THE TOPOGRAPHY OF 4 SUBTRACTION ERP-WAVEFORMS DERIVED FROM A 3-TONE AUDITORY ODDBALL TASK IN HEALTHY YOUNG ADULTS

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Five components were studied in 4 subtraction waveforms derived from ERPs obtained in passive and active conditions of a 3-tone oddball task (common = 70%, C, 0.8 KHz; deviant = 15%, D, 2 KHz; 1.4 KHz = 15%, t, also used as a target (T)). These waveforms reflect different stimulus-mismatch processes and thus their topography could be revealing of different brain regions mediating them. The following mismatches were studied: stimulus-mismatch (deviant – common, D/C, rarity and pitch confounded), pitch-mismatch (T – deviant, T/D, rarity not target features controlled), attention-mismatch (T – t), T/t, controlled for pitch and rarity to show the influence of target features). These are compared with Goodin's procedure [G–wv, (T – common (active)) – (t – common (passive))]. There were main site effects in normalized data in all cases (not P2 and N2 latency). There were separate frontal and posterior contributions to P1, with the former emphasized where target comparisons were involved. Frontal N1 peaks, largest in D/C, spread posterior and to the right where target matching was involved. P2 posterior maxima were also less localized where target features were involved in the comparison. N2 topography was similar between waveforms but spread slightly more to each side in the T/t comparison. Onset was earlier in the D/C comparison. Parietal P3 peaks in waves based on target-ERPs showed a left temporal shift (vs D/C), though in T/D P3 was in fact maximal on the right. Thus an attentional effect is evident as early as 60 ms. Target features modify the anteroposterior distribution of positivity and negativity for the early components and in the lateralization of P3-like positivity. A comparison of waveforms by latency of potential shift (running t-test) vs peak identification (MANOVA) is illustrated and discussed. D/C and T/t (rather than T/D or G–wv) waveforms are recommended for distinguishing comparator mechanisms for stimulus- and task-relevant features.

Keywords: mismatch negativity, processing negativity, negative difference, Goodin-wave, topography, attention

Studies of the N1 potential elicited by common and deviant tones have attempted to distinguish between the different components of this wave and led to the idea of subtracting the event-related potential (ERP) elicited by the one from that elicited by the other. The resulting negative peak had a latency around 200 ms, lay characteristically between the conventional N1 and N2 components and was termed the *mismatch negativity* (MMN: Ford et al., 1973; review Näätänen, 1990). This component in the D/C waveform reflects neuronal activity (a "trace") representing the disparity between two stimuli.

Later the idea of subtracting ERPs was applied to task situations. The aim has been to differentiate the contribution of physical stimulus differences (salience) from task-related features (relevance) on both earlier negative as well as later negative (Shelley et al., 1991) and positive components such as the P3 (e.g., Oades et al., 1988; Johnson, 1993). It had long been appreciated that mismatches involving a target stimulus in a task situation pro-

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duced an N2-like wave, similar but different to the MMN, which was called processing negativity (PN; review Näätänen, 1982).

However, it should be noted that while the term PN was intended to refer to the *task-related* difference in two stimuli, the physical features by which they differ have often been confounded in actual measures of PN. This has occurred through using common tones and targets, both in the 2-tone oddball and dichotic listening paradigms, that confound stimulus- and task-related features (e.g., pitch and rarity, see critique Breton et al., 1988). The waveform that attempts to control for stimulus features has been called the negative difference (Nd; Hansen & Hillyard, 1980). It is best seen as the ERP elicited by a target less that elicited by the same stimulus before it was designated a target (e.g., T – t, here called T/t).

Thus it should be apparent that it is important for the interpretation of subtraction waves in terms of intervening variables related to psychological matching processes to control for the features associated with each stimulus. Therefore a 3-tone paradigm was chosen in which a primary comparison could be made between subtraction waves reflecting stimulus features (MMN-like, deviant and common tones, D/C) and waveforms reflecting task-related features (i.e., processing negativity in the Nd-like waveform, T/t). A secondary comparison was made with subtraction waveforms more or less confounding these two sets of features (i.e., deviant and target, T/D). The waveform attributed to Goodin et al. (1978), appropriate for a 2-tone paradigm used in many clinical applications, was also studied as it has been claimed to discriminate schizophrenics on the basis of the P3 component [Faux et al., 1988: (Target – common, active) – (t – common, passive)].

The waveforms studied can be summarized as follows: D/C (deviant – common) confounds the stimulus-features of rarity and pitch not task-relevance, T/D (T – deviant) confounds task relevance and pitch but not the frequency of stimulus presentation and T/t (T – t) is specific for task relevance (controlling for pitch and presentation frequency). The G-wave attempts to counter the confounds of frequency and pitch with relevance in the active condition by subtracting the same confounds in the passive condition; but these cannot be assumed to be equivalent.

It would be expected that these "mismatch" waveforms would share many features as do the analogous subtraction procedures used in tomographic studies of attention (Corbetta et al., 1990). But we would predict that the focussed attention distinction between stimulus-features (D/C) and other waveforms involving task-related features would reveal ERP component differences and that the T/t waveform would show this best. The 3-tone paradigm was preferred to the widely used dichotic task that usually uses stimuli varying on more dimensions as the proposed extension to psychotic patients resulted in too many failing the discrimination.

Topographic recording was employed to increase the likelihood of picking up regionally specific contributions to the different matching processes and showing potential anomalies in future psychiatric applications. While the principal ERP components of interest concern the "mismatch-related" negativity (here termed N2) and P3 we were encouraged to examine earlier components in the P1, N1 and P2 latency range firstly because we had noted consistent potential shifts in this latency range (at 1:2 to 1:3 of the better studied N2 and P3 components) and secondly because they have received some (see Novak et al., 1992) but very little study in investigations of subtraction-waves. Lastly if the components have significantly different latencies as well as amplitudes, this would indirectly support the possibility that the subtraction waveforms from which the ERP components are derived represent different processes.

