



COLD CHAMBER EXPOSURES (-67,3°C, 3 MIN) IN FIBROMYALGIA SYNDROMES CHR. GUTHENBRUNNER 1,2, G. ENGLERT 3, M. NEUES-LAHUSEN 3, A. GEHRKE 2

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ABSTRACT:

There are only a few studies looking at the analgesic effect of cold chamber exposures in patients suffering from fibromyalgia.

However, in addition to the pain symptoms, patients with this syndrome also frequently suffer from an increased sensitivity to cold. Thus, the effect of cold chamber exposures (-67°C, 1-3 min) on the sensitivity to pain, thermal comfort and actual pain intensity was examined in 17 female patients with fibromyalgia (ACR criteria) and compared with a control group without applications. The measured parameters were pressure, heat and cold pain thresholds (pressure algometry, Peltier thermode), thermal comfort (local thermal cutaneous stimulation applied by a Peltier thermode; systematically varied stimulation sequence) as well as the actual pain intensity and feeling of general well-being (visual analogue scales, VAS).

The thermal pain thresholds were determined on the inner surface of the forearm, and the sensitivity to pressure pain at the styloideus radii. The thermal comfort measurements were carried out at the forehead. After cold chamber exposures, cold and pressure pain thresholds were significantly or very significantly increased while no shifts of the threshold were evidenced for heat pain. In the range of the applied thermode temperatures of 17.5 – 27.5 °C the subjective temperature sensation curve was significantly increased after cold chamber exposure as compared to initial values and control period. The mean thermal tolerance range calculated from the intersection points of comfort curve and temperatures applied showed a statistically significant increase. Such an improvement of the thermal tolerance could not be evidenced for the control group. The mean values of the actual pain scores (VAS) were also significantly reduced after cold chamber exposures, and the overall-being improved. It is concluded that cold chamber exposures have an analgesic effect in patients suffering from fibromyalgia and that in addition the thermal tolerance is increased. Now, further studies have to be carried out to determine if repeated cold chamber applications yield in stable adaptive improvements of pain sensitivity and thermal discomfort.

INTRODUCTION:

Cold chamber therapy was introduced into rheumatology in the 1980th by Fricke (also refer to Yamauchi 1986). Startz et al. (1991a) as well as Samborski et al. were the first to report of the analgesic effect of this therapy form and who discovered an increase in the serum dopamine

concentration, a significant decrease of the β -endorphin-serotonin and cortisol concentrations (Startz et al., 1991b). As a direct effect of cold chamber therapy also the known analgesic effects of local tissue cooling including inhibition of the C-fiber system as well as muscle relaxation effects have to be taken into account (lit. transl. see Schnizer and Schöps 1995). Due to the short exposure time it is rather likely, however, that the clinically observed effects of cold chamber therapy (Birwe et al. 1989) are caused by a reflex inhibition of the pain perception by stimulation of other afferent systems.

The fibromyalgia syndrome is a chronic clinical picture which is characterized by hardly manipulable pain of the skeletal muscles and capsule-ligament apparatus as well as by frequent sleep disorders (lit. transl. see Yunus 1991). Dysfunctions of the vegetative regulatory mechanisms often cause a shift of the thermal comfort in patients with fibromyalgia syndrome, which is primarily characterized by a reduced tolerance to cold (lit. transl. see Yunus 1991); (Kosek et al. 1996). This also restricts the tolerance to the different physical therapeutic applications such as hydrotherapy, kinetherapeutic baths etc. (Piso et al. 1999).

The currently discussed pathomechanism of this disease with disturbances of the neurotransmitter metabolism (serotonin, substance P; lit. transl. see Russel 1998; also refer to Zimmermann 1991) offers a plausible explanation for the generalized shift of sensitivity thresholds. A standard treatment for this problem is not yet been known.

