Summary

Pain thresholds through thermal stimulation are determined in patients with a chronic pain syndrome of different etiology and a healthy control group. For this purpose, heat is applied to the skin of the hand and lower arm at 5 different points using a modified Marstock thermode.

The threshold values of pain sensation on heat stimulation show good intraindividual reproducibility and are independent of age, sex and time of the day. The pain patients do reach significantly higher thermal pain thresholds but also rate their intensity higher than healthy subjects on a visual analog scale. As the expression of increased sympathetic activity, pain patients show a vasoconstriction that is manifested in the form of a lower skin temperature. Right-handed subjects display significantly higher threshold values on the dominant side of the body irrespective of their sex.

Pain patients differ only negligibly from healthy test subjects with respect to their depressiveness (Beck's depression inventory). The threshold elevations for painful thermal stimuli in chronic pain syndromes are probably the expression of central inhibitory mechanisms; an altered reaction pattern of the sympathetic nervous system is also evident.

Pain threshold measurements are based on the algesimetric methods; some fundamental remarks will thus be made on this topic.

A distinction is drawn between objective algesimetry, which examines involuntary reactions triggered by nociceptive stimuli (e.g., reflexes), and subjective algesimetry, which covers conscious and voluntary responses to pain. The latter may be regarded as a special area of psychophysics. This interdisciplinary field composed of physiology and psychology primarily attempts to measure sensation thresholds. One experimental approach consists in the registration of diverse threshold values, whereby the following parameters are defined (70):

- Pain threshold: the stimulus intensity at which pain just becomes perceptible.
- Intervention threshold: the pain intensity at which the test subject would seek treatment if the pain did not occur in the laboratory but in daily life ("drug request point").
- Pain tolerance threshold: the point at which the pain becomes so strong that the test person demands a termination of the stimulus.
- Pain sensitivity range: the difference between the pain threshold and the tolerance limit.
- Difference threshold: that difference in stimulus intensity at which an interval can just barely be perceived between two pain stimuli (Hardy's DOL scale).

Some stimulus methods hitherto applied for determining thermal threshold values are listed in the following. Radiation heat induced by an infrared source (Hardy 1952) or a halogen lamp (Beck et al. 1974), Hiedl et al. 1979) excites to functional activity a homogeneous nociceptor population of the skin without concomitant stimulation of mechanical afferences. Contact thermodes that are fluid-perfused or equipped with Peltier elements and differ in their stimulus surface can also be used to produce a heat stimulus (12, 13, 14, 21, 28, 39, 49, 59, 63, 66).

One problem encountered in pain measurement is the inadequate comparability between clinical and experimentally induced pain (43, 62). The latter is controllable by intensity adjustment and the possibility of intervention and thus lacks the characteristic elements of clinical pain that play a central role in the subjective pain perception of the person affected, as, for example, fear and helplessness. The fact that adequate quantification is hampered by the multidimensionality of the pain process represents a further problem involved in algesimetry. The validity of experimental pain measurement is therefore difficult to determine (33).

The aim of the present study is to standardize an algesimetric method for threshold-value determination in thermic stimulation and to subsequently verify its validity in a group of test subjects. A modified Peltier thermode was used for heat stimulation. With the aid of standardized stimulus patterns, experimental pain is to be generated which can then be measured according to meaningful psycho-physical criteria and checked for reproducibility.

METHODS AND TEST SUBJECTS

The group of test subjects (n = 48) was divided as follows: 32 subjectively healthy persons (18 males, 14 females) without neurological symptoms or psychiatric irregularities (test with Beck's depression inventory) ranging in age from 21 to 46 years; 16 patients (9 males, 7 females) who had been suffering from chronic pain conditions for at least 6 months and who were instructed to take no analgetics or only low doses of peripherally acting types for at least 5 days prior to measurement. These patients suffered from: low-back syndrome (3), cervical syndrome (2), phantom pain of the upper extremity (2), phantom pain of the lower extremity (1), trigeminal neuralgia (2), zoster neuralgia (1), intercostal neuralgia (1), rupture of the brachial plexus (1), syringomyelia (1), severe osteoporosis (1), headaches of the tension type (1).

