Brain and Human Pain: Topographic EEG Amplitude and Coherence Mapping

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Summary: Nineteen young healthy volunteers (8 males and 11 females) participated in an experimental ice-cube cold pressor test to study topographic changes of EEG parameters in response to painful stimulation. EEG was recorded with 19 electrodes and quantified by amplitude and coherence analyses. Mean amplitudes and values for local (between adjacent electrodes) and interhemispheric (between electrodes on homologous sites of both hemispheres) coherences were computed for six frequency bands. For the evaluation of changes between EEG at rest (baseline) and EEG during painful stimulation (right or left hand), non-parametric paired Wilcoxon tests were performed. The obtained descriptive error probabilities were presented in probability maps. In the behavioural pain tolerance and subjective pain ratings, no difference in gender or stimulation condition was observed. Under painful stimulation the results showed: (A) most pronounced decrease of Alpha amplitude in the central areas and some increase of high Beta amplitude; (B) increase of local coherence for Alpha and Beta2 mainly in central regions and centro-frontal leads; and (C) increase of interhemispheric coherence for Alpha and Beta2 in the central areas. The results of this study indicate clearly that peripheral painful stimulation is reflected by EEG changes. Decrease of EEG amplitude and simultaneous increase of EEG coherence in the central regions can be cortical correlates of human pain.

Key words: Pain; EEG; Spectral analysis; Local coherence; Interhemispheric coherence; Topographic mapping.

Introduction

How brain processes noxious information is central to our understanding of neurophysiology of human pain. Since human pain is an integration of sensory, perceptual, affective and cognitive processing in the brain, studying of brain activities in animals and man naturally comprises the essential step towards the exploration of brain mechanisms for pain. Conventionally, almost all the neurophysiological investigations of pain are relying on brief activation (in ms) of electrical or thermal stimulations, mainly due to technical and ethical considerations. Our understanding of basic physiological mechanisms of pain is often built on the phasic pain model, which largely lacks ethological validity.

It has been argued that the longer lasting and diffused type of tonic pain may exert different subjective experience and subserved by different physiology than those in the short brief phasic pain (Chen and Treede 1985; Vaccarino and Melzack 1992). Cold-pressor tonic pain can closely simulate the subjective properties of a wide variety of clinical pain (Chen et al. 1989a). Therefore, we suggested to examine systematically the psychophysiogical mechanisms of tonic pain and it was demonstrated that topographic brain activities can index the human pain experience and differentiate the pain responsiveness (Chen et al. 1989b). In these two previous reports, it was observed that human pain reactivity can be naturally dichotomized into the distinct pain sensitive (PS) and pain tolerant (PT) subjects, based on their behavioural endurance to the ice water cold-pressor test. Under the tonic pain test, both groups exhibited heightened low frequency Delta and high frequency Beta EEG power densities, and the PS subjects showed significant higher Delta, but not Beta power, than the PT subjects. The issues of EEG and clinical pain has been well reviewed recently (Chen 1993a) and the EEG effects of experimental pain are now an issue of dispute (Chen et al. 1989b; Backonja et al. 1991; Veerasarn and Stohler 1992; Backonja and Howland 1993; Chen 1993b; Stohler 1993).

In the previous study (Chen et al. 1989b), topographic brain activities were limited to 8 EEG channels, 4 positions in each hemisphere, and only power spectrum densities were computed. Both limitations hamper a close

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examination of cortical events in pain state. 8 electrodes on the skull yield a much too coarse spatial resolution and EEG power may reflect physiological events only partially. Other parameters may show much closer relevance to cortical information processing than EEG power. Among the computations of such parameters is the central role of coherence analysis (Shaw et al. 1978; Shaw 1984; French and Beaumont 1984; Tucker et al. 1986).

Coherence analysis of the EEG may depict cortical coupling of neural ensembles, anatomically and/or physiologically, during processing of information. Both local and distal (e.g., interhemispheric coupling) coherences may occur, simultaneously or in isolation, depending on the activation of the mental state. EEG coherence studies have covered a wide range of signal processing, modeling in neurophysiology, ontological development and aging, sleep/awake states, sensory activation, cognitive processing, learning, stress and emotionality, mental disorders, effects of psychotropic agents, traumatic brain injury, seizures, neurosurgery, and the functions of split brain. Functional brain activity mapping, especially coherence mapping (Rappelsberger and Petsche 1988; Rappelsberger et al. 1993), has proved highly sensitive and specific for cortical EEG activities in profiling mental events, such as silent reading, mental arithmetic, problem solving (Petsche et al. 1986), mental imagery (Rappelsberger et al. 1987), musical perception (Petsche et al. 1985), and thinking (Petsche et al. 1992). Consequently, current study was conducted to explore the sensitivity and specificity of functional brain electrical activity mapping in pain state.

To extend our previous findings on brain and pain, the tasks of this study were: (a) to employ both amplitude and coherence analysis in pain study, (b) to expand the EEG recording channels and replications of pain stimulation, and (c) to display and analyze the cortical events of noxious experience in topographic maps. We expected that both the methodology applied and the comprehensive results emerged in this work may constitute a new perspective and a fresh look how cortical activities changed during the well controlled tonic pain state in man.

Methods

Subjects and procedures

Healthy young female (n=11, age 22.5 ± 2.2) and male (n=8, age 22.6 ± 3.3) students participated in the study which was approved by the Ethics committee of the University of Vienna. A single session lasted about two hours and consisted of four test procedures:

(1) RH-EO: pain stimulation: ice cube on right hand (RH), eyes open (EO)

(2) LH-RO: pain stimulation: ice cube on left hand (LH), eyes open (EO)

(3) RH-EC: pain stimulation: ice cube on right hand (RH), eyes closed (EC)

(4) LH-EC: pain stimulation: ice cube on left hand (LH), eyes closed (EC)

In every experiment the tests were performed in random order and counter-balanced as closely as possible. EEG was recorded for up to two minutes when the subject endured the entire two minutes of ceiling time in the pain test or less than two minutes when the subject could not endure the entire pain tolerance time. Both behavioural pain endurance times and subjective ratings of pain intensities were recorded.

