ACTA NEUROBIOLOGIAE EXPERIMENTALIS

Acta Neurobiol. Exp. 1998, 58: 55-64

The effect of tonic pain on processing the non-painful stimuli indexed by late components of event-related potentials

Andrzej Michalski

Department of Neurophysiology, Nencki Institute of Experimental Biology, 3 Pasteur St., 02-093 Warsaw, Poland, Email: michan@nencki.gov.pl

Abstract. Event-related potentials (ERPs) evoked by light flashes and auditory tones in a standard odd-ball procedure were recorded from Fz, Cz and Pz scalp sites. Tonic pain was evoked by immersion of the hand in cold water (5°C). Significant effects of pain were found in responses to target stimuli but not in responses to non-target stimuli. P300 wave was affected more than the earlier P200 component. The reduction of P300 amplitude was the strongest effect, both in auditory and visual tests. P300 latency was not significantly affected. Difference curves (target minus non-target ERPs) showed the additional effects: latency of P200 component was elongated and its amplitude enlarged but only in auditory experiments. In control experiments with warm water stimulation no significant alterations of P300 or P200 components were found. The results show that the effect of tonic pain is specific: it predominantly affects the processes that manifest themselves as amplitude changes of P300 components in responses to target stimuli.

Key words: human ERP, P300, P200, cold stimulus

INTRODUCTION

A physiological index of pain has been sought for a long time. Among the investigators that focused their attention on event-related potentials two basic strategies prevailed:

1. In the majority of experiments somatosensory potentials were evoked directly by painful stimuli. Many papers reported good correlation between late potential amplitudes and the painfulness of the sensation. (Chudler and Dong 1983, Dowman and Rosenfeld 1985, Bromm and Treede 1987, Handwerker and Kobal 1993). It was found, however, that these components depended also on factors such as the subject's attention, stress situation, stimulus expectancy or emotional aspects of pain (Chapman et al. 1981, Zaslansky et al. 1996).

2. The effect of tonic pain on processing neutral, non-painful stimuli was studied. This approach directly addressed the problems of every-day life of patients suffering from chronic pain but relatively few studies followed this strategy. Rosenfeld and Kim (1991) reported the decreased amplitude and no effect on latency of P300 wave during pain generated by fingernail pressure. In subsequent experiments with an ischemia cuff as a pain-generating device Rosenfeld and co-authors (1993) found both the reduction of P300 amplitude and the elongation of its latency. More experiments were done on patients suffering from chronic pain but the results were highly inconsistent. Mazzotta and co-authors (1995) found the increased latency and increased amplitude of P300 wave during headache attacks in patients with migraines. Tandon and Kumar (1993) found the increased latency but no alterations in P300 amplitude in patients suffering from chronic pain.

The aim of the present experiment was:

1. to provide data for the comparison of different models of tonic pain that could help to resolve the existing discrepancies,
2. to compare the effects of tonic pain on potentials evoked by non-painful stimuli of different modalities,
3. to analyze the effects of pain on target and non-target responses,
4. to compare the effects of pain on P300 component and the preceding waves.

The immersion of the hand in cold water was chosen as a model of tonic pain. It has been shown that cold stimulus produced a number of responses typical for pain rather than for the sensation of cold. During immersion a diffuse, aching pain is usually perceived. Since both low and high threshold cold receptors can produce only transient responses to cold stimulus (Darian-Smith et al. 1973, Duclaux et al. 1980) it was suggested that the response was secondary to the activation of C nociceptors rather than cold receptors (Wolf and Hardy 1941). This conclusion was supported by the fact that the pattern of changes in blood pressure, pulse volume and rate, cardiac output and total peripheral resistance recorded in response to cold stimulus was very similar to that recorded in response to pain (Lovallo 1975, Musante et al. 1994, Turner et al. 1994).

METHODS

Subjects

Sixteen volunteers of both sexes (7 males and 9 females), aged 27-43 years participated in the experiment. Informed consent was obtained from all participants. Participants were also informed that they should feel free to terminate the sessions at any time. Before the experiment each participant was asked to evaluate his/her level of anxiety and mood state on a ten point scale.

Recording and stimulation

Three 10 mm disc electrodes were glued on the scalp at the Fz, Cz and Pz positions, according to the 10-20 system, with the linked mastoids as a reference. Electrode impedance did not exceed 5 kΩ. Vertical EOG was recorded from an electrode above and below the right eye. Horizontal EOG was recorded from the outer canthi. Signals were amplified, digitized and stored with Elmiko Paperless EEG system. All channels were sampled with 2048 Hz frequency, 12 bit resolution, digitally filtered 0.16-30 Hz, reduced to 256 Hz by averaging the adjacent points and stored in epochs containing 250 ms of recording before stimulus presentation and 1 s after the stimulus onset. The epoch was rejected and replaced with a new one if EOG amplitude exceeded 40 μV. The number of rejected epochs never exceeded 3%.

