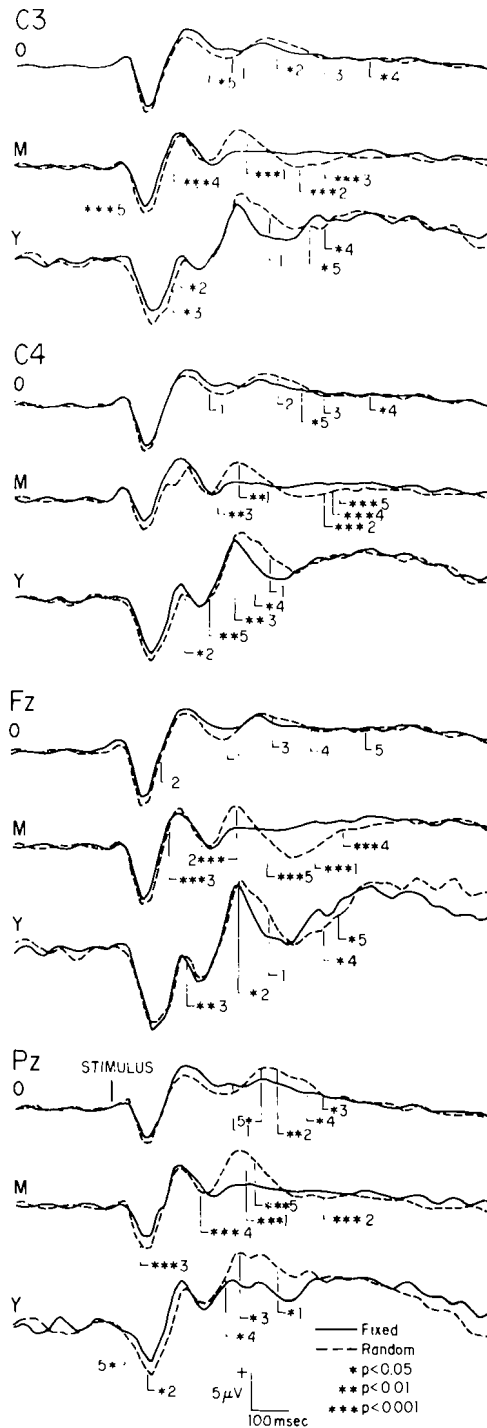


FIGURE 1 Comparison of grand average ERPs to rare tones for fixed and random conditions within each age group. Subjects between the ages of 20–60 displayed the most significant condition-wise differences in the P3 latency range. Subjects under 20 years of age had the largest amplitude P3 response in both conditions. Arrows indicate variables of the waveforms selected as discriminators in 5-step discriminant analysis. Order of entry into the discriminant equation is indicated by numbers. Statistically significant points are indicated.

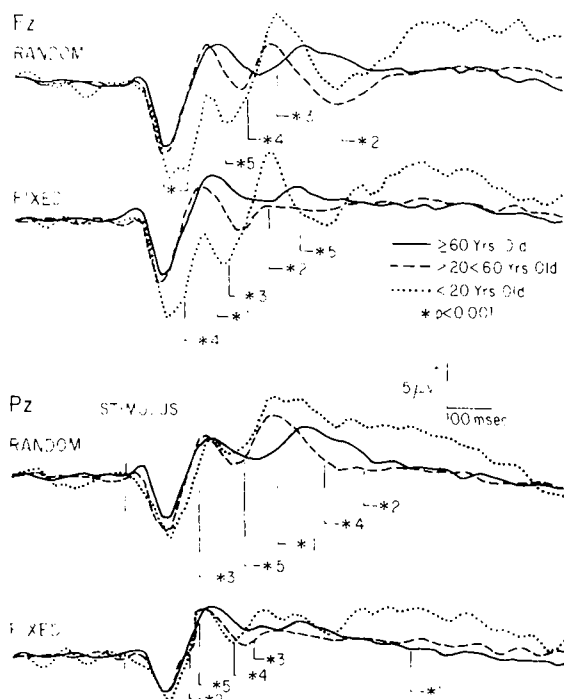


FIGURE 2 Comparison of grand average waveforms to rare tones for the three age groups at Fz and Pz for random (upper trace) and fixed (lower trace in each panel) condition.