Control EEG were recorded with eyes open and eyes closed before the pain tests, between the pain-tests, and after the pain-tests. During the control records the subjects were asked to relax.

Pain test was a simplified ice-water cold-pressor test; instead of immersing both hands into the 1 ± 0.3°C ice-water bath, the subjects held the test palm up, half-open, and an assistant placed one ice-cube into the palm. The ice-cube measured 2x1x1.5 cm^3 in dimension. Subject was instructed to (a) hold the ice-cube as long as he/she could tolerate, (b) drop the ice-cube when he/she could no longer endure the pain, and (c) rate the pain intensity, after completion of pain endurance test, on a 0-10 scale, 0 = no pain at all, and 10 = pain as unbearable as could be.

EEG Recording, Artifact Rejection and Parameter Selection

According to the international 10-20 system, 19 gold-disc electrodes were glued to the scalp. Recordings were made against the averaged signals at both ear lobe electrodes (TC 0.3s, Filter 35 Hz). The EEG was displayed on paper and simultaneously stored on hard disk (sampling rate 128/s) for off-line processing.

The subjects were seated comfortably in an arm chair. All records were separated from one another by a period of rest while the subjects were allowed to move head and limbs. After each ice-cube test, the resting period lasted several minutes to dry and warm up the hand.

Conspicuous artifacts were eliminated from further computation by visual inspection. Beside the visual screening a quality control program was used to detect further artifacts mainly caused by muscle activities. This was based on amplitude and slope parameters (John et al. 1983). As many as possible artifact free 2 s epochs were chosen for further processing. Dependent on the artifact rejection, in total 10 to 60 epochs (median 39, mean 38) were used. Each epoch was Fourier transformed to compute averaged power and cross-power spectra with a frequency resolution of 0.5 Hz. Nineteen power spectra and 38 cross-power spectra were obtained for each record. Averaged cross-power spectra were calculated between adjacent electrodes along the transverse and longitudinal electrode rows (local cross-spectra) and also between electrodes on homologous sites of both hemispheres (interhemispheric cross-spectra). Data reduction of the spectra was performed by averaging adjacent spectral lines to obtain broad band parameters for six frequency bands: Delta (0.5-3.5 Hz), Theta (4-7.5 Hz), Alpha (8-12.5 Hz), Beta1 (13-18 Hz), Beta2 (18.5-24 Hz), and Beta3 (24.5-31.5 Hz). The final step was the computation of amplitude and coherence per frequency band. In total 6*19=114 amplitude values and 6*38=228 coherence values were obtained for each record and stored in a data base. Details of coherence computation are described in Jenkins and Watts (1968).

The baselines for the evaluations of pain-test dependent amplitude and coherence changes were obtained by merging all control recordings of a subject with eyes open and eyes closed, respectively. Dependent on the artifact rejection, the resulting amplitude and coherence values were based on 30 to 148 epochs (median 75, mean 81).

Statistical Procedure and Topographic Mapping:

To test whether the obtained coherence values were significantly different from zero, 95% confidence intervals were computed. Since coherence values are correlation coefficients per frequency band with unknown distribution, the z-transformation towards normal distribution as proposed by Fisher was applied (Rappelsberger et al. 1986). The theoretical variance of the normal distribution is inversely proportional to the number of epoches used for averaging. Confidence intervals were estimated in the z-plane, bias corrected according to Benignus (1969) and transformed back into the coherence plane. Coherence values were indicated as significantly different from zero if the confidence intervals did not include zero coherence.

Changes of the chosen parameters during pain with respect to the corresponding baselines were averaged over all subjects and presented in spectral parameter maps. Each frequency band is represented by three maps: amplitude, local coherence and interhemispheric coherence. In the presentations, "red" means an increase of the corresponding parameter during pain and "blue" indicates a decrease.

For the evaluation of significant differences between chosen parameters, paired Wilcoxon tests were applied. The obtained rank sums were converted to error probabilities (IBM-Scientific Subroutine Package 1970) which were presented in probability maps. A significant amplitude change is presented by a square at the corresponding electrode position. A black square means an increase and an empty square a decrease. The size of a square corresponds to the obtained error probability. A significant local coherence change is presented by a square drawn between the two electrodes involved. A significant interhemispheric coherence is marked by squares at both electrodes connected by a line. It should be mentioned that for reasons of many parallel statistical tests the results presented in the maps are purely exploratory. A more detailed description of the procedures can be found in Rappelsberger and Petsche (1988).

Confirmatory statements for amplitude comparisons at preselected positions and for coherence comparisons between preselected pairs were made using the significance level adjustment according to Holm (1979). This procedure is also described in Abt (1988). From the total number N = 6*19 = 114 (6 frequency bands, 19 positions) a subset of n = 2*6 = 12 (positions C3 and C4) were preselected and each null hypothesis was tested at error probability α using the adjusted significance levels $\alpha_i^* = \alpha/(n-i+1)$, i = 1, 2, ... n. All null hypotheses were rejected at α as long as $p_i \leq \alpha_i^*$, and where the obtained p-values according to the paired Wilcoxon tests were rank-ordered as $p1 \leq p2 \leq ... \leq pn$.

The same procedure was used to obtain confirmatory statements for coherences F3-C3 and F4-C4.

Results

Pain State, Pain Endurance Time, and Pain Rating

Usually at the beginning, the ice-cube test produced a cold sensation in the palm. Within a few seconds, the chilling sensation grew intense and a throbbing, aching pain resulted after about 10-15 seconds. The pain changed from moderate to strong or unbearable for the subject within 1-2 minutes.

Table I indicates that, behaviourally, there was a consistent pain endurance time of a little less than two minutes of ceiling time.

