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BIOFEEDBACK AND CONTROL OF SKIN CELL
PROLIFERATION IN PSORIASIS

THESIS

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By

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The present study was designed to determine the effect of skin-temperature-biofeedback training on cellular proliferation in three psoriasis patients. It was hypothesized that (a) psoriasis patients would be able to consciously decrease skin temperature of psoriatic tissue, and (b) there would be a positive correlation between rate of cellular proliferation and temperature change.

Results obtained indicated biofeedback training to be effective in decreasing the surface temperature of psoriatic tissue. A 2 X 7 analysis of variance for two repeated measures indicated the change in skin temperatures as a function of sample period to be significant, $F(6,26) = 3.29, p < .02$. Generalization of temperature-training effects from the biofeedback to the no-feedback condition were observed. Rate of proliferation decreased from pretraining to posttraining biopsies.

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BIOFEEDBACK AND CONTROL OF SKIN CELL
PROLIFERATION IN PSORIASIS

Biofeedback has been shown to be effective with a great number of diverse physiological functions. If control could be established at the cellular level, the possibilities for medical and psychological applications would be virtually unlimited. In addition, the theoretical implications of such a breakthrough would make clear the amount of influence mental functioning has over physical health. One of the purposes of the present investigation is to determine if cellular activity can be affected through biofeedback techniques.

Biofeedback research over the past few years has led to many discoveries which have not only proven to be clinically useful, but have produced data which may have resolved certain theoretical issues and perhaps opened new areas of controversy -- one most directly affected concerns the autonomic nervous system (ANS) functions. The ANS has been viewed as reflexive or involuntary, and regarded as the principal source of control over such bodily functions as heart rate, blood pressure, and a wide range of gastrointestinal processes. Until only recently, the majority of researchers agreed with Kimble's (1961) conclusion that autonomic functions could be modified by classical (but not

by instrumental) training methods. However, DiCara and Miller (1968) worked with rats paralyzed by curare (to eliminate mediation through the skeletal muscles) and showed not only that animals could learn to control one of these "automatic" responses--but that they could do so with a great degree of specificity. For instance, one rat learned to increase blood flow in one ear at a time.

Recently it has been found that humans are able to voluntarily increase or decrease the amplitude and percentage of specific electroencephalographic (EEG) patterns (Kamiya, 1969; Peper & Mulholland, 1970). It has also been shown that through electromyographic (EMG) biofeedback training, humans are quickly and effectively able to control muscle tension (Budzynski, Stoyva, & Adler, 1973). This control has been achieved at the level of the single motor unit, as demonstrated by Harrison and Mortensen (1962). Basmajian, 1969 (as cited in Brown, 1974), states that:

Normal human beings can quickly, in a manner of 15 or 20 minutes, isolate only one motor unit from the population of perhaps a hundred or two hundred which are within an area of pick-up of an electrode pair. They can suppress all of the units, turn them on and off easily, suppress the one they started with, pick up another one, train it, suppress it, turn to a third, and then, on

command, they can respond with signals from the unit that you choose for them to respond.

(p. 164)

Basmajian and Simard (1967), in fact, did teach a single subject to isolate and fire each of 11 different motor units upon command.

As Green (1973) points out, blood pressure, blood flow, heart rate, lymph flow, muscle tension, and EEG patterns have already come under conscious control through biofeedback techniques. It has also been demonstrated that pulse volume (Snyder & Noble, 1968; Volow & Hein, 1972), diastolic blood pressure (Shapiro, Schwartz, & Tursky, 1972), galvanic skin response (Crider, Shapiro, & Tursky, 1966, Fowler & Kimmel, 1962; Kimmel & Hill, 1960; Kimmel & Kimmel, 1963; Rice, 1966; Senter & Hummel, 1965), and other visceral responses such as heart rate, intestinal motility, arterial pressure, urine formation and contractions of the uterus (Dicara, 1973; Pappas, DiCara & Miller, 1970) can be voluntarily manipulated by human and nonhuman subjects. In a review of the potential clinical applications of biofeedback, Shapiro and Schwartz (1972) include essential hypertension, cardiac arrhythmias, tension and migraine headaches, rumination, Raynaud's disease, anxiety and fear reduction, pain reduction, attention and learning, and sexual behavior.

Recently it has been found that humans are able to voluntarily control skin temperature through visualization and

imagery (Green, Ferguson, Green, & Walters, 1970; Zimbardo, Maslach, & Marshall, 1970). This control has been made more efficient and specific through biofeedback (Surwit, Shapiro, & Feld, 1975; Taub & Cleeve, 1973). Roberts, Kewman, & MacDonald (1973) trained participants in their study to control skin temperatures differentially in the digits of the two hands with the aid of hypnosis. Later, the same results were obtained without hypnosis (Roberts, Schuler, Bacon, Zimmerman, & Patterson, 1975). Apparently, the degree of response specificity depends upon the pattern of feedback used (Schwartz, 1972). Surwit, Shapiro, and Feld found no evidence for response specificity to the site of feedback even after nine days of training, when absolute (as opposed to differential) temperature feedback was delivered to the participants.

There exists the definite possibility that any physiological process that can be detected and displayed in the form of objective feedback can be self-regulated to some extent--if the feedback meets certain criteria. The feedback must be: (a) representative of very small changes, (b) accurate in its indication of changes, and (c) delivered immediately (ideally, in a continuous fashion). These criteria would seem essential for the most efficient control of physiological processes which can be manipulated through biofeedback training.

Various procedures have been employed to study differences in skin temperature. These procedures are collectively referred to as thermography. Infrared thermography has been used for some time in the detection and assessment of such conditions as skin burns and frostbite (Barnes, 1963; Hochligetti, 1959; Lawson, Wlodek, & Webster, 1961; Lloyd-Williams, Lloyd-Williams, & Handley, 1961). As Barnes pointed out,

Human skin is an almost perfect emitter of infrared radiation in the spectral region beyond 3 microns. This energy may be recorded as a thermogram to yield a quantitative temperature map of the skin. If the nude [subject] has remained quiet in a cool room for 10 to 15 minutes prior to thermography, the skin temperatures are determined largely by the vascularity of the skin itself and by the heat conducted from within the body. Since, under these conditions, the contrasts which appear arise essentially from the internal sources of heat, the resulting thermograms yield information concerning certain pathological conditions within the body.