In summary differences of amplitude and latency of 5 components in 4 subtraction wave-forms were analysed to see if the waveforms could represent different attention-related mismatch processes on the basis of their topographic representation. On the basis of a 3-tone oddball paradigm this report considers, 1) briefly, the main effects of waveform at the vertex for raw amplitude and latency measures of 3 positive (P1, P2 & P3) and 2 negative ERPs (N1, N2): 2) the topographical main effect of recording site and its interaction with waveform for these components in the D/C, T/D, T/t and G-wave [where a significant interaction is required for interpretation in terms of separate topographical localization (Johnson, 1993)]: and lastly 3) in contrast to the foregoing analysis of peaks identified with variable latencies between waveforms, a running comparison of the variation of amplitude between waveforms over time is considered.

METHODS

Recordings were made with 23 young healthy subjects as in the preceding report. ERPs were evaluated at 15 electrode sites F7, F3, Fz, F4, F8; T3, C3, Cz, C4, T4; T5, P3, Pz, P4, T6; referenced to linked ears with ground at Fpz and Oz, (see also Table 1 in accompanying paper). ERP latencies and peaks were not evaluated at the ground electrodes Fp and O sites, but these data contributed to the 19 sites providing data for the linear interpolation algorhythm used for establishing the topographic maps (see accompanying paper).

The auditory stimuli were a common tone (0.8 KHz, p = 0.7), a deviant standard (2 KHz, $p = 0.15$, and a target, only identified to the subjects as such after the passive stimulus presentation (t or T, 1.4 KHz, 65dBSL, $p = 0.15$) presented in a Bernoulli sequence (rise/fall time 10 ms, duration 50 ms, 1.2–1.7 interstimulus interval). Four difference waves were calculated by subtracting the waveforms elicited by the stimuli as follows: D/C (MMN-like) = deviant – common, T/D (PN-like) = T – deviant, T/t (Nd-like) = T – t and the Goodin-wave (G-wv) = (T – common (active)) – (t – common (passive)).

ERP Definitions

P1 was recorded as the largest positive-going dip immediately preceding the N1 (20–120 ms). N1 was the largest negative-going wave after P1 and before N2 (60–180 ms post-stimulus). (Pilot work suggested there was usually a negative deflection (N1) preceding the major negative-going wave (N2; Fig. 1). P2 was the largest positive-going dip between N1 and N2 (120–240 ms). N2 was the largest negative peak after N1 and before P3 (latency 150–300 ms). In some cases when it was not the largest negative peak, (a larger peak occurred outside the window), there was always a clear preceding P2. The P3 component was the largest post-P2 positive going wave (240–540 ms).

Grand mean maxima across waveforms for the components (in micro-volts) were P1/Pz + 2.24, N1/F3 –2.3, P2/Pz +2.42, N2/Cz –4.23, P3/Pz + 7.61 (see also Figs. 2–6).

Data Analysis

Data were normalized by vector analysis (McCarthy & Wood, 1985; Naumann et al., 1992) separately for each waveform for the 15 sites studied in order to test for the potential independent effect of each waveform. Thus the mean value of the peak at each site for each subject was divided by a vector obtained by taking the square root of the sum of the squared mean measures obtained for each of the 15 sites studied (see also accompanying report).
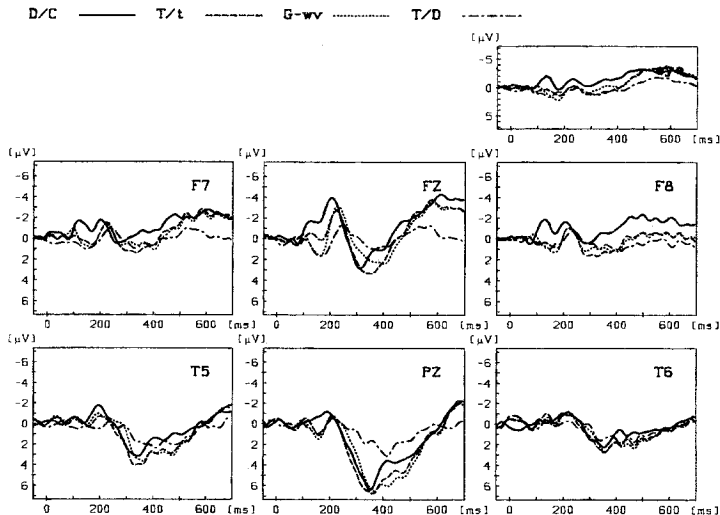
FIGURE 1   Grand mean ERP waveforms for D/C, T/D, T/t and G-wave at lateral and midline frontal and posterior recording sites (bin = 4 ms).

A 2-way MANOVA was conducted for 4 difference-waves (D/C, T/D, T/t, G-wave) at 15 sites with repeated measures for each ERP component, separately. A multivariate analysis was employed with electrode-site treated as a within-subjects factor as a precaution against between subject variability. After briefly referring to the main ANOVA effect of waveform at Cz (raw data) *in the text*, we concentrate on reporting on the topography of component measures (main effects of site and site-waveform interactions). Statistical results are reported after Greenhouse-Geisser (1959) correction of the degrees of freedom with the appropriate epsilon (e) factor for SPSSX "averaged" tests for 15 sites and Hotellings T2 test as an assessment of potential between-measure differences (Faux & McCarley, 1990: *see appendix*).

Significant site effects were followed by selected paired Student t-tests (for dependent variables) for 6 selected comparisons between anterior/posterior (F7/T5, Fz/Pz, F8/T6) and left/right lateral sites (F7/8, T3/4, T5/T6) to determine the source of the difference. Alpha was corrected according to the Bonferroni procedure. Significant interactions were followed by conservative Scheffe tests for putatively independent variables, cited at the 5% level *in the text*. Insignificant interactions ($p > 0.1$) are not reported. The terms "tend, tendency and trend" refer to either statistical significance of 5–10% or where Hotellings and averaged tests provided contradictory evidence of significance. For the amplitude and latency of each of the 5 components in the following text we consider first the main effect of waveform at Cz in the raw data, then the main effect of site followed by the interaction with waveform in the normalized data (if present).