Classification of handedness:
The test person is classified as right- or left-handed if the same hand is used to write, throw a ball and use a hammer and as ambidextrous if this is not the case.

The stimulating device is equipped with a Peltier element consisting of semiconductor components that build up a temperature difference between the upper and lower thermode side as soon as it is connected to a power source. On the back of the stimulator, there is a metal block perfused with water drawn from a water bath (volume 1 l; room temperature at 22 ± 2°C) by means of an electropump and tubing system. This allows the stimulation surface (2 x 2 cm) to be either cooled or heated depending on the flow direction. Temperature is measured with the aid of a thermoelement (iron-constantan) fixed in the center of the thermode. The measuring range is 0-99.9°C; the display offers a precision of 0.1°C. The analog ports of the interface yield 100 mV / °C. With digital control, the function generator produces, through a D/A transducer via a time function (rectangle, slope), an amplitude in the 0-9.99 V range with the corresponding start impulses. Thus the thermode offers the possibility of both achieving a linear temperature increase at variable speeds and maintaining a particular temperature value for any given time. The specified functions may be controlled either with the keyboard on the device or via an external trigger pulse. The value of the digital display can be stored by a holding signal and recorded via the analog ports.

Based on the criterion of rapid and direct accessibility, five measuring points were selected on the hand and lower arm which permit as plane as possible a contact of the thermode surface in order to achieve an equivalent energy release into the tissue at all points: tabatière anatomique, thenar, hypothenar, volar wrist joint and medial elbow. Left and right stimulation was done in each case so that a statement could be made about possible lateralization of the pain sensation.

Recording of the measured values is carried out via the analog ports of the stimulators after interpositioning an analog/digital transducer online in a personal computer. The 100 data of each session were recalled in the order of the measuring points and subsequently transferred into a statistics program (ANOVA) for evaluation.

The room temperature is kept constant at 22 ± 2°C throughout the experiment. The test subject sits opposite the investigator with forearms extended towards him on a small table. The thermode is now applied to the respective skin areas with a pressure kept as constant as possible and only slightly exceeding its own weight. Finally, heating is begun at an initial temperature of 35°C and an increase rate of 1°C/sec. As soon as the test person has reached his "pain threshold" (instruction to intervene at the transition from the sensation "hot" to the sensation "just barely painful"), he can interrupt the stimulus by pressing a button. The thermode is then removed immediately and placed on the next measuring point, while, in the intervening period (about 4 sec), the temperature will have returned to the initial value of 35°C. At one session, each of the ten measuring sites is stimulated ten times, thus yielding ten runs with ten test values each. The sequence is specified by the computer in a randomized manner under the

additional condition that at least four measuring points of another localization are selected between the same measuring sites in order to avoid an immediate stimulus repetition. Before and after each session, the skin temperature is measured in the stimulated areas as well as on the finger pad of digitus III and on the forearm as reference points in order, on the one hand, to be able to detect pathological processes with regard to the circulation and, on the other, to obtain information on the sympathetic activity.
The intraindividual range of variation and the circadian rhythm were checked by measuring the test subjects at three different times with different intervals and times of the day.

For each of the 10 measuring points, the descriptive parameters arithmetic mean value, standard deviation, variance, etc. are intraindividually calculated for each session. From the respective mean values of the individual test subjects, the statistical values are calculated for the interindividual comparison. The comparative statistics (variance analysis, t-test, correlation, etc.) are done using the corresponding programs (e.g., ANOVA).

RESULTS

1. Healthy test subjects

Inter- and intraindividual observations. The pain threshold measurements in 32 test persons (18 males, 14 females) ranging in age from 21 to 46 years ($x = 27.9$, $SD = 5.6$ years) are shown in Table 1 and Figure 1.

A noteworthy finding was the highly significant ($p \geq 0.0001$) difference between the pain thresholds of the individual measuring points with the exception of the tabatière anatomique and the thenar ($p = 0.732$). The elbow and wrist joint have the highest sensitivity in contrast to the distally situated areas (tabatière anatomique, thenar, hypothenar), which display the highest threshold values. The latter also show the greatest variance, whereas the test data of the proximal points deviate the least. Male and female test subjects did not differ significantly ($p = 0.8342$) with respect to their mean threshold values ($x_{males} = 51.78°C \pm 0.92$; $x_{females} = 51.68°C \pm 1.32$).