An essential diagnostic criterion for the fibromyalgia syndrome consists in the increased pressure sensitivity of the tendinous attachments (lit. transl. see Fischer 1991a, b; Lautenschläger 1991; Wolfe 1991). Also, the disturbances of the thermal tolerance have been objectified as compared to healthy test persons (Kosek et al. 1996). Since it is difficult to influence fibromyalgia symptoms therapeutically and no causal treatment has yet been found polypragmatic treatment approaches are currently recommended employing analgesics and antidepressants as well as physical therapy methods (Miehle 1991). Thus, the potential analgesic effect of physical therapeutic therapy forms to cure fibromyalgia is still a question of great importance. The current experimental study examines the potential effects of cold chamber exposures on thermal and pressure sensitivity as well as pain intensity and wellbeing in patients with fibromyalgia as compared to a control group without cold chamber application.

METHOD:

Based on the ACR criteria (Wolfe et al. 1990, Wolfe 1991) the inclusion criteria for participation in the study were as follows: diagnosis of existing primary fibromyalgia syndrome (syn. generalized tendomyopathy), between 30 and 70 years of age, and female sex. The latter criterion was chosen to eliminate potential sex-dependent inhomogeneities regarding pain perception and assessment (cf. Offenbaecher et al. 1998). Patients with isolated tendomyopathies, inflammable and severe degenerative spine and joint disorders, polymyositis, rheumatic polymyalgia as well as neurological and psychiatric disorders were excluded from the study. In addition, patients with severe metabolic and cardiovascular diseases were also not included in the study. The diagnosis of fibromyalgia which was made primarily by the attending rheumatologist was verified on the basis of an initial clinical examination according to the ACR criteria.

The examined patient collective consisted of 17 women aged between 42 and 70 years (mean age 54.2 ± 7.0 years). All patients were recruited from a local group of the rheumatology league. They were fully informed about the goal, method and possible risks of the examination and



participated voluntarily in the study. All patients took non-steroid antirheumatics on the basis of an on demand medication. 82% of the patients were additionally treated with Amitryptilin medicaments.

All patients participated in two comparative tests (control, cold chamber exposure). The order of the individual examinations was systematically varied according to a Latin square design. All examinations were carried out between 9:00 and 13:00 in the morning. The minimum interval between individual examinations was 7 days.

Cold chamber exposures were performed according to the commonly used method. The used cold chamber (*CRIO Space Cabin*) was manufactured by CRIO Medizintechnik and had an internal diameter of 2m². The chamber temperature was set to -67°C and varied between tests between -65°C and -68°C. Exposure time was 3 minutes. The patients entered the cold chamber wearing bathing costumes and nose masks, extremities were protected by gloves, shoes and head bands. Increased physical activities during cold chamber exposure were prohibited. Through a glass window and an intercom the test persons were in continuous contact with the investigator. Before and after the application, patients rested in a constant lying position covered with a wool blanket. The control examination consisted in an equally long resting phase in constant lying position during which identical measurements were performed as during therapy tests.

Determination of the pressure pain threshold was performed using a gauged pressure algometer (pd&t: Measurement range: 0.5 – 5.0 kg) using a rounded pressure tip with a diameter of 0.5 cm and a pressure speed of 1kg/sec (Fischer 1987). Evaluation of this study was limited to the pressure point values measured on both sides of the styloideus radii. Additional measurement points were the epicondylus humeri radialis, acromio and costal junction.

The same Peltier thermode was used to determine the subjective temperature sensation and thermal comfort (cf. Fruhstorfer et al. 1976; Verdugo & Ochaba 1992; Yarnitzky & Sprecher 1994; Yarnitzky et al. 1995). The measurements were carried out at the patient's forehead. The patients received applications with ten different temperatures set prior to treatment. The duration of a single stimulus was 5 seconds. Between the individual stimuli a break of at least 10 seconds was made.

