Effect of peppermint and eucalyptus oil preparations on neurophysiological and experimental algesimetric headache parameters

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The effects of peppermint oil and eucalyptus oil preparations on neurophysiological, psychological and experimental algesimetric parameters were investigated in 32 healthy subjects in a double-blind, placebo-controlled, randomized cross-over design. Four different test preparations were applied to large areas of the forehead and temples using a small sponge and their effect was evaluated by comparing baseline and treatment measure. The combination of peppermint oil, eucalyptus oil and ethanol increased cognitive performance and had a muscle-relaxing and mentally relaxing effect, but had little influence on pain sensitivity. A significant analgesic effect with a reduction in sensitivity to headache was produced by a combination of peppermint oil and ethanol. The essential plant oil preparations often used in empiric medicine can thus be shown by laboratory tests to exert significant effects on mechanisms associated with the pathophysiology of headache. • *Cantingent negative variation, eucalyptus oil, experimental headache, exteroceptive suppression, mood states, peppermint oil*

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Essential oils such as peppermint oil and eucalyptus oil are present in a large number of medicaments for external application and have long been used in empirical and traditional medicine for the treatment of various pain conditions, including headache syndromes (1). Few studies have been carried out of the analgesic efficacy mechanisms of action of this form of therapy. The rationale for using essential oils to alleviate headache is based on several assumptions. Via peripheral mechanisms, essential oils could exert an analgesic effect by inhibiting the influx of nociceptive impulses due to afferent, segmental inhibition in the region of the posterior horns in accordance with the gate-control theory of pain (2). Owing to the additional stimulating central effect, efferent inhibition as a result of activation of endogenous anti-nociceptive mechanisms is also possible (3). The two effects could combine to produce an intrinsic analgesic effect of the essential oils. Assuming that such an intrinsic action exists, this should be observable in algesimetric human tests. In this study, therefore, the aim was to analyse the effects of essential oils on neurophysiological, psychological and experimental algesimetric parameters in a multidimensional approach using a double-blind, placebo-controlled randomized cross-over design. The study was to make use of methods designed to investigate headache mechanisms in earlier studies. Accordingly, contingent negative variation (4), EMG activity of pericranial muscles, and exteroceptive suppression of the temporal muscle (5-8) were investigated. To record possible changes in psychological factors, current mood states were measured on a standardized basis using the adjective list (9). The pain sensitivity of head structures was analysed by means of standardized recording of psychophysical stimulus-pain-functions for mechanical, thermal and ischaemic pain induction (10). The study addressed the question of whether the application of essential plant oil preparations to the skin of the head can exert effects on the above experimental headache measures.

Method

Subjects

The study was conducted on 32 healthy subjects with an average age of 25 ± 2.1 years (mean ± SD). Their average body weight was 77.2 ± 7.3 kg, their average height 176 ± 30.3 cm. To exclude the possibility of menstrual cycle effects, only men were included in the study. After being informed about the experimental procedure the subjects gave their consent to participating in the study. The personality characteristics of the subjects were recorded before the start of measurements using the Freiburg Personality Inventory (11); all were in the normal range. To rule out illness, a medical history was taken and a general and neurological examination was performed. Consumption of tobacco and alcohol was forbidden for 72 h before and 24 h after the test.

Inclusion and exclusion criteria

The inclusion criteria were as follows: healthy male subjects aged between 20 and 30 years, body weight not more than 10% above or below normal weight, physical examination findings normal, no serious prior illnesses, and voluntary written consent given. Any of the following criteria resulted in exclusion: more than 10 days with tension-type headache per year, other primary or secondary headache disorders, skin injuries or skin changes in the region of the forehead and temples, regular nicotine consumption, alcohol and drug abuse, taking of medicaments within 72 h of the start of the test, and basic diseases ascertained from the medical history. Headache occurring during the study disqualified subjects.

Medicaments

Four different test preparations were used (Table 1). Preparation 1 (LI1701) consisted of 10 g peppermint oil and 5 g eucalyptus oil plus ethanol 90% to 100 g; preparation 2 (LI1702) of 10 g peppermint oil and traces of eucalyptus oil plus ethanol 90% to 100 g; preparation 3 (LI1703) of traces of peppermint oil and 5 g eucalyptus oil plus ethanol 90% to 100 g; and preparation 4 (placebo) of traces of peppermint oil and traces of eucalyptus oil plus ethanol 90% to 100 g. The addition of traces of the substances to preparations 2, 3 and 4 was to prevent subjects distinguishing between the preparations by differences in smell.