RESULTS

P1

Amplitude. There was no waveform effect at Cz. A positive shift to right (vs left) frontal and left (vs right) temporal areas (t −2.3/2.7 p = 0.03–01) was mainly seen in the D/C waveform. P1 was least marked in the raw data for D/C (contrast the distribution in the normalised data, Fig. 2). Positivity was less widely distributed than in the constituent ERPs (accompanying paper). The apparent frontal contribution to waveforms involving target comparisons was not reflected by a significant interaction.
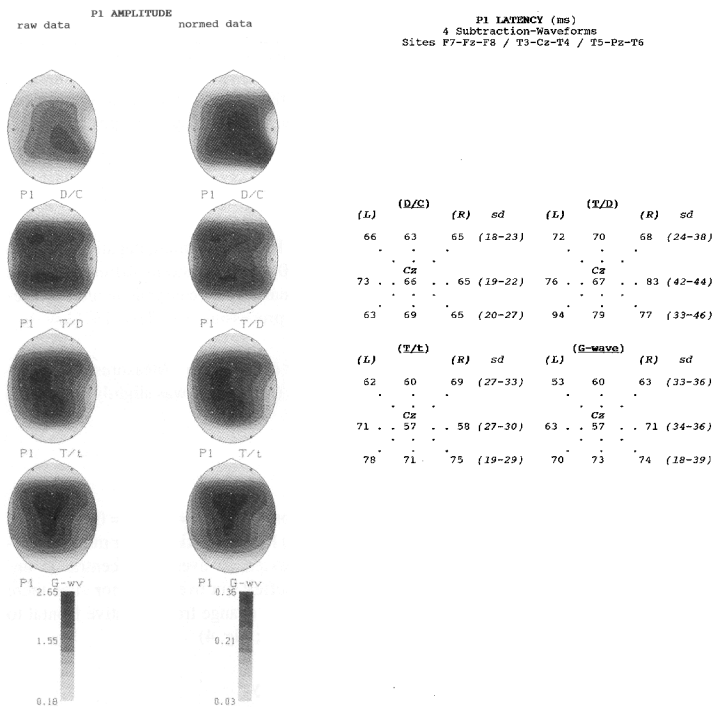

P1 AMPLITUDE
raw data   normed data

P1 LATENCY (ms)
4 Subtraction-Waveforms
Sites F7-Fz-F8 / T3-Cz-T4 / T5-Pz-T6

	(D/C)				(T/D)		
(L)		(R)	sd	(L)		(R)	sd
66	63	65	(18-23)	72	70	68	(24-38)
	.	.			.	.	
	Cz	.			Cz		
73 . .	66	. . 65	(19-22)	76 . .	67	. . 83	(42-44)
	.	.			.	.	
63	69	65	(20-27)	94	79	77	(33-46)

	(T/t)				(G-wave)		
(L)		(R)	sd	(L)		(R)	sd
62	60	69	(27-33)	53	60	63	(33-36)
	.	.			.	.	
	Cz	.			Cz		
71 . .	57	. . 58	(27-30)	63 . .	57	. . 71	(34-36)
	.	.			.	.	
78	71	75	(19-29)	70	73	74	(18-39)

FIGURE 2 (Left) *Topographic distribution of raw and vector-normalized peak amplitudes (uv) in 4 subtraction waveforms (D/C, T/D, T/t & G-wv) with anterior sites uppermost in each map.* Normalized P1 amplitudes reflected the raw data in size and distribution except for D/C. A broader distribution of positivity can be seen than after the constituent ERPs, shifted to the left side over anterotemporal regions, with frontal maxima in the G-wave, parietal maxima in D/C and T/t and over both regions in T/D. (Right) *Topographic representation of latencies (ms) from selected sites in 4 subtraction waveforms (D/C, T/D, T/t & G-wv) with standard deviation range (sd) on the right.* Latencies were shorter frontally than posteriorly and tended to be longer in T/D.

Table 1

Summary of analyses of variance on the *amplitudes* and *latencies* of 5 ERP components in 4 difference-waveforms derived from a 3-tone oddball task: raw data at Cz for main effects of condition (condn; i.e., waveform) and normalized data for topographic data (site) after Greenhouse-Geisser correction.

Amplitude: Component: Factor	P1	N1	P2	N2	P3
wave (raw)	–	–	**	a	a
site	**?	*?	*?	***	***
wave × site	–	–	?	–	*?
Latency:					
wave (raw)	–	–	–	*	**
site	*?	?	–	–	***
wave × site	–	–	–	–	–

a 0.1 > p > .05, * p < .05, ** p < .01, *** p < .001 (averaged tests), ? = conflict on degree of significance between averaged tests and Hotellings-

Latency. Latency was similar across the 4 waveforms, but was on average slightly delayed in T/D. Peaks occurred 10–15% earlier at anterior with respect to posterior sites (t –2.8 to –3.6, p = .006–.001).

N1

Amplitude. There was no effect of waveform at Cz. Peaks were more negative over the left than the right anterior temporal region (t –4, p = .000). Anteroposterior differences were *not* significant. Figure 3 shows that the frontocentral maxima were complemented by secondery posterior peaks in waveforms involving target processing (i.e., T/D, T/t, G-wv).

Latency. There was no effect at Cz nor of site (after e-correction). Measures were variable showing no lateral or antero-posterior differences (Fig. 3). N1 was slightly delayed in the T/D vs the other waveforms.

P2

Amplitude. At Cz P2 was smallest in the D/C waveform (F(3,88) = 4.9, p = 0.004). (The T/D and G-wave showed the most positive deflections.) P2 was maximal over midline parietal regions (t –2, p < .05). The effect seen at Cz extended over frontocentral to anterotemporal sites (i.e., D/C < G-wave, p < 0.05, Scheffe); but over posterior sites there was a tendency for this to reverse (i.e., there was a sharp change from negative frontal to positive parietal values for D/C, compared to the G-wave; Fig. 4).

Latency. There were no significant effects for P2 latency.

N2

Amplitude. At Cz N2 tended to be least negative in the T/D and most negative in the D/C or G-wave (F(3,88) = 2.3, p = 0.8; Fig. 5). Frontal peaks were largest, especially in the midline (t –7.0, p = .000). N2 peaks (like N1) were more negative over the left than right anterotemporal region (t – 2.6, p = .012); but waveform did not interact with site.