Tones of 1,000 Hz and 2,000 Hz (80 db, 100 ms duration) were used as auditory stimuli. Flashes of spatially overlapped arrays of red and yellow LED diodes (2 deg x 2 deg of the visual angle, 10 cd/m^2 luminosity on 1 cd/m^2 background, 100 ms duration) were used as visual stimuli. Two stimuli of the same modality were presented in random order. The subjects were asked to mentally count one of them (target stimulus) and report

the number at the end of the recording (standard "odd-ball" procedure). If the error in counting was bigger than an arbitrarily set threshold of 20%, it was assumed that subject attention was poor and the data were rejected. Three percent of the recordings were rejected.

Four pairs of stimuli were tested in separate experiments: each tone was tested as a target combined with the other tone as a non-target and each color of LED was tested as a target with the other color as a non-target. Stimuli were presented at intervals of 1,250 ms. Probability of occurrence of target stimulus was 0.12. The minimal number of target stimulus presentations was 30.

Procedure

All subject participated in "cold water" sessions, during which they were asked to immerse one hand, up to the wrist, in a water of 5°C. In 9 subjects all four combinations of visual and auditory stimuli were tested. Seven experiments were terminated earlier, due to subject fatigue. In two subjects three combinations and in five subjects two combinations of stimuli were tested (visual tests only). The order of the recordings was randomized, but each stimulus combination was always preceded or followed by a control test, recorded with the same visual or auditory stimuli but without the cold water stimulation.

Nine subjects participated also in control "warm water" sessions held on different days at the same time, starting at 11 a.m. In these sessions an identical procedure was repeated but with water kept at 30°C. Recordings were also accompanied by control tests, performed without the warm water stimulation. The selection of cold and warm water temperatures was based on the ratings of pain and neutral-pleasant warmth sensations obtained in preliminary tests. Only one stimulus combination was used in experiments with warm water: yellow light was a target and red light was a non-target stimulus. This stimulus combination produced the biggest effect in cold water tests.

Data analysis

Epochs of EEG were averaged, stored and printed. Difference waveforms were computed for each pair of target and non-target ERPs. P200 and P300 waves were identified as components sensitive to cold water stimulation. Amplitudes and latencies of these components were measured using cursors on the computer screen and transferred to SYSTAT program for statistical analysis (ANOVA).

For each pair of stimuli the grand-averaged target, non-target and difference waveforms were computed. Corresponding points of grand-averaged curves recorded with and without painful stimulation were expanded into a sets of paired data (points of individual difference curves) and compared with Student *t*-test. Points were selected every 24 ms within the range between 102 ms and 582 ms after the stimulus onset. Twenty one points were analyzed in each pair of grand-averaged difference curves. The analysis of corresponding points did not duplicate the results of ANOVA. In the process of grand-averaging, points of the same latency were added together, whereas amplitudes measured for ANOVA were "latency corrected" ,i.e., the highest value within the specified region was selected irrespective of its latency.

RESULTS

Only the data from experiments when level of anxiety and mood state measured on ten point scale varied between 4 and 6 were included into the analysis.

Cold water stimulation did not produce a significant difference in the number of errors in counting the target stimuli. Mean error was 1.7 counts in cold water experiments and 1.5 in control tests.

Figure 1 shows the grand-averaged potentials recorded with Pz electrode. This electrode recorded the biggest P300 waves. Potentials were evoked by target stimuli in visual and auditory experiments. Visual ERPs were grand-averaged over 16 subjects and auditory ERPs were grand-averaged over 11 subjects. Besides the early components, all the waveforms clearly show two long latency peaks:

1. the P300 peak, identified for further analysis as the most positive value between 290 ms and 400 ms after the stimulus onset,

2. the P200 peak, identified as the most positive value between 150 ms and 290 ms after the stimulus onset.

Dotted lines in Fig. 1 show the ERPs obtained in control recordings and solid lines show the effect of the immersion of the hand in cold water. In both auditory and visual experiments, for all combinations of stimuli, the amplitudes of P300 components were clearly reduced during cold water stimulation. There was a clear difference between the effects of cold water stimulation on P200 and P300 waves: the amplitude of P200 component