Design

The test was conducted on a double-blind, placebo-controlled, randomized design with repeated measurements (fourfold cross-over). The four test preparations were administered individually on four test days according to a double-blind balancing plan (Latin squares), so that by the end of the study each test preparation had been tested with the same frequency on each of the four test days in order to exclude sequence effects. The treatment effects of the preparations tested were evaluated by comparing

Table I. **Composition of the four test preparations.**

	Peppermint oil	Eucalyptus oil	Ethanol 90%
Preparation 1 (LI1701)	10 g	5 g	ad 100 g
Preparation 2 (LI1702)	10 g	in traces	ad 100 g
Preparation 3 (LI1703)	in traces	5 g	ad 100 g
Preparation 4 (placebo)	in traces	in traces	ad 100 g

baseline and treatment measurements. To this end, a baseline measurement to determine the initial intensity of the relevant variables was made before each medication. Then the test preparation in question was applied to large areas of the skin of the forehead and temples for a period of 3 min using a small sponge. This application was made three times: immediately after, 15 min after, and 30 min after the baseline measurement. After 45 min the treatment effect was recorded by fresh measurement of the dependent variables. This interval was chosen because a clinical effect of the substances can generally be observed within this period. The question of whether the preparations in question could exert a significant effect on the dependent variables was investigated, and the extent of these effects was compared. The various methods were used in the order in which they are described below. Each subject received the four different test preparations on four different test days separated by at least one day without a test (wash out). The tests were scheduled to take place between 03.00 and 06.00 h to keep any possible influence of circadian rhythms on the dependent parameters constant.

Apparatus and measurement methods

EMG activity of temporal muscle under relaxation. After a 5 min relaxation period, the resting activity of the right temporal muscle was measured for 1 min with surface electrodes and the integral of the activity was determined with a Nihon Kohden neuropack 4.

Exteroceptive suppression periods of temporal muscle activity. In order to measure the exteroceptive suppression periods an electrical stimulus (20 mA, 0.2 ms) was applied to the right labial commissure and the EMG of the temporal muscle was measured during maximum contraction of the masticatory muscles. An early (ES1) and a late (ES2) suppression period were observed. The periods were defined as an 80% reduction in baseline EMG activity. Ten responses were registered at a stimulus frequency of 0.1 Hz, and the means of the latencies or durations were determined (for details of method see 6, 8).

Contingent negative variation (CNV). Spontaneous EEG (Cz-A1; referential monopolar lead) and binocular EOG were recorded with a time constant of 5 sec using Ag/AgC1 electrodes. A warning stimulus S1 (acoustic click for 50 ms) announced an imperative stimulus S2 appearing after 2 sec (15 Hz LED flash) which the subjects terminated by pressing a switch. The purpose of the additional measurement of EOG was to rule out artifacts due to eye movement. EEG and EOG were recorded triggered by the SI stimulus and the CNV was determined by taking the average of 30 runs. The time interval between indi-

vidual runs was varied between 10 and 30 sec on a randomized basis. CNV amplitude and CNV integral were determined using the difference between pre-S1 baseline level and 1800-2000 ms post-S1 level (for details of method see Schoenen and Timsit-Berthier [4]).

Sensitivity to experimentally induced pain. Three different pain stimuli were used for pain induction. Details of the methods have been described elsewhere (10) and are therefore only outlined briefly here. Pressure was exerted with a mechanical pressure algesimeter standardized to Cz. The circular pressure pad had a bearing surface area of 2.56 mm^2 and thus exerted a pressure of 2.6 Megapascal on the scalp. This pressure was not reported as painful until a few seconds had elapsed, an increasing pain intensity becoming very strong within about I min. The same stimulus was also applied to the middle phalanx of the middle finger of the right hand. The start of the stimulus was defined by the application of the pressure pad.

For thermal pain induction a 15 ohm ceramic resistance was used, to which a constant voltage of 4.5 volt was applied. The ceramic resistance was fixed to the forehead I cm above the root of the nose using an elastic band. The increasing resistance temperature induced pain of gradually increasing intensity, which became very strong within about 2 min. The start of the stimulus was defined by the application of the electrical voltage.