Each temperature stimulus had to be rated by the patients on a scale from +10 to -10 (meaning „very comfortable“ to „very uncomfortable and „very cold“ to „very hot“ respectively) (for information on the method of thermal comfort measurement see Cabanac et al. 1976; Attia et al. 1980; Hildebrandt et al. 1981, Demuth et al. 1984). Due to the permanently stored stimulation sequence a continuous increase or decrease of the temperature stimuli could be eliminated. Hyperthermal and hypothermal stimuli were applied in an alternating order. All tests were performed at room temperature (20°C – 22°C) and in a lying position.

		Heat pain threshold	Cold pain threshold	Pressure pain threshold
Controls	Ipsilateral	99,5 ± 0,51100,1 ± 0,37	102,0 ± 1,29102,1 ± 1,11	91,8 ± 1,8490,3 ± 3,15
	Contralateral			
Cold chamber	Ipsilateral	102,4 ± 1,4198,4 ± 1,11	53,2 ± 6,8291,0 ± 7,70	177,8 ± 13,7011,7 ± 5,75
	Contralateral			



Tab. 1

Mean changes (in percent) of heat, cold and pressure pain thresholds at exposed and non-exposed arm after application and control test: the stated scatterings represent the ranges of mean errors of the mean values: significance specification (ipsi vs. contralateral) after variance analysis.

Before and after the therapeutic applications or control phase a 10 cm line, the visual analog scale designed by Piso, was presented to the patients. One end of the line was labeled “no pain” and the other “the worst pain ever felt”. Patients were inquired about their pain at rest, kinesiophobia and exertion pain as well as general musculoskeletal pain. The scales conformed to the accepted and evaluated method of pain progression measurement (lit. transl. see Anton 1993). Furthermore, patients were asked to rate their general physical wellbeing on a 10cm analog scale with one end marked “I feel very unwell” and the opposite end “very well”.

The statistical analysis of the results was performed using the variance analysis for repeated measurements. An error probability of under 5% was determined as significance limit.