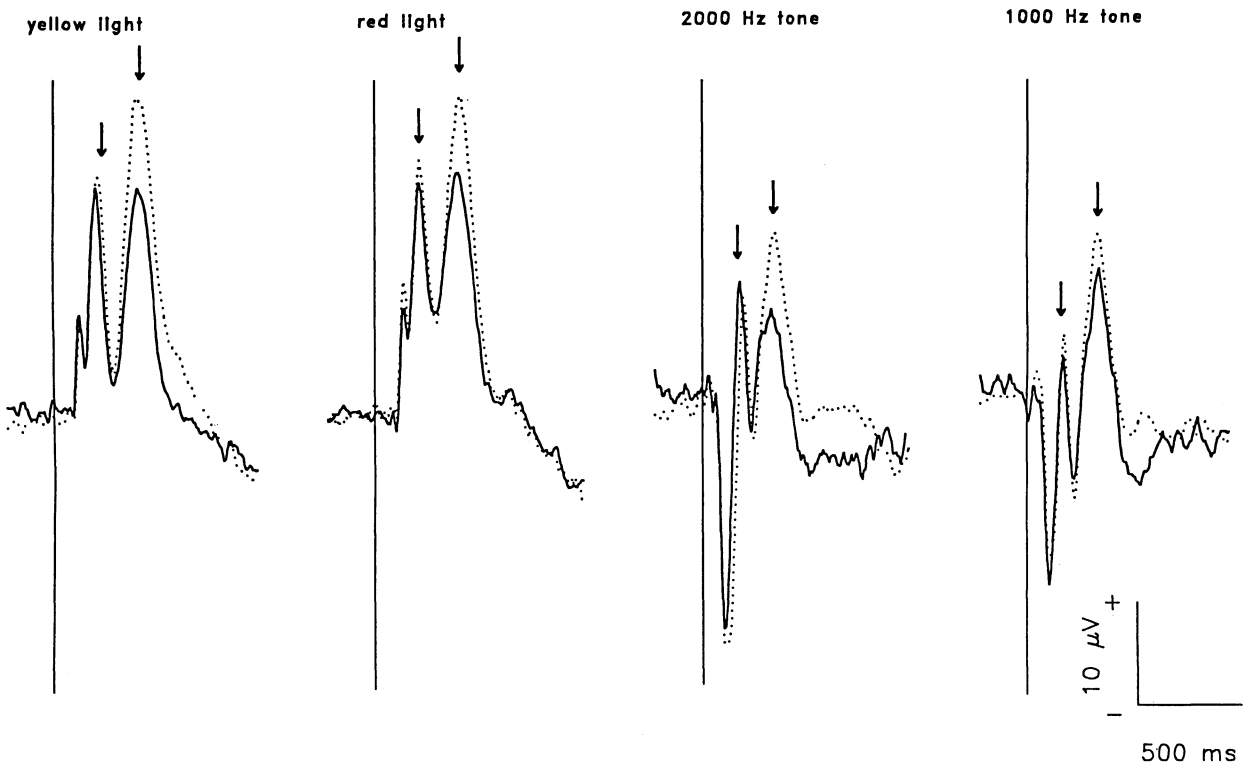

Fig.1. Grand-averaged ERPs evoked by target stimuli. Potentials were recorded with Pz electrode. Target stimuli are given above each graph. Solid lines show the ERPs recorded when one hand of the subject was immersed in cold water. Dotted lines show the control ERPs recorded in the absence of cold water stimulation. Arrows indicate P200 and P300 peaks.

was much less affected. The identical effects were seen in Fz and Cz recordings.

Amplitudes of P300 and P200 components, recorded with all three electrodes, were measured relative to 250 ms pre-stimulus baseline and analyzed with a three way ANOVA ("pain" x "electrode" x "stimulus modality"). Identical analysis was used for latencies of both peaks.

The effect of cold water stimulation on P300 amplitude in target ERPs was highly significant ($F = 17.131$, $P<0.001$). In contrast, the alterations of P200 amplitudes were insignificant. Both components were significantly higher in visual than in auditory experiments ($F = 32.497$, $P<0.001$ for P300 and $F = 91.773$, $P<0.001$ for P200).

The effects of cold water stimulation on P300 and P200 latencies in target ERPs were insignificant. Both latencies were shorter in auditory than in visual experiments ($F = 179.291$, $P<0.001$ for P300 and $F = 249.637$, $P<0.001$ for P200).

Figure 2 shows the grand-averaged Pz potentials evoked in the same experiments, by non-target stimuli. Figure conventions are the same as in Fig.1. The most clear difference between ERPs shown in Figs. 1 and 2 is the absence of P300 components in the latter. P200 components, on the other hand, are still relatively big. It is also apparent from Fig. 2 that cold water stimulation practically did not alter the ERPs evoked by non-target stimuli. The only components that could be attenuated were the small remainders of P300 waves recorded in the experiment with yellow light as a non-target stimulus. Again the results obtained with Fz and Cz electrodes were the same.

Since P300 waves could not be reliably identified in the majority of ERPs evoked by non-target stimuli, statistical analysis was limited to P200 component. A three way ANOVA ("pain" x "electrode" x "stimulus modality") showed that cold water stimulation did not produce significant changes either in amplitudes or in latencies of this component. As in the responses to target stimuli, the P200 amplitudes were higher in visual than in auditory experiments ($F = 22.313$, $P<0.001$).