A second group-wise discriminant analysis indicated that the age groups were significantly discriminated from each other Table II. In the random condition, the primary loci of age separation were early negative components at Fz (N140) and late positive components at Pz (P300) (Fig. 2). Differentiation of the fixed response was due mostly to the robust response of the young subjects at Fz with less clear discriminations (late positive response in the young subjects) at Pz.

TABLE II
Comparison of Jackknifed Percent Correct Classification Scores for All Three Age Groups at Fz and Pz Within Fixed and Random Conditions Using 2-Way SWDA.

Condition	Groups	Placements	
		Fz	Pz
Fixed	Young	78	67
	Middle	73	68
	Elderly	81	62
Random	Young	78	78
	Middle	77	67
	Elderly	85	89

TABLE III
F-Ratio and Significance Levels for Amplitude of the Major ERP Components of the Major ERP Components.

Independent Variables	Degrees of Freedom	Dependent Variables: Components of the ERP			
		N1	P2	N2	P3
Age (A)	2/49	1.53	.68	.49	14.52***
Condition (C)	1/49	4.02*	.53	.12	9.63**
Placement (P)	1/49	80.11***	6.03*	7.65**	59.14***
(Fz-Pz)					
AC	2/49	.12	1.17	.09	1.52
AP	2/49	2.52	7.09**	.20	24.25***
CP	1/49	.01	.00	.28	7.48**
ACP	2/49	2.17	.19	1.90	1.17

* $p < .05$

** $p < .01$

*** $p < .001$

Analysis of Variance

Since the three age groups were differentiated at Fz and Pz, a 3 (age group) $\times$ 2 (condition; random-fixed) $\times$ 2 (placement; Fz-Pz) analysis of variance was computed for the major ERP components. (A larger analysis including C3 and C4 was computed but did not alter the results.) The results, presented in Table 3 illustrated that the majority of the significant effects were for P3.

The only significant main effect ($F_{2,49} = 14.62, p < .001$) for age was the amplitude of P3, consistent with the findings of the SWDA. In addition, there were significant main effects for condition and placement indicating larger P3's in the random condition and over Pz. The significant interaction (age $\times$ placement; $F_{2,49} = 24.25, p < .001$) was the result of especially large P3s in young subjects over Fz compared with equal amplitude responses at Pz and Fz in the other two groups. Larger P3's were recorded at Fz than Pz in the fixed condition (condition $\times$ place-

TABLE IV
F-Ratios and Significance Levels for Latency of the Major ERP Components

Independent Variables	Degrees of Freedom	Dependent Variables: Components of the ERP			
		N1	P2	N2	P3
Age (A)	2	2.22	1.15	19.95***	14.45***
Condition (C)	1	3.02	.07	1.47	.11
Placement (P)	1	.63	1.86	.01	.03
(Fz-Pz)					
AC	2	.24	.90	1.09	1.67
AP	2	2.01	.20	1.46	3.47*
CP	1	1.96	.16	.01	3.65
ACP	2	.36	.24	.21	1.11
Error	49				

* $p < .05$

** $p < .01$

*** $p < .001$

ment; $F_{1,49} = 7.48, p < .01$) across age groups. The age $\times$ condition interaction failed to achieve statistical significance ($p < .10$) even though age differences by condition were detected with SWDA. This may be due to analysis of absolute differences with ANOVA and absolute values with SWDA.

The significant age $\times$ placement ($F_{1,49} = 7.09, p < .01$) effect (Table 3) for P2 was reversed from the P3 findings because it was greater at Pz than Fz in the young subjects. The main effects of placement for each component in each case was due to increased amplitude over Fz ($F_{1,49} = 6.03, p < .05$).

