Electroencephalography and Clinical Neurophysiology, 1981, 52: 553–570
Elsevier/North-Holland Scientific Publishers, Ltd.

NON-CEPHALIC REFERENCE RECORDING OF EARLY SOMATOSENSORY POTENTIALS TO FINGER STIMULATION IN ADULT OR AGING NORMAL MAN: DIFFERENTIATION OF WIDESPREAD N18 AND CONTRALATERAL N20 FROM THE PREROLANDIC P22 AND N30 COMPONENTS [1]

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(Accepted for publication: October 1, 1981)

The recent surge of interest for early somatosensory evoked potential (SEP) components is providing a wealth of clinically relevant data (e.g., Desmedt 1971; Noël and Desmedt 1975, 1980; Colon et al. 1977, 1978; El-Negamy and Sedgwick 1978; Anziska and Cracco 1980; Chiappa et al. 1980; Eisen and Odusote 1980; Small et al. 1980; Mauguière et al. 1982) while raising new issues that call for special investigations. For example, the early negativities recorded from the posterior neck after median nerve stimulation (Liberson and Kim 1963; Matthews et al. 1974; Cracco and Cracco 1976; Hume and Cant 1978; Small et al. 1980; Desmedt and Cheron 1980a; Mauguière and Courjon 1981) have recently been analysed with pre- and post-vertebral electrode arrays whereby they could be resolved into an N11 component that is propagated from spinal entry up the dorsal column, and an N13 component that is related to a fixed generator in the dorsal horn of the cervical spinal cord (Desmedt and Cheron 1981). On the other hand, there is still a problem with the proper evaluation of the early cortical responses.

Most current studies have considered the SEPs recorded from the parietal scalp while neglecting the SEP components that can be picked up in front of the central sulcus. The latter present a distinct profile which undergoes dissociated changes with aging (Desmedt and Cheron 1980b). Moreover the early frontal components P22 and N30 have now been shown to involve independent cortical generators with a separate thalamocortical input since they persist in patients with postrolandic cortical lesions that eliminate the early parietal SEP components (Mauguière et al. 1982). Therefore the SEP studies in which a frontal electrode was connected to grid 2 of the amplifiers as reference have been complicated by the unwanted interference of the frontal generators. A thorough examination of these problems requires that a non-cephalic electrode be connected to grid 2 of the amplifiers whereby the subcortical far-field components P9-P11-P13-P14 have indeed been studied (Cracco and Cracco 1976; Anziska and Cracco 1980; Cracco et al. 1980; Desmedt and Cheron 1980a; Grisolia and Wiederholt 1980; Wiederholt 1980). However, it is much less known that the SEP components following the P14 far-field display quite unexpected features with non-cephalic reference recording. One of these is an apparently bilateral distribution of the early SEP negativity (Kritchevsky and Wiederholt 1978) which would appear to conflict with the current interpretation of the N20 SEP compo-

[1] This research has been supported by grants from the Fonds de la Recherche Scientifique Médicale and the Fonds National de la Recherche Scientifique, Belgium.

0013-4649/81/0000–0000/$02.75

nent as reflecting the contralateral cortical 'primary' response to median nerve stimulation.

The present paper analyses the early SEP components recorded with non-cephalic or with earlobe electrodes connected to grid 2 as reference and also tackles the issue of individual variabilities of SEP components in normal subjects. Such variabilities and the consistent changes occurring with normal aging have proven invaluable in the proper evaluation of genuine SEP components (cf., Desmedt and Cheron 1980b). Consistent new features have now been disclosed, namely the occurrence of a rather widespread N18 component that must be distinguished from the 'primary' contralateral postrolandic N20, and that interacts with the prerolandic P22 and N30 generators to produce the topographical features of SEP wave forms.

Material and methods

The data were collected from 40 normal adults (20 males and 20 females) of 20—35 years (37 subjects between 20 and 25 years and 3 between 30 and 35 years), and 35 healthy octogenarians (17 males and 18 females) of 80—91 years (mean age 84.6 ± 3.8 S.D.). About half of the subjects had been used for a previous paper in which the criteria for selection of the older subjects have been discussed (Desmedt and Cheron 1980b, p. 405). All subjects were in good health, free from neurological disease and non-addicted to tobacco or alcohol. No subject had any evidence or history of trauma to upper limb, neck or skull. They had given informed consent and many of them agreed to return for repeat SEP studies. Besides freedom from disease, the criteria for subject selection involved ability to fully relax in order to minimize muscle or eyeblink interference and good yields in SEP averaging. The subjects laid comfortably on a couch in a soundproofed, electrically shielded and air-conditioned room at 24°C.

The stimuli were square electrical pulses of 0.2 msec delivered through a pair of Beckman cup electrodes to the left median nerve (cathode proximal) just above the wrist. The intensities checked by a current probe were 3—7 mA (about 3 times the subjective threshold) and elicited small thumb twitches. In other runs the stimuli were delivered through silver rings to fingers II and III of the left hand, also at about 3 times subjective threshold. When the thumb was also stimulated to increase the afferent volley, its stimulus was delayed by 0.5 msec to make up for the shorter distance to the spinal cord (cf., Debecker and Desmedt 1964). The time intervals between stimuli varied at random between 0.5 and 1.0 sec, and the mean stimulation rate never exceeded 2/sec. The left upper limb was warmed by infrared and its skin temperature was normal at 35—36.5°C.

Each experiment included several runs with 14 simultaneous recordings that involved two 8-channel FM magnetic recorders, operated at 7 in./sec. Scalp, earlobes and posterior neck sites were recorded from with unvarnished stainless steel needles 0.2 mm diameter. The non-cephalic reference was a silver plate on the dorsum of the right hand. Electrode impedance was maintained under 3000 Ω. Differential amplifiers with 10 MΩ input impedance were used. The overall bandpass extended from 2.5 kHz to 0.5 Hz (Desmedt et al. 1974). For each run 1024 or 2048 samples were averaged off-line with a Nicolet model 1074 computer (4096 words of 9 bits) after editing the FM-taped data to exclude blockings, excess EMG or other interference (cf., Desmedt 1977, for details of methods). The bin width was 80 or 160 μsec and 1024 points were used for each of the 4 traces simultaneously averaged. All figures present original records, that is unsmoothed traces drawn on paper by the averaging computer through an X-Y plotter, to allow detailed scrutinization of the responses. Several writings of the same trace (with a 0.2 mm shift along the ordinate) were used to obtain a thicker line for identification purposes when two different records

were superimposed. Component profiles and latencies were consistent in repeat runs on any given subject. The SEP components were labelled from the positive (P) or negative (N) polarity and their modal peak latency, as recommended by an international committee (Donchin et al. 1977).

Results

In order to clarify the presentation, all SEP components are given standard labels with the model peak latency for median nerve stimulation in a young subject of mean arm length: thus, the labels for the positive scalp far fields P9-P11-P13-P14, for the postcentral N20-P27-P45 and for the precentral P22-N30 are used irrespective of the actual peak latency (which may be about 3 msec longer in the case of finger stimulation, for example). The records illustrated for each subject are from both sides of the scalp at a parietal site 70 mm from the midline and 30 mm behind Cz and at a frontal site 50 mm from midline and 60 mm in front of Cz (Fig. 1). The emphasis is on the inter-subject differences in those SEP features which were consistent in any given subject.

With a non-cephalic reference on the right hand, the contralateral parietal SEP disclosed several inflections on the rising limb of N20, after the P14 far field (Fig. 1B). The first inflection also occurred ipsilaterally at the frontal (Fig. 1A) and earlobe electrodes (Fig. 1C). This phenomenon differed from a mere return of the P14 positivity and we propose to designate it as the widespread N18 component (hatched). In this subject the N18 was fairly consistent in size and profile ipsilaterally. For lack of any other specific reason, we consider that it terminated or decreased at the time of onset of the frontal N30 (Fig. 1A).

The N18 is thought to be present at the contralateral electrodes where its interaction with postcentral N20 and precentral P22 generators resulted in typical wave forms. The onset of N20 could be estimated from the divergence time of the contralateral trace from the ipsilateral (Fig. 1B) or after electronic subtraction of these two traces whereby the early far fields are removed and a fair approximation of the early 'primary' cortical negative response is directly displayed (Fig. 2D) (cf., Desmedt and Cheron 1980a, Fig. 10). A similar profile of N20 was seen with earlobe (instead of non-cephalic) reference (Fig. 2C), obviously because the N18, being roughly similar at earlobe and ipsilateral parietal electrodes, canceled out. In these traces the rising limb of N20 displayed a second inflection whose significance remained obscure.