The P300 waves were recorded almost exclusively in responses to target stimuli but P200 components were present in both target and non-target ERPs, possibly with

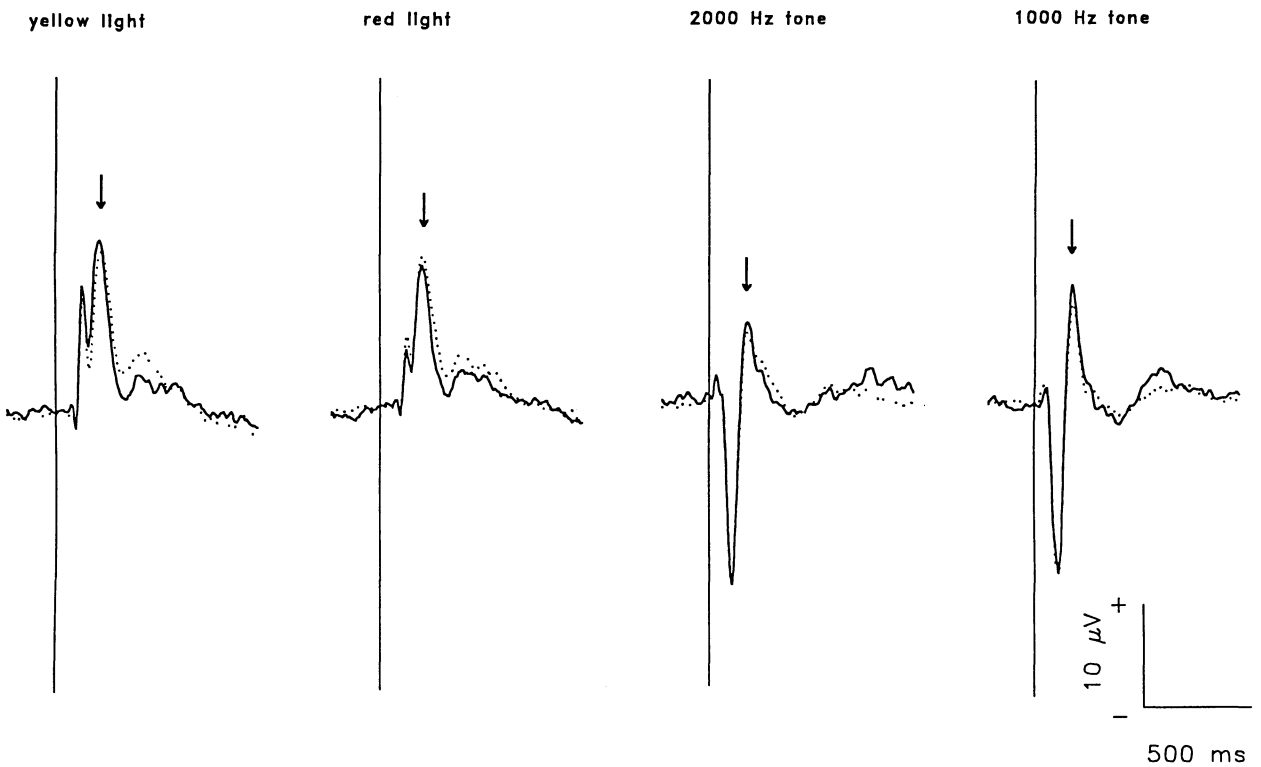

Fig. 2. Grand-averaged ERPs evoked by non-target stimuli. Figure conventions are the same as in Fig. 1. Since P300 component was not visible on these recordings, arrows show only P200 waves.

different parameters. To isolate the components specific for target stimulus responses, the difference curves were computed by subtracting non-target ERPs from target ERPs. These curves were chosen for a more detailed analysis of the effects of pain. Figure 3 shows the difference curves computed from Pz recordings. It is apparent that P200 components are preserved in these curves indicating that, in spite of their presence in non-target recordings, they have the attributes of endogenous components. On the other hand, P300 components clearly dominate all difference curves. The effect of cold water stimulation is also much stronger within the P300 region than anywhere else.

Amplitudes and latencies measured in difference curves computed from ERPs recorded with all three electrodes were analyzed with three way ANOVA ("pain" x "electrode" x "stimulus modality"). The effect of pain on P300 amplitude was highly significant (F = 40.9, P<0.001). Post-hoc hypothesis tests showed that the reduction of P300 amplitude was significant in both visual and auditory experiments (F = 27.6, P<0.001 for visual and F = 15.7, P<0.001 for auditory tests). As in the analysis of target responses P300 amplitudes recorded with visual stimulation were significantly higher than those recorded with auditory stimulation (F = 65, P<0.001). Latencies of visually evoked P300 waves were significantly longer than those recorded in auditory experiments (F = 42.320, P<0.001).

Table I shows the mean amplitudes and latencies of P300 components measured in difference curves in visual and auditory experiments. Since the latency differences between electrodes were below the estimated accuracy of peak detection in broad P300 waves, Table I shows only the mean latencies for all electrodes.

Surprisingly, the ANOVA indicated that P200 amplitudes measured in difference curves significantly increased during cold water stimulation (F = 12.046, P<0.001). The interaction between the effect of pain and stimulus modality was significant (F = 16.5, P<0.001). Post-hoc hypothesis tests showed that the increase of P200 amplitude was significant in auditory tests (F = 22.22, P<0.001) but not in visual tests.