The average pain intensity rated was around 6 in a 0 - 10 scale, corresponding to "moderate" pain range. Further statistical analyses with 2 x 2 x 2 repeated measure ANOVA indicated: a) no gender difference between male and female subjects in behavioural pain endurance on subjective pain rating; b) no difference between eyes open and eyes closed condition; and c) no special difference between right and left hand stimulation.

Consistency of individual pain measures were in-

Table I. Pain Endurance Time and Pain Ratings: Mean ± SEM.

		Pain Endurance Time (seconds)		Pain Rating (0-10)	
Pain Test		Male	Female	Male	Female
<RH-EO>		116	120	5.87	5.54
	±	2.16	1.85	0.65	0.55
<LH-EO>		113	116	6.00	6.27
	±	5.27	4.50	0.64	0.55
<RH-EC>		109	116	6.00	5.27
	±	7.04	5.61	0.69	0.55
<LH-EC>		112	114	6.75	6.22
	±	6.00	4.78	0.69	0.51
Grand Mean:		112.5	116.5	6.15	5.82

spected in two aspects. For the behavioural pain endurance time, all but two (one male, one female) out of the 19 subjects could endure the entire 2 min of ice-cube test in each of the 4 study conditions. For the subjective pain ratings, cross correlations of the group across the 4 conditions were all statistically significant. The pain ratings of both hands showed a correlation of .829 under eyes open condition, comparing to the correlation of .631 under eyes closed condition. For the right hand, the correlation was .753 between eyes open and eyes closed conditions; for the left hand, the correlation was .811 between these two conditions. These results indicate that ice-cube test induced reliably painful activations across conditions.

EEG changes

The computation of averaged spectral parameters using the control records before, between and after the pain tests yielded the baselines for the comparisons. By averaging a great number of epoches (30 to 148, median 75) amplitude and coherence fluctuations between the epochs cancelled largely. This was examined extensively and is part of a thesis at the University of Vienna (Weiss 1994).

The maps of amplitude and coherence changes between the control baseline and pain state in eyes open condition are illustrated in figure 1 (right hand stimulation) and figure 2 (left hand stimulation), respectively. Similar maps of EEG changes were observed in the eyes closed condition.

(a) EEG Amplitude

The results here describe the systematic effects of EEG changes across the 4 study conditions. Theta and Alpha amplitude reductions were observed in both hemispheres but these effects were accentuated in the contralateral hemisphere to the stimulated hand. In the probability maps, the statistically significant reductions within the Theta and Alpha band were observed mainly in the central and precentral regions. In contrast, in the upper Beta bands amplitude enhancement was observed.

(b) Local Coherence

Local coherence values were in all cases highly significant different from zero. This was tested by the computation of confidence intervals. For the Alpha band e.g., local coherence differences presented in figure 1 are based on coherence values in the range of 0.43 to 0.86. For the other frequency bands and eyes closed conditions similar values were obtained.

In the Delta band coherence decreased in the frontal and fronto-temporal regions (figure 1 and figure 2). Theta coherence showed reductions in left anterior and temporal regions. Local Alpha coherence displayed great enhancement in the vertex region but reduction in both posterior parietal regions. The Beta2 band exhibited similar coherence changes but to a lesser degree than the Alpha band. In the Beta3 band coherence enhancement was found in the fronto-central and parietal areas.

(c) Interhemispheric Coherence

Interhemispheric coherence values Fp1-Fp2, F3-F4, C3-C4, P3-P4 and O1-O2 were in all cases highly significant. For the Alpha band e.g., interhemispheric coherence differences presented in figure 1 are based on coherence values between 0.52 and 0.76. For the other frequency bands and eyes closed conditions similar values were obtained. In contrast, interhemispheric coherences F7-F8, T3-T4 and T5-T6 were frequently below the level of significance. Therefore, no description and interpretation of coherence changes between these locations is attempted.

In the Delta and Theta bands no systematic interhemispheric coherence change was exhibited. In contrast, in the Alpha band interhemispheric coherence reduction anteriorly but strong interhemispheric coherence enhancement in the central region were found. The Beta2 band exhibited marked enhancement in the central and parietal areas.