The two groups ($n = 8$ in each) exhibited no significant differences ($p = 0.4022$) in the pain thresholds ($x_{morning} = 51.36°C \pm 1.12$; $x_{afternoon} = 51.77°C \pm 0.76$). A significant change in the pain thresholds through different intervals between the 3 sessions was not detectable ($p = 0.5450$; $x_{short} = 51.77°C \pm 0.76$; $x_{long} = 52.08°C \pm 1.22$). An age dependence of the pain threshold cannot be demonstrated. The correlation for the pair of values (age / cross-sectional value) is r = - 0.09 (Fig. 2).

The temporal course of the measurements (Fig. 3) shows a distinct habituation of the pain sensation after 10 min. The first two runs of each session are 2°C lower on the average than the values of runs 3-10. Only 3 of the 32 test subjects evidenced significant differences on the 95% level between the 3 sessions at maximally 2 of 5 skin points in each case.

The wrist joint and elbow show the lowest intraindividual variations; the hypothenar, on the other hand, deviates most. No significant differences in cross-sectional values can be demonstrated between male and female test subjects (x_{males} = 0.76°C ± 0.12; $x_{females}$ = 0.77°C ± 0.11; p = 0.93). Morning and afternoon measurements show no standard deviations that differ significantly (p = 0.4862; $x_{morning}$ = 0.79°C ± 0.11; $x_{afternoon}$ = 0.74°C ± 0.13). Different session intervals do not significantly affect the intraindividual variations (p = 0.5879; x_{short} = 0.74°C ± 0.13; x_{long} = 0.77°C ± 0.11). The variation of test values is likewise independent of age. The correlation (age / cross-sectional value of SD) is r = - 0.15.

Subjective pain assessment. With the VAS applied here, the pain intensity was specified numerically in a range from 0 (no pain) to 10 (unbearable pain). Here the test persons gave ratings from 2 to 6 ($x_{controls} = 3.71$, SD = 1.27). This evaluation discloses no differences between the sexes ($x_{males} = 3.77 \pm 1.30$; $x_{females} = 3.64 \pm 1.29$; $p = 0.80$). The assessment based on the VAS does not permit any conclusion to be made about the threshold values reached. The correlation (scale value VAS / cross-sectional value of the pain thresholds) is $r = 0.17$ (Fig. 4). The examined collective showed no age-dependence in the pain rating ($r = -0.22$). The p-values for the correlation coefficients are, in each case, ≥ 0.05.

For the verbal description of the pain quality, a ranking list was set up according to the frequency of the designations (multiple designations possible): burning (14), hot (12), stabbing (8), sharp (7), limited (5), dragging (4), pricking (3), biting (3), light (2), superficial (2), circumscribed (2), diffuse (2), creeping (1), enjoyable (1).

Skin temperatures. There are no significant sex differences in the cross-sectional values of the initial temperature: $x_{males} = 28.17 \pm 1.97$, $x_{females} = 27.38 \pm 1.80$; $p = 0.2984$ (Fig. 5). It is not possible to demonstrate a dependence of the heat pain thresholds on the initial temperature prior to the start of stimulation ($r = -0.17$; $p \geq 0.05$), see Fig. 6.

Temperature differences before and after stimulation. The cross-sectional values of the skin-temperature differences (Δ T) between stimulated and nonstimulated skin areas differed significantly by 0.95°C ($p \leq 0.0001$) in favor of the stimulated regions (Table 2). Though male and female test subjects show no significant differences, females tend more towards cooling at the nonstimulated measuring points ($p_{stimulated} = 0.82$; $p_{nonstimulated} = 0.15$). The measured temperature differences are not dependent on the pain thresholds reached. The correlation (cross-sectional value of the pain threshold /cross-sectional value of Δ T) yields $r_{stimulated} = -0.04$ and $r_{nonstimulated} = 0.42$ for the stimulated and non-stimulated areas respectively. The subjective pain evaluation of the test persons on the VAS is reflected to an equally low degree in the measured skin temperatures. The correlation (scale value VAS / cross-sectional value Δ T) is $r_{stimulated} = 0.29$ and $r_{nonstimulated} = 0.28$ for the stimulated and non-stimulated areas respectively. Valid for all coefficients is $p \geq 0.05$.