The latencies of P200 components were significantly elongated by painful stimulation (F = 10.1, P<0.002). Interaction between the effect of pain and stimulus modality was significant (F = 7, P<0.009). Post-hoc hypothesis tests

TABLE I

The effect of pain on amplitude and latency of P300 component measured in difference curves. Standard deviations are shown in parentheses beneath the mean values

Electrode	Visual test				Auditory test			
	Amplitude (μV)		Latency (ms)		Amplitude (μV)		Latency (ms)	
	Control	Pain	Control	Pain	Control	Pain	Control	Pain
Cz	25.3	19.2			18.1	13.7		
	(7.9)	(8.3)			(7.5)	(7.5)		
Pz	27.4	20.7	391.2	391.4	18.9	12.4	333.9	335
	(8.9)	(7.7)	(32.9)	(43.7)	(9.5)	(5.7)	(35.9)	(46.3)
Fz	25.1	19.5			17.7	11.3		
	(10.1)	(8.2)			(8.1)	(6.2)		

showed that latency elongation was significant in auditory experiments ($F = 13.1$, $P<0.001$) but not in visual recordings.

Black diamonds in Fig. 3 show the results of the analysis of corresponding points. Diamonds indicate the differences between curves that were significant at the 0.05 level. The concentration of diamonds within the P300 region is apparent.

Figure 4 shows the potentials recorded with Pz electrode in control experiment in which the pleasantly warm

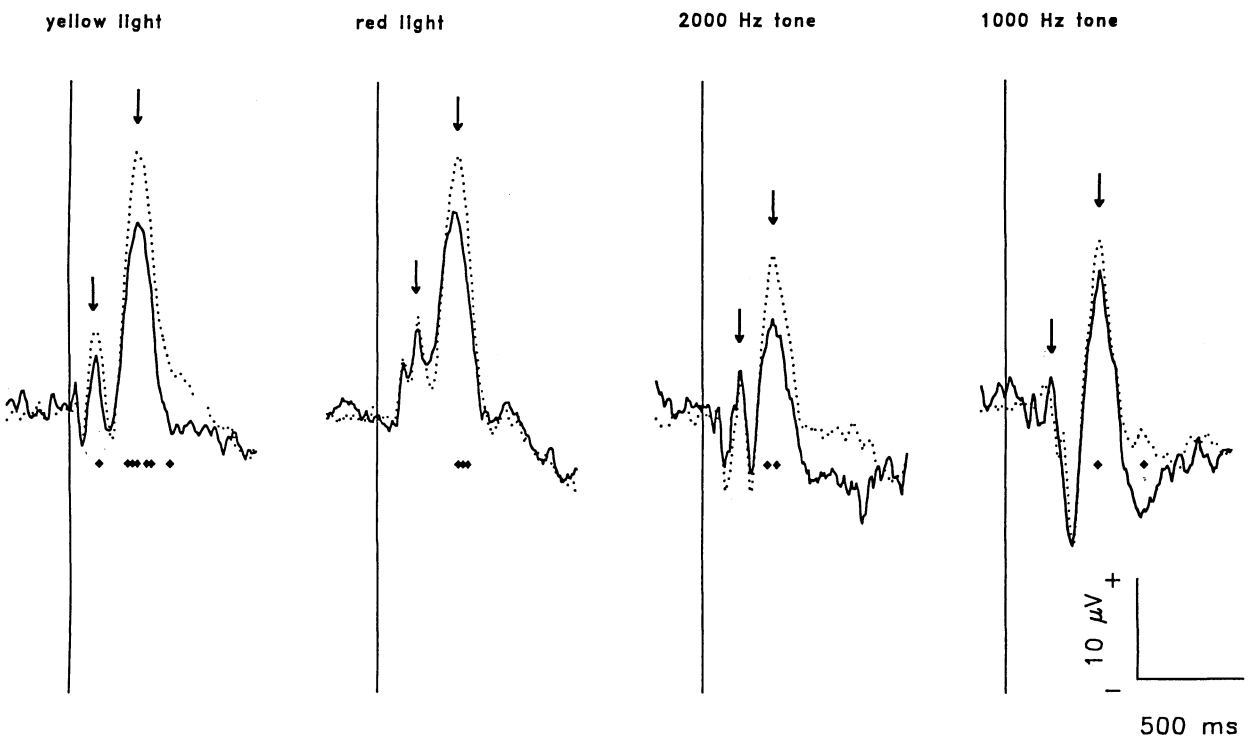

Fig. 3. Grand-averaged difference curves computed by subtracting ERPs evoked by non-target stimulus from ERPs evoked by target stimulus. Figure conventions are the same as in Fig. 1. Black diamonds beneath the curves show the points where curves recorded with cold water stimulation differed significantly from control curves (Student *t*-test for paired data).