N1 AMPLITUDE
raw data   normed data

N1 LATENCY (ms)
4 Subtraction-Waveforms
Sites F7-Fz-F8 / T3-Cz-T4 / T5-Pz-T6

	(D/C)				(T/D)		
(L)		(R)	sd	(L)		(R)	sd
109	111	117	(32-44)	126	124	114	(41-44)
.	.	.		.	.	.	
	Cz				Cz		
121.	. 113 .	.116	(38-42)	132.	. 118 .	.135	(47-55)
.	.	.		.	.	.	
110	113	127	(19-37)	133	137	123	(48-62)

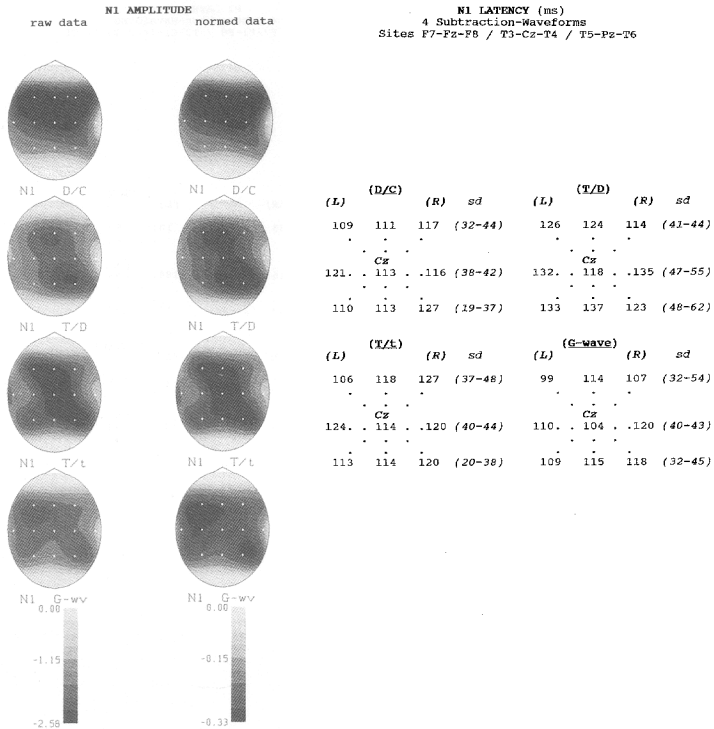|	(T/t)				(G-wave)		
(L)		(R)	sd	(L)		(R)	sd
106	118	127	(37-48)	99	114	107	(32-54)
.	.	.		.	.	.	
	Cz				Cz		
124.	. 114 .	.120	(40-44)	110.	. 104 .	.120	(40-43)
.	.	.		.	.	.	
113	114	120	(20-38)	109	115	118	(32-45)

FIGURE 3   *See Fig. 2.* (Left) Normalization did not alter the distribution of N1 peaks seen in the raw data. Primary frontal peaks were seen in all waveforms and secondary posterior peaks in T/D, T/t and G-wave. Potentials were more negative at T3 with respect to T4. (Right) Latencies were longer than in constituent ERPs and did not show topographical differences. Latencies tend to be slower in T/D.

Latency.   At Cz negativity peaked c.20% earlier in the D/C than in the T/D waveform ($F(3,88) = 3.8$, $p = .013$; Fig. 5). There were no significant topographical effects.

P3

Amplitude.   At Cz P3 tended to be less marked in T/D than in the other waveforms (F(3,88) = 2.4, $p = .07$). In all waveforms peaks were larger at posterior sites bilaterally and in the midline (t −2.5 to −4.5, $p = .02$–.000).

The D/C P3 component was smaller on the right (F8, T4) than in the T/D and G-waves (Scheffe $p < .05$ and $p < .01$, respectively). Indeed P3 over *left* anterior temporal areas was larger than on the right for D/C, T/D and T/t (t 3–5.4, $p = .007$–.000; Fig. 6). Further, larger amplitudes on the left tended to extend to posterior temporal regions in the T/t waveform (t 2.1, $p = .048$).
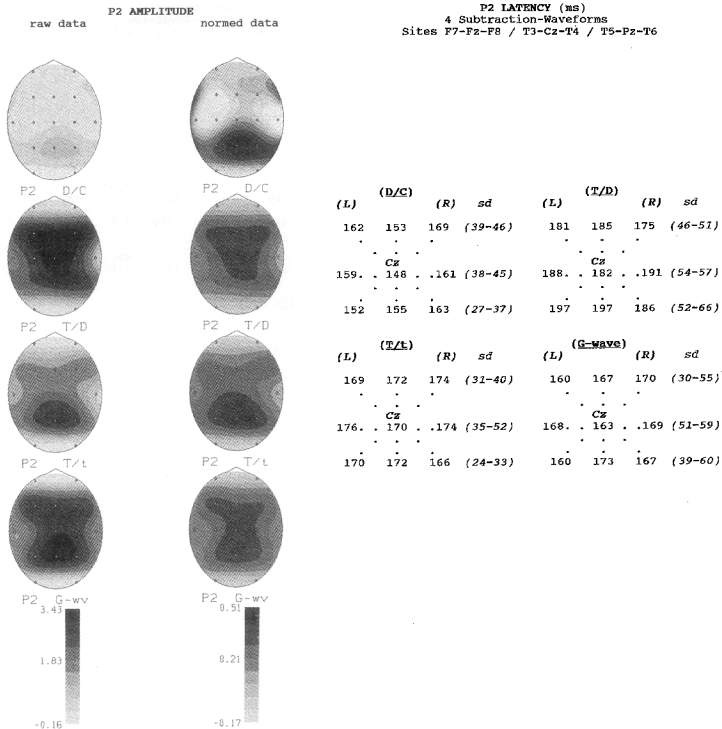
P2 AMPLITUDE
raw data   normed data

P2 LATENCY (ms)
4 Subtraction-Waveforms
Sites F7-Fz-F8 / T3-Cz-T4 / T5-Pz-T6

	(D/C)				**(T/D)**		
(L)		**(R)**	**sd**	**(L)**		**(R)**	**sd**
162	153	169	(39-46)	181	185	175	(46-51)
	Cz				Cz		
159.	. 148	. .161	(38-45)	188.	. 182	. .191	(54-57)
152	155	163	(27-37)	197	197	186	(52-66)

	(T/t)				**(G-wave)**		
(L)		**(R)**	**sd**	**(L)**		**(R)**	**sd**
169	172	174	(31-40)	160	167	170	(30-55)
	Cz				Cz		
176.	. 170	. .174	(35-52)	168.	. 163	. .169	(51-59)
170	172	166	(24-33)	160	173	167	(39-60)

FIGURE 4   *See Fig. 2.* (Left) Peaks were maximal parietally and D/C showed a contrasting negative shift over frontotemporal areas probably reflecting MMN onset. (Right) Latencies continued to be delayed in T/D, did not vary topographically and are now overall shorter than in constituent ERPs.