Blood circulation in the pericranial muscles was reduced by means of an inflatable collar which was placed around the cranium and inflated to 2O0 mm Hg. By rhythmically biting on a crib in time with a metronome (1 Hz) an increasing dull, oppressive headache on both sides was ischaemically induced in the pericranial musculature, and reached a strong intensity in approximately 3 min. The start of the stimulus was defined by inflation of the collar.

During experimental pain induction the subjects were seated in a chair with a headrest. A numeric scale from 0 to 50 was used to scale the experimentally induced pain intensity. This scale was also subdivided into the following verbal categories: 0 = no pain, 1-10 = very slight pain, 11-20 = slight pain, 21-30 = moderate pain, 31-40 = strong pain, and 41-50 = very strong pain. At the edge of the scale a pointer was attached which the subjects could slide to correspond to the continuously increasing pain intensity. The test was discontinued if the pointer reached 50. The position of the pointer was recorded as a function of time. The pain intensity for the pain threshold was operationally defined in terms of time by dividing the number of pain intensity units per category by the stimulus time necessary to induce it. (Unit: induced pain units per second, IPU/sec.) To arrive at a total score for supraliminal pain sensitivity, the scores of the five pain sensitivity ranges were added together [calculation: total score = (10/time taken to reach category limit 10) + (20/time taken to reach category limit 20) + (30/time taken to reach category limit 30) + (40/time taken to reach category limit 40) + (50/time taken to reach category limit 50)]. The larger the value of this quotient, the faster the pain intensity units were induced and hence the greater the pain sensitivity.

Current mood states. The subjects' current mood states were determined with the Janke and Debus (9) adjective list standardized in accordance with the instructions. The list covers 15 important aspects of current disposition using 60 items and makes it possible to describe them in quantitative terms.

Statistical analysis. Group averages were stated as arithmetic mean and standard deviation. To determine treatment effects the differences between base-line and treatment measurements were tested using the paired *t*-test.

Results

Effects on resting activity of temporal muscle

The combinations peppermint oil plus eucalyptus oil plus ethanol and peppermint oil plus ethanol resulted in a significant reduction in EMG surface activity of the temporal muscle (by 30.6% [$p < 0.001$] and 28.8% [$p < 0.001$] respectively) (Table 2). The combination of eucalyptus oil plus ethanol and ethanol alone produced no significant changes in EMG. The effect of the combination peppermint oil plus eucalyptus oil plus ethanol proved significantly greater than the effects of the combination eucalyptus oil plus ethanol ($p < 0.05$) and ethanol alone ($p < 0.001$).

Effects on duration of late exteroceptive suppression (ES2)

Only the combination peppermint oil plus ethanol produced a significant reduction (7%; $p < 0.05$) in the duration of ES2; the other preparations did not (Table 2). No significant differences were observed in the effects of the various combinations on the duration of ES2.

Effects on amplitude of contingent negative variation (CNV)

Only the combination peppermint oil plus eucalyptus oil plus ethanol brought a significant reduction in CNV amplitude (35.3%; $p < 0.05$) (Table 2). The effect of this combination proved to be considerably greater than the effects of the preparations

Table 2. **Arithmetic mean ± SD of neurophysiological measures before and after treatment**.

	Prep. 1 P + Eu + E	Prep. 2 P + E	Prep. 3 Eu + E	Prep. 4 E
Resting EMG temporal muscle (µV/sec)				
before	150.3 ± 84.3	156.3 ± 90.9	122.9 ± 64.1	125.5 ± 50.9
after	104 ± 66.0	111.3 ± 63.6	108.6 ± 71.9	112.3 ± 54.5
significance	***	***	ns	ns
ES2 duration (ms)				
before	41.5 ± 6.7	42.4 ± 8.2	41.9 ± 5.7	42.9 ± 6.9
after	41.3 ± 6.4	39.9 ± 6.5	40.1 ± 5.7	41.1 ± 4.7
significance	ns	*	ns	ns
CNV amplitude (µV)				
before	11.6 ± 7.9	9.9 ± 10.5	8.8 ± 7.3	10.4 ± 8.7
after	7.5 ± 6.6	10.2 ± 8.8	10.7 ± 9.0	9.9 ± 7.6
significance	*	ns	ns	ns