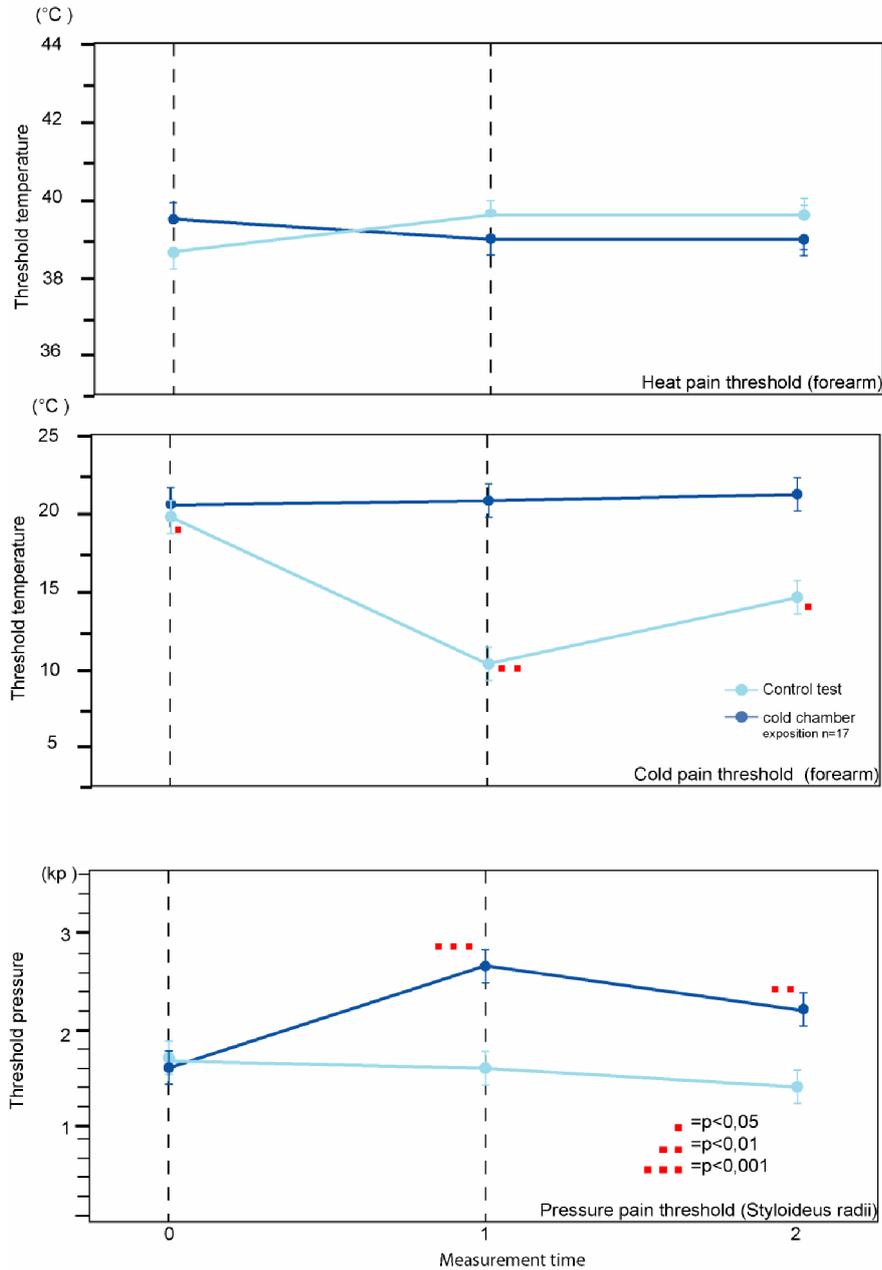


Table 1: Mean changes (in percent) of heat, cold and pressure pain threshold at exposed and non-exposed arm after application and control test. The stated scatterings represent the ranges of mean errors of the mean values: Significance specification (ipsi vs. contralateral) after variance analysis.

RESULTS:

As illustrated in Fig. 1, the mean heat pain threshold showed no noteworthy changes until the end of cold chamber application and during the resting phase after application. In contrast,

threshold temperature during cold pain provocation was decreased significantly until the end of cold chamber exposure, but slightly increased in the resting phase following application. The mean decrease was approx. 8°C, corresponding to approx. 40% (Tab. 1). Threshold temperature did not change during the control tests. A significant shift of the pressure threshold could also be observed. The mean threshold pressure increase until the end of application was 1kg, equaling approx. 60–80% ($p < 0.0001$ as compared to the control test). During the post-application resting phase this increase was also declining. It can thus be concluded that cold chamber exposures have an analgesic effect in patients with fibromyalgia. This was clearly evidenced by the chosen pain threshold determinations.

The mean data of temperature and comfort temperature sensation in dependency to the applied thermode temperatures (Fig. 2) show the typical characteristic prior to application. In contrast to the healthy test persons, patients with fibromyalgia assessed lower temperatures to be colder than they actually were (cf. Kosek et al. 1996). The resulting break in the progression between thermode temperature and sensation score was completely eliminated by cold chamber exposure thus causing a diagram that equals that of a healthy test subject.

The diagram of the mean thermal comfort sensation presented in the lower part of Fig. 2, however, showed no noticeable changes.

For statistical evaluation of the thermal sensitivity during cold chamber exposure as compared to the control group, the different temperature sensitivity values before and after application – as described above – were calculated for each thermode temperature (Fig. 3) (for information on the methodic procedure cf. Gutenbrunner et al. 1999).

It became apparent that particularly under low thermode temperatures, the temperature sensitivity was increased considerably by cold chamber exposure with the results from 20°C to 27.5°C being of statistical significance. In contrast, no difference was observed between application and control test in those cases where the thermode temperatures were above the thermoneural point. From this can be followed that cold chamber exposures cause a significant decrease of cold sensitivity in the hypothermal range.