A close negative correlation ($r = - 0.59$; $p \leq 0.001$) is displayed by the initial temperature prior to the start of stimulation and the temperature increase at the stimulated measuring points at the end of the session (Fig. 7).

Pain lateralization. Pain thresholds of the corresponding measuring points are evaluated as left- and right-lateralized if they differ significantly (criterion : $p \leq 0.01$, t-test) and as indifferent if they do not (Fig. 8).

Altogether, 42% of the measuring points can be regarded as indifferent in right-handed subjects, while significantly higher thresholds are found for 36% on the right and 22% on the left. If the regions are considered individually, however, it is noteworthy that three loci (tabatière anatomique, thenar and hypothenar) have an above-average frequency of right lateralization; the wrist joint and elbow evidence the same irregularity to the left (Fig. 9). These results are both age- and sex-independent ($p = 0.7130$ and $p = 0.9027$ respectively).

In the group of ambidextrous subjects, there are more measuring points lateralized to the left (33.3%) than to the right (26.7%), while 40% show no lateral preponderance. Left-handedness is associated with a continued trend to the left (43.3%); see Fig. 8.

The above observation that the three distal measuring points (tabatière anatomique, thenar and hypothenar) differ distinctively from the wrist joint and elbow with respect to lateralization in right-handed subjects proved to be significant ($p \leq 0.0135$) in the variance analysis (ANOVA). On the other hand, the individual measuring points do not differ significantly in either the ambidextrous ($p \geq 0.1218$) or the left-handed ($p \geq 0.2094$) subjects (Table 3).

Beck's depression inventory (BDI)

The depression profile (Table 4) of the healthy test subjects showed no significant sex difference ($x_{males} = 8.88 \pm 3.40$ vs. $x_{females} = 10.44 \pm 4.16$; $p = 0.4113$). Individual items do, however, evidence significant differences at the 5% level: lack of appetite, weight loss and reduced concentration power show higher values in women, while men frequently report a reduced enjoyment of life. Crying tended to gain more points with greater frequency among female test subjects ($p = 0.1236$), whereas social isolation affected the men more often ($p = 0.1857$). The total BDI score is independent of age in the examined population ($r = - 0.25$) and shows no correlation to either the heat pain threshold ($r = - 0.09$) or the VAS scale ($r = -0.04$); the p values are ≥ 0.05 in each case.

2. Chronic pain patients

Inter- and intraindividual observations. 16 patients (9 males; 7 females), aged 29 - 78 years ($x = 48.0$, $SD = 9.4$ years), who suffered from a chronic pain syndrom evidenced a pain-threshold distribution as depicted in Fig. 10. The mean cross-sectional value of the pain thresholds is significantly increased ($p = 0.0169$) by 1.07°C compared to healthy controls. At the individual measuring points, the tabatière anatomique, thenar and hypothenar differ in favor of pain patients at the 95% significance level; the elbow ($p = 0.0719$) and wrist joint ($p = 0.3453$) show only a tendency towards higher values.

Between the 3 sessions, significant changes at the 95% level are found in 3 patients and at maximally 2 of the 5 measuring points in each case. The mean values of the standard deviations compared to healthy subjects are shown in Fig. 11: the mean cross-sectional value of the standard deviations is significantly increased ($p \leq 0.0001$) by 0.29°C in the chronic pain patients.

Subjective pain assessment. Chronic pain patients tend to give higher intervention points on the VAS than healthy controls ($x_{pain\ pat.} = 4.60 \pm 1.41$; $p = 0.0935$); see Fig. 12. In this connection, the assessment is significantly higher ($p = 0.0187$) in female than in male pain patients ($x_{females} = 5.14 \pm 1.11$, $x_{males} = 3.83 \pm 0.87$). Clinical pain is rated significantly higher ($p \leq 0.0001$) by the patients than experimental heat pain: $x_{clinical} = 6.91 \pm 1.27$; $x_{heat} = 4.60 \pm 1.41$. The correlation between the VAS ratings of the clinical and heat pain is very close ($r = 0.94$). The verbal assessments are comparatively limited: hot (9), burning (7), sharp (3), diffuse (2), dragging (1).