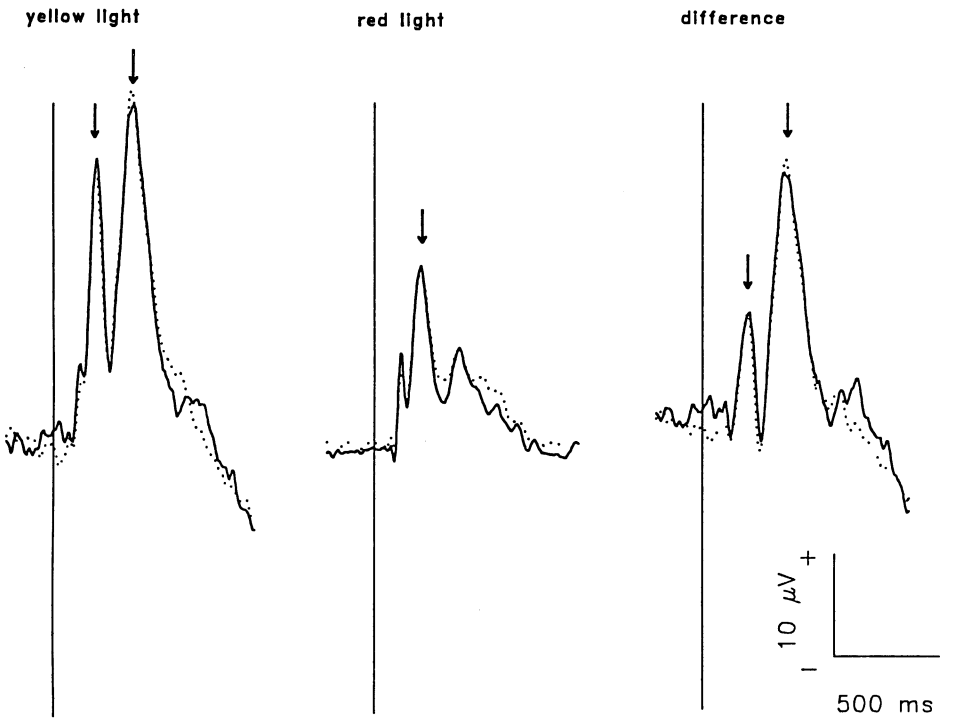

Fig. 4. Grand-averaged ERPs and difference curves recorded in the control warm water experiment. Yellow light was used as a target and red light as a non-target stimulus. Potentials were recorded with Pz electrode. Solid lines show the waveforms recorded when one hand of the subject was immersed in warm water and dotted lines show the recordings obtained without the warm water stimulation.

instead of cold water was used. A control experiment was performed on nine subjects using one set of stimuli: yellow light was a target and red light was a non-target stimulus. Unlike the cold water, the warm water stimulation did not produce the differences in responses to target stimuli. Consequently, there were no differences in grand-averaged difference curves. Identical results were obtained with Fz and Pz electrodes.

Potentials recorded with all three electrodes in the control experiment were analyzed with x two way ANOVA ("warm water" x "electrode"). As in the main experiment, target responses, non-target responses and difference curves were analyzed separately. In all cases warm water stimulation did not produce significant differences in amplitudes or latencies of P300 or P200 components. The analysis of corresponding points of grand-averaged waves also did not show any points of significant differences.

DISCUSSION

The main result of the experiment was the reduction of P300 amplitude during cold water stimulation. The effect was clear, visible in all tests, and the differences were significant when tested with an ANOVA and when corresponding points of grand-averaged curves were compared. The control experiment with warm water stimulation produced clearly different results: not only were the differences in amplitudes insignificant, but the curves were practically identical.

The decline in P300 amplitude confirms the data of Rosenfeld and co-authors (1991, 1993) obtained in their experiments with fingernail pressure and ischemia cuff. These authors suggested that pain could be treated as a drain on processing resources of the brain just as any other concurrent activity. P300 component is an exceptionally good measure of such re-allocation of processing resources in the brain. It was suggested that the degree of demand of additional experience could be assessed by measuring the decrement of P300 amplitude (Isreal et al. 1980a,b, Donchin et al. 1986a,b, Kramer et al. 1987, Polich 1989). Can the intensity of pain be measured by analogous decrement?

Present findings differ from the results of Mazzotta and co-authors (1995) who reported not only larger amplitude but also elongation of latency of P300 wave during migraine attacks. They also differ from the results of Tandon and Kumar (1993) who found increased latency but no alterations in P300 amplitude in patients suffering from chronic pain. It should be remembered, however, that the present results and the results of Rosenfeld and co-authors (1991, 1993) were obtained from healthy

subjects exposed to painful stimulation, whereas in the above-mentioned experiments the brain itself could be in a pathological state. Such a pathological state could produce a number of changes with pain as a manifestation of only some of them. Thus, the direct comparison of the results may be very difficult.