At the frontal electrodes recorded with non-cephalic reference, the trace diverged downward contralaterally with the onset of the P22 (Fig. 1A). This was virtually absent ipsilaterally in this subject. Electronic subtraction of the two traces removed the early far fields and displayed a well-delineated P22 (Fig. 2A) which was rather similar to the one seen in the earlobe reference recording (Fig. 2B). The actual onset time of P22 may have to be negotiated, but a clear positive transition seemed to occur about 1 msec after the onset of the postcentral N20. The duration of P22 could only be surmised. It was taken to decrease or disappear as the frontal negativity N30 took off: this was clearly indicated in the non-cephalic recording (Fig. 1A). Some N30 activity was usually present ipsilaterally, as indeed suggested by the added negativity at the same latency in the ipsilateral record (Fig. 1A). If so, the electronic subtraction of the two frontal traces underestimated the true size of the contralateral N30 (Fig. 2A), whereas the earlobe reference recording disclosed more appropriately a larger N30 (Fig. 2B) because the earlobe itself presented little 'N30' activity (Fig. 1C).

In this subject, postcentral positivities were virtually absent with non-cephalic reference recording (Fig. 1B). A P27 appeared to be riding on a steady negativity and was revealed either by subtraction of the parietal traces (Fig. 2D) or by earlobe reference recording

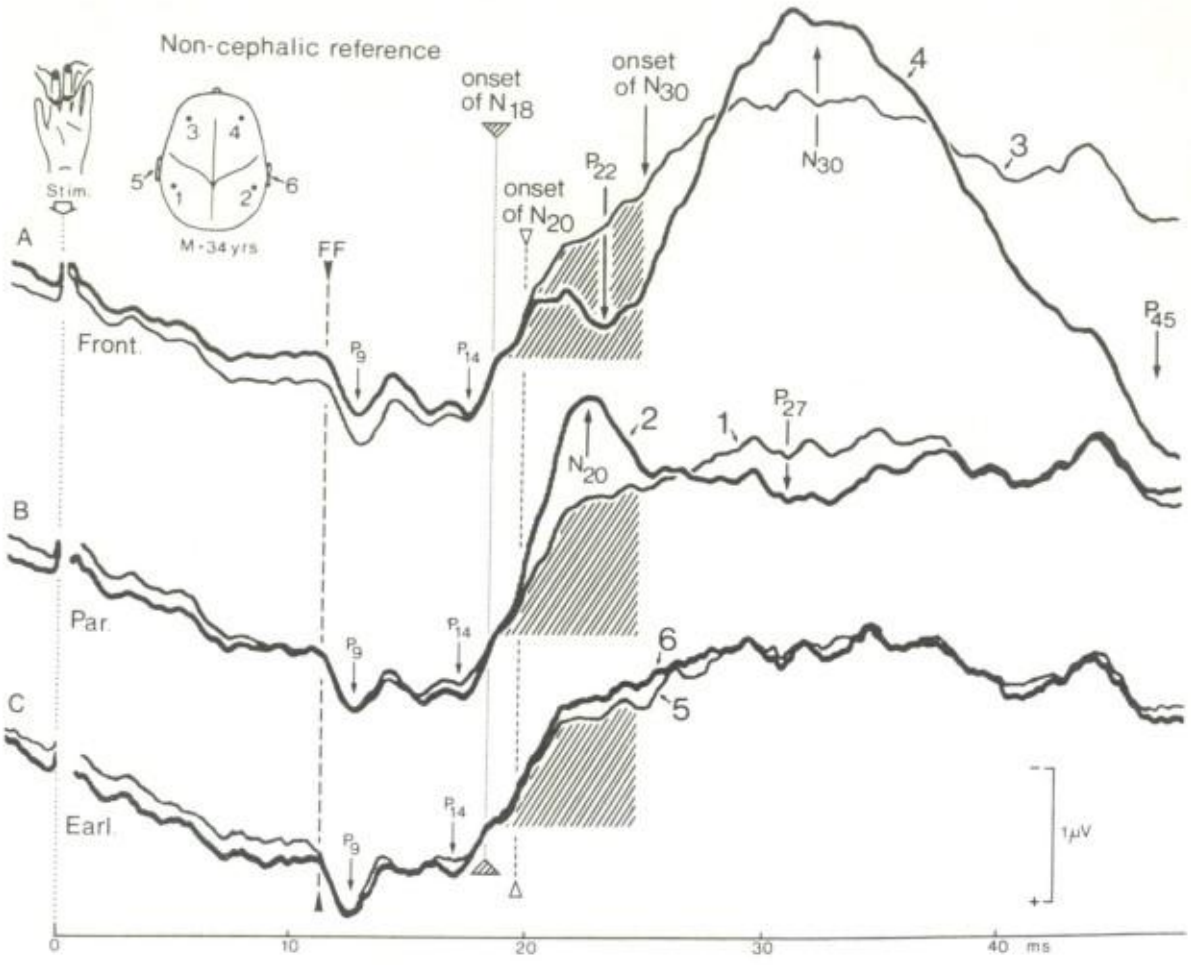

Fig. 1. Normal male subject of 34 years. Non-cephalic reference recording of SEP components recorded at the frontal scalp (A), at the parietal scalp (B) and at the earlobes (C). Negativity of the active electrode produces an upward movement of the trace in this and all subsequent figures. The traces from the contralateral side are presented by thicker lines (drawn by several writings of the computer) and are superimposed on the traces from the ipsilateral side. Electrode positions and traces are numbered from 1 to 4. The electric stimulus is delivered to the left fingers II and III. The far-field onset and the P9 and P14 far fields are well delineated. After P14, a first inflection on the negative-going traces indicates the onset of component N18 (vertical fine-dotted line) while the onset of the parietal N20 is indicated as corresponding to the divergence of the contralateral and ipsilateral parietal traces in B. The N18 phenomenon is represented by hatched area which is arbitrarily terminated at the onset of the frontal N30 component (A). The N18 is present at all electrodes ipsilaterally, and is supposed to underlie the focal SEP components N20 (B) or P22 (A) on the contralateral side.

(Fig. 2C). Both manipulations indeed removed much of the N18 phenomenon and subsequent negativity. The onset time of P27 was well defined and quite different from the onsets of the precentral P22 or N30. It was surprising that a large P45 appeared precentrally (Figs. 1A and 2B) while none was recorded postcentrally (Fig. 2C,D).

When comparing recordings from either earlobes, P14 far field was larger contralateral