RH - EO

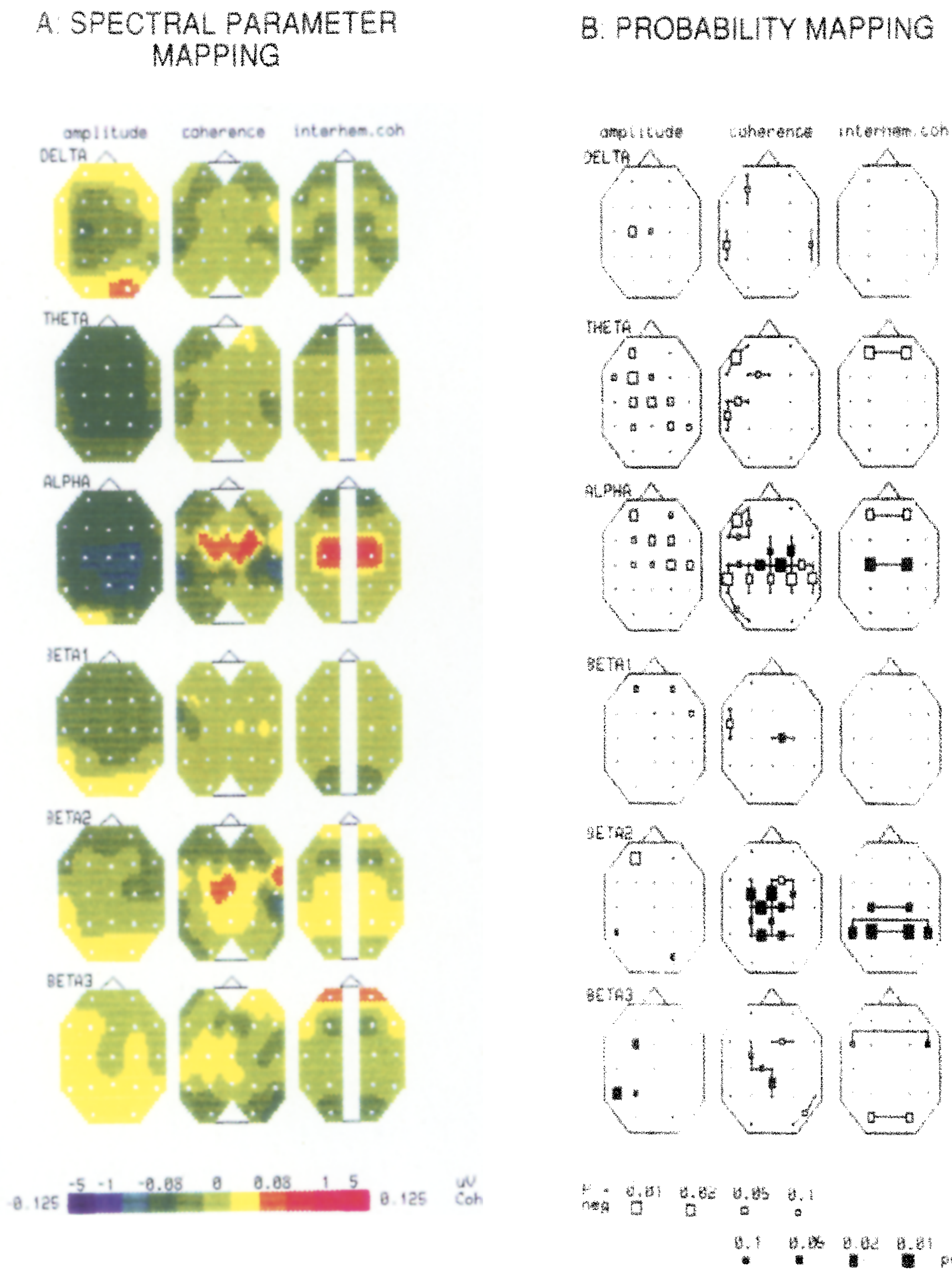

Figure 1A. Spectral parameter maps. Pain stimulation induced topographic EEG changes (average over 19 subjects; right hand stimulation - eyes open condition, RH-EO). Amplitude changes are presented in the left column, local coherence changes in the middle column and interhemispheric coherence changes in the right column. The six rows correspond to the six frequency bands examined. Red colour means an increase of thecorresponding parameter during pain state with respect to the baseline. Blue colour means a decrease of the corresponding parameter. Figure 1B. Error probability maps according to paired Wilcoxon tests (N = 19). Significant changes are indicated by squares as described in the text. Empty squares mean a decrease and black squares an increase of the corresponding parameter.