(p. 877)

There is a great deal of data to indicate that variations in skin temperature correlate with abnormalities in the skin and underlying tissue. Lawson (1956) observed in two cases of metastatic breast cancer that the skin overlying the affected areas was definitely hotter than

that of surrounding areas. He then used this observation as a basis for identifying malignant tumors in the breast by the elevated skin temperature, as compared to a symmetrically identical area in the opposite breast. These findings have subsequently been supported by others (Lawson, 1957; Lloyd-Williams, Lloyd-Williams, & Handley, 1960) which indicated that in the case of malignant tumors, the overlying skin appeared to be hot--while in the case of cysts, the skin temperature appeared to be cooler. It has been found that the temperature rise due to malignancy is variable, but ranges from 2 to 3° C (Lawson, Saunders, & Cowen, 1956; Lloyd-Williams, et al., 1960). The suggestion has also been made that there is a correlation between the amount of temperature rise and the degree of malignancy (Lawson & Chughtai, 1963). Selawry, Neubauer, Selawry, and Hoffmeister (1966) have even used decreases in temperature in certain areas of tumors to predict central tumor breakdown prior to overt clinical changes.

Soon after these observations, medical researchers began to investigate the possible causes of this increase in temperature. As early as 1945, Algire and Chalkley had hypothesized that tumors were capable of elaborating vasoproliferative substances to insure adequate blood supply to the constantly hungry neoplastic tissue. This hypothesis was later supported by clear demonstrations of rich vasculature in the body of many transplantable experimental neoplasms and spontaneous

human tumors (Lasser & Schobinger, 1955). This substance (tumor angiogenic factor) was isolated from several human and nonhuman tumors by Folkman, Merler, and Abernathy in 1970. The necessity for such a mechanism is logical since the survival of tumor implants is premised on the evolution of a nutritionally adequate blood supply (Wolf & Hubler, 1975).

The difference in temperatures, therefore, has been accounted for by the obvious increased blood and lymphatic vascularity. However, local increases in temperature over tumors may be due not only to increased blood supply, but also to heat production in the tumor itself--either by an increase in its metabolic activity or by a decrease in the efficiency of its metabolism, or both. This is shown by observations made by Lloyd-Williams, et al. (1960).

In several examples of inflammation and neoplasm, skin temperature over the lumps were found to be higher than the rectal temperature by as much as 1.5 degrees C. A rise of temperature in an area of skin caused solely by increased transference of heat to that area by the blood stream could not surpass that of the interior of the body.

(p. 958)

Further indications of tumors generating heat independently of the blood and lymphatic supply were reported in the same study.

An observation [was] made on a 'hot' melanoma of a limb in which occlusion of the blood supply led to a general cooling of the limb during the 5 minutes of the test, without affecting the difference in temperature between the melanoma and the surrounding skin. When the same thing was done with a 'hot' haemangioma there was a rapid decrease in the differential temperature.

(p. 958)

These conclusions are supported by the results of investigations of Lawson and Chughtai which suggest that the function of the increased vascularity is actually to drain off the heat energy and thus cool the tumor, in spite of serving its increased metabolic demands.

Although there is evidence that the large number of capillaries in tumor tissue does not necessarily provide an abundant supply of nutrient materials and that the rich vascular bed is functionally inefficient (Urbach & Noell, 1958), it has been shown that there is a high rate of cell proliferation in well-vascularized tumor regions (Hendrickson & Skypeck, 1963). This has been further supported by the findings of Caspersson and Santesson (1942). They summarized evidence which suggests three possible causes for the development of necrosis in tumors: lack of glucose, lack of oxygen, and high concentrations of lactic acid. It has also been demonstrated (Tannock, 1968) that the concentration of oxygen

plays an important role in controlling the rate of cellular proliferation. Algire and Legallais (1951) presented evidence that hemorrhaging and partial destruction of tumor cells resulted from the slowing of blood flow and the development of stasis in vessels of both the tumor and surrounding tissue of the host. This decrease in blood flow was brought about by tourniquet shock, injection of hypotonic glucose, mechanical obstruction, and injection of histamine (Algire, Legallais, & Park, 1947; Barrett, 1942).

One of the most outstanding characteristics of psoriatic tissue is an extremely rapid rate of cell proliferation. Van Scott and Ekel (1963) described psoriasis as a disease of epidermal hyperplasia (excessively rapid growth). Weinstein and Frost (1968) concluded that "the kinetics of epidermal cell proliferation in psoriasis determined in this study support and further extend the concept of cellular hyperplasia as a significant factor in this disease" (p. 258). As a result of their observations of cell proliferation kinetics in hyperplastic psoriatic tissue, Weinstein and Frost make the further conclusion that "it is apparent that . . . psoriasis provides an accessible model system for studying rapid cell proliferation in humans" (p. 258). In psoriasis, the number of cells in mitosis has been shown to be as much as 50 times greater than normal epidermis (Fry & McMinn, 1968, 1970). Cell proliferation of involved tissue differs from normal tissue--not only in rate, but also in that mitoses are

not limited to the basal layer (Van Scott & Ekel, 1963). Psoriasis also results in increased vascularity and abnormal amounts of heat production (Herndon, 1975). This increased heat is accounted for by increased metabolic activity as indicated by an elevated oxygen consumption at rest (Zoon & Mali, 1957) without changes in thyroid function (Krook, 1960).

Psoriasis is a chronic, noninfectious skin disease characterized by "brownish-red papules and plaques. The lesions are sharply demarcated, dry, and usually covered with layers of fine silvery scales" (Lever & Schaumburg-Lever, 1975, p. 136). If the scales are removed by gently scraping the surface of the plaque, fine bleeding points (the so-called "Auspitz sign") appear. The histopathology of psoriasis, as described by Soltani and Van Scott (1972) includes (a) regular elongation of the rete ridges, (b) elongation and edema of the papillae, (c) presence of a very small "spongiform pustule," (d) parakeratosis, and (e) presence of Munro microabscesses. Finally, capillary dilatation and formation of new capillaries in the affected area also occur (Mom, 1971). Vasoproliferation is important to cell growth as clearly demonstrated by Baxter and Stoughton (1970) when occlusion alone was shown to decrease the mitotic index as compared to the unoccluded and untreated control.