P: peppermint oil, Eu: eucalyptus oil, E: ethanol. Significance in *t*-test: ns: not significant; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

Table 3. **Arithmetical mean ± SDs of dimensions of current psychological mood states before and after treatment.**

	Prep. 1 P + Eu + E	Prep. 2 P + E	Prep. 3 Eu + E	Prep. 4 E
Performance-related activity				
before	-1.3 ± 2.5	- 1.0 ± 1.9	-0.58 ± 2.0	-0.62 ± 3.8
after	-0.28 ± 2.8	-1.2 ± 2.1	-0.77 ± 2.0	-0.96 ± 3.3
significance	***	ns	ns	ns
Inactivity				
before	4.2 ± 4.0	4.5 ± 3.5	5.5 ± 3.8	4.9 ± 3.6
after	4.1 ± 3.6	4.2 ± 3.6	4.7 ± 3.7	4.3 ± 3.5
significance	ns	ns	ns	ns
Extroversion/Introversion				
before	14.3 ± 3.4	14.8 ± 3.2	14.9 ± 3.1	15.3 ± 3.4
after	13.8 ± 2.9	14.6 ± 3.7	14.4 ± 3.3	15.0 ± 3.2
significance	ns	ns	ns	ns
Mood (well-being)				
before	12.5 ± 3.6	13.0 ± 3.5	13.0 ± 3.7	13.2 ± 3.7
after	12.1 ± 3.7	12.8 ± 3.6	13.7 ± 3.7	13.0 ± 3.8
significance	ns	ns	ns	ns
Emotional irritation				
before	7.1 ± 4.9	6.7 ± 3.6	6.9 ± 3.1	6.6 ± 3.8
after	6.1 ± 4.7	5.8 ± 3.7	6.4 ± 3.0	6.3 ± 3.7
significance	*	***	ns	ns
Timidity/depression				
before	2.2 ± 2.9	2.0 ± 3.6	2.3 ± 4.1	1.8 ± 3.2
after	2.0 ± 2.9	1.6 ± 3.6	2.1 ± 3.7	1.5 ± 3.1
significance	ns	ns	ns	ns
Dreaminess				
before	2.6 ± 2.1	2.9 ± 2.4	3.0 ± 2.5	3.1 ± 2.6
after	2.5 ± 2.0	2.3 ± 2.0	2.8 ± 2.2	3.0 ± 2.4
significance	ns	ns	ns	ns

P: peppermint oil; Eu: eucalyptus oil; E: ethanol. Significance in *t*-test: ns - not significant; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

peppermint oil plus ethanol ($p < 0.05$) and eucalyptus oil plus ethanol ($p < 0.05$).

Effects on dimensions of current mood states

The dimension performance-related activity, formed by the attributes activity and concentration, was statistically significantly increased by 78% ($p < 0.001$) with the combination of peppermint oil plus eucalyptus oil plus ethanol (Table 3). The effect of this combination was also significantly greater than the effects of the other combinations. The dimension emotional irritation, comprising the characteristics excitability, sensitivity, and annoyance, was statistically significantly reduced by 14% ($p < 0.05$) with the combination peppermint oil plus eucalyptus oil plus ethanol, and by 13.4% ($p < 0.01$) with peppermint oil plus ethanol (Table 3). The other preparations had no effects, and no significant differences were found between the effects of the four preparations.

Effects on experimental pain sensitivity parameters

Experimental pain sensitivity to pressure stimuli on the middle phalanx of the middle finger and on the head (Cz) was not significantly altered by any of the four preparations investigated (Table 4). Experimental pain sensitivity to a head stimulus was diminished by the three preparations containing essential oils, but only the combination peppermint oil plus ethanol produced a statistically significant reduction of 40.3% ($p < 0.001$), while the other two oil preparations had no effect. Ethanol alone, unlike all other preparations, caused a significant increase of 38.9% ($p < 0.05$) in thermal pain sensitivity. This sensitization was not present when the three oil preparations were applied, which resulted in significant differences between the effect of ethanol and that of the other preparations. Pain sensitivity to experimental ischaemia of the pericranial musculature was significantly reduced (by 27%; $p < 0.01$) with the combination peppermint oil plus ethanol, whereas the other three preparations produced no significant differences (Table 4). The differences between the effects of the four preparations were not significant.