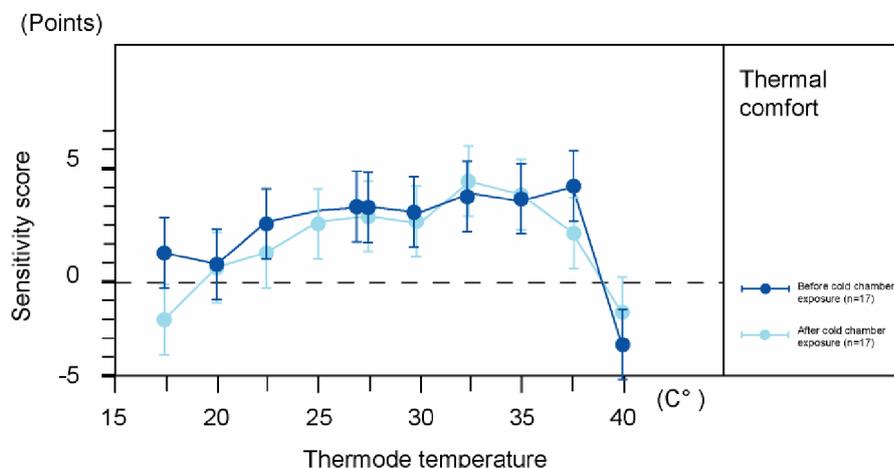


Fig. 2: Mean subjective temperature sensitivity and mean thermal comfort sensitivity during local application of different temperatures on the skin using a Peltier thermode before and after cold application in patients with fibromyalgia syndrome. Parenthesis mark the areas of mean errors and values.

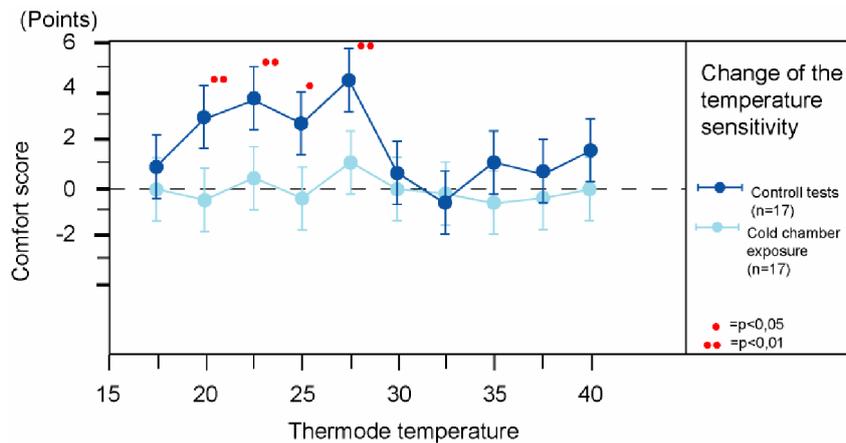


Fig. 3: Mean change of the subjective temperature sensitivity (difference of the sensitivity score) before and after and during 3-minute cold chamber exposure respectively (closed symbols) as compared to control group without therapeutic application (open symbols). Parenthesis mark the areas of mean errors of mean values. Significance information after variance analysis.