Skin temperatures. The initial temperatures of healthy controls and pain patients do not differ significantly: $x_{controls}$ = 27.77°C $\pm$ 1.89, $x_{pain\ pat.}$ = 27.12°C $\pm$ 1.06, $p = 0.3169$.

The cross-sectional value of ΔT for stimulated areas does not differ significantly in pain patients from that in healthy controls ($x_{controls}$ = 1.62°C $\pm$ 0.66, $x_{pain\ pat.}$ = 1.91°C $\pm$ 0.83, $p = 0.3208$); Fig. 13. However, there is a distinct significance for the nonstimulated reference points: $x_{controls}$ = 0.63°C $\pm$ 0.53, $x_{pain\ pat.}$ = 0.12°C $\pm$ 1.08, p = 0.0374. Consideration of the temperature span widths ($T_{stim.}$ - $T_{n.stim.}$) of 0.99°C in healthy controls and 1.79°C in patients discloses an even higher significance level (p = 0.0028).

Pain lateralization. Only the hypothenar and the elbow differ significantly (p = 0.0284), while the p values $\geq$ 0.1232 at the other measuring sites. However, no significant differences from healthy right-handed subjects are found in the lateralization (p = 0.3247).

Beck's depression inventory. The pain patients differ immaterially from the healthy controls in their depression profile ($x_{pain\ pat.}$ = 10.86 $\pm$ 2.97, $x_{controls}$ = 9.71 $\pm$ 3.79; p = 0.4818). Significant differences with higher point values in the patients are found for the following items: reduced enjoyment of life, reduced concentration power and loss of libido. Interestingly, the total score for these at r = - 0.75 shows a good negative correlation to the pain threshold; i.e., the higher the depression profile, the lower the threshold value reached. There is no relation to the assessment on the VAS (r = 0.22). Evidently there appears to be an increase in depressiveness among pain patients as they grow older (r = 0.64).

DISCUSSION

1. Healthy subjects

Three different techniques have thus far been applied for the application of thermic nociceptor stimuli in algesimetry: radiation heat (e.g., halogen lamp, infrared source) (13, 31, 32, 45, 48), contact thermodes (e.g., Peltier element) (13, 14, 15, 21, 39, 49, 59, 63, 66) and laser stimuli (60).

There are several measured variables for specifying the pain threshold: 1. the period of time at constant heat application or skin temperature, 2. the amount of energy per area of the stimulated zone and 3. the skin temperature. The latter appears most useful for practical reasons and has in the meantime also been given preference by most authors. A further obstacle to the comparability of the heat pain thresholds reported in the literature is the difference in experimental conditions with the variability of three decisive influence parameters: stimulus site, application surface and stimulation rate. Chart 1 gives a brief summary of this.
The choice of different measuring points alone under otherwise identical experimental conditions results in variations of up to 11.5°C (low back: 42.2°C, heel: 53.7°C) (32). Different stimulation rates (0.3 - 2.0°C/sec) give rise to threshold values of 46.9 - 50.3°C at the same stimulation site. Furthermore, stimulus surfaces of 0.96 - 12.5 cm^2 hamper the comparability. The greatest influence on the variability of

sensory thresholds (thermal and mechanical), however, appears to be exerted by central mechanisms - e.g., the psychological variability (51).

Our results with a mean heat pain threshold of 51.88°C for the thenar are most comparable to those of Croze (13, 14), who describes values of 47.9 and 49.2°C at a stimulation rate of 0.8 and 1.4°C/sec and an application surface of 6.5 cm^2 (contact thermode). The wide interindividual variations of 32 - 50°C and the mean pain threshold of about 40°C on the thenar found by Fruhstorfer are striking. His procedure offers a possible explanation: he determines the heat pain thresholds directly subsequent to the cold pain thresholds and repetitive stimulation up to ten times at the same measuring point. Here temperatures partially ranged to about 10°C, so that, on subsequent heat stimulation, pain perception could already start several degrees earlier. To my knowledge, no study thus far has investigated the influence of the initial skin temperature on the heat pain thresholds under such wide temperature variations. Moreover, some authors report a slight decrease of threshold values on repeated thermal stimulation. After electric tooth stimulation, on the other hand, there is a reduction of pain sensitivity on repetitive stimulation (19). A compilation of the effects on the pain threshold with different influence factors is presented in Chart 2.