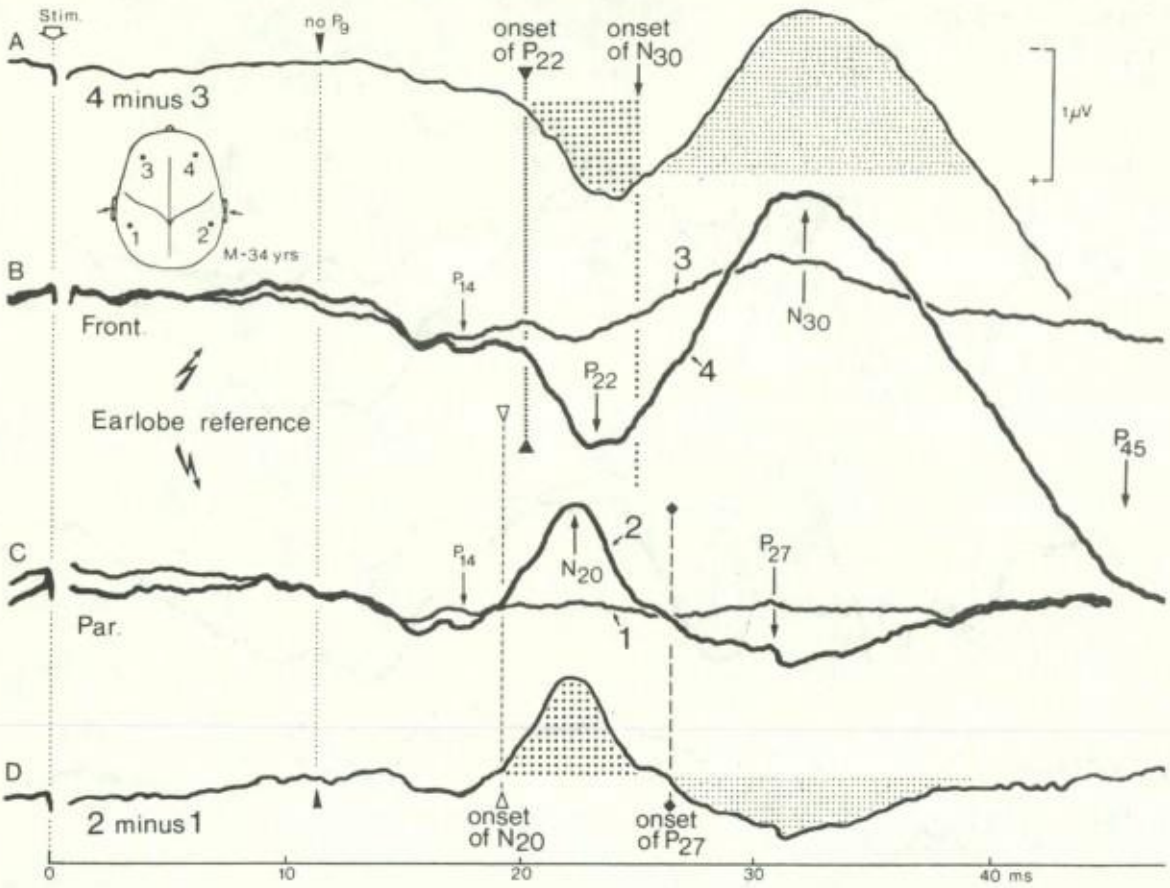

Fig. 2. Same experiment as in Fig. 1. The same averaged data are here presented with earlobe reference (B and C) or after subtraction of the ipsilateral front (A) or parietal (D) trace from the symmetrical contralateral trace. These traces present little, if any, far-field and N18 components and the positivities are better delineated (such as the P22 at the front and the P27 at the parietal electrodes). There is virtually no early negativity at the ipsilateral parietal electrode.

to the hand stimulated as previously described (Desmedt and Cheron 1980a, Figs. 5 and 6) while the subsequent negativities were fairly similar (Figs. 1C and 3C). It is difficult to decide whether the transient upward deviation at the contralateral earlobe between about 18 and 24 msec related to a slight increase of either N18, or N20, or both on that side.

The next adult subject also disclosed clear inflections on the negative-going trace after the P14 far field and the N18 and N20 components were easily differentiated (Fig. 3B). The contralateral frontal electrode presented a typical P22-N30-P45 sequence, but the ipsilateral front showed definite P22 activity (Fig. 3A) in contrast to the previous subject (Fig. 1A). The subtraction of the frontal traces thus tended to underestimate the P22 (Fig. 4A). At the contralateral parietal electrode, large P27 and P45 were seen, even with the non-cephalic reference (Figs. 3B and 4C). These components were virtually absent from the ipsilateral trace so that the subtraction displayed quite prominent 'W' profiles (Fig. 4D).

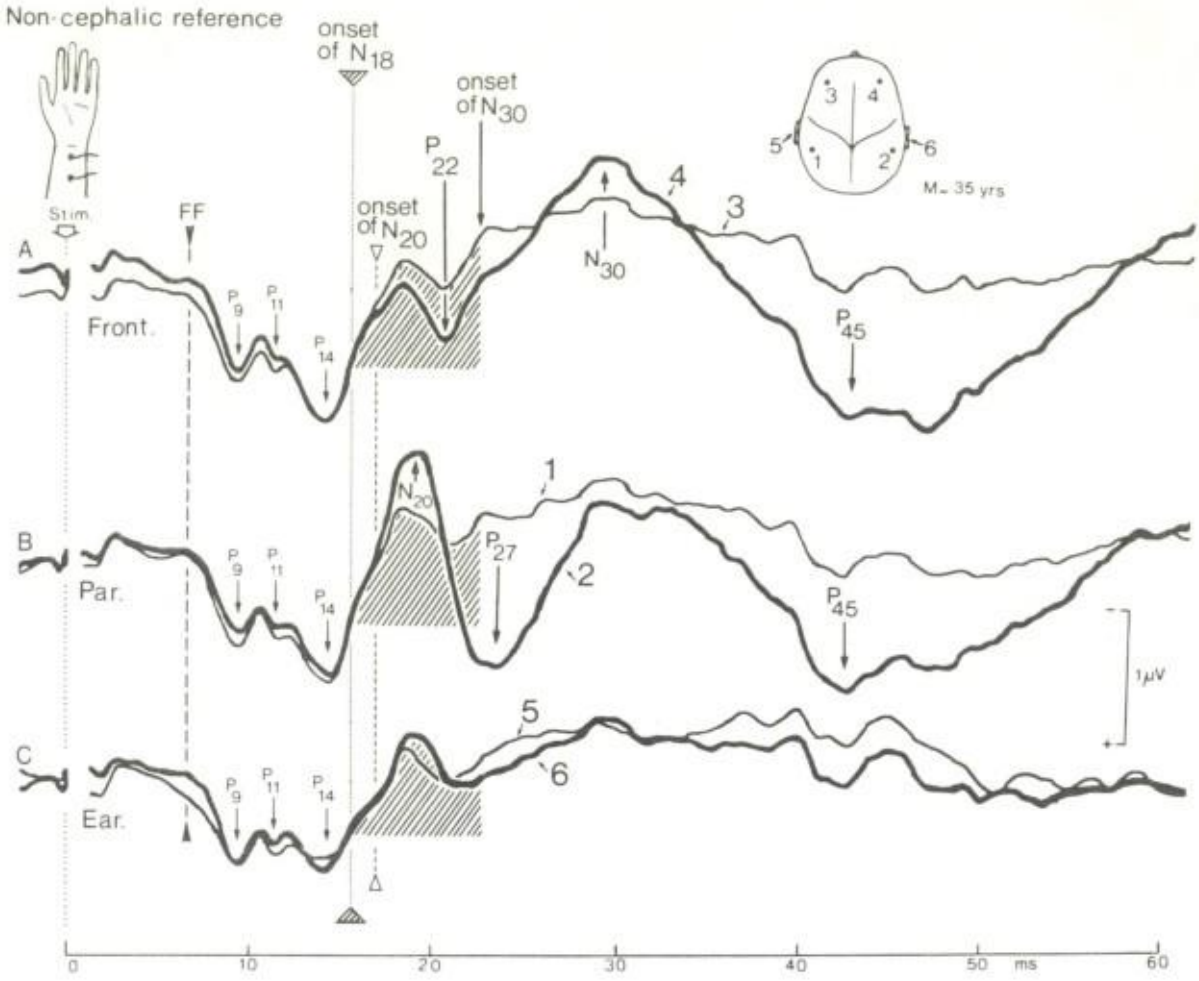

Fig. 3. Normal male subject of 35 years. Same presentation of non-cephalic reference recordings of SEP components at the frontal scalp (A), at the parietal scalp (B) and at the earlobes (C). The contralateral traces are presented with thicker line. The electric stimulus is delivered to the left median nerve at the wrist. The N18 component is indicated by hatching.

The next normal adult subject presented characteristic P9, P11 and P14 far fields followed by a clear inflection corresponding to the onset of the widespread N18 (Fig. 5). The amplitude of N18 was definitely smaller than in previous subjects at all sites compared. Moreover the prerolandic P22 was quite large contralaterally and present with a smaller size ipsilaterally (Fig. 5A). In fact the traces at the front were rather similar on both sides so that their subtraction resulted in very small deflexions (Fig. 6A) that underestimated the true size of P22 and N30. These were better displayed with earlobe reference recordings in which the P9 and N18 effects virtually canceled out (Fig. 6B). The onset of the parietal N20 and P27 was clear in all montages (Figs. 5B and 6C,D). The P45 was present at the contralateral parietal.

Fig. 7 illustrates a normal adult in whom the N18 was rather large while the prerolandic P22 was quite small. The frontal N30's were very large on both sides frontally, but not at the ipsilateral parietal electrode (Fig. 7C).