LH - EO

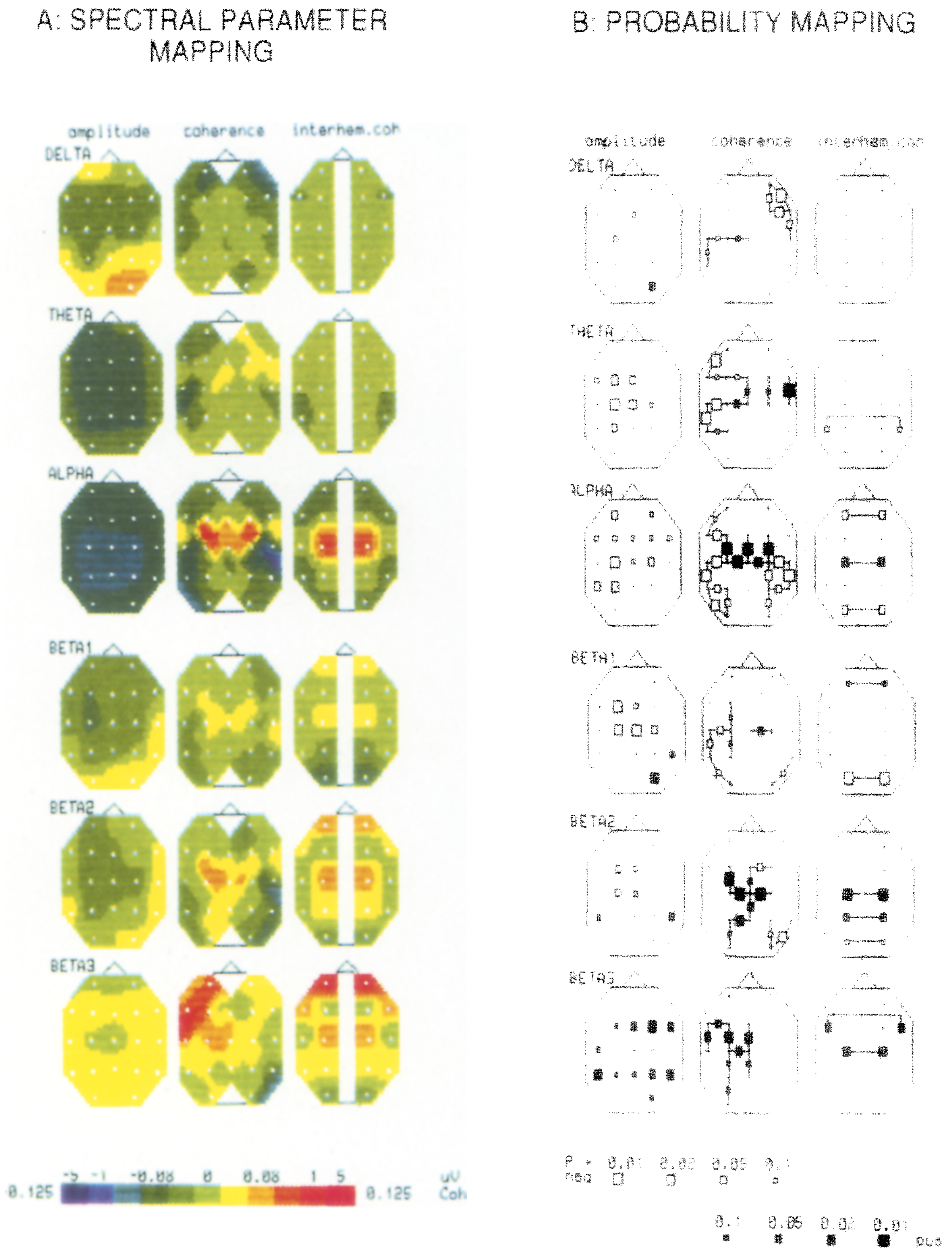

Figure 2. Spectral parameter maps and probability maps of EEG changes between baseline and pain state under the left hand stimulation - eyes open condition (LH-EO). Legend as in figure 1.

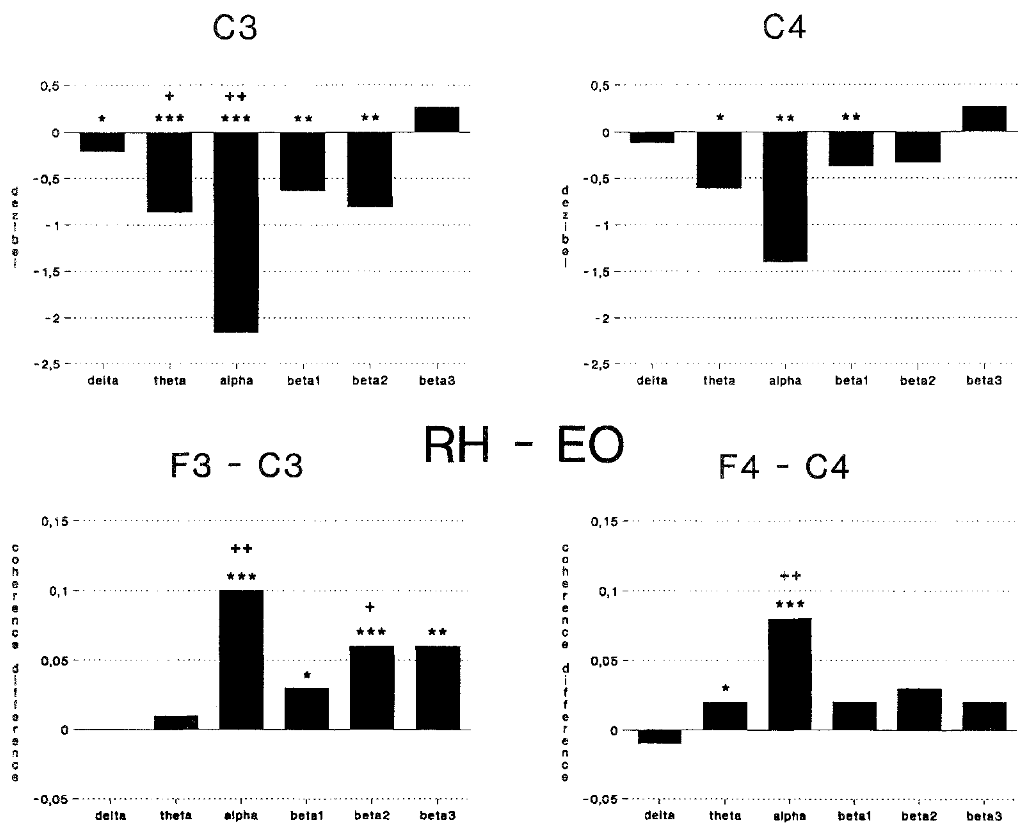

Figure 3. Lateralization effect, right hand stimulation - eyes open condition (RH-EO). Left upper part: amplitude relations at location C3 between stimulation and baseline condition. Frequency bands are on the x-axis. Downward bars mean a decrease of amplitude during pain, upward bars mean an increase. Right upper part: same as left part but amplitude relations at location C4. Left lower part: coherence differences between F3-C3 between stimulation and baseline condition on a linear coherence scale. Right lower part: same as left lower part but coherence differences between F4-C4. Exploratory statistical results according to the paired Wilcoxon tests are indicated by * ($p \leq 0.10$), ** ($p \leq 0.05$) and *** ($p \leq 0.01$), respectively. Confirmatory statistical results are indicated by + ($\alpha \leq 0.10$), ++ ($\alpha \leq 0.05$) and +++ ($\alpha \leq 0.01$), respectively. Right hand stimulation shows greater Alpha amplitude reduction on the contralateral than on the ipsilateral side. The reduction at C3 is statistically significant ($\alpha \leq 0.05$). Additionally, Alpha coherence increase between F3-C3 is higher than between F4-C4, however, both are statistically significant ($\alpha \leq 0.05$).

(d) Contralateral EEG Effects to Hand Stimulations

To explore the sensitivity of EEG parameters for the contralateral somatosensory lateralization effects in response to the stimulated hand additional analyses were conducted.

Under the right hand stimulation - eyes open condition, comparisons of the EEG amplitude changes at scalp locations C3 and C4 and EEG coherence changes F3-C3 and F4-C4 over the somatosensory cortex showed (figure 3): (a) greater Alpha, Theta, Beta1 and Beta2 amplitude reductions in the left hemisphere. Alpha amplitude reduction at C3 was statistically significant ($\alpha \leq 0.05$); (b) larger coherence increase in the left hemisphere for Alpha and Beta bands. A logarithmic scale in decibel is used ($20\log[A_{pain}/A_{baseline}]$; A_{pain} = amplitude under pain stimulation, $A_{baseline}$ = amplitude of baseline condition). Alpha coherence increase was statistically significant on both hemispheres ($\alpha \leq 0.05$). About reversed patterns of results emerged under the left hand stimulation - eyes open condition (figure 4): (a) greater Alpha amplitude reduction in the right hemisphere; (b) corresponding greater Alpha coherence increase in the right hemisphere.