The fact that pain thresholds apparently vary to a considerable degree at different skin areas is primarily explained by partially marked variations in the density of nociceptors (35). Further influence factors are the tissue quality (hairy or hairless skin)(44) and the perspiration rate (55), whereas the cutaneous circulation is reported to exert no influence on the threshold values (15, 48).

Göbel et al. (23) describe a highly significant ($p = 0.008$) sex difference in experimentally induced headache, women reaching their pain thresholds considerably earlier. Levy (46) and Severin (63), on the other hand, report no significant sex differences ($p = 0.7$ and $p = 0.92$) for heat pain thresholds. Our results also substantiate the latter investigations ($p = 0.92$).

A number of studies have already addressed the question as to the existence of a circadian rhythm of pain sensitivity. A survey is presented by Göbel (23): some authors report significant circadian variations in the pain threshold, mostly with a maximum in the early morning hours and a minimum in the evening (62). Other groups (54, 66) found no circadian dependence. Our measurements, performed comparatively in the morning and afternoon, disclosed no significant differences.

The training effect with regard to the pain thresholds reached is likewise discussed controversially. For the ischemia pain test (27), a slight tendency towards tolerance of painful stimuli has been reported, but a space of twice 2 weeks was chosen in each case without comparison to shorter intervals.

Our results show no noteworthy differences between the session intervals (2 days vs. 2 weeks).

Some authors report that the pain thresholds after heat stimulation increase with age; they explain this phenomenon by a progressive reduction of the nerve fibers and/or a decrease of nociceptors per nerve fiber (35, 46, 62). Our results confirm those of Fruhstorfer, who was not able to demonstrate a significant correlation with age (29), but only a restricted statement is possible due to the narrow age distribution of our group.

Lynn (48) gets mean standard deviations of 1.2 - 1.7°C when using radiation heat. Fruhstorfer (29) also reports good intraindividual reproducibility using the Marstock method, but without giving precise information. With a mean scattering of values from 0.68°C (wrist joint) to 0.90°C (hypothenar), our investigations likewise show very slight variations. The variance of the intraindividual pain thresholds is independent of sex, age, and session intervals and evidences no differences between morning and afternoon sessions. There is thus far only little data in the literature regarding these connections. Fagius found a positive correlation of the standard deviation with the age (20). On repeated stimulation of a measuring point at intervals of at least 4 minutes, the first three stimulations are followed by a distinct habituation of the pain perception in the form of a pain-threshold increase (also see Fig. 3). The threshold values of the next 7 stimulations scatter very narrowly, however, so that there is no question of either a habituation or a sensibilization of the nociceptor perception.

The visual analog scale (VAS) is an instrument for measuring pain intensity that distinguishes itself by temporal reliability and low variance in the face of psychomotor factors and has in the meantime become established in algesimetry (17, 27, 36, 41, 61). The objection may be raised that, in determining the pain threshold, the intensity rating of the test subjects will, by definition, probably only range between 0 and perhaps 10% of the maximal value. Since the definition of the pain threshold is very difficult and, in addition, a subjective experience, test subjects rate the beginning of pain perception very differently. The following explanations are necessary here. For most test subjects, heat pain is made up of two components: it is first perceived as a slightly stabbing pain with a rather superficial character, followed by a burning quality after one to two seconds. This phenomenon is described by many authors and loses some of its significance on stimulation of proximal skin sites (6, 7). In the evaluation of the test person, this "double pain" is rated higher on the affective-emotional reaction level than at the time the pain threshold was first indicated by pressing a button. This renders the mean intensity rating of 37% somewhat more understandable. Women and men did not differ here in their scoring behavior ($p = 0.80$). The ratings on the VAS are independent of age ($r = -0.22$) and of the pain thresholds reached ($r = 0.17$), i.e. a test subject with a high threshold value has not necessarily marked this in the upper range of the VAS.