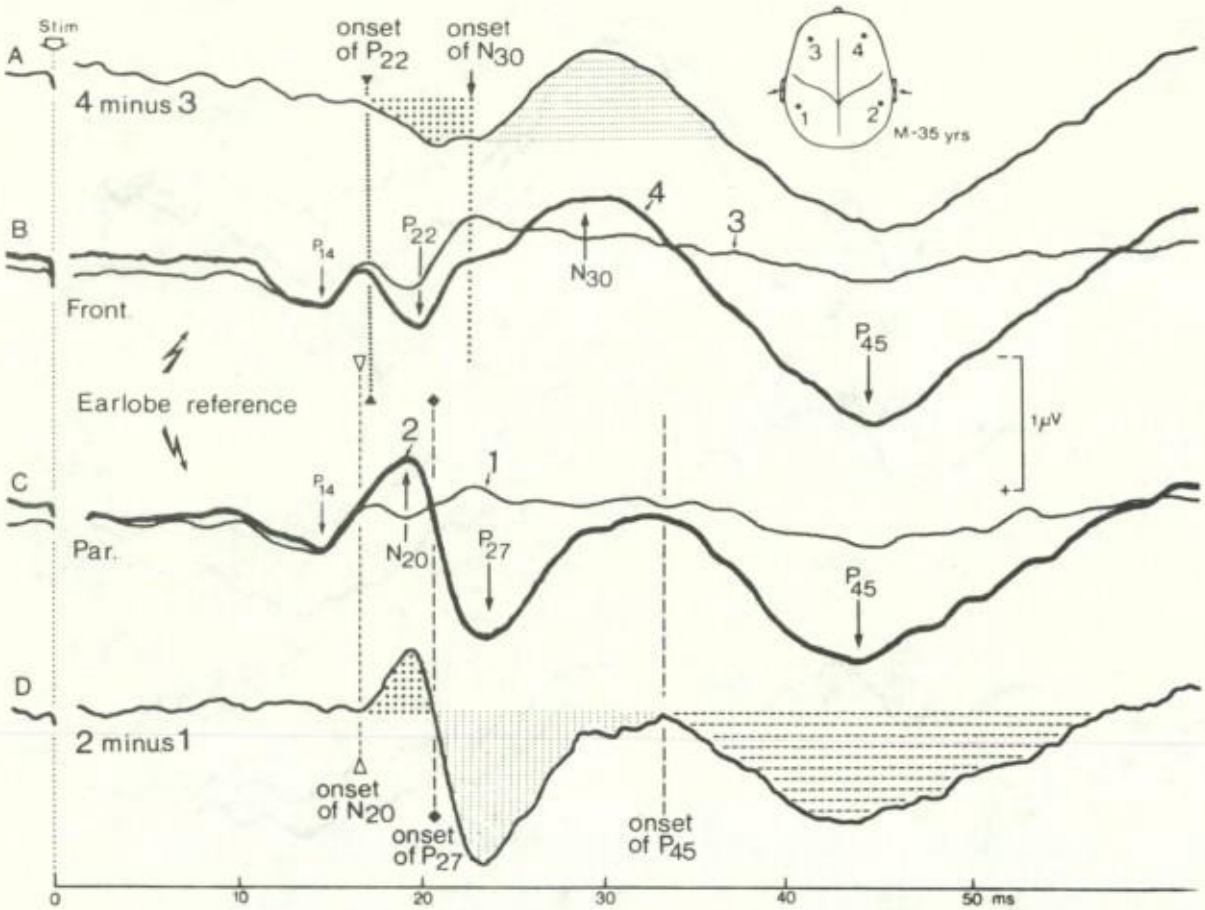

Fig. 4. Same subject as in Fig. 3. Earlobe reference recording (B,C) and subtraction of the ipsilateral from the contralateral SEPs (A,D) as indicated by the electrodes labels.

There was a steady negativity prolonging the N18. The onset of N20 was clearly indicated but its amplitude was small and it required good quality records to identify the N20 riding over the large N18 phenomenon (Fig. 7B). The subtraction displayed the N20 without ambiguity and also the P27 (Fig. 7D). If considered independently of the N18 and steady negativities identified in the ipsilateral trace, the contralateral trace would have been difficult to interpret correctly (Fig. 7B). In this subject subtraction of the frontal record yielded a spurious 'N14' (because the P14 far field was larger at the front, now used as a reference; see Desmedt and Cheron 1980a, Fig. 9) and larger N20 and P27 (because the front reference connected to grid 2 of the amplifier picked up the P22 and N30) (Fig. 7E). The posterior neck trace identified the spinal entry time from the onset of N11 (Fig. 7F) which coincided with the onset of the P11 scalp far field (cf., Desmedt and Cheron 1980a, 1981).

Fig. 8 illustrates another young adult with rather small N18 and a large P22 which appeared at the contralateral front only (A). The frontal N30 presented an earlier onset ipsilaterally, presumably because of the lack of competing P22 on that side in this experiment. The true onset of N30 was taken as

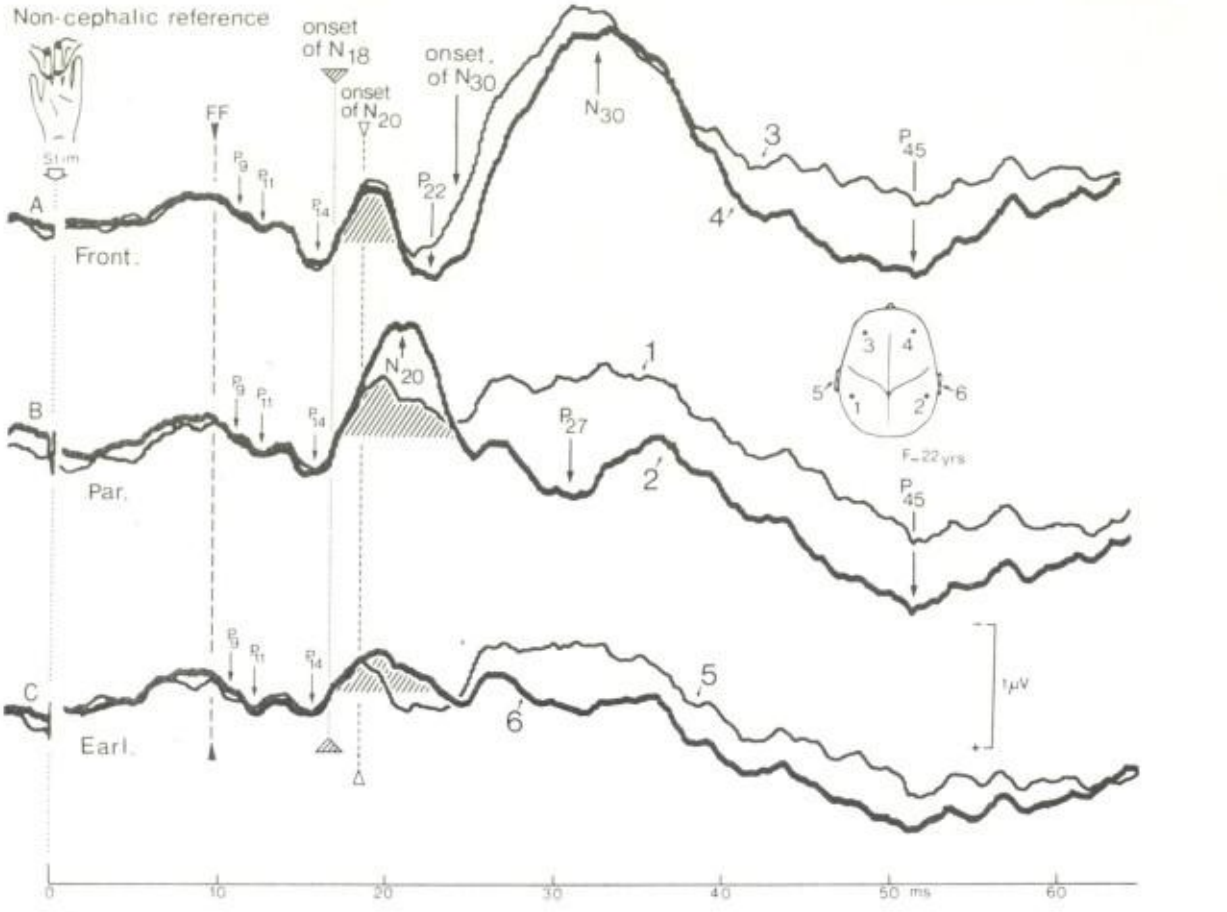

Fig. 5. Normal female subject of 22 years. Non-cephalic reference recordings of SEP components at frontal (A), parietal (B) and earlobe electrodes (C). Electrical stimulation of the left fingers II and III. The N18 is indicated by hatching.

indicated at the trough of P22 and onset of ipsilateral N30. The difference in onset latencies for N20 and P22 was rather important in this subject (Fig. 8C).

Comparison with healthy octogenarians

Fig. 9 presents similar data for a female subject of 85 years who was selected as discussed before (Desmedt and Cheron 1980b) for lack of any interfering disease state. With non-cephalic reference large far-field potentials were recorded (Fig. 9A,B) and the onset of the spinal N11 at the posterior neck (Fig. 9D) matched the onset of the scalp-recorded P11 far field. A feature of aging is the enhancement of the parietal SEP components N20, P27 and P45. The N18 was also present with the same profile and onset at the first upward inflection as in the young adults. The frontal negativity tended to be reduced in the older subjects.