Latencies of Major Components

The latencies of the major components also were compared by age, condition and electrode placement (C3 vs. C4 and separately, Fz vs. Pz). The influence of age on latency only was apparent after 250 ms (see Table 4). Accordingly, N2 ($F_{2,49} = 19.95, p < .0001$) and P3 ($F_{2,49} = 14.45, p < .0001$) were significantly delayed for the elderly group.

Regression Analysis: Age and P3 Amplitude

The relationship between age and P3 amplitude was significant and negative at Fz but not Pz, for both fixed and random conditions. These data suggested that the greatest amplitude of P3 at Fz was evident in subjects below 18 years of age although the small number subjects in this group limits generalization. A progressive decline in P3 at Fz (both random and fixed conditions) continued until 60 years of age. After 60, considerable variation was apparent as evidenced by near zero correlation. Subanalysis of the three age groups indicated that the largest age-related changes in P3 amplitude occurred in younger subjects in the random condition at Fz and Pz. At Pz, the major contribution to the negative relationship between P3 amplitude and age for both fixed and random conditions was due to large responses in the youngest subjects.

TABLE V
Linear Correlation Coefficients for Amplitude and Latency for Pz and Fz in Fixed and Random Conditions.

Groups	Pz-Random		Pz-Fixed	
	Amplitude	Latency	Amplitude	Latency
Young	-.755*	.573	-.353	.408
Middle	.128	.401	.088	.040
Over 60	.147	.016	.103	.290
Overall	.251	.573	.252	.558
Groups	Fz-Random		Fz-Fixed	
	Amplitude	Latency	Amplitude	Latency
Young	.777*	-.514	.353	.437
Middle	.343	.376	.259	.016
Over 60	.008	.044	.130	.308
Overall	.463	.527	-.398*	.522*

* $p < .05$

** $p < .01$

The differential responses by age to the fixed and random rare events was of primary importance in this study. A supplemental analysis was computed of the relationship between age and the *difference* between P3 in the fixed and random condition. At Pz the relationship was significant ($r = -.28, p < .05$) but at Fz it was not ($r = -.06, p > .10$). Thus, the differences in P3 responses in the fixed and random conditions diminished at Pz as a function of age.

Regression Analysis: P3 Latency and Age

For both the fixed and random conditions a significant, positive relationship existed for age and P3 latency at Fz and Pz. Separate correlations computed within age groups suggested differential contributions to the overall coefficient. For instance, coefficients for the middle aged group roughly approximated the overall coefficient only in the random condition at Fz and Pz. The correlation in the fixed condition for this group was near zero. This response pattern was reversed for the elderly since a significant relationship existed between P3 latency and age in the fixed but not random condition. Further, the relationship in the young group was negative for both conditions. Clearly, some of the inconsistency was due to arbitrary age grouping, however, the general overall trend was made more positive by the skewed distribution and the much greater variance in the elderly group.

DISCUSSION

Predictable and unpredictable sequences of common/rare tones were presented to subjects ranging in age from 5 to 84. The linear relations between chronological age, P3 latency and amplitude found for rare stimulus sequences essentially confirmed the findings of previous investigators (Beck, Swanson, & Dustman, 1980; Brown, Marsh, & Larue, 1983; Courchesne, 1978; Goodin et al., 1978; Podlensky, & Dustman, 1982; Pfefferbaum, Ford, Roth, & Kopell, 1980a, 1980b). Across the lifespan, P3 latency increased and P3 amplitude decreased. However, subanalyses of the three age groups revealed differences in the rate of age-related change (slope) for both amplitude and latency. Young subjects had decreased latency and amplitude with advancing age. During middle age and in elderly groups advancing age was related to increased latency, and either no change in amplitude (middle-aged) or decreased amplitude (elderly). This apparent nonlinearity, also reported by Brown et al., (1983) with a more limited age range, suggested that neural processes responsible for P3 undergo different rates and direction of change with age.