The gradations in characterizing pain intensity are influenced by many factors (education, culture, ethnic background (53), etc.), and, in addition, verbal pain description possesses only low sensitivity (5, 22, 26). Various verbal assessment scales and pain questionnaires have been developed in the meantime, the most widely applied being the McGill Pain Questionnaire introduced by Melzack in 1975. For the description of experimentally induced pain, such questionnaires play a subordinate role, since, compared to clinical pain, they possess a more circumscribed character of less far-reaching consequences. Nevertheless, the listing of quality designations by the test subjects (see page 26) discloses a wide spectrum.

The influence of the initial skin temperature on the thermic stimulation was examined by several groups (15, 33). Hardy (31) reports decreasing heat pain thresholds with increasing skin temperature. With initial temperatures of 25°C and 39°C, Croze (15) found no effect on the threshold values. Our measurements with mean skin temperatures within the range of 23° to 31°C showed no correlation ($r = 0.17$) with the the pain thresholds. Women had a slightly lower initial temperature than the men (27.38°C vs. 28.17°C).

There has been little data in the literature thus far on comparative measurements of skin temperature before and after heat stimulation. Within the framework of microneurographic studies in healthy subjects, Blumberg (30) found that distinctly noxic heat stimulation (score on the VAS at least 50%) leads to activation of sympathetic vasoconstrictor neurons followed by a cutaneous vessel constriction - and thus to a reduction of the skin temperature. Our heat-stimulation results with a significantly higher (0.95°C, $p \leq 0.0001$) temperature increase in the stimulated skin areas (1.62°C) than at the nonstimulated measuring points still fail to demonstrate a sympathetic influence in the form of a blood-pressure reduction; only female test subjects already show a tendency towards cooling at nonstimulated measuring points. The difference in the temperature increase from the nonstimulated skin areas can doubtless only be explained by the local heat application.

Göbel (24) gives a summary of the hitherto existing studies on pain lateralization (a distinction was not made according to the stimulation methods) which demonstrates that the nondominant hand or left side of the body is described as the more sensitive (3, 16, 52, 60). The cause of this is ascribed to the dominance of the right hemisphere for emotional processes. Other authors fail to detect in their studies a lateral asymmetry of pain perception (28) or report on observations to the contrary (e.g., on electric stimulation) (57, 58). Our investigations show higher threshold values on the right for dextrals and on the left for sinistrals; the ambidextrous subjects lie in between. These results, as opposed to those of Göbel (24), are sex- and age-independent. A consideration of the individual measuring points in the dextrals reveals that the more distally situated areas (tabatière anatomique, thenar and hypothenar) most frequently show higher pain thresholds on the right, but the wrist joint and elbow often reach higher values on the left side. It could be conjectured, on the basis of this observation, that the lateralization tendency is less pronounced for proximal skin points. Unfortunately, there have been no studies thus far examining this question in various body regions.

The literature has hardly any data concerning the influence of depressiveness on the pain threshold. The test subjects were questioned before the session with a modified Beck's depression inventory, which has thus far proven to be a reliable and valid psychometric instrument (34). This revealed an only negligibly higher value for women ($p = 0.4113$), as also described by Hautzinger (34). There is also conformity with the literature in the female preponderance for the items inappetance and crying and the male preponderance for reduced enjoyment of life and social isolation (34). There is no significant correlation with respect to the age and the heat-pain threshold.

2. Chronic pain patients

Not only patients with a chronic pain syndrome wonder about the connection between the experimental laboratory pain and their suffering. This problem of applying algesimetric results to the clinical pain condition has always been given. As the following results show, the acute pain generated experimentally under standard conditions is definitely suited as a building block for better understanding the function of the nociceptor system and thus also the pathophysiology of chronic pain syndromes. The question of whether pain patients have lower or higher pain thresholds than a healthy control group has thus far been controversially discussed in the literature. In the following, a representative description is given of two considerations that lead to opposing assumptions. Cogan (11) postulates that pain patients evaluate experimental pain within the context of their own experience with clinical pain, and this would have to result in a higher pain threshold. According to Chapman's hypothesis, on the other hand, pain patients evidence a hypervigilance towards unpleasant body stimuli and have lower pain thresholds due to an exaggerated fixation on pain sensations (4).
Scholz (64) found a tendency towards higher pain thresholds in female patients with progressive systemic sclerosis.