Discussion

This study examines the effects of different essential oil preparations on neurophysiological, psychological, and experimental algesimetric parameters in humans. The dependent variables used have proved to be closely associated with headache mechanisms. Increased tension of the pericranial musculature with increased surface EMG activity levels is described as a concomitant symptom of tension-type headache, though there is also some evidence of increased pericranial muscle activity in migraine patients as well (12). More recent studies report reduced or non-existent late exteroceptive suppression of temporalis muscle activity (ES2) in cases of chronic tension-type headache putatively as an expression of faulty serotonin mediated muscular inhibition (5, 10). Contingent negative variation (CNV) displays significantly increased amplitude in patients with migraine without aura by contrast with healthy control subjects (4).

Table 4. **Arithmetical mean ± SD of experimental algesimetric parameters before and after treatment. Unit: induced pain units per second.**

	Prep. 1 P + Eu + E	Prep. 2 P + E	Prep. 3 Eu + E	Prep. 4 E
Pressure stimulus hand				
before	1.2 ± 0.80	1.2 ± 1.0	1.2 ± 1.1	1.2 ± 0.81
after	1.5 ± 1.7	1.3 ± 0.81	1.3 ± 1.4	1.1 ± 0.74
significance	ns	ns	ns	ns
Pressure stimulus head Cz				
before	1.4 ± 1.1	1.2 ± 1.0	1.2 ± 1.0	1.2 ± 0.90
after	1.2 ± 1.0	1.2 ± 1.0	1.2 ± 1.1	1.1 ± 0.84
significance	ns	ns	ns	ns
Heat stimulus forehead				
before	0.165 ± 0.20	0.196 ± 0.22	0.181 ± 0.18	0. 159 ± 0.20
after	0.139 ± 0.19	0.1174 ± 0.16	0.124 ± 0.16	0.221 ± 0.24
significance	ns	***	ns	*
Ischaemic stimulus head				
before	2.6 ± 2.2	3.3 ± 3.0	2.7 ± 1.9	2.7 ± 2.6
after	2.4 ± 2.3	2.4 ± 2.1	2.3 ± 2.2	2.3 ± 2.2
significance	ns	**	ns	ns

P: peppermint oil; Eu: eucalyptus oil; E: ethanol. Significance in *t*-test: ns - not significant; * p £ 0.05; ** p £ 0.01; *** p £ 0.001.

Table 5. **Synopsis of effects of essential oil preparations on experimental headache mechanisms.**

	Prep. 1 LI1701 P + Eu + E	Prep. 2 LI1702 P + E	Prep. 3 LI1703 Eu + E	Prep. 4 Placebo E
Neurophysiology				
Relaxation pericranial muscles	‾‾ ‾ (3,4)	‾‾‾	-	-
Duration ES2	-	‾	-	-
Contingent negative variation	‾ (2,3)	-	-	-
Mood states				
Performance-related activity	--- (2,3,4)	-	-	-
Inactivity	-	-	-	-
Extraversion/introversion	-	-	-	-
Mood (well-being)	-	-	-	-
Emotional irritation	‾	‾‾‾	-	-
Timidity/depression	-	-	-	-
Dreaminess	-	-	-	-
Algesimetry				
Pressure, hand	-	-	-	-
Pressure, head	-	-	-	-
Heat, head	-	‾‾‾	-	- (1,2,3)
ischaemia, head	-	‾‾	-	-

No significant effect; - : increase (p £ 0.05); ---: increase (p £ 0.001); ‾: decrease (p £ 0.05); ‾‾‾ : decrease (p £ 0.01); : decrease (p £ 0.001). The figures in parentheses indicate significant differences in effects compared with the preparations stated. P: peppermint oil; Eu: eucalyptus oil; E: ethanol.

This has been interpreted as an expression of dopaminergic or noradrenergic hyperactivity. An association between mood and the triggering and maintenance of pain is well documented (10). When various pain stimuli are employed as in this study, experimental pain sensitivity measures can provide direct information about the effects of the substances used on nociceptive mechanisms.