Latency.   At Cz P3 latencies were 15–20% shorter in the D/C than in T/D and G-waves ($F(3,88) = 5.3$, $p = .002$). Latencies at posterior sites were c.8% longer than anteriorly in all cases (t –4.4 to –7.0, $p = .000$). They were longer over left vs right frontal areas (t 2.5, $p = .016$). Compared to the constituent ERPs latencies were longer posteriorly but similar anteriorly (see Fig. 6 and accompanying paper).

Waveform Comparisons

Differences between waveforms were compared for successive time bins. Such an analysis ignores the different peak latencies found in the grand means and thus forms a contrast to an analysis of variance of peak amplitude irrespective of latency (above). The grand mean waveforms have been compared with running (paired) *t*-tests taking into account the Guthrie-Buchwald (1991) criterion for the number of successive time bins (4ms) where the
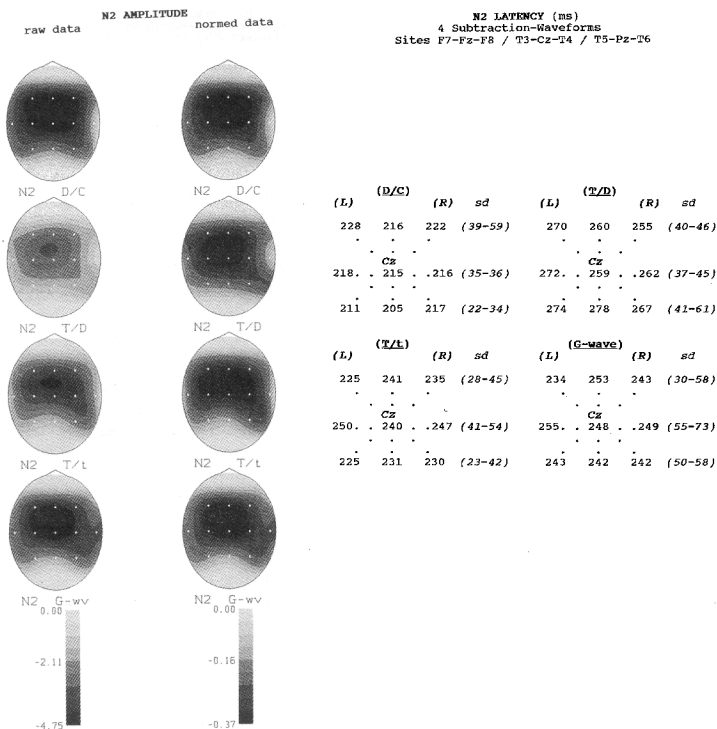
N2 AMPLITUDE
raw data   normed data

N2 LATENCY (ms)
4 Subtraction-Waveforms
Sites F7-Fz-F8 / T3-Cz-T4 / T5-Pz-T6

N2   D/C   N2   D/C

N2   T/D   N2   T/D

N2   T/t   N2   T/t

N2 G-wv   N2 G-wv
0.00   0.00

-2.11   -0.16

-4.75   -0.37

(D/C)					**(T/D)**		
(L)		(R)	sd		(L)	(R)	sd
228	216	222	(39-59)		270	260	255	(40-46)
.	.				.	.		
	Cz					Cz		
218.	. 215	. .216	(35-36)		272.	. 259	. .262	(37-45)
.	.				.	.		
211	205	217	(22-34)		274	278	267	(41-61)

(T/t)					**(G-wave)**		
(L)		(R)	sd		(L)	(R)	sd
225	241	235	(28-45)		234	253	243	(30-58)
.	.				.	.		
	Cz					Cz		
250.	. 240	. .247	(41-54)		255.	. 248	. .249	(55-73)
.	.				.	.		
225	231	230	(23-42)		243	242	242	(50-58)

FIGURE 5   *See Fig. 2.* (Left) The large N2 in the raw data for D/C and G-wave and small N2 in the T/D do not show topographic differences after normalization. Peaks were maximal over a large part of the frontocentral region. There is a relative positive shift over anterotemporal areas on the right compared to the left (as with N1) which is not evident in the G-wave. (Right) Latencies were shorter in D/C than for other waveforms.

95% criterion for significance is exceeded: (i.e., over the windows studied 20 ms is considered as a trend and over this (e.g., 40 ms) as significant).

Prior to 100 ms, in the P1 latency range, there were no significant differences with one exception. In the 50–100ms range where T/t showed a "late P1" the G-wave showed an "early N1". This was significant for 20–40 ms at the 5 frontal sites, C3 and T3 (Fig. 7).

Over the latency range 100–150 ms D/C was more negative than T/t (F7, F3, F4, F8 for > 20 ms) and T/D and the G-wave (at all frontal and central sites for 50 ms). At the 6 more mesial frontocentral sites T/t was clearly more negative than the G-wave over the whole period and tended to be more negative than T/D. T/D and G-waves showed no differences (Fig. 7).