The present study on a larger number of subjects replicated the data of the previous paper (Desmedt and Cheron 1980b) to document the significant increase of the N20, P22, P27 and P45 SEP components and the decrease of the frontal N30 component (Table I). It was interesting to enquire whether

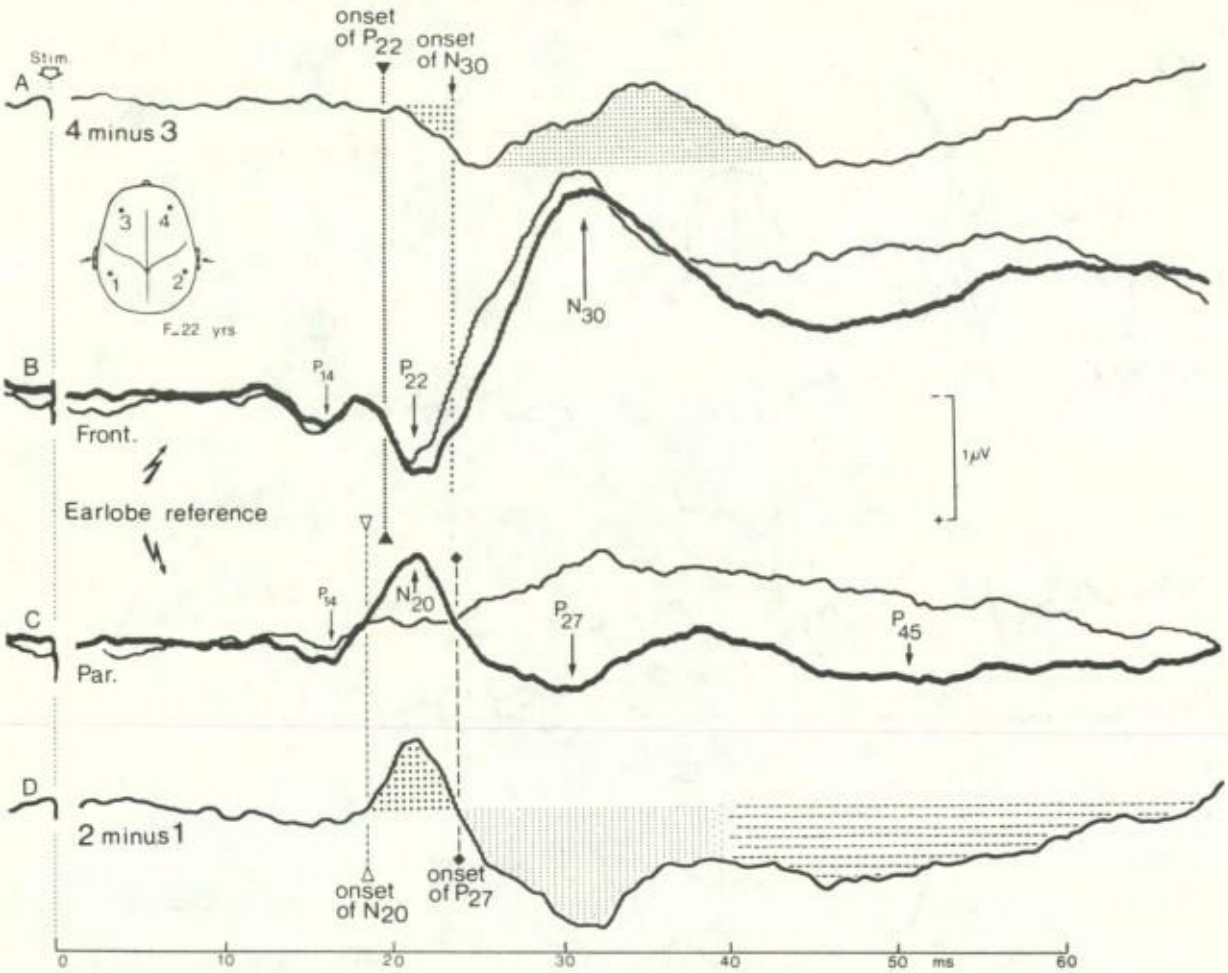

Fig. 6. Same subject as in Fig. 5. Earlobe reference recordings (B,C) and subtraction of ipsilateral from contralateral records (A,D).

the differences of SEP with aging were also present to the same extent when a non-cephalic reference electrode was used. When measured from baseline, the contralateral parietal negativity (which is shown in the present paper to include in fact the N18 and N20 components) was clearly larger in octogenarians (Table II). The difference was substantiated by the N20 measures obtained after subtraction of the ipsilateral parietal response. By contrast the amplitude of the widespread N18 was not significantly different between the young adults and the healthy octogenarians (Table II).

The transit times from onset of N20 to the onset of the other cortical SEP components were also re-measured with the notion that an N18 component was present underneath the N20, and a larger number of subjects considered. There is one new feature in these updated measures, namely that we considered now the P22 at the frontal electrodes about 60 mm in front of Cz in order to avoid the interference from the postcentral N20. The latter sometimes diffused to some extent towards the front (although with smaller am-

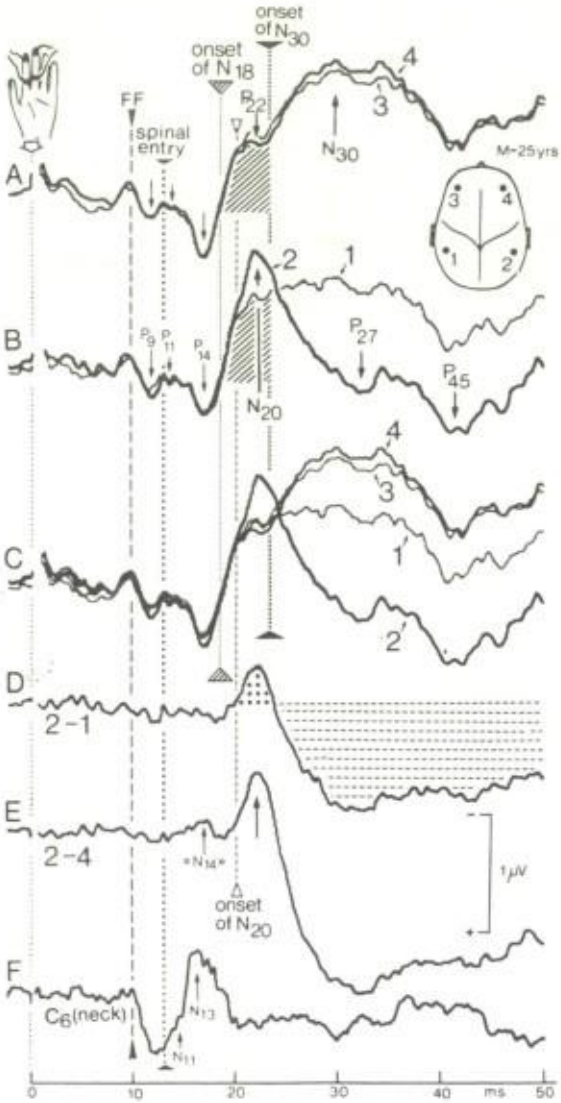

Fig. 7. Normal male subject of 25 years. Non-cephalic reference recordings of frontal (A) and parietal (B) electrodes. Electrical stimulation of left fingers II and III. C: superposition of the 4 traces displayed in A and B. D: subtraction of the ipsilateral parietal from the contralateral parietal record. E: subtraction of the contralateral frontal from the contralateral parietal record. F: posterior neck recording at C6.