According to the Merck Manual (Holvey, 1972), the prognosis for psoriasis sufferers depends on the extent of severity of the initial involvement and the age of onset. Acute attacks usually clear up, but complete remission is rare. Early lesions are more amenable to treatment, while long-standing ones have a poor prognosis. No known therapeutic method assures a complete cure.

One additional problem suffered by psoriasis patients is a failure to vasoconstrict normally on cooling (Shuster & Marks, 1970). Since the skin provides the principle site for physiologic heat exchange, widespread skin disease invariably causes loss of temperature control (Herndon, 1975). This inability to restrict heat loss causes the patient to complain of feeling constantly cold. That this is a very serious condition is indicated by Fox, Shuster, Williams, Marks, Goldsmith, and Condon (1965) in their discussion of the relationship between peripheral blood flow and hypothermia (excessive loss of body heat). They conclude that "the unexplained high mortality of patients with erythrodermic skin disease may in large part be due to the haemodynamic and thermoregulatory problems we have discussed" (p. 622).

In summary, pathology in psoriasis is characterized by elevated local temperature, increased vascularity, and increased cellular proliferation. Blood flow and oxygen concentration are directly related to rate of cellular proliferation. Surface temperature of diseased tissue often

exceeds internal temperature. Thus, the function of the vastly increased bloodflow is to provide oxygen and other nutrients, and to cool the cell through heat transfer. Increased blood flow can result in hypothermia. Therefore, it may be possible that voluntary reduction of heat production in psoriatic plaques will result in decreases in cellular activity. This could occur either directly (by acting on the metabolism of the cell itself), or indirectly (through changes in the local vascular system causing reduction in blood flow and a resultant lack of oxygen and nutrient materials).

The effect of temperature control on cellular proliferation may be determined through biopsy and use of the tritiated thymidine (H^3T) labeling procedure which allows identification of cells in the process of division. It is now generally accepted that cells which are multiplying by mitotic division pass through a series of physiological and biochemical events which constitute the so-called "cell mitotic cycle." One of these phases is characterized by new DNA synthesis (the S-phase) and this process can be detected by exposing S-phase cells (Lachapelle & Gillman, 1969) to isotopically labeled DNA precursors. Tritiated thymidine is considered to be a specific precursor of DNA. Thus, should tritiated thymidine, proferred to cells, be incorporated into DNA (as one would expect) in S-phase nuclei, this event and the nuclei involved could be precisely determined through

the use of high-resolution radioautography on appropriately prepared histological sections of the labeled tissues (Baserga, 1968). Therefore, the result of tritiated-thymidine labeling is a count of the number of cells preparing for mitosis. The number of labeled cells in the process of mitosis divided by the total number of germinative cells in a particular sample will then yield the rate of cellular proliferation of that sample.

In psoriasis, the duration of the S-phase has been experimentally determined (Weinstein & Frost, 1968) as 8.5 hours. According to the same study, the complete germinative cell cycle lasts approximately 37.5 hours in involved psoriatic epidermis. This compares with a duration of 163 hours for the germinative cell cycle of normal skin.

Only two methods for the incorporation of radioactive tracers into the skin can be seriously considered for routine clinical use in man--the local in vivo method and the in vitro method. These two methods yield very similar results (Lachapelle & Gillman, 1969), but the in vivo method requires injection of radioactive materials directly into the skin of the subject. The local in vivo method is described by Epstein and Maibach, 1965; Goodwin, Hamilton, and Fry, 1973; and Weinstein and Frost, 1968. The in vitro method involves removing a portion of skin through biopsy, then subjecting this skin to the radioactive material. Because it is much safer to the subject, the in vitro method has been selected for determining rate of proliferation.

The present research was designed to determine the effect of skin-temperature-biofeedback training on cellular proliferation. The first hypothesis was that psoriasis patients would be able to decrease skin temperature of psoriatic tissue through biofeedback. The second hypothesis was that there would also be a decrease in rate of cell proliferation corresponding to decreases in temperature.

Method

Subjects

Subjects were one male (age 60) and two female (ages 28 and 21) psoriasis patients who were referred through the dermatology clinic of a hospital where they were diagnosed as having severe chronic psoriasis vulgaris. They were selected on the basis of location and size of psoriatic plaques with the a priori criteria as (a) a psoriatic plaque on either the hand, forearm, lower leg, or foot; and (b) a plaque of equal size on a symmetrically identical area on the contralateral limb. Selection was made by a physician uninvolved with the study and unaware of its specific purpose or design.

No payments or promises were made to the participants except that the results would be made available to them. They were simply told that this was an experimental procedure that had never before been tried and it might or might not have any beneficial effect on their condition.

Apparatus

The basic recording system was a biofeedback thermometer (BFT 302). One electrode was placed in the center of the experimental plaque (feedback condition) and another in the center of the control plaque (no-feedback condition). This electrode placement allowed immediate detection of the absolute temperature of both experimental and control plaques. Auditory and visual feedback on the current absolute temperature of the experimental plaque was presented to the patient during training via a tone-and-meter display. The tone varied in frequency with temperature variations, increases in frequency indicating decreases in temperature. The meter display (12.1 X 5.5 cm) indicated temperature variations of 2.5° F (1.39° C) in either direction from baseline, in graduations of .1° F (.06° C).

Patients were seated in a comfortable armchair to preclude bodily movement and possible artifact. Each participant sat facing a table upon which was placed the BFT thermometer. The experimenter sat to the side and somewhat behind the patient to avoid distracting him/her from the task. This seating arrangement also allowed easy access to the thermometer from which temperature data were collected at 5-minute intervals and recorded on a training log.