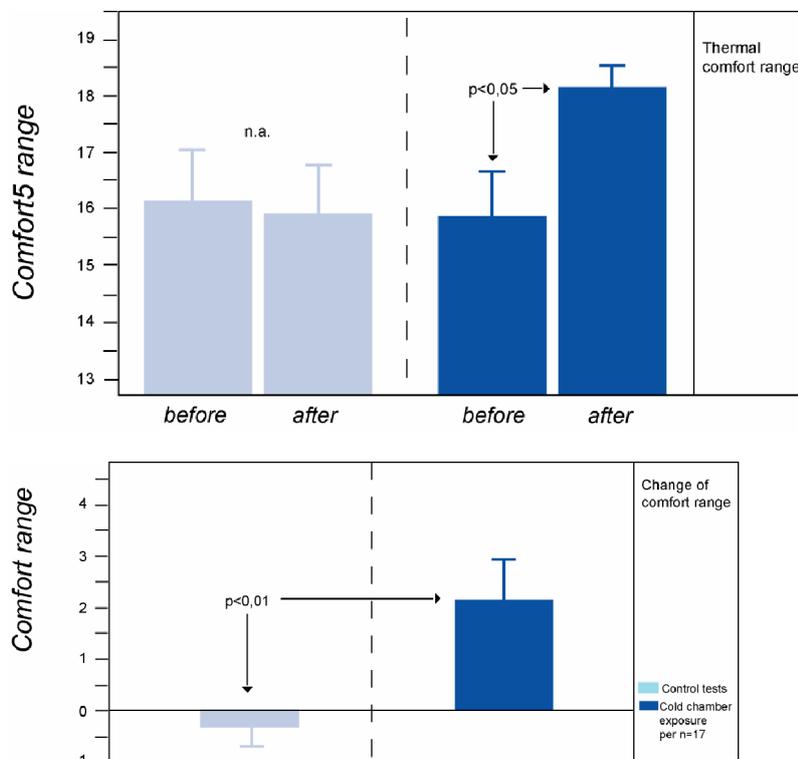


Fig. 4: Mean thermal comfort range before and after cold chamber application as well as at the beginning and end of the control phase. The mean changes of this parameter for the respective application are displayed in the lower part of the diagram. Parenthesis mark the areas of mean errors of mean values. The significance data in the upper part of the diagram refer to the difference between the values before and after application and control phase respectively; data in the lower part of the diagram represent the result of a variance analysis.

For analysis of the thermal comfort scores and their respective changes, those temperatures were determined for each individual examination at which a negative score was transformed into a positive score and vice versa. These temperatures were defined as upper or lower comfort threshold respectively (Gutenbrunner et al. 1999). The mean values and scattering ranges of these comfort thresholds before and after application or control test are shown in Tab. 2. As expected, no changes were observed in the control group while the lower comfort threshold was decreased during cold chamber application ($p < 0.01$). In contrast, the upper comfort thresholds showed no statistically relevant changes. It should be noted, though, that the tests were performed up to a thermode temperature of 40°C max. and that a significant change in an upper range could not be registered for the medium upper comfort threshold of 38.4°C.

To analyze the overall effect, the difference between upper and lower comfort threshold was defined as the thermal tolerance range. As shown in Fig. 4, no significant change was observed for this parameter during control examinations. During cold chamber exposure, however, it increased by approx. 2°C. This increase was statistically highly significant both in comparison with the values before and after application as well as when comparing the differences (tolerance range changes). The evaluations thus confirm the changes which have been observed for the temperature sensitivity, and they demonstrate that the thermal tolerance in patients with fibromyalgia can be improved by cold chamber exposure.

Parameter	Application	Point of time	Mean value ± Standard error
Lower comfort threshold	Control test	Before application	22,2 ± 1,00
		After application	22.4 ± 1.04 ns
		Change	+0.14 ± 0.34 ns
	Cold chamber exposure	Before application	22,2 ± 1,00
		After application	20,1 ± 0,95 *
		Change	-2,1 ± ,65**
Upper comfort threshold	Control tests	Before application	38,4 ± 0,42
		After application	38.2 ± 0.51 ns
		Change	-0.14 ± 0.26 ns
	Cold chamber exposure	Before application	38,1 ± 0,46
		After application	38.1 ± 0.46 ns
		Change	0.0 ± 0.30 ns

* $p < 0.01$ (t-test comparison of pre/ post application)

** $p < 0.01$ (ANOVA comparing the control group)

ns not significant: bold = significant changes or differences

Tab 2: Mean values of the lower and upper comfort threshold before and after cold chamber exposure and control test respectively as well as mean changes of the respective parameter (difference between values before and after application) in 17 patients with fibromyalgia syndrome.



Mean values and standard errors are indicated. Significance information refer to the t- test (comparison between pre/post application) or a variance analysis (comparisons of the applications).