In the present experiment P300 latency was not affected by pain. This was in contradistinction to the findings of other authors reporting latency elongation as an effect of painful stimulation. Rosenfeld and co-authors (1993) reported latency elongation during pain generated by ischemia cuff. Similar elongation was found in patients suffering from chronic pain (Tandon and Kumar 1993). Migraine attacks were also correlated with elongated P300 latency (Mazzotta et al. 1995). However, Rosenfeld and Kim (1991) did not find latency changes in their experiments with fingernail pressure. It is very difficult to measure the intensity of tonic pain and the experimenters report only qualitative data, but the comparison of different pain-producing stimuli indicates that latency changes can indicate higher pain levels. Rosenfeld and co-authors (1993) evaluated pain produced by ischemia cuff as much more intense than that generated by fingernail pressure. After the longer period of cuff application it was described as "excruciating". In the present experiment this level of pain was never reported.

The clear presence of P200 component on the difference curves shows that it also differs in target and non-target ERPs, supporting the earlier findings that both P200 and P300 waves reflect endogenous processes (Hillyard and Picton 1979, Miltner et al. 1989). It was demonstrated for example, that the amplitudes of both waves increased if the subject attended to the stimulus (Velasco et al. 1980, Farthing et al. 1984). Instead, P200 component was clearly present in both target and non-target ERPs whereas P300 appeared virtually only in responses to target stimuli.

The increase of P200 amplitude in the difference curves should be treated with caution. It was found only in auditory experiment. In the visual experiment only a slight increase of this amplitude was found in one electrode recording. Grand-averaged difference curves obtained in the visual experiment show a slight decrease of P200 amplitude during cold water stimulation (Fig. 3). Thus, the clear result of this experiment concerning P200 amplitude was only that painful stimulation affected it much less than the amplitude of P300 wave.

The elongation of latency of P200 component during painful stimulation was more consistent. It reached the level of statistical significance only in auditory tests, but smaller elongations could be seen also in the visual data. Latency changes were bigger in P200 than in P300 component. But this comparison can be very misleading since the accuracy of peak detection in the broad P300 wave was much lower than in the narrower P200.

The difference between the effects of pain on target and non-target responses was dramatic: non-target responses were practically immune to painful stimulation. It should be noted, however, that peak parameters could be reliably measured only in P200 waves that were well developed on non-target recordings. P300 components, on the other hand, were too small on these recordings to ensure reliable measurements, especially in individual ERPs. Similar discrepancy between the effects of pain on target and non-target responses to auditory stimuli was found by Rosenfeld and co-authors (1993). It would be premature to conclude that non-target responses are completely insensitive to environmental manipulations because their small changes were reported in subjects watching films of different engagingness (Rosenfeld et al. 1992). But the difference in strength of the effect on target and non-target responses seems to be evident. Such result indicate that early and middle latency processes, probably up to the level of passive stimulus perception, are little affected. The pain affects mostly processes which come next, especially when the stimulus is meaningful.

The occurrence of P300 wave was linked with decision-making, categorization of target stimulus or "context updating" mechanisms, active whenever one's model of environment needs updating as a result of the new meaningful stimulus (Donchin 1981). Alternatively, it was suggested that P300 wave reflected an extensive inhibitory brain deactivation that followed the perceptual identification of target stimulus (Desmedt and Debecker 1979, Desmedt and Tomberg 1995). This hypothesis suggested that more stimulus specific processes should be reflected in components preceding P300. The present experiment did not address these questions directly, but the finding that P300 component is much more sensitive to pain than the preceding P200 indicates that P300 wave reflects more complicated processes than neuronal deactivation after the event. Thus, the present data indirectly support the hypotheses of Donchin (1981) rather than those of Desmedt and coauthors (Desmedt and Debecker 1979, Desmedt and Tomberg 1995).

ACKNOWLEDGEMENTS

The technical assistance of Mrs Janina Rokicka is gratefully acknowledged. This research was supported by statutory grant of Nencki Institute.

REFERENCES

Bromm B., Treede R.D. (1987) Human cerebral potentials evoked by C02 laser stimuli causing pain. Exp. Brain Res. 67: 153-162.

Chapman C.R., Colpitts Y.H., Mayeno J.K., Gagliardi G.J. (1981) Rate of stimulus repetition changes evoked potential amplitude: dental and auditory modalities compared. Exp. Brain Res. 43: 246-252.

Chudler E.H., Dong W.K. (1983) The assessment of pain by cerebral evoked potentials. Pain 16: 221-244.

Darian-Smith I., Johnson K.O., Dykes R. (1973) Cold fiber population innervating palmar and digital skin of the monkey: responses to cooling pulses. J. Neurophysiol. 36: 325-346.

Desmedt J.E., Debecker J. (1979) Wave form and neural mechanism of the decision P350 elicited without prestimulus CNV or readiness potential in random sequences of near-threshold auditory clicks and finger stimuli. EEG Clin. Neurophysiol. 47: 648-670.