Design

The experimental design of this study involved two dependent variables: (a) changes in rate of cellular

proliferation, and (b) changes in surface temperatures of psoriatic tissue. Changes in cellular proliferation were measured by a before-and-after procedure. Changes in skin temperature involved repeated measures over time. These parameters were recorded for both the feedback and no-feedback conditions. Temperature feedback on one plaque was delivered via an electronic thermometer which was also used to record absolute temperature changes of both plaques. The participants received information as to the temperature variations on one plaque (feedback condition), but no temperature feedback was available on a plaque of identical size and location on the contralateral limb (no-feedback condition). Determination of the effect of temperature control on cellular proliferation was made through biopsies taken before and after training, and cell count using a tritiated-thymidine labeling procedure.

Previous research indicates that temperature control often results in generalized effects. This is especially applicable to the present study since absolute temperature was employed. Therefore, temperature data could be compared to cellular proliferation data in one of two ways. (1) If no generalization occurred, the design would consist of three experimental plaques and three control plaques. In this case, temperature control would have been established and temperature decreases achieved in the former; no voluntary control would have occurred in the latter. (2) Conversely,

if generalization did occur from the feedback to the no-feedback condition, the design would consist of six experimental plaques, each with its own temperature and cell proliferation data. In consideration of these possibilities, the terms experimental plaque (or limb) and feedback condition, and the terms control plaque (or limb) and no-feedback condition will be used interchangeably.

It was decided prior to selection of patients that the nondominant limb would be subject to the feedback condition for the first and third participants. Accordingly, the second participant would receive feedback on the dominant limb.

Procedure

The patient was seated in a temperature-controlled room where the apparatus had been previously assembled. At the beginning of the first training session the workings of the thermometer were explained and the following instructions read:

Through all sessions please relax, remain as quiet as possible, and breathe evenly. The tone you hear from the thermometer will go up as the temperature of the plaque on this (experimental) limb goes down. Also, the needle on the meter will move to the left. All you have to do is listen to the tone and notice the movement of the needle.

Just let the tone go up and let the needle move to the left.

You might find it helpful to think of the thermometer as another part of your body. You don't have to think about what you are doing, just let your body do it. Also, it sometimes helps to think of your arm as getting cooler--as if you'd just put it in a bucket of ice water.

There's really no one way to do this. Just do whatever works for you.

After the patient was prepared by attachment of the thermometer, there was a delay of 5 minutes to allow for adjustment of equipment, followed by a 10-minute rest period to allow for adaptation to the situation. The instrument was placed so the participant could not see the meter. Next, it was turned "on" with the audio mode in the "off" position. Three samples of (baseline) temperature data were collected on both the experimental and control plaques. The thermometer was then rotated so that the patient was able to read the meter and the audio mode turned "on." Over the next 30 minutes, six more samples of (training) temperature data were collected. These nine sample periods (baseline and training) occurred at 5-minute intervals. Each session lasted approximately one hour--of which 30 minutes were spent in training. Each patient participated in seven sessions spaced over a period of approximately one month.

Data on the feedback condition were read directly from the meter being observed by the participant. Data on the no-feedback condition were collected in the following manner.

(1) The instrument was turned "off." (2) The cabinet was rotated 90° (to prevent observation by the participant). (3) The electrode attached to the experimental plaque was replaced by the electrode attached to the control plaque (i.e., control electrode plugged into the operational jack of the recording instrument). (4) The instrument was again turned "on" (audio mode remained "off"). (5) Data were recorded. (6) Steps 1-4 were reversed to resume training. Unfortunately, this procedure involved a brief (approximately 10-second) interruption in training. An attempt was made to minimize the effects of such discontinuity by instructing the participants to expect regular interruptions throughout the sessions.

Biopsies were performed on the experimental and control plaques of each participant before the first and immediately following the last training session by a physician (naive as to the experimental design of the study) who was simply requested to take the pretraining biopsies on a given patient from symmetrically identical locations on the two limbs (within boundaries of specific plaques). He was requested to take the posttraining biopsies as close to the pretraining biopsies as possible.

Labeling procedure. Biopsies were analyzed to determine rate of cellular proliferation through the use of in vitro tritiated-thymidine labeling which was as follows for each biopsy. (1) A skin biopsy 3 mm in diameter was taken from the experimental and the control plaque. (2) These were immediately placed into containers of saline solution labeled "left" and "right" for transportation to the laboratory. (3) The specimens were then removed from the saline and cut into slices 1 mm thick or less. (4) The slices were placed into 50-ml conical Erlenmeyer glass flasks containing isotope (H^3T) in culture medium 100 so the concentration of H^3T was 2 μ c/ml. (5) A mixture of 95% oxygen and 5% carbon dioxide was bubbled continuous through the culture medium at 37° C during a two-hour incubation period. (6) The tissue was washed in several changes of isotope-free tissue-culture fluid to remove unincorporated excess isotope. (7) The slices of skin were then flattened on a coverslip and slid into fixative. (8) After appropriate fixation, the tissue slices were dehydrated, embedded in wax, and several 5-7 μ sections were prepared for radioautography.

Radioautographic technique. The radioautography consisted of dipping each slide in nuclear track emulsion (Eastman Kodak NTB3) at 43°-44° C in a completely dark room. The slides were allowed to dry for at least 3 hours before being placed in sealed boxes and put into the refrigerator at 4°-8° C for 14 days.

After developing (Eastman Kodak D19) and fixing the radioautography, the sections were treated with Wright's stain to set off one cell from another.

Counting procedure. The rate of proliferation was determined by counting the total number of epidermal cells along the basal layer (stratum germinativum) and the two layers immediately above--then dividing this number into the total labeled cells in these same layers. In this way, a ratio of the labeled cells to the total number of germinative epidermal cells was computed, yielding the percentage of cells in the process of mitosis. All counting was done by the experimenter. A naive technician placed the prepared slides into a slide-box with numbered compartments. The slides had been labeled by this time, but the labels were covered with opaque paper. The slides were not identified as to their respective conditions (feedback or no-feedback, dominant or nondominant) until all counting had been completed for all biopsies of each subject.

Results

The data obtained from the experimental manipulations of the present study indicate decreases in the surface temperature of psoriatic tissue as well as decreases in temperature for both the feedback and no-feedback conditions. Cell turnover rate decreased in biopsies from pretraining to posttraining. No systematic changes were observed in initial baseline temperature from session to session.

Each session consisted of nine sample periods for the collection of temperature data. During each respective sample period, an identical task was presented to the patient from session to session. For instance, period 1 was always the first baseline sample, period 4 always occurred immediately after the first 5 minutes of training, and period 9 was always the last temperature sample. By compiling the data separately for periods 1 through 9 across all sessions for each patient, it was possible to compute the mean value of each individual sample period. This computation yields a representative, or average, session for each participant. As shown in Figure 1, baseline temperature appears to fluctuate at random, while training temperature shows consistent decreases from one sample period to the next with only one exception (period 7 of Subject C's experimental limb). It may be noted also that for each participant, the feedback and no-feedback conditions show a roughly symmetrical downward trend (indicating decreases) in temperature during training.

A 2 X 7 analysis of variance for two repeated measures used experimental versus control plaque and sample period, beginning with the last baseline measurements (period 3) to the last training measurements (period 9) across all participants. Results showed nonsignificant F values for experimental versus control plaque and interaction. In this particular comparison, data from only three subjects were

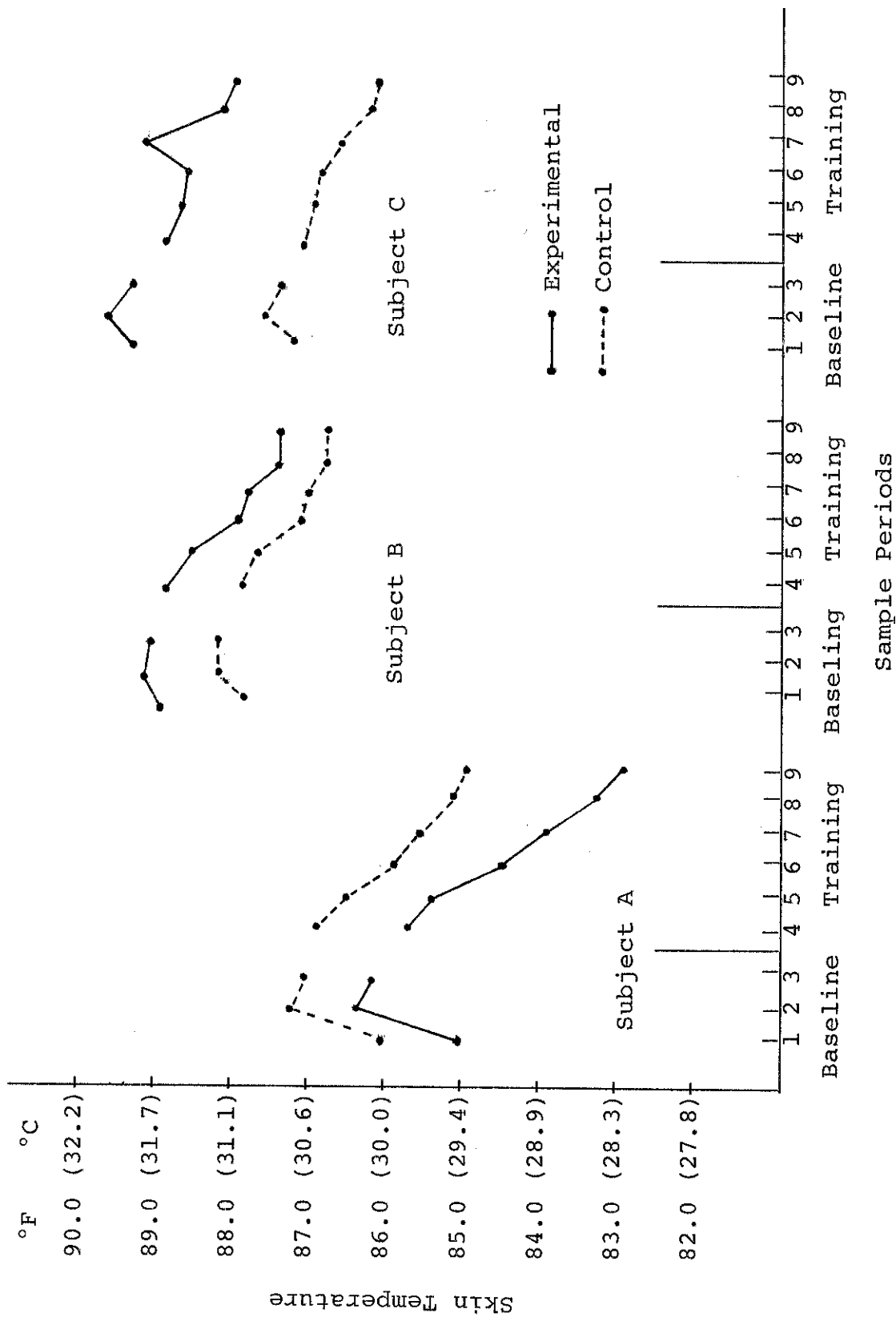


Figure 1. Mean temperature per sample period across all sessions for each subject.

analyzed. Therefore, even a significant F would have been difficult to interpret. The main purpose for completing this analysis was to demonstrate that skin temperature changes occurred over sample periods. The change in skin temperature as a function of sample period ($n = 6$) was significant, $F(6,26) = 3.29$, $p < .02$ (Table 1, Appendix A).

All the temperature data collected from the first three baseline periods (1, 2, and 3) and the last three training periods (7, 8, and 9) were separately compiled for each participant under both conditions in order to get an overall representation of the effects of training. As presented in Figure 2, mean-training temperatures are consistently lower than mean-baseline temperatures in every case. Comparison of the slopes of the feedback and no-feedback curves (within subjects) indicates similar temperature changes in both conditions.

Figure 3 is a representation of the total temperature change accomplished during each session by each patient for both conditions. These values were determined by computing the difference between the last baseline-temperature sample (period 3) and the last training-temperature sample (period 9) of each session.