From 150 to 200 ms significant negative differences followed the sequence D/C > T/t > T/D > G-wv, with emphasis on the 6 mesial frontocentral sites. This reflected the onset of N2 rather than P2 amplitude (Fig. 8). (Waveforms were less differentiated at T6 than T5).
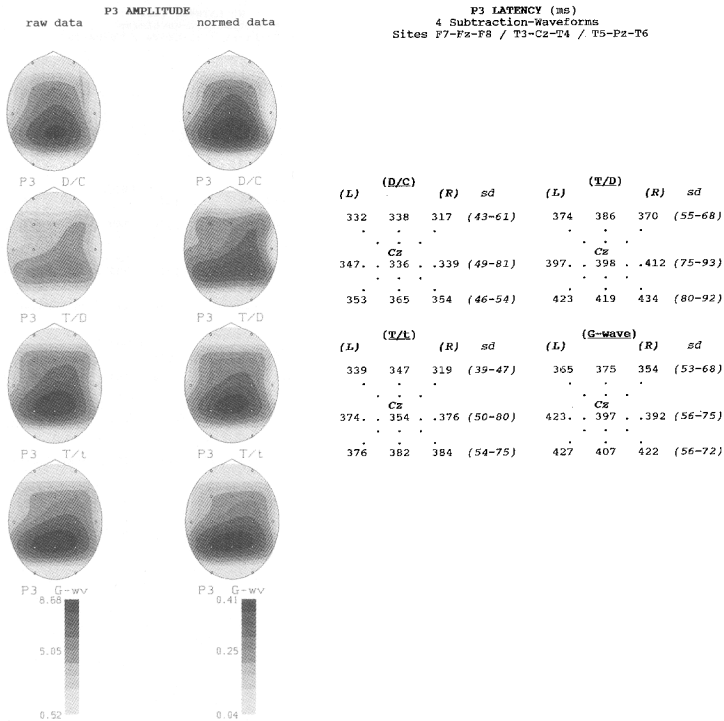
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        P3 AMPLITUDE                              P3 LATENCY (ms)
  raw data        normed data                 4 Subtraction-Waveforms
                                          Sites F7-Fz-F8 / T3-Cz-T4 / T5-Pz-T6


              (D/C)                                    (T/D)
         (L)        (R)    sd              (L)        (R)    sd
         332  338   317  (43-61)           374  386   370  (55-68)
          .    .     .                      .    .
               Cz                                Cz
      347. . 336 . .339  (49-81)        397. . 398 . .412  (75-93)
          .    .     .                      .    .
         353  365   354  (46-54)           423  419   434  (80-92)


              (T/t)                                   (G-wave)
         (L)        (R)    sd              (L)        (R)    sd
         339  347   319  (39-47)           365  375   354  (53-68)
          .    .     .                      .    .
               Cz                                Cz
      374. . 354 . .376  (50-80)        423. . 397 . .392  (56-75)
          .    .     .                      .    .
         376  382   384  (54-75)           427  407   422  (56-72)
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FIGURE 6   *See Fig. 2.* (Left) The modest T/D-P3 amplitude in the raw data contrasts with the broadly similar P3 topography between waveforms after normalization: but a positive shift is biased to left anterotemporal regions. D/C-"P3a" was particularly small over right anterior areas. (Right) Latencies were shorter over frontal areas for all waveforms, especially on the right.

With respect to the N2 component D/C continued more negative than T/D until 220 ms (>95%) but the running t-test fell below criterion at 200 ms for the comparison with T/t and G-wave. T/t and G-waves remained more negative and above criterion with respect to T/D until 220 ms. The emphasis again was on the 6 mesial frontocentral sites but trends for similar differences were evident at T3 and T4.

In the P3 latency range 250–500 ms the most interesting comparisons were between D/C and T/t. There were short-lasting differences at all frontal sites with the D/C component the more positive for about 40 ms, reflecting the earlier D/C peak and perhaps *the P3a component*. While there were no differences parietally, T/t was more positive for 40–80 ms around 400 ms post stimulus over anterior temporal sites (and for a shorter period over far lateral frontal sites). The G-wave was also more positive than D/C over anterotemporal sites (400–450 ms).
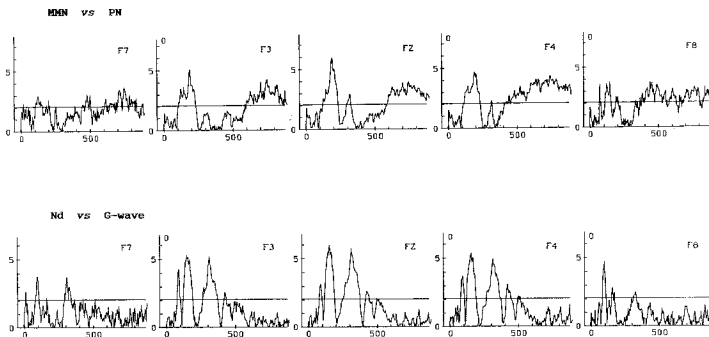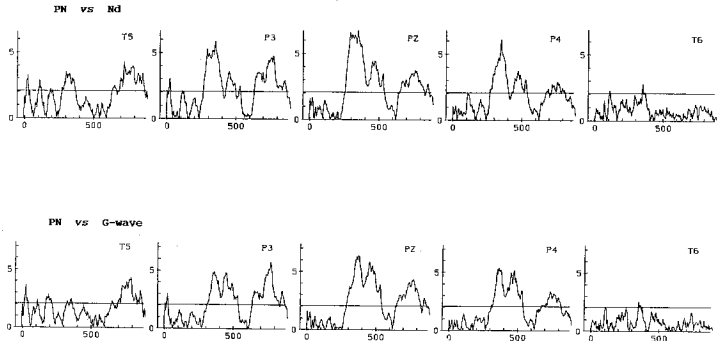
FIGURE 7 Running paired t-tests for each 4 ms bin (F-value vs time) for MMN in the D/C vs PN in the T/D waveform (above) and Nd in the T/t waveform vs G-wave (below) at the 5 frontal sites where 5% significance (F(1,22) = 2.1) is represented by a line from the vertical axis.

D/C was more positive than T/D from 280 to 360 ms at the vertex and parietal sites. Here T/t was much more positive than T/D from 250 to 500 ms, as was the G-wave over 350–500 ms (Fig. 9: i.e., T/D showed less positivity in the P3a *and P3b* latency range than waveforms where the mismatch process emphasized rarity (D/C) or task-features (T/t).

DISCUSSION

General

In the 3-tone discrimination, main effects of site for amplitude and latency were seen for P1 and N1; over 100–150 ms D/C was more negative. With P2 amplitude an interaction
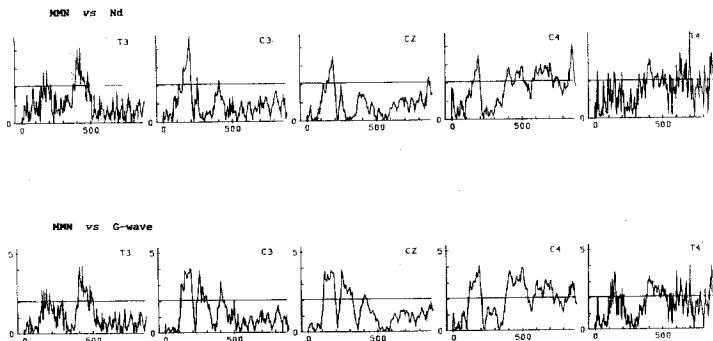
FIGURE 8 Running paired t-tests for each 4 ms bin (F-value vs time) for MMN in the D/C waveform vs G-wave (above) and MMN in the D/C vs Nd in the T/t waveform (below) at T3, C3, Cz, C4 and T4 where 5% significance (F(1,22) = 2.1) is shown by a line from the vertical axis.