Desmedt J.E., Tomberg C. (1995) Consciousness and cognitive brain potentials. In: Pain and the brain: from nociception to cognition. Advances in pain research and therapy (Eds. B. Bromm and D.J. Desmedt). Vol 22. Raven Press Ltd., New York, p. 61-71.

Donchin E. (1981) Presidential address 1980. Surprise!... Surprise? Psychophysiology. 18: 495-513.

Donchin E., Karis D., Bashore T.R., Coles M.G.H., Gratton G. (1986) Cognitive psychophysiology and human information processing. In: Psychophysiology: systems, processes and applications (Eds. M.G.H. Coles, E. Donchin and S.W. Porges). Guilford Press, New York, p. 244-267.

Donchin E., Kramer A., Wickens C. (1986) Applications of brain event-related potentials to problems in engineering psychology. In: Psychophysiology: systems, processes and applications (Eds. M.G.H. Coles, E. Donchin and S.W. Porges). Guilford Press, New York, p. 702-718.

Dowman R., Rosenfeld J.P. (1985) Operant conditioning of somatosensory evoked potential (SEP) amplitude in rats. I. specific changes in SEP amplitude and a naloxone somatotopically specific change in facial nociceptive. Brain Res. 333: 201-212.

Duclaux R., Shafer K., Hensel H. (1980) Response of cold receptors to low skin temperatures in the nose of the cat. J. Neurophysiol. 43: 1571-1578.

Farthing G.W., Venturino M., Brown S. (1984) Suggestion and distraction in the control of pain. J. Abnorm. Psychol. 93: 266-276.

Handwerker H.O., Kobal G. (1993) Psychophysiology of experimentally induced pain. Physiol. Rev. 73: 639-671.

Hillyard S.A., Picton T.W. (1979) Event-related brain potentials and selective information processing in man. In: Cerebral evoked potentials in man (Ed. J.E. Desmedt). Karger, Basel, p. 71-93.

Isreal J.B., Chesney G.L., Wickens C.D., Donchin E. (1980) P300 tracking difficulty: evidence for multiple resources in dual-task performance. Psychophysiology. 17: 259-273.

Isreal J.B., Wickens C.D., Chesney G.L., Donchin E. (1980) The event-related potential as an index of display monitoring workload. Hum. Factors 22: 212-224.

Kramer A., Sirevaag E., Braune R.A. (1987) Psychophysiological assessment of operator workload during simulated flight missions. Hum. Factors 29: 145-160.

Lovallo W. (1975) The Cold Pressor Test and automatic function: a review and integration. Psychophysiology. 12: 268-282.

Mazzotta G., Alberti A., Santucci A., Gallai V. (1995) The event-related potential P300 during headache-free period and spontaneous attack in adult headache sufferers. Headache 35: 210-215.

Miltner W., Johnson R.Jr., Braun C., Larbig W. (1989) Somatosensory event-related potentials to painful and non-painful stimuli: effects of attention. Pain 38: 303-312.

Musante L., Raunikar R.A., Treiber F., Davis H., Dysart J., Levy M., Strong W.B. (1994) Consistency of children's hemodynamic responses to laboratory stressors. Int. J. Psychophysiol. 17: 65-71.

Polich J. (1989) P300 from a passive auditory paradigm. EEG Clin. Neurophysiol. 73: 312-320.

Rosenfeld J.P., Bhat K., Miltenberger A., Johnson M. (1992) Event-related potentials in the dual task paradigm: P300 discriminates engaging and non-engaging films when film-viewing is the primary task. Int. J. Psychophysiol. 12: 221-232.

Rosenfeld J.P., Johnson M.M., Koo J. (1993) Ongoing ischemic pain as a workload indexed by P3 amplitude and latency in real versus feigned pain conditions. Psychophysiology. 30: 253-260.

Rosenfeld J.P., Kim M. (1991) Ongoing pain as a mental workload indexed by P300 depression: discrimination of real and feigned pain conditions. Psychophysiology. 28: 336-343.

Tandon O.P., Kumar S. (1993) P3 event related cerebral evoked potential in chronic pain patients. Indian J. Physiol. Pharmacol. 37: 51-55.

Turner J.R., Sherwood A., Light K.C. (1994) Intertask consistency of hemodynamic responses to laboratory stressors in a biracial sample of men and women. Int. J. Psychophysiol. 17: 159-164.

Velasco M., Velasco F., Olvera, A. (1980) Effect of task relevance and selective attention on components of cortical

and subcortical evoked potentials in man. EEG Clin. Neurophysiol. 48: 377-386.

Wolf S., Hardy J.D. (1941) Studies on pain. Observations on pain due to local cooling and on factors involved in the "cold pressor" test J. Clin. Invest. 20: 521-533.

Zaslansky R., Sprecher E., Katz Y., Rozenberg B., Hemli J.A., Yarnitsky D. (1996) Pain-evoked potentials: what do they really measure. EEG Clin. Neurophysiol. 100: 384-392.

Received 28 May 1997, accepted 20 January 1998