The possible manipulation of the actual pain status is of particular clinical importance as well as the changes in well-being which may also reflect a possible positive influence on the mental strain. As shown in Fig. 5, statistically high significant reductions of the pain at rest, kinesiopia and exertion pain amounting to 12–21% were observed after cold chamber exposure as opposed to the control test. In all tested parameters, these changes were statistically significant or high significant as compared to the control examinations. This demonstrates that the analgesic effect verified by pain threshold determination is also of clinical relevance for patients with fibromyalgia.

DISCUSSION

METHOD:

Generally accepted and evaluated methods have been used for testing the pain threshold sensitivity and actual pain intensity. The used measurement methods also served for testing both the sensitivity on the skin surface (thermal pain threshold) and in the deeper layers of the tissue (pressure pain threshold). Reference values for the thermal pain threshold values can be found in studies by Fruhstorfer et al. (1996), Verdugo & Ochoa (1992), Yarnitzky & Sprecher (1994) as well as Yarnitzky et al. (1995). Determination of the pressure pain using an appropriately gauged pressure algometer represents a standard procedure in pain diagnostics of the fibromyalgia syndrome and has been used in numerous examinations for the therapy of this disease (lit. transl. cf. Fischer, 1987, 1991 a,b; Lautenschläger 1991; Wolfe 1991). Piso's (1998) modified 10-cm visual analog scale which is used for pain assessment also represents a commonly used and valid procedure applied for patients with fibromyalgia (lit. transl. cf. Anton, 1993). The modification made by Piso (1998) merely applies to the separate recording of pain at rest and exertion pain; a procedure that has proved itself in multiple cases for assessment of pain in patients with degenerative spine and joint disorders (Gutenbrunner et al. 1997, 1998).

In the early 1980's Hildebrand et al. (1981) already indicated that the measurement of tissue temperatures is not sufficient to prove the impact of thermally effective physical applications but that it is rather necessary to take parameters of thermoregulation into account.

Therefore, the authors suggested to use the method described by Cabanac (1969, 1973, 1979) which determines the thermal comfort sensation. Standardized measurement instruments are now available for use with this method (cf. Fruhstorfer et al. 1976; Verdugo & Ochoa 1992; Yarnitzky & Sprecher 1994; Yarnitzky et al. 1999). The method has also proved itself to determine disturbances in patients with fibromyalgia syndrome (Kosek et al. 1996).

In patients with fibromyalgia syndrome, cold chamber exposures have a clinically relevant analgesic effect, as shown by the results, and also act in favor of experimentally defined pain threshold as well as actual pain symptoms. Corresponding results have already been reported earlier; however, lower temperatures had been applied (Stratz et al. 1991 a; Samborski et al. 1992). As demonstrated by a parallel examination, the shift of pain thresholds cannot be evidenced in a thermally isolated extremity (Gutenbrunner et al.). This suggests that the analgesic effect of cold chamber therapy equals the effects of locally applied cold applications such as cold air stream or liquid nitrogen. These effects are caused by direct tissue cooling and the resulting inhibition of the conduction velocity of sensitive neurons (lit. transl. cf. Schnizer &

Schöps 1995). It is also quite conceivable that the strong stimulation of the cold afferences – in the sense of a counter irritation – causes an inhibition of the pain perception (cp. Handwerker 1995). Due to the limited local effect, a central effect has to be regarded as rather unlikely.