FIGURE 9   Running paired t-tests for each 4 ms bin (F-value vs time) for PN in the T/D waveform vs Nd in the T/t waveform (above) and PN in the T/D waveform vs G-wave (below) for the 5 posterior sites where 5% significance (F(1,22) = 2.1) is shown by a line from the vertical axis.

developed separating D/C from the other waveforms. N2 had an earlier onset in the D/C waveform. For the N2-P3 complex interactions developed showing P3a-like activity (D/C) and lateral P3b-like differences over temporal areas (T/t more widespread on the left and in D/C smaller on the right). These largely confirm our prediction of a difference between subtraction waveforms referring and not referring to target features, whereby the D/C and T/t waveforms show the clearest difference.

Methods

In the accompanying report we have discussed the merits of vector normalized data for topographic analyses, along with the use of a statistical filter (averaged tests and Hotelling's T2 test) as a conservative criterion preceding posthoc tests. More controversial is the introduction of the results of running t-tests. This has been regarded as an exploratory statistic until the introduction of criteria for accepting a sequence of successive results as being unlikely to constitute a type I error (Guthrie & Buchwald, 1991; Javitt et al., 1993). In accepting low values for the autocorrelations calculated by Guthrie & Buchwald we do not question the validity of the criterion but its interpretation.

In contrast to the MANOVA analysis, the running t-tests performed here for every 4ms bin cannot be directly related to named components. They compare positive and negative potential shifts between difference waveforms standardised to a zero time point of stimulus presentation. But the sequence of named peaks vary in latency between waveforms, albeit not always significantly. For example the N2 peak around 200 ms in the D/C wave is larger than that occurring later in the T/D, but after 250 ms N2 negativity is larger in T/D (Fig. 1). On the one hand one may argue that because the T/D is derived from responses to different stimuli than the D/C, the negative peak refers to a different information processing mechanism. On the other hand the general similarity of the geometry of the waveform allowing the peaks to be named and the similar topography seen after the analysis of variance would suggest that what the D/C-N2 and T/D-N2 have in common overrides (i.e., the psychological process is essentially the same).

We cannot answer this question here, but suggest a solution. If a combination of task parameters can elicit, for example, "N2" peaks with a similar amplitude and latency in the D/C and T/D waves, even though the constituent ERPs are derived from different stimuli, then there is reason to consider that the same psychological process is represented. Further if defined parameters elicit dipoles with different loci or orientation for D/C- and T/D-N2 then the psychological processes can be differentiated on physiological-anatomical grounds.

Difference Waves: "P1, N1 and P2"

The ANOVA (Cz) and MANOVA (15 sites) analysed amplitudes of defined ERP components irrespective of the actual latency of the specific component and the latencies of these peaks are compared.

P1 peaks in subtraction waves have been noted (Woods & Alain, 1993) and may be seen elsewhere (e.g., Woldorff et al., 1991) but have not been analysed. Here P1 peaked 20–30 ms later and with a broader distribution than in the constituent ERPs. A small delay was already evident in the T/D waveform. Like the constituent ERPs, latencies were marginally shorter frontally. The appearance of two maxima (frontal & parietal, Fig. 2) in waveforms derived from target responses (T/D, T/t & G-wave) but not D/C was not confirmed statistically. However this would bear further study as the implication is of the use of a template or cortical feedback on stimulus relevance as early as 60 ms post-stimulus, as reported by Hackley et al. (1987) and Woods and Alain (1993). In contrast Mangun and Hillyard (1988) claimed that an enhancement of visual P1 and N1 amplitudes with focussed attention did not involve changes of scalp distribution or onset latency.

The component designated N1 preceded the larger negative shift well-known from subtraction waves and may be similar to the "NA1" that preceded the MMN in the report from Novak et al. (1992). They suggested that it reflected initiation of an attention-like process prior to the MMN which makes the comparison of traces necessary to determine potential stimulus relevance. The size and early onset in the D/C (MMN-like) waveform was noted in the running comparisons (below). In general N1 peaked 10–15 ms later than in the constituent ERPs, but like the constituent ERPs there were no local latency differences.

N1 maxima were frontocentrally distributed in the D/C, but in waveforms based on target responses negativity extended posterotemporally (Fig. 3). This shift was not confirmed by a topographic interaction, but received support from the absence of an anteroposterior main effect (contrast N1 in constituent ERPs). This should be the subject of further study. An extension of the negative shift temporally was observed by Woods and coworkers (1992) in intermodal subtraction waves vs those derived from dichotic auditory stimuli. The distribution of our data suggests that their shift may have reflected the subjective valence of the targets rather than the change of modality.

P2 peaks may be small (e.g., D/C) or not visible in all difference waveforms (O'Donnell et al., 1993) but under our conditions the post-N1 positive dip attained mean maxima of 3.43 µv (40% of P3) in waveforms based on target ERPs (Fig. 4 and main effect). These showed local parietal maxima in normalized data (cf. in constituent ERPs maxima were close to the vertex). The latencies were *shorter* than in the constituent ERPs and at 150–190 ms were shorter than the pre-P300 positive deflection seen in other published curves (O'Donnell et al., 1993). P1 and P2 peaks were least differentiated in the D/C reflecting the earlier onset and larger negative shift over the N1-N2 period.

Inspection of the D/C-waveform in Figure 4 shows a sharp negative shift for "P2" over anterior temporal regions. This may reflect the observation of Novak and colleagues (1990) that the MMN inverts in posterolateral loci, a feature that is not so apparent in subtraction waves de-

rived from target ERPs (Teder et al., 1993). The changes noted here in P1-N1-P2 topography emphasize the rapid dialogue between frontal, anterior temporal and posterior temporo-parietal loci that occurs 100–200 ms poststimulus in the evaluation of task-relevant stimulus features.