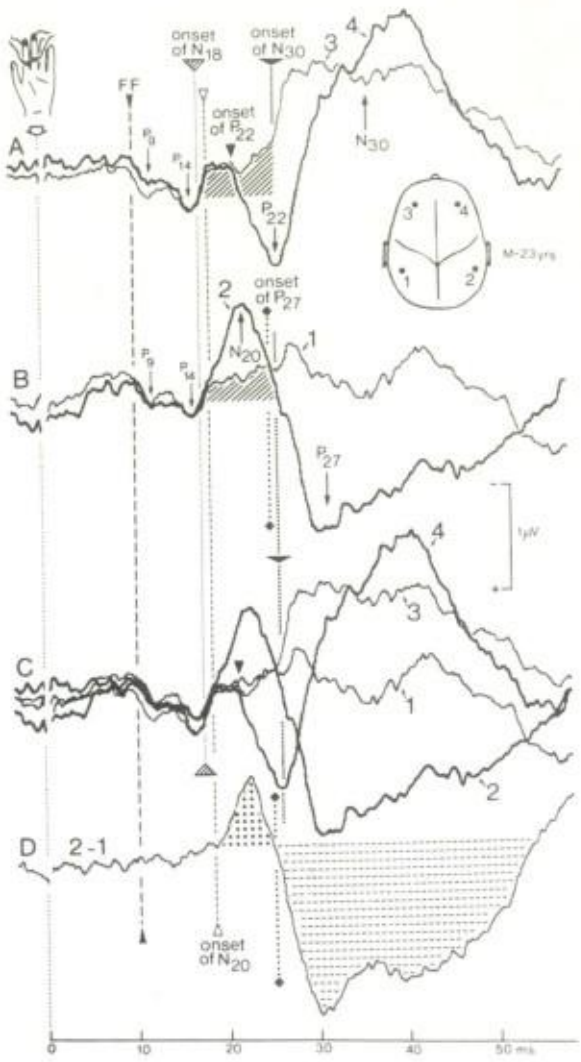

Fig. 8. Normal male subject of 23 years. Non-cephalic reference recording of SEP of frontal (A) and parietal (B) electrodes. Electrical stimulation of left fingers II and III. C: superposition of the 4 traces displayed in A and B. D: subtraction of the ipsilateral parietal from the contralateral parietal record.

plitude) and this effect was found to contribute to unduly delaying the apparent onset of the prerolandic P22. When measuring the P22 onset further in front, as we now recommend, a shorter transit time was found for this component, namely 0.62 ± 0.7 msec (instead of 2.5 ± 1.1 msec in Desmedt and Cheron 1980b, Table III) for the young adults and 0.95 ± 0.94 msec (instead of 3.4 ± 0.8 msec in the same paper) for the octogenarians. The increase in transit time from onset of N20 to

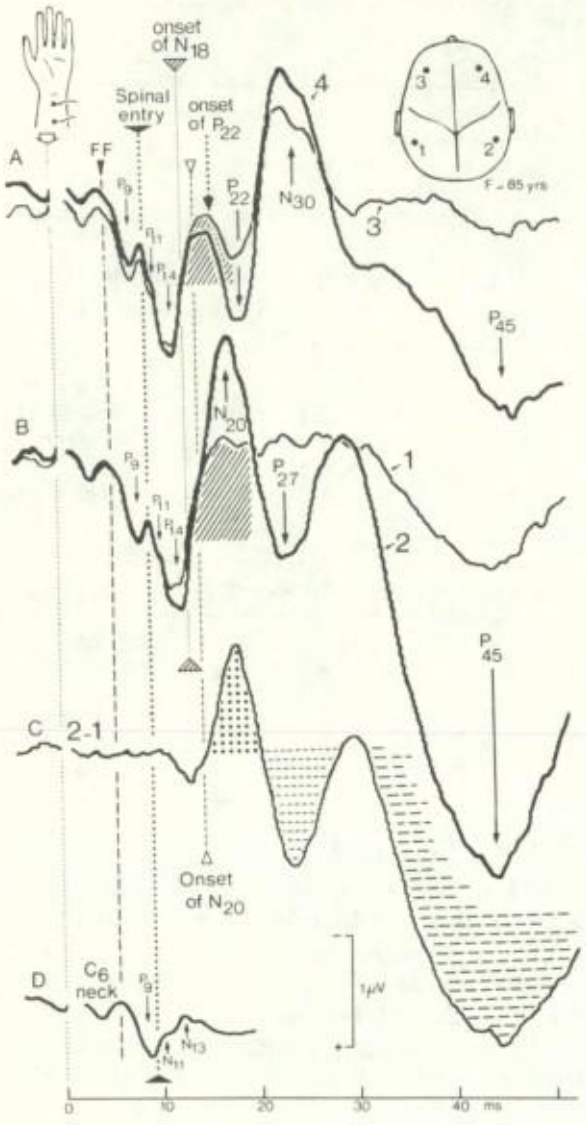

Fig. 9. Healthy octogenarians female of 85 years. Non-cephalic reference recording of SEP of frontal (A) and parietal (B) electrodes. Electrical stimulation of the left median nerve at wrist. C: subtraction of the ipsilateral parietal from the contralateral parietal record. D: posterior neck recording at C6.

onset of P22 remained significant at $P < 0.02$ (Table III). There is also a slight change in the mean transit time from onset of N20 to peak of P22, while the other measures are in good agreement with the previous study. The reasons for measuring P22 at more frontal electrodes will become clear from detailed SEP maps (in preparation).

Time features of N18 and early SEP components

With non-cephalic reference recording, the characteristic pattern of the positive scalp far-field potentials P9, P11, P13-P14 was recorded in 38% of the subjects (Figs. 3 and 10A,B). Intersubject variations affected mainly the P11 (absent in 32% of the subjects; Figs. 8 and 10D) or the P13 (absent or doubtful in 44%; Figs. 3, 10C and 11A). In some subjects the P13 was larger than P14 (Fig. 10D).

The duration of P14 up to the onset of N18 (Fig. 11A) had a mean value of 1.66 ± 0.58 msec and P14 tended to be somewhat shorter when it was preceded by a clear P13 (stippled area in Fig. 11D). The duration of P11 was 1.56 ± 0.77 msec (Fig. 11C). These durations of scalp far fields were significantly shorter at $P < 0.001$ than the duration of the spinal N13-P13 component (4.19 ± 0.64 msec; Fig. 11E) which was best measured in

TABLE I

Voltage of SEP components recorded with earlobe reference (μV).

Component	Young adults (n = 40)	Healthy octogenarians (n = 35)	Difference (%)	*t* test
N20	0.78 ± 0.4	1.30 ± 0.4	+67	$P < 0.001$
P27	1.41 ± 0.7	2.10 ± 1.0	+49	$P < 0.02$
P22	0.74 ± 0.4	1.27 ± 0.7	+71	$P < 0.02$
P45	1.61 ± 0.7	3.64 ± 1.2	+126	$P < 0.001$
N30	2.49 ± 0.9	1.54 ± 1.0	−38	$P < 0.02$

TABLE II

Voltage of early negative SEP components (μV).

Component	Reference	Young adults	Healthy octogenarians	Difference (%)	*t* test
Contralateral parietal (N18 + N20)	Non-cephalic	0.98 ± 0.2 (n = 17)	1.43 ± 0.4 (n = 9)	+46	$P < 0.001$
N18 Ipsilateral parietal	Non-cephalic	0.58 ± 0.2 (n = 17)	0.61 ± 0.3 (n = 9)	+5	$P > 0.2$
N20 Contralateral parietal	Ipsilateral parietal	0.54 ± 0.1 (n = 17)	0.92 ± 0.3 (n = 9)	+70	$P < 0.001$
N20 Contralateral parietal	Earlobe	0.78 ± 0.4 (n = 40)	1.30 ± 0.4 (n = 35)	+67	$P < 0.001$

TABLE III

Transit times from the onset of N20 to various components (msec) (mean ± S.D.).

	Young adults (n = 40)	Healthy octogenarians (n = 35)	Difference (%)	*t* test
Onset of P22	0.62 ± 0.7	0.95 ± 0.94	+53	$P > 0.1$
Peak of P22	4.3 ± 1.4	6.0 ± 1.4	+39	$P < 0.02$
Peak of P27	8.0 ± 2.9	10.0 ± 3.0	+25	$P > 0.1$
Onset of N30	4.9 ± 1.0	7.3 ± 1.2	+49	$P < 0.001$
Peak of N30	11.0 ± 2.7	15.1 ± 6.1	+37	$P < 0.02$
Peak of P45	24.2 ± 2.6	29.5 ± 3.8	+22	$P < 0.01$

TABLE IV

Mean transit times from spinal entry estimated as onset of neck N11 or scalp P11 (mean ± S.D. in (msec).

To onset of P13-P14 scalp far fields	1.75 ± 0.30
To peak of P14 scalp far field	3.71 ± 0.55
To onset of scalp N18	4.74 ± 0.27
To onset of parietal N20	6.4 ± 0.45
To onset of prerolandic P22	7.02 ± 0.51
Mean interval from onset of P13-P14 far fields to peak of P14	1.96 ± 0.27
Mean interval from peak of P14 far field to onset of scalp N18	1.03 ± 0.27

prevertebral (oesophageal) recordings and which was recently shown to be related to a fixed generator in the dorsal horn (Desmedt and Cheron 1981, 1982).