When oil preparations were externally applied to the head in our study, there were statistically significant effects on several of the dependent variables described. An overview of the results is given in Table 5. The application of eucalyptus oil alone had no effects. The same was the case for ethanol alone, except that there was significant sensitization to thermal pain stimuli. This was counteracted by the oil preparations tested.

The effects of the combination peppermint oil, eucalyptus oil, and ethanol were significantly superior to other preparations for the parameters pericranial muscle relaxation, contingent negative variation, and performance-oriented activity. This combination by a muscle-relaxing and mentally relaxing effect can increase cognitive performance, but has little influence on pain sensitivity. The greatest effects on the reduction of pain sensitivity, by contrast, were exerted by the combination peppermint oil and ethanol.

The mode of action of the essential oil preparations tested is of interest, but few studies exist to date. In a human test with a combination of 10 g peppermint oil, 5 g eucalyptus oil, 5 g natural menthol and ethanol 90% to 100 g, a long-lasting cooling effect was shown as a result of long-term activation of cold fibres in the skin which could be differentiated from the physical effect resulting from the heat of evaporation (13). Possibly the rough ascending inhibition (2), the cold stimuli transmitted by the A-d fibres reduces pain information transmitted by the C fibres. In addition to this neurophysiological action, increased skin blood flow may occur, as is the case for external use of the menthol present in peppermint oil (1). The effects on contingent negative variation described in our study indicate that there could be an influence on central noradrenergic activity.

The reduction in ES2 corresponds to a peripheral conditioning of the brainstem reflex that is invoked on exposure to external stimuli and peripheral anaesthesia of the stimulus side at the lips. If in addition to the triggering stimulus continuous electrical stimuli are applied to the periphery or the CNS is stimulated electromagnetically there is a reduction in ES2 as the conditioning stimuli increase (4). These effects are seen in association with an influence on the central serotoninergic system (5, 7). The changes in current mood states with increasing performance-related activity and decreasing emotional irritability point to CNS effects of the essential oil preparations.

References

1. Saller R, Hellstein A, Hellenbrecht D. Klinische Pharmakologie und therapeutische Anwendung yon Cineol (Eukalyptusöl) und menthol als Bestandteil atherischer Öle. Internistische Praxis 1988;28:355-64

2. Melzack R, Wall P. Pain mechanisms: a new theory. Science 1966:150:971-9

3. Fields HL, Basbaum AI. Brain stem control of spinal pain-transmission neurons. Annu Rev Physiol 1978;40:217-248

4. Schoenen J, Timsit-Berthier M. Contingent negative variation: methods and potential interest in headache. Cephalalgia 1993;13:28-32

5. Schoenen J, Jamart B, Gerard P, Lenarduzzi P, Delwaide P. Exteroceptive suppression of temporalis muscle activity in chronic headache. Neurology 1987;37:1834-6

6. Schoenen J. Exteroceptive suppression of temporalis muscle activity: methodological and physiological aspects. Cephalalgia 1993;13:3-11

7. Göbel H, Dworschak M, Wallasch TM. Exteroceptive suppression of temporalis muscle activity: perspectives in headache and pain research. Cephalalgia 1993;13:15-19

8. Göbel H, Schoenen J. Exteroceptive suppression of temporalis muscle activity. Discussion summary. Cephalalgia 1993; 13:20

9. Janke W, Debus G. Die Eigenschaftswörterliste. Göttingen, Toronto, Zürich: Hogrefe, 1984

10. Göbel H. Schmerzmessung. Theorie, Methodik, Anwendungen bei Kopfschmerz. Stuttgart, Jena, New York: Gustav Fischer, 1992

11. Fahrenberg J, Selg H, Hampel R. Freiburger Persönlickeitsinventar. Göttingen: Hogrefe, 1973

12. Bischoff C. Wahrnehmung der Muskelspannung. Göttingen, Toronto, Zürich: Hogrefe, 1989

13. Bromm B. Gutachten zum Nachweis einer physiologischen Wirkung von Euminz. Research Report, Department of Physiology, University of Hamburg, Hamburg, 1990

14. Rassmussen BK, Jensen R, Schroll M, Olesen J. Epidemiology of headache in a general population-a prevalence study. J Clin Epidemiol 1991;44:1147-57