Difference Waves: "N2 and P3"

ERP and magnetoencephalographic studies report that the "N2" in subtraction waves derives from supratemporal primary auditory cortex anterior to the N1 sensu stricto, whereby the dipole orientation depends on stimulus pitch (Novak et al., 1990; Tiitinen et al., 1993). While our data are broadly consistent with this, maxima are not localized anterior to the N1 and the negative shift is not distributed as far laterally as in the N1. A right hemisphere bias has been reported independent of the ear stimulated in a dichotic paradigm (Paavilainen et al., 1991), but the present binaural data show a slight left hemisphere bias. However the distribution was broadly symmetrical as has been reported for D/C and T/t (Woods et al., 1993).

"N2" latencies were similar to those in the constituent ERPs and, as with P2, were slowest in the T/D waveform. Latencies tended to be 10% shorter in the D/C waveform which is consistent with the finding that MMN has a shorter latency in the unattended than the attended ear in dichotic paradigms (Woldorff et al., 1991). The running t-tests emphasized the earlier onset and larger size of "N2" in D/C compared to other waveforms around 200 ms (cf. T/t and G-wv, Figs. 9 & 10).

"N2" amplitude was least marked in the T/D waveform. This supports the role of N2 in processing rare stimuli (Ritter et al., 1979) and suggests that discrimination difficulty (effort) is associated with this process. "N2" was largest in the D/C and G-wave, perhaps reflecting the relative ease of the comparison required (t vs common: pace Alho et al., 1992). The topography was remarkably similar between waveforms suggesting that the main negative mismatch component in these waveforms may represent similar information processing activity.

P3 latencies were shorter anteriorly, but in contrast to earlier components, particularly on the right. Similar relatively symmetrical P3 parietal maxima were found in all waveforms as reported elsewhere (Woods et al., 1993). But this disguises a few subtle features: 1) all waveforms (only G-wv not significant), were biased to left antero-temporal regions; a left bias was reported for the G-wave by Faux et al. (1988): 2) over right anterior areas P3 in D/C (P3a?) was least positive: the small peak in the T/D wave continued to emphasize the need for effort in the discrimination of the rare tones (cf. N2 above). T/t provided the most distinct P3 among the subtraction waves, again with a left temporal bias.

Difference Waves—Running Tests and Comparative Utility

The D/C was better than the other subtraction waves for differentiating positive and negative shifts upto the latency range of the P3a; (i.e., evaluation of stimulus-features). T/t components were marked in the N2-P3b latency range where stimulus significance is important. The G-wave seemed better than T/D for measuring processing negativity (stimulus deviance reflected in early ERP components) and was similar to T/t with respect to the later P3b. The more modest differentiation afforded by G-wv vs T/t may be attributable to it confounding two measures,—PN (T – common) and Nd (task-relevance, T – t).

Components were least marked in the T/D waveform throughout the evaluation period. But T/D and G-wave may be appropriate to studies of the P2 which has been linked to the inhibitory processes associated with the augmenting-reducing phenomenon (Hegerl & Juckel, 1993).

Finally it may be noted that although P3 maxima were parietally located (main effect) there was an interaction for anterotemporal sites also seen in the running analysis, especially on the left (Fig. 10). Here the T/t and G-wave were more positive than the D/C waveform. This is of interest in view of the discussion over multiple (temporal) sources for the P3 (Halgren, 1988) and the source of a schizophrenic impairment (McCarley et al., 1993).

Conclusions

Our results suggest that the study of subtraction waves and their topography leads to a better description of elementary psychological processes and their localization than the study of the constituent ERPs. In particular differences appear between waveforms embracing non-target ERPs (D/C) and those where a constituent ERP is elicited by the target (T/D, T/t, G-wave). For the differentiation of task-related processing the T/t provides the strongest contrast followed by the G-wave. In general T/D measures seemed less useful. Detailed consideration of conventionally described peaks indicates that the present 3-tone oddball task is not ideal for the study of early components but it may be effective for studies of psychiatric patients where differential impairments in the processing of salient and task-relevant stimuli are suspected, especially if running analyses are performed (Oades et al., 1993; 1994).

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Appendix of analysis of variance results for amplitude and latency of 5 ERP components in 4 difference-waves (3-tone oddball task); 1) averaged tests with Greenhouse-Geisser df-correction. 2) Hotelling's T2 test.

Component measures and factors:	site-averaged tests	Hotellings T2 test
P1		
amplitude: $e = .338$;		
site,	$F(5, 416) = 10.6, p = .000$;	T2 $F(14, 75) = 3.5, p = .000$:
latency: $e = .437$;		
site,	$F(6, 538) = 5.2, p = .000$;	T2 $F(14, 75) = 2.6; p = .004$:
N1		
amplitude: $e = .349$,		
site,	$F(5, 430) = 6.3, p = .000$;	T2 $F(14, 75) = 3.3, p = .000$:
latency: $e = .423$,		
site,	$F(6, 521) = 1.7, p = .05*$;	T2 $F(14, 75) = 2.0, p = .03$:
P2		
amplitude: $e = .308$;		
site,	$F(4, 379) = 3.0, p = .000$;	T2 $F(14, 75) = 6.1; p = .000$:
waveform × site,	$F(13, 379) = 1.3, p = .08$;	T2 $F(42, 221) = 2.1, p = .000$:
no topographical latency effects.		
N2		
amplitude: $e = .379$,		
site,	$F(5, 467) = 21.7, p = .000$;	T2 $F(14, 75) = 14.2, p = .000$:
no topographical latency effects.		
P3		
amplitude: $e = .326$,		
site,	$F(5, 402) = 66.1, p = .000$;	T2 $F(14, 75) = 18.5, p = .000$:
waveform × site,	$F(14, 402) = 1.6, p = .009*$	T2 $F(42, 221) = 1.9, p = .002$:
latency: $e = .407$,		
site,	$F(6, 501) = 15.8, p = .000$;	T2 $F(14, 75) = 5.2, p = .000$:

Notes: Results are cited if averaged *or* Hotellings test gave a clear or borderline significant result: the degrees of freedom (df) cited for the averaged tests are corrected by the epsilon value given; * = not significant after Greenhouse-Geisser correction.