Our investigations show that chronic pain patients have significantly ($p = 0.0169$) higher pain thresholds than healthy subjects. This finding strongly varies in degree at the different measuring points: significant ($p \leq 0.05$) for the distal regions (tabatière anatomique, thenar, hypothenar) and tendential for the wrist joint and elbow. These results are supported by studies in patients with progressive systemic sclerosis (64), patients with chronic back pain (12, 71), hand amputees (injured and not damaged extremity) (68) and persons with endogenous depression (69), where heat stimulation led to tendentially or significantly higher pain thresholds than in one healthy control collective each. Higher values are likewise described by Lipman in unselected pain patients (47), though the experimental instruction here does not specify whether threshold or tolerance values are measured. Ekenvall et al. (18) examined patients with Raynaud's disease and found elevated thresholds only for the damaged extremity, while other body regions evidenced normal values. In a study by Langemark et al. (42), patients with chronic tension headache showed significantly lower heat-pain thresholds. He interprets this result as an indication of a central dysmodulation: either through an insufficient antinociceptive modulation at the spinal/trigeminal level or through an enhanced perception of noxic stimuli at the cortical level. Cohen reports on a different psychic profile in various etiological groups of pain patients (12). Patients with temperomandibular symptoms, for example, complained most about emotional stress and anxiety, while depression was the most frequent symptom among patients with back pain (the latter had significantly higher thresholds). This observation surely represents an important aspect in interpreting the different pain thresholds in pain patients.

The intraindividual standard deviations are, on the average, significantly ($P \leqq 0.0001$) elevated in pain patients compared to the healthy controls. This would suggest that they have reduced perceptivity for an identical pain stimulus. A parameter representing a related dimension, the so-called discrimination capacity, was found by Cohen et al. (12) to be reduced in patients with back pain compared to healthy subjects. However, this observation may perhaps be only the expression of reduced vigilance. The patients' self-selected pain threshold, which is significantly higher than in healthy subjects, is also rated markedly higher by them in the VAS ($P = 0.0935$). They describe the quality of pain, on the other hand, with a limited vocabulary, perhaps because the character of the laboratory pain is perceived as relatively monotonous. The intensity of the patients' pain plays an important role in the depiction of their suffering; the ratings for the clinical pain evidence a mean value of 69.1% (SD = 13.1%) on the VAS. The correlation between clinical and laboratory pain is very good ($r = 0.91$), whereas other authors (25) found no connection at all between the experimental pain threshold and clinical pain. Though the heat pain induced by thermic stimulation is perceived as distinctly less pronounced by comparison, it is seen by the pain patients against the background of their everyday experience and rated correspondingly higher in relation to the assessment of the healthy subjects, who were usually only confronted with intensities from the lower range of the scale. Similar observations are reported by Clark (8), who found that, compared to patients, healthy subjects placed more emphasis on the emotional dimension than on the intensity of the pain.

The initial temperatures prior to starting thermic stimulation are only slightly lower than in the control group. The change in skin temperature at the stimulated measuring points after the stimulation likewise differs only negligibly in pain patients. A marked difference is found, however, in considering the nonstimulated reference sites: here the value is significantly lower than in the healthy subjects. This absence of the skin warming measured in the control group could already be interpreted as a slight vasoconstriction in the sense of a sympathicotonic reaction (as also found by Blumberg (2)).

Regarding pain lateralization, no significant differences exist among the right-handed patients ($p = 0.3247$). However, the distribution is somewhat more homogeneous with respect to the individual measuring points, i.e. there is no stimulus-site dependence of the lateralization as in healthy subjects.

In contrast to a study by Hautzinger (34), the pain patients show no significantly higher <u>depression profile</u> compared to healthy subjects. This discrepancy may be explained, for example, by the 5 distinct items and/or the different definition of the "pain patient". Depression is not necessarily the result of longstanding pain, though depressive symptoms are more frequent during chronic pain symdromes. For example, Pilowsky and Spence found only 10% of their pain patients to be depressive (1).