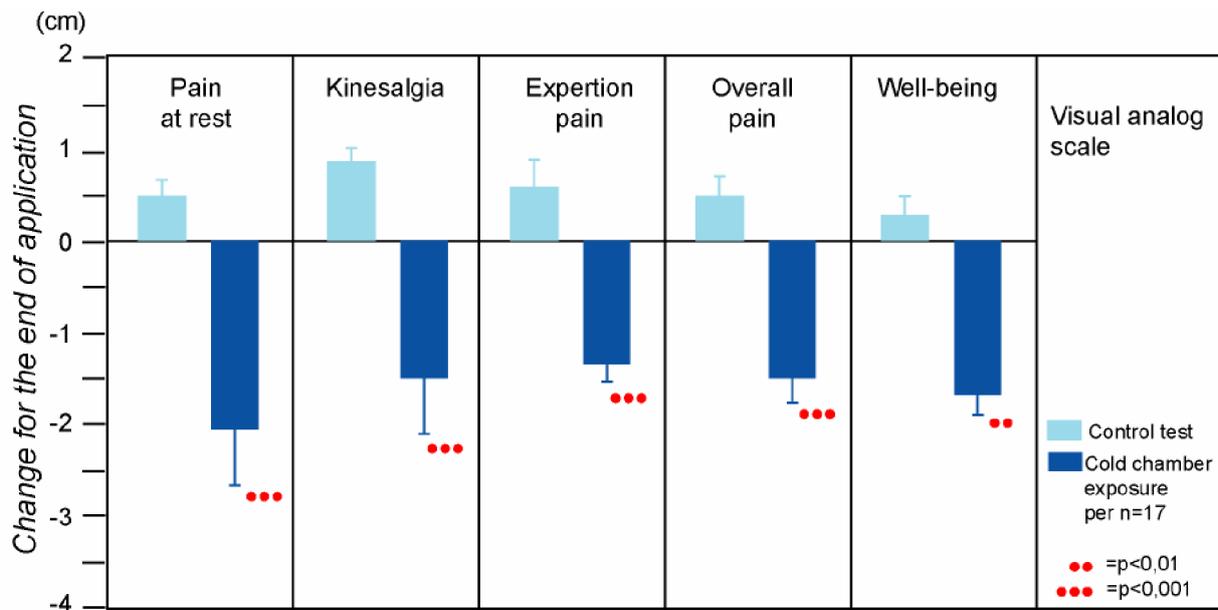


Fig. 5: Mean changes of the actual pain assessed using visual analog sales (10 cm) and general well-being shortly after application as compared to the situation before application. Absolute changes are indicated in cm. Parenthesis mark the areas of mean errors of mean values. Significance information after variance analysis.

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In the literature, mainly temperatures between -110°C to -120°C are requested for cold chamber exposures (Yamauchi 1986; Fricke 1989). According to the present results, a temperature of approx. -65°C is apparently sufficient to obtain at least an analgesic effect.

The fact that cold chamber exposures are capable to improve the tolerance to thermal stimulations may be of clinical importance for a therapy of the fibromyalgia syndrome. This diagnosis is in so far of clinical relevance as these patients – as already mentioned – also suffer from thermally effective paralgnesia and have a reduced tolerance to thermally effective physical therapies. Piso et al. (1999) proved that kinetotherapeutic baths with a temperature of 29°C –

30°C are tolerated less well by patients with fibromyalgia syndrome than those with a temperature of 35°C–36°C. The disturbed tolerance to thermal stimulation has also been experimentally evidenced by Kosek et al. (1996). This also explains the recently evidenced therapeutic effect of thermal adaptations on the clinical symptoms and general condition of patients with fibromyalgia syndrome (Piso et al. 1998).

Besides the already mentioned local cold effects in the sense of local thermally related sensitivity changes of thermal receptors, adaptive level shifts in the sense of cold habituation have to be discussed as an operating principle for reducing the cold tolerance (lit. transl. cf. Hildebrandt 1998). These habituated sensitivity dampings have been described repeatedly for vegetative cold reactions (Stempel & Stroh 1982). According to Glaser (1968) they are controlled by the central nervous system on the level of the formatio reticularis (lit. transl. cf. Hildebrandt 1998).

The presented results may be of great practical importance to the treatment of the fibromyalgia syndrome because fibromyalgia, as already mentioned, not only impairs the pain symptoms but also the general well-being due to thermal paralgia. As cold chamber applications are by nature not suited for permanent therapy, the question is of particular importance as to whether a serial application over several weeks via functional adaptations may cause a longterm change of the pain sensitivity and thermoregulation as well as thermal comfort sensation.

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