The results of right hand stimulation - eyes closed condition show figure 5: (a) greater Alpha and Beta1 amplitude reductions in the left hemisphere. Amplitude reductions in the Theta, Alpha and Beta1 band were statistically significant on both hemispheres ($\alpha \leq 0.05$); and (b) larger Alpha coherence increase in the left hemisphere, but significant Beta2 coherence increase on the ipsilateral side ($\alpha \leq 0.05$). In contrast, left hand stimulation depicted (figure 6): (a) greater Alpha and significant ($\alpha \leq 0.01$) Beta1 amplitude reduction in the right hemisphere; (b) corresponding and significant ($\alpha \leq 0.05$) Alpha as well as Beta2 coherence increases in the right hemi-

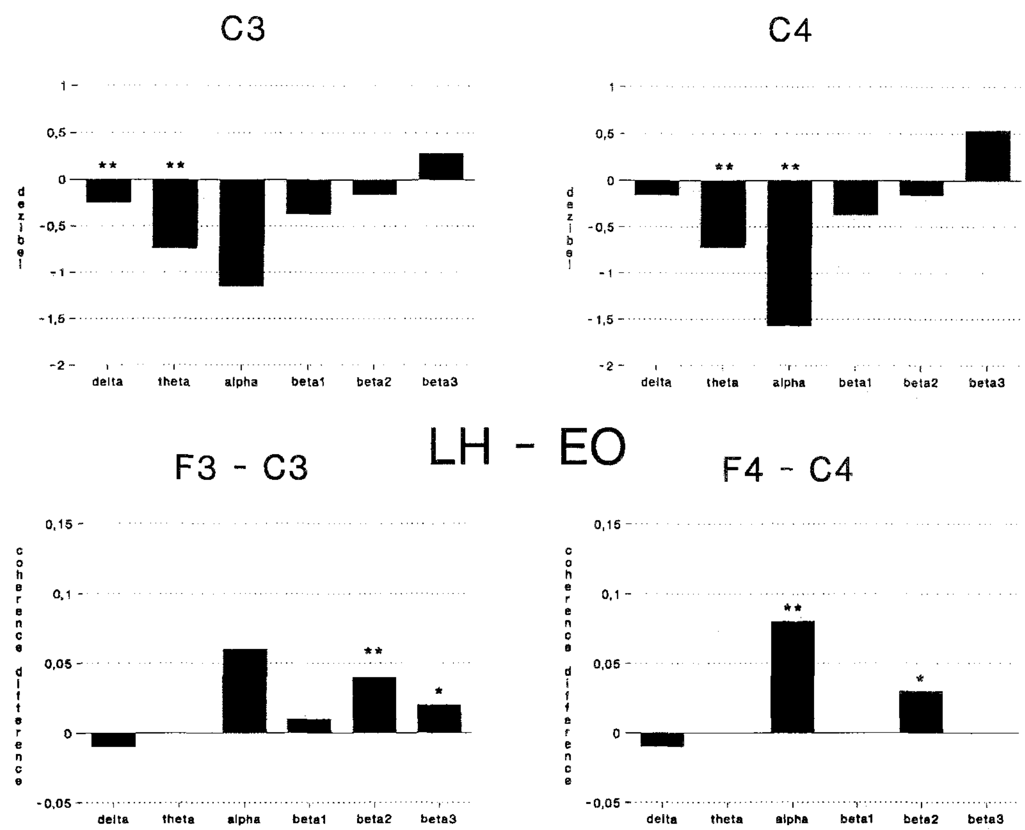

Figure 4. Lateralization effect, left hand stimulation - eyes open condition (LH-EO). Explanation of the graphs as in figure 3. The results show greater Alpha amplitude reduction and Alpha coherence increase on the right side. Both changes are significant in the exploratory but not in the confirmatory sense.

sphere.

Considering the Theta amplitude reductions across the 4 study conditions (figures 3 to 6) no clear lateralization effect is observed. Moreover, almost no Theta coherence changes can be seen.

Discussion

Methodological Issues

(a) Pain Test

The ice-cube cold test can be considered as a variation of the ice-water cold pressor test. This ice-cube test proved to be convenient and consistent across the testing conditions. As a tonic pain model, the ice-cube test poses a spatial and temporal summation of pain stimulation. Even though the pain stimulation is focal, the sensation of pain and numbness seems to be diffused and spreading in the testing palm. In the previously published cold pressor test (Chen et al. 1989a) with hands immersion into the 1 ± 0.3 C of ice-water baths, there is a consistent dichotomy of behavioural pain endurance. The pain sensitive (PS) subjects could merely tolerate the tonic pain for a mean of one minute, while the pain tolerant (PT) group could endure the whole 3 or 5 min of upper limit ceiling. There was no such dichotomy in behavioural endurance under the ice-cube test because of both spatial and temporal summation, 2 min. in the ice-cube test vs. hand immersion for 3 or 5 min. in the cold pressor test. Only two out of 19 subjects could not endure the whole 2 min of ceiling time. However, the averaged pain ratings of intensity (grand mean VAS - visual analogue scale - in pain rating of 5.99, see table I above) by subjects under the ice-cube test were to the same magnitude as those by PT group under the cold pressor test (grand mean VAS score of 5.97, see Chen et al. 1989a).