Table IV provides a replication and update based on 40 normal adults for the transit times along the central somatosensory pathway (cf., Desmedt and Cheron 1980a,b, 1981). Evidence suggests that the afferent volley arrives at the thalamus at a mean of about 3.71 ± 0.58 msec after spinal entry, thus at about the peak of the P14 scalp far field. The onset of the widespread N18 is only 1.03 ± 0.31 msec thereafter, while the onset of the parietal N20 is 2.69 ± 0.42 msec thereafter (Table IV).

Discussion

This paper replicates and extends several points recently made about the functional organization of the somatosensory system in man and its changes with normal aging (Desmedt and Cheron 1980a,b, 1981). It emphasizes the sharp and consistent differences recorded in front or behind the central sulcus contralateral to the hand stimulated (Desmedt and Cheron 1980b; Papakostopoulos and

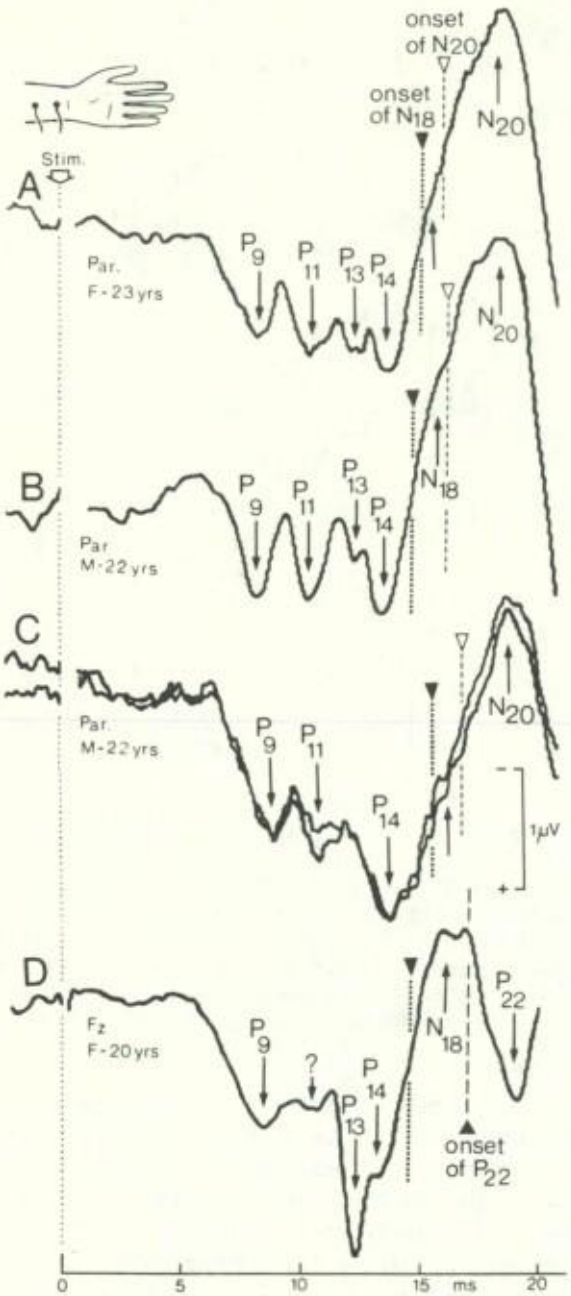

Fig. 10. Examples of different patterns of positive scalp far-field potentials recorded with a non-cephalic reference in normal young adults. Electrical stimulation of the left median nerve at wrist. The active electrode is placed at the contralateral parietal scalp (A,B,C,) and at midfront Fz (D). The onset of the N18 is indicated in all traces, as well as the onset of N20 (A—C) or P22 (D). A: female of 23 years. B: male of 22 years. C: male of 22 years. D: female of 20 years.

Crow 1980). In addition, the use of non-cephalic reference recording helped resolve current issues about the early SEP negativities through the demonstration that an N18 phenomenon with widespread scalp distribution must be distinguished from the cortical N20 SEP component which is restricted to the contralateral parietal region.

SEP components disclose a number of consistent features varying within a reasonably restricted range (Tables I—III), but they also present intriguing intersubject variabilities that have confused a number of questions and that have certainly not been given adequate consideration, at least in published reports. We think that both the intersubject variabilities and the changes associated with normal aging offer considerable opportunities for a more realistic evaluation of the genuine SEP components (Desmedt and Cheron 1980b). Clinical applications of SEPs are to be upgraded through such detailed information in order to better identify the characteristic changes associated with specific disease conditions.

Subcortical SEP components

With non-cephalic reference recording, all scalp and neck electrodes record first a positive P9 far-field potential that is related to action potential volley of peripheral nerve fibres near the entrance into the brachial plexus. The spinal N11 recorded at the posterior neck is related to the ascending volley in dorsal column and its onset, coinciding with that of the scalp-recorded P11 far field (Figs. 7 and 9), corresponds to the arrival of the peripheral nerve volley at the spinal cord C6-C7 segments (Desmedt and Cheron 1980a, 1981). N11 is eliminated as well as the subsequent SEP components by spinal root avulsion in brachial plexus lesions (Anziska and Cracco 1980). The onset of the P13-P14 scalp far-field potential is thought to correspond to the

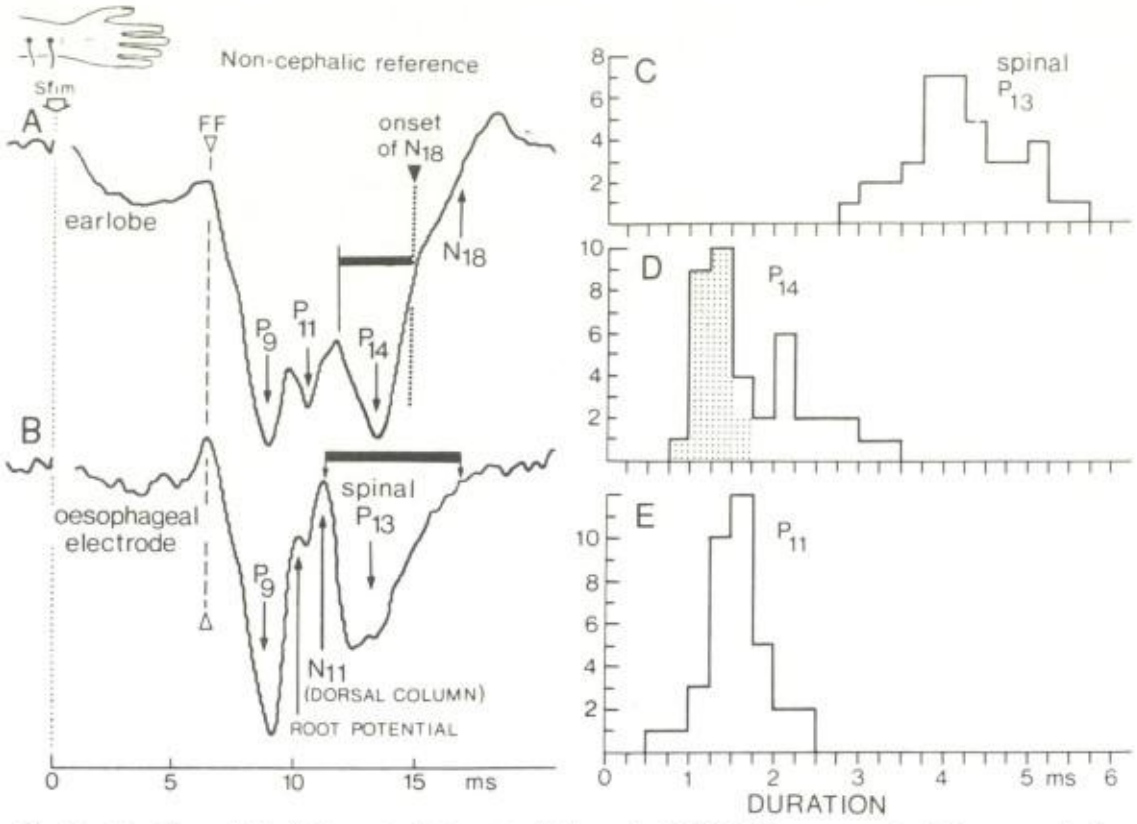

Fig. 11. Duration of far-field potentials and of the spinal P13-N13 component. A,B: non-cephalic reference recordings of SEP to median nerve stimulation in a young adult subject. A: earlobe derivation showing far fields P9, P11 and P14 (no P13 can be clearly identified in this experiment). The duration of P14 is taken from its onset to the onset of the N18 component. B: prevertebral (oesophageal) recording from the level of C5 showing after the P9 nerve far field a spinal root action potential, then a small negativity N11 from the dorsal column, and the P13 wave whose duration is indicated. The graphs C to E present pooled data in different adult subjects for the duration of the spinal P13 (C), of the scalp or earlobe recorded P14 (dotted area corresponds to P14 when preceded by clear P13 while the white area corresponds to P14 when P13 is apparently lacking) (D), and of the scalp P11 (E).

activation of the ascending volley in the medial lemniscus since its timing at a mean of 1.75 ± 0.30 msec after spinal entry (Table IV) corresponds fairly well with the dorsal column conduction time (70 mm at 58.5 m/sec, that is 1.2 msec) plus a synaptic delay of 0.3—0.5 msec for the synapses between dorsal column axons and cuneate neurones (Desmedt and Cheron 1980a).