Data presented in Figure 3 are consistent with those presented in Figures 1 and 2, in that there seem to be similar changes in temperature during training for the two conditions. This similarity is again less striking for Subject A than for

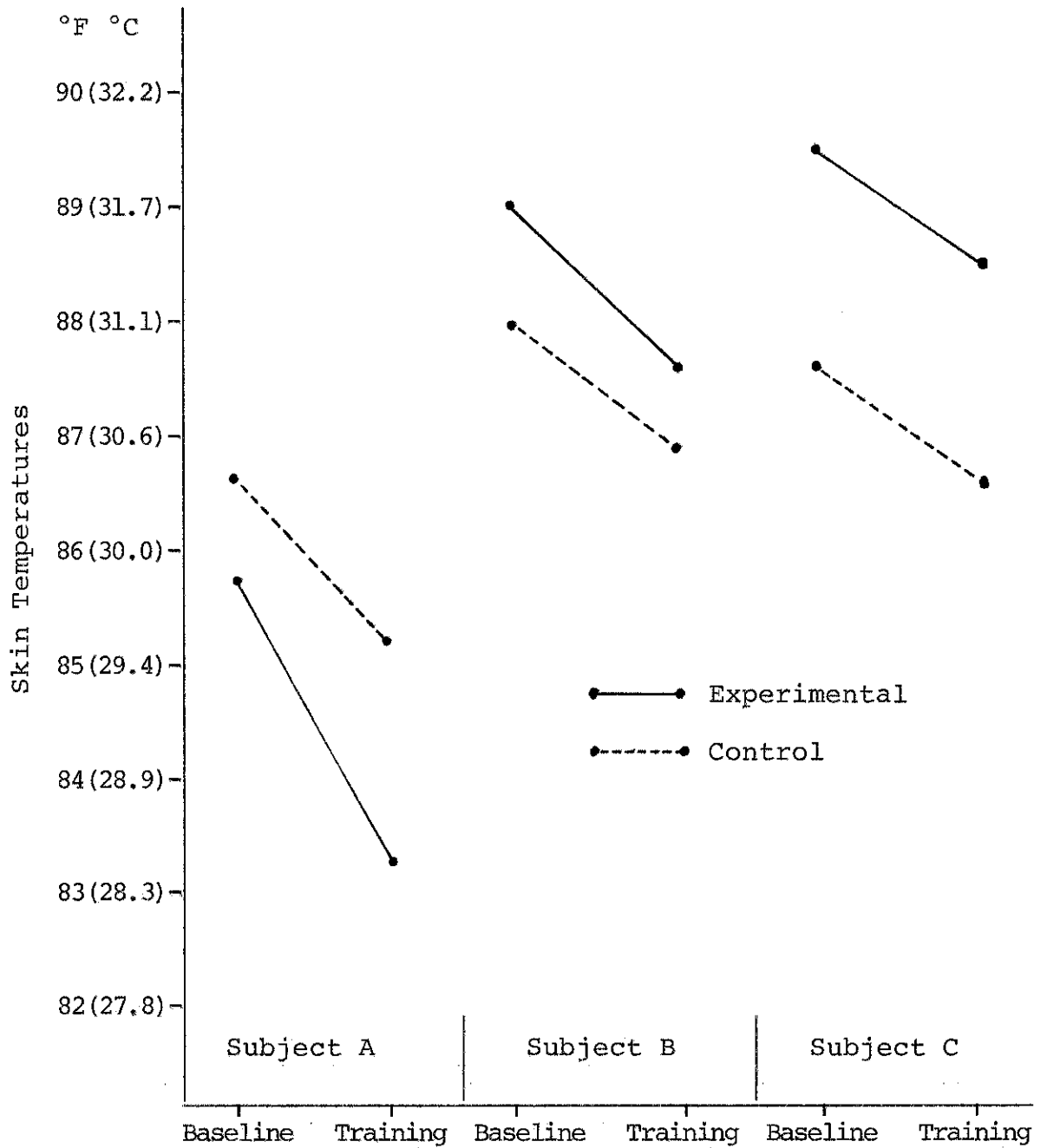


Figure 2. Mean of the first three baseline and the last three training sessions.