The primary hypothesis of this study was that with increasing age, the ability to distinguish predictable and unpredictable rare tones would decrease. That is, elderly subjects would be less able to detect and track fixed sequences of events than younger subjects, and would have ERPs governed by global rather than local events. This hypothesis was confirmed with SWDA but only partially with ANOVA procedures due possibly to the fact that absolute values (negative and positive) were used in the computations of SWDA and absolute amplitude differences between adjacent peaks were used for the ANOVA.

In support of the hypothesis, ERPs to predictable and unpredictable rare events were significantly different at all electrode placements in middle-aged but not elderly subjects. For the middle-aged subjects, the P3 region was selected as the best discriminator at all placements except Fz. At Fz, N140 was the primary discriminator. For the elderly group, discrimination of the ERP to fixed and random conditions was near

chance at all electrode placement. The ERPs from young subjects were of large amplitude and did not differ for the fixed and random targets at C3, C4 and Fz. However, at Pz, only the random target P3 was large and the difference with the fixed target was significant. The age-dependency of response to the fixed and random conditions was supported by correlations of different responses with age. Over Pz, absolute differences in P3 to fixed and random conditions diminished as a monotonic function of age.

The different responses to fixed and random targets may be related to memory function. In the fixed condition, sensitivity to local sequences of events (i.e.: the "ability" to track and remember recent sequences), insulated the subject from surprise by the predictable but rare event. Subjects who are not sensitive to local sequences of events may not benefit from information contained in the immediately preceding ordered sequences. For these subjects, the fixed target cannot be predicted. Immediately preceding events are less informative about the random target and the rare tone should evoke a P3 response. By this reasoning, subjects unable to recall (i.e.: are insensitive) to immediate (local) sequences, will have P3 responses to fixed and random targets. However, subjects who are sensitive to local sequences should have large P3's to the random target but "suppressed" responses to the fixed target. Thus, greater differences in the P3 response to the fixed and random targets may reflect greater integrity of short term memory processes.

This putative memory-dependent pattern was diffusely distributed over the scalp in the middle-aged group. The absence of memory-dependence in elderly subjects also was reflected over all electrode placements. Topographic localization was apparent only in young subjects, perhaps depicting development of the memory dependent patterns. In the young group, responses in the P3 region separated the fixed and random targets only over Pz. It can be inferred that mature memory functioning, as measured in this study, is associated with expression of response inhibition over frontal areas of the brain. These findings extend Courchesne's (1978) observation that with age, emergence of a frontal P3 may reflect development of sophisticated neuro-cognitive networks. As this process regressed in elderly subjects, the response to predictable targets became disinhibited, diffuse, and undifferentiated at all placements, perhaps reflecting impaired short-term memory.

However, these findings can be interpreted differently. As suggested above, elderly subjects may be guided by global models or schemas (Perlmutter *et al.*, 1987) and because of this adopted "strategy," are less sensitive to episodic changes. Events that do not conform to global expectations may be ignored. In the present study, the two global models were identical (1:4) but the composition of local (episodic) events in the two conditions was different. Responses of the elderly subjects were identical in both conditions and at all electrode placements supporting the possibility of an exclusive focus on global patterns with age. A shift in focus may occur with age from concern with the recent past to general patterns or schemas of events. Adaptive schemas validated over a lifetime encourage dismissal of immediate or episodic perturbations and instead guide behavior with global and general models of the environment. Obviously, poor memory is one consequence of ignoring immediate events in favor of general models, but the mechanism may not be pathological.

The N1 Response

Finally, the significant increase in amplitude of N1 in the random condition suggested that processes in the brain, sensitive to local sequences were engaged as early as 100–120 ms after the stimulus. Because this effect was seen at N1 and P3 but not P2

or N2 suggested that N1 and P3 share critical information and perhaps memory-dependent processes. However, the N1 response did not share with P3, age sensitivity. This dissociation between two processes, one age sensitive and the other not, which participated in detection of unpredictable targets invites new studies of the ERP and age-related decline in memory.

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