(b) Statistical Test and Interpretation of EEG Data

The non parametric Wilcoxon statistics used in the EEG analyses need no requirement of the homogeneity of variance as in the parametric statistics. However, statistical tests of many variables, such as the 6 EEG bands over 19 electrode positions, with 30 transverse and longitudinal local coherences and with 8 interhemispheric coherences poses problems of the Type I error due to the inflation of the α-value (Abt 1983). Therefore, the

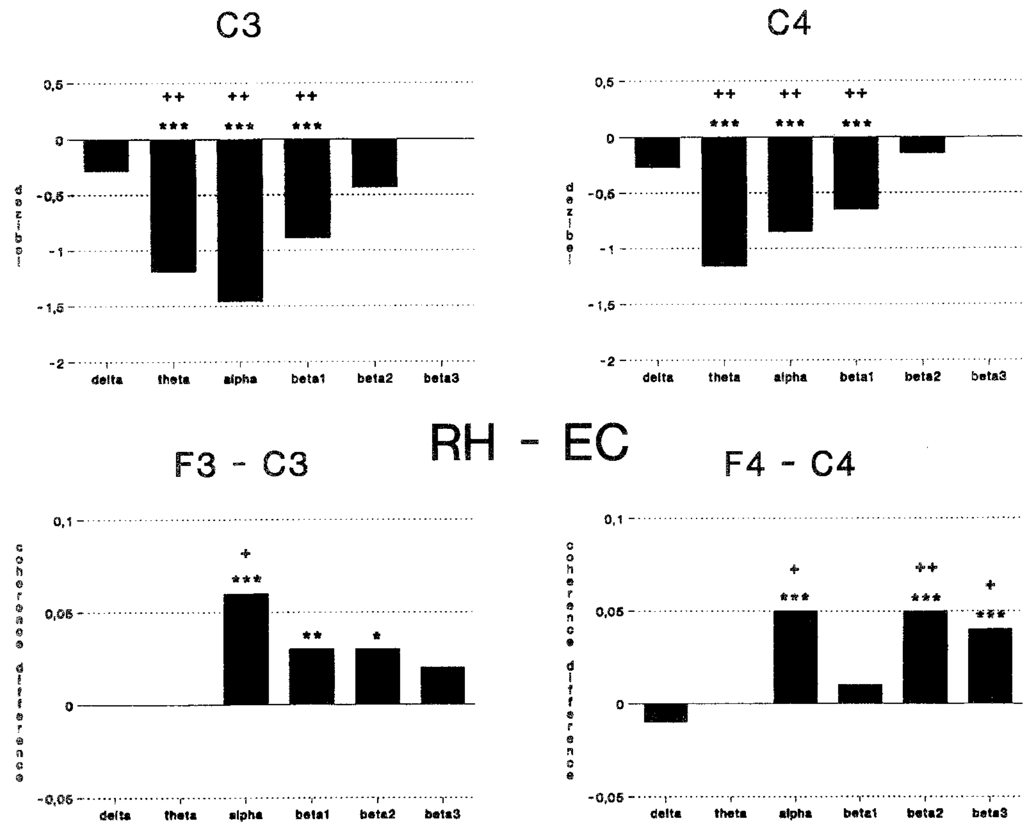

Figure 5. Lateralization effect, right hand stimulation - eyes closed condition (RH-EC). Explanation of the graphs as in figure 3. Amplitude reductions in the Theta, Alpha and Beta1 band are statistically significant on both hemispheres although a little more pronounced at C3. Significant Alpha coherence increase is observed on both sides. However, error probability is relatively high ($\alpha \leq 0.10$). Additionally, marked increase of right Beta2 and Beta3 F4-C4 coherence is observed.

statistical results in the probability maps should be considered as exploratory (i.e., hints at the potential difference existed over the many comparisons), but not confirmatory (i.e., reject or accept the null hypotheses). To make confirmatory statements particularly important electrode positions C3 and C4 and coherence pairs F3-C3 and F4-C4 were selected and the significance level was adjusted according to Holm (1979).

Topographic Measures of EEG Amplitude and Coherence in Human Pain

The major focus of this investigation is to extract or identify the common features of brain activities from the pain stimulations across the 4 testing conditions. EEG amplitude and coherence are mutually independent. However, for the measurement of coherence an appropriate reference must be used. There does not exist an ideal site for a reference without any local signal and therefore a compromise has to be taken. For our recordings the average of both ear lobe signals turned out to be suitable (Rappelsberger 1989) for the proper interpretation of coherence data.

(a) Amplitude

Increased frontal Delta activity was observed in the spectral parameter maps in spite of careful rejection of eye movement artifacts from further analyses. These Delta activities may result from involuntary eye-movements masked by the EEG activity. Significance of the increased Delta activity in posterior regions is not clear. However, Delta EEG can be connected with emotionality (Pribram 1981) and our previous report (Chen et al. 1989b) indicated that Delta enhancement was higher in the PS than PT subjects under noxious stimulation.

There was a consistent decrease of EEG amplitude in Theta, Alpha, Beta1 and Beta2 bands across the 4 testing conditions. The decrease of EEG amplitude in Alpha was centred in the vicinity of central gyrus and exhibited some contralateral effect to the stimulation side. Such contralateral effect was also shown in the Beta1 band and to a less degree in the Beta2 band but not in the Theta band. The lateralized changes shown in figure 3 to figure