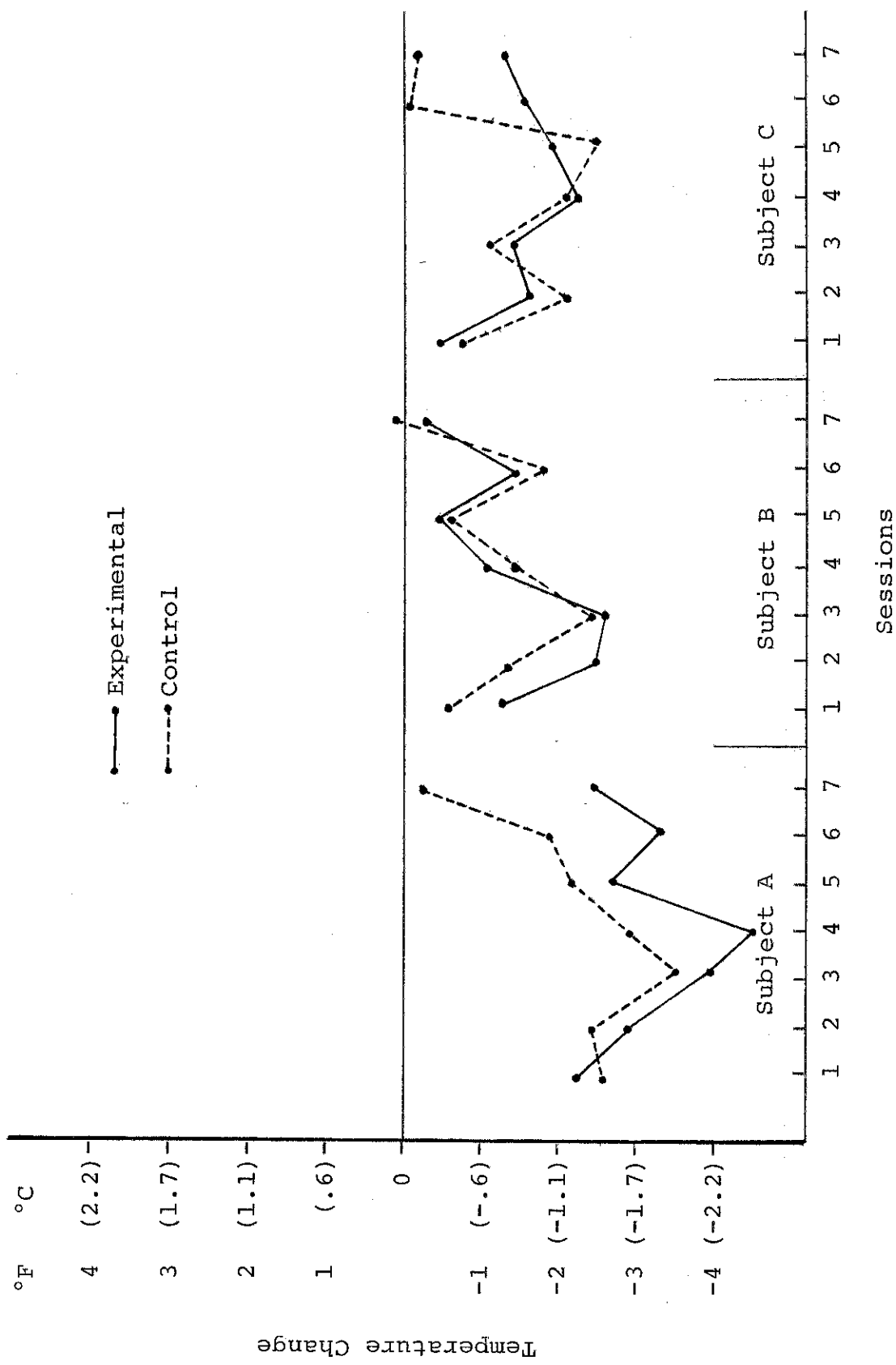


Figure 3. Mean change from baseline during training.

Subjects B or C. As may be noted in Figure 3, Subject A's experimental and control curves intersect only once throughout the seven sessions. On the other hand, experimental and control data points show considerably more correspondence and intersections for Subjects B and C.

Cell proliferation data, presented in Figure 4, show cell turnover rate to have decreased after training in all but one instance. This figure indicates cell turnover rate computed from biopsies taken before training and immediately after training. As shown in Figure 4, changes in rate of proliferation for the feedback and no-feedback conditions are approximately equal for Subjects B and C. In the case of Subject A, the changes in rate of cellular proliferation are quite different from one condition to the other. Subject A's control limb shows a slight increase in turnover rate. Subject B's cell proliferation data show reductions from the pretraining biopsy in the feedback and no-feedback conditions of 10.3% and 8.2%, respectively. The reductions for Subject C are 4.0% and 4.8%, respectively. In the case of Subject A, however, a reduction of 3.7% was attained under the feedback condition, while a 1.3% increase occurred under the no-feedback condition.

Initial baseline measurements (period 1) from session to session are presented in Figure 5. These data show no consistent trend from one session to the next.

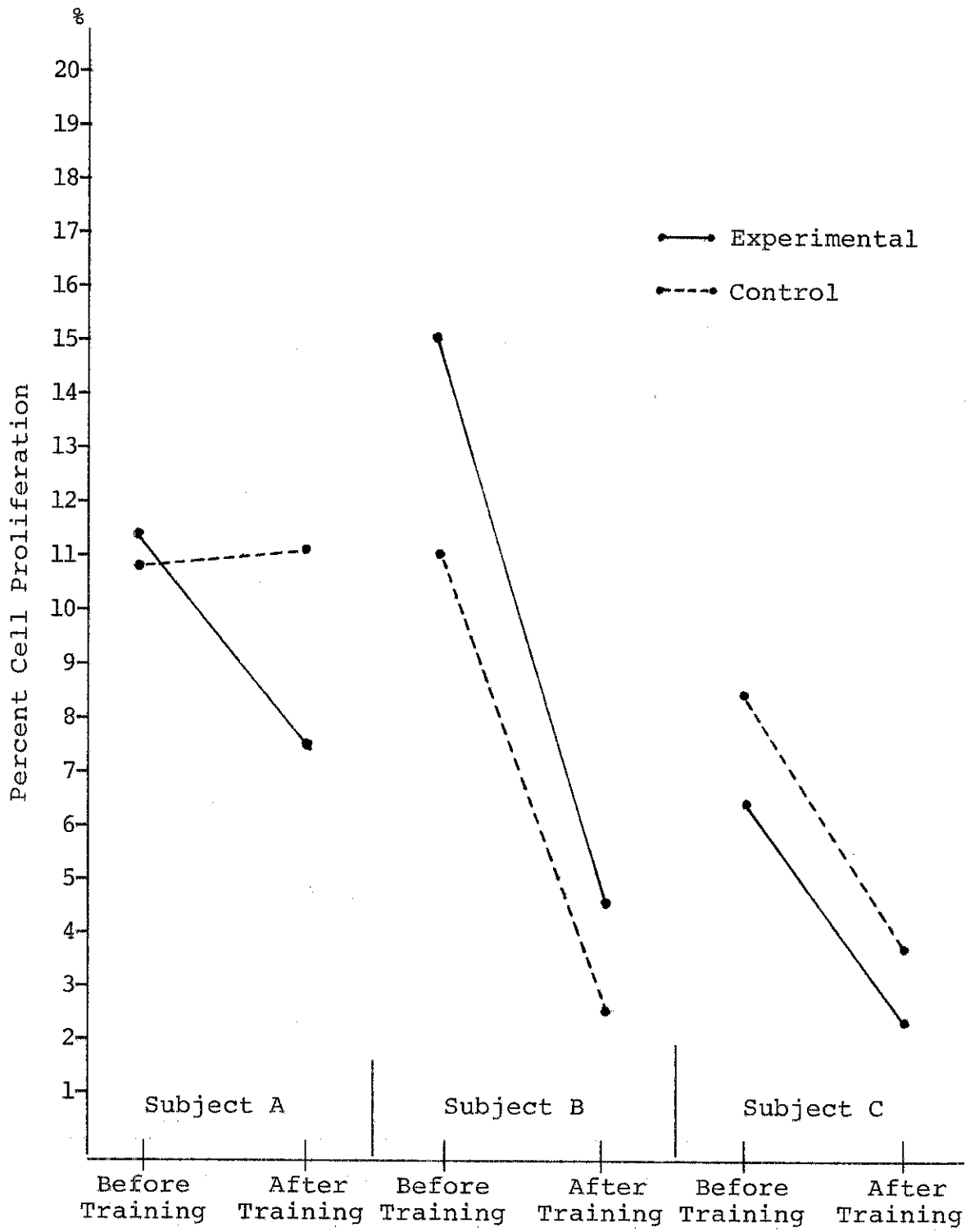


Figure 4. Percent cell proliferation before and after training.

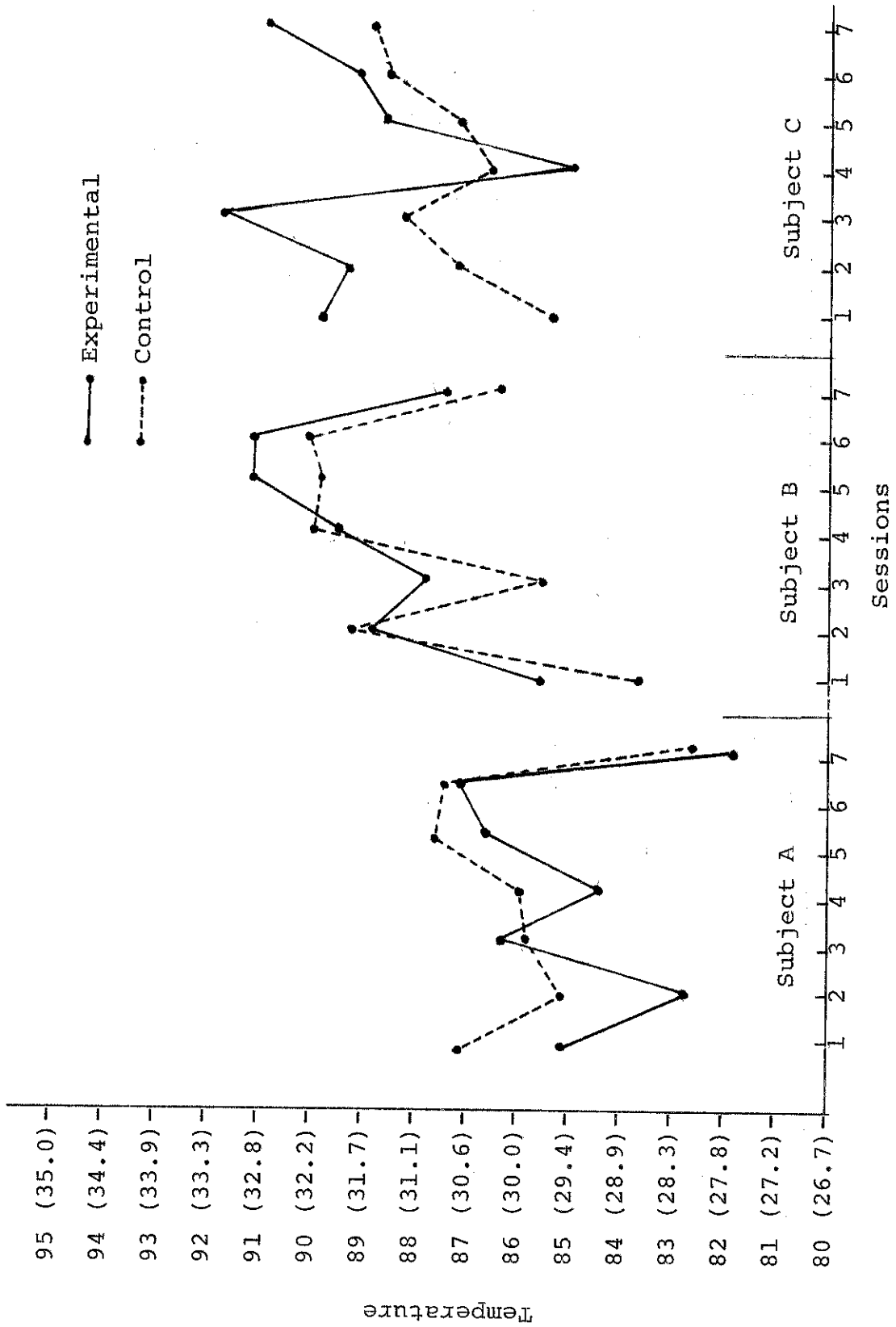


Figure 5. Initial baseline measurements (sample period 1) per session.

All plaques showed obvious clinical improvement in Subject B and Subject C. During the course of training (as early as the fourth session), their plaques underwent noticeable changes in appearance. It was noted that for these two patients, each plaque began as a clearly demarcated area of red tissue covered with layers of scales. By the end of the last training session all four of these plaques appeared only slightly pinker than uninvolved surrounding tissue. Scales were eliminated with few exceptions. In each case, however, a faint demarcation remained.

Subject A's plaques appeared as deep red areas covered with scales. The experimental plaque changed in color to a dark pink. Scales were still apparent, but clearly decreased in number. The control plaque showed very little change in appearance.

In an informal follow-up conducted four months after training, each of the participants reported that the improvements were still evident, but were beginning to show return to their original condition.

Discussion

Analysis of data collected during the course of this investigation would seem to present evidence in support of the first hypothesis--that psoriasis patients would be able to decrease skin temperature of psoriatic tissue through biofeedback, and at least tentative support of the second hypothesis--that there would be a decrease in rate of cell

proliferation corresponding to decreases in temperature. Comparison of baseline and training temperatures clearly indicate biofeedback training to have been effective in enabling patients to voluntarily decrease surface temperature of psoriatic tissue. The average temperature change per session of 1.3° F (.7° C) is quite small in comparison to what might have been expected from training subjects to increase skin temperature. This, however, was not unexpected. A comparable degree of temperature change was obtained by the only other published investigation which trained decreases in skin temperature (Johnson & Turin, 1975).

Due to the extremely small number of participants, statistical analysis of cell proliferation data is not presented. Nevertheless, the drastic reduction in cell proliferation lends considerable support to the hypothesis that voluntary temperature reduction of psoriatic tissue would correspond with decreases in rate of cellular proliferation. Training seems to have resulted in a generalized response