Since the larger axons in the medial lemniscus have a diameter of 8—9 μm, this corresponds to a conduction velocity of about 36 m/sec if the conversion factor of 4.5 m/sec/μm applies (see Discussion in Desmedt and Cheron 1980a). With a conduction distance of about 70 mm in medial lemniscal axons, the conduction time can be calculated as 70 : 36 = 1.94 msec. Such data would be rough estimates which we consider valid ±10—20%. In any case this value is remarkably close to the mean time from onset of the scalp far-field P13-P14 up to the peak of the P14 (Table IV). Therefore we interpret the P13-P14 far field (which is not recorded below foramen magnum) as a volume-conducted potential related to the summation of the travelling activity in medial lemniscus: the far-field onset corresponds to the activation of the caudal

lemniscal fibres while its peak at P14 reflects the arrival of the fastest lemniscal action potentials at the thalamus. These data show internal consistency and they exclude the possibility that P14 could be generated at or above the thalamus (Desmedt and Cheron 1980a). This interpretation is actually supported by clinical evidence that the P14 far field is preserved in patients with a thalamic vascular lesion that eliminates all subsequent SEP activity (Nakanishi et al. 1978; Mauguière and Courjon 1981).

We can now consider the transit time from the arrival at the thalamus to the onset of the N18 which has a mean value of 1.03 ± 0.31 msec (Table IV). Since a synaptic delay of no less than 0.3 msec must be allowed for in thalamus between the lemniscal axons and the ventrobasal neurones, this would only leave about 0.74 msec for conduction along the nerve fibres that elicit the N18. This rules out N18 being generated at the cortex for the thalamocortical conduction distance is about 60 mm and, with only 0.74 msec available, the conduction velocity would have the unreasonably high value of 81 m/sec. Another argument for denying a cortical origin to N18 is its widespread occurrence all over the scalp: this seems to preclude any specific regional or areal generator that would be consistent with the known anatomy of somatosensory connections (Jones and Powell 1969; Jones 1981).

This N18 probably reflects subcortical activities such as delayed potentials in the thalamus itself, or action potentials in the lower part of the thalamocortical axons. The observation that N18 presents a sizeable amplitude on the ipsilateral scalp also invites questions since the thalamocortical radiation potentials are elicited only from the hemithalamus contralateral to the side stimulated (Albe-Fessard et al. 1963; Ohye et al. 1972). Another intriguing point is the negative sign of N18 since all other far-field potentials present a positive deflexion, as indeed to be expected for volume conduction beyond the structure generating the nerve volley (Lorente de Nó 1947; Arezzo et al. 1981).

The disclosure of widespread N18 negativity appears to resolve at least in part the issue raised by Kritchevsky and Wiederholt (1978) who studied SEP with non-cephalic reference recording and found that there is no clear difference between the parietal derivations on the two sides of the head. We propose that, at the ipsilateral electrodes, a sizeable N18 is recorded with non-cephalic reference that must be distinguished from the contralateral N18 + N20. Measurements presented in Table II clarify this problem, as do also the figures illustrating the intersubject variations of these negativities. In all cases it was obvious that a surplus negativity (N20) was present at the contralateral parietal cortex. In view of its restricted location behind the central sulcus, this N20 must represent the earlier ('primary') cortical response in the projection areas 3–1–2 of somatosensory cortex (cf., Desmedt and Cheron 1980a,b). N20 is large and of longer duration in normal newborn babies (Desmedt and Manil 1970) and it shows a remarkable increase (not present for N18) during normal aging (Table II). N20 can also be recorded with a high amplitude of several microvolts by electrodes placed directly on the postcentral gyrus (Domino et al. 1965; Papakostopoulos and Crow 1980).

The present data also replicate and emphasize that the ipsilateral parietal cortex does not generate a specific early response similar to N20, in addition to the widespread N18. The lack of ipsilateral early SEP components for stimulation of distal upper limb was documented by Desmedt and Robertson (1977) and confirmed since (Desmedt and Cheron 1980a,b). This has probably to do with the lack of callosal connections for the primary receiving areas representing the distal limb (Jones and Powell 1969; Pandya and Vignolo 1969; Karol and Pandya 1971).

The cortical SEP component P22 described by Cheron and Desmedt (1980b) has been further delineated in the present data. Due to blurring of contours of regional potentials,

the postcentral N20 contributes to some delay in the recorded onset of the prerolandic P22 when the latter is recorded at about the level of Cz. This interference of potential fields is no longer present at more frontal positions (60 mm in front of Cz) that were used here (cf., Cheron and Desmedt in preparation). It was thus possible to re-estimate the transit times and amplitude for P22 in a larger series of subjects (Tables I and II). We find that there is a rather short interval between the onset of N20 and P22, namely 0.62 msec. This finding supports the view that P22 is related to a separate generator (Papakostopoulos and Crow 1980; Desmedt and Cheron 1980b, 1982) and cannot be reduced to a simple mirror image (phase reversal) of N20. While there are important cortico-cortical connections from parietal areas 2 and 5 to precentral areas 4 and 6 (Jones and Powell 1969; Jones et al. 1978; Jones 1981), it now appears that P22 must be generated by separate thalamocortical connections because the interval between onset of N20 and P22 is rather short. Decisive evidence for this view comes from recent results of Mauguière et al. (1982) showing that the prerolandic P22 and N30 components persist in patients with a parietal lesion that eliminates the N20-P27-P45 components.

The present study also confirms that SEP components are generally larger and better delineated in the healthy old subjects than in the young adults. For example a clear 'W' pattern with clear P27 and P45 components after the N20 at the contralateral parietal cortex was recorded in 47% of the young adults, but in 83% of the octogenarians.

Summary

Prerolandic and parietal SEPs to electrical stimulation of fingers or median nerve were studied with non-cephalic reference in 40 normal young adults and in 35 healthy octogenarians. Limb temperatures were 36—37°C. Intersubject variations of SEP components were analysed. A new widespread component N18 was identified and shown to be generated below the cortex. This N18 is about the only early component recorded at the parietal ipsilateral region after the positive far-field potentials P9, P11 and P13-P14. Transit times along the central somatosensory pathway were replicated and discussed as well as other evidence about the sequential activation of the various neural structures involved. The N20 potential representing the earliest cortical response is recorded from the contralateral parietal region, but is absent ipsilaterally. The prerolandic potential is related to distinct generators and is elicited by a separate thalamocortical pathway rather than by cortico-cortical connections from areas 2 and 5 in parietal cortex. The changes associated with normal aging have been confirmed and extended.

Résumé

Enregistrement avec référence non-céphalique des potentiels somesthésiques précoces déclenchés par la stimulation des doigts chez l'adulte ou le sujet âgé normal: différenciation de la composante diffuse N18 et de la composante contralatérale N20 des composantes prérolandiques P22 and N30

Les potentiels évoqués somesthésiques (PES) frontaux et pariétaux à la stimulation des doigts ou du nerf médian ont été étudiés avec l'utilisation d'une référence non-céphalique chez 40 sujets adultes normaux et chez 35 octogénaires en bonne santé. La température du membre stimulé était de 36 à 38°C. Les variations interindividuelles des composantes PES ont été analysées. Une nouvelle composante diffuse N18 a été identifiée (origine sous-corticale) et différenciée du N20 contralatéral. Aucune composante précoce à part le N18 n'a été observée ipsilatéralement après les potentiels de champ éloigné P9, P11 et P13-P14. Les temps de transit le long de la

voie somesthésique ont été confirmés et discutés sur un plus grand nombre de sujets. Les composantes prérolandiques ont été mises en relation avec des générateurs corticaux distincts qui sont activés par une voie thalamocorticale séparée. Les modifications des PES liées au vieillissement normal ont été confirmées et étendues.

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