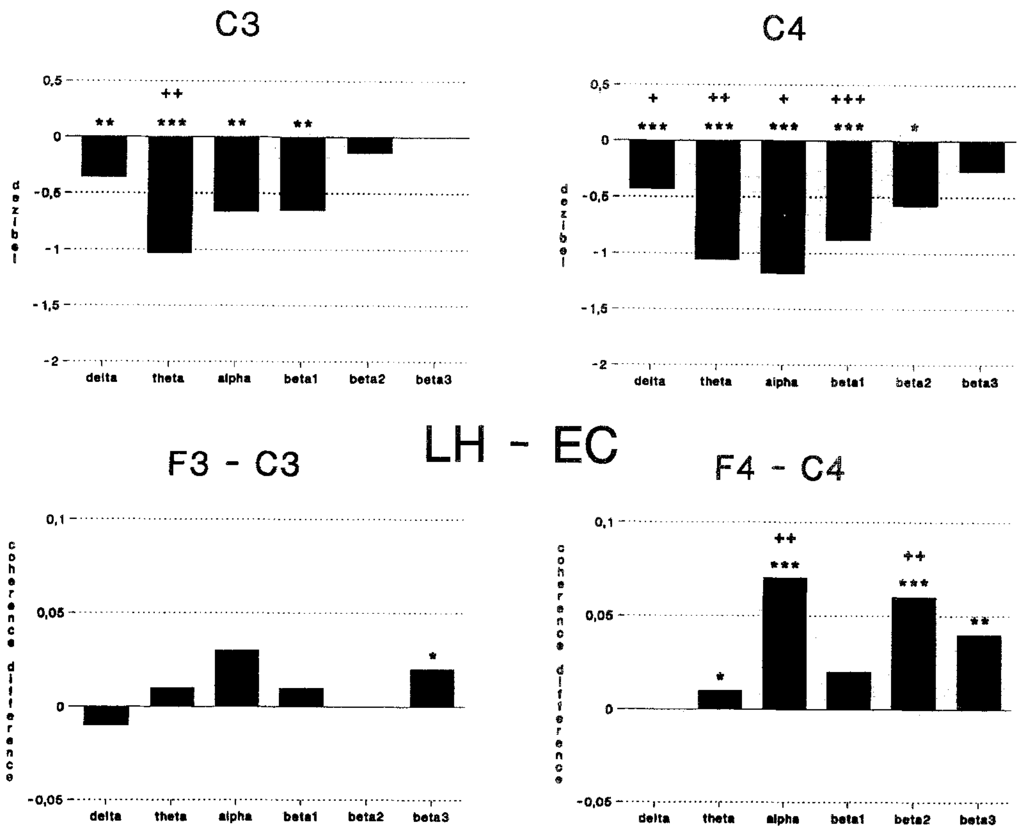

Figure 6. Lateralization effect, left hand stimulation - eyes closed condition (LH-EC). Explanation of the graphs as in figure 3. Clear amplitude reduction in Theta, Alpha and Beta1 is shown on the right hemisphere whereas on the left hemisphere only the Theta band is concerned significantly. Significant increase of coherence is observed in F4-C4 in the Alpha and Beta2 band.

6 are closely related to somatosensory activation of cold stimuli, but less likely related specifically to the cortical processing of noxious perception.

In contrast, there was also some enhancement of EEG amplitude across the 4 testing conditions in the Beta3 band. These increases were largely away from the central gyrus and no meaningful contralateral effect was shown. The increase of high EEG Beta was reported in the previous pain study on EEG power density (Chen et al. 1989b).

The decrease of Alpha amplitude is considered a nonspecific desynchronization effect in the brain under novel activation, a general arousal effect. However, the decrease of Theta amplitude and Beta1 amplitude may be related to the special activation of nociception under the tonic pain test. The specific nature of such cortical changes requires further investigations.

(b) Local Coherence

The most conspicuous findings are the significant increase of vertex and near-vertex coherences in the Alpha and Beta2 bands across the 4 testing conditions. In addition, there is some increase of coherence in the Beta3 band. The major decrease of local coherence was observed posteriorily in the Alpha band, under the eyes open condition, but rarely under the eyes closed condition.

The patterns of coherence changes are different from those of the changes in EEG amplitudes. This result indicates that cortical areas in the brain exhibits various forms of information processing during the noxious stimulation. The result of noxious stimulation is often a combination of pain and stress. The physiological commonality and differentiation between these two events are open for clarification. The interpretation of local coherence may be linked to functional activation of underlying neural ensembles. Therefore, the results from this study suggests a prominent synchronization of neural activities in the central regions under the pain state, consistent to the results in the studies of pain-related evoked potentials (e.g., Chatrian et al. 1975; Chen et al. 1979; Bromm 1984), where the largest evoked potential amplitude to phasic pain stimulation is invariably observed at the vertex area. We consider that this heightened coherence at the vertex may index the neurophysiology of arousal-related pain processing in the brain in man.

(c) Interhemispheric Coherence

A most consistent effect of pain stimulation in the 4 testing conditions on interhemispheric coherence was the enhancement of C3-C4 coherence in the Alpha and Beta2 bands. The frequent observed behaviour of Alpha and Beta2 may be due to the second harmonic of Alpha frequency which falls within the Beta2 range (e.g., Alpha = 10 Hz, then the second harmonic is 20 Hz). The enhancement of C3-C4 coherence may reflect the primary activation of somatosensory action of cortex in noxious processing.

Considering both amplitude and coherence changes in pain activation, there was a consistent decrease in amplitude, most pronounced in the alpha range, and simultaneously an increase of coherence. This shows that coherence is an additional measure independent of amplitude. In contrast to the changes in the Alpha band, Theta amplitude was not accompanied by remarkable coherence changes.

In conclusion, the results of this study indicate that (a) ice-cube pain test was a variation of the ice-water cold pressor test for the subjective pain rating measure; (b) significant consistency in behavioural pain endurance and subjective pain rating was observed across the 4 pain testing conditions (eyes open or closed, stimulation of the left or right hand); (c) gender difference was not observed in both behavioural pain endurance and pain rating; (d) upon painful stimulation, decrease of EEG amplitude in Theta, Alpha, Beta1 and Beta2 bands as well as increase of Beta3 amplitude occurred. Alpha amplitude exhibited contralateral effect in amplitude reduction. The increase of Beta3 amplitude was diffusely localized; (e) upon painful stimulation, local coherence and interhemispheric coherence enhancement were observed, most pronounced in the Alpha range; (f) potential physiological markers for clinical pain are feasible if EEG measures of noxious experience, albeit attention, arousal and anxiety are controlled, can be reliably identified and quantified; and, (g) both amplitude and intra-/interhemispheric coherence indices examined in this study may reflect differential processing of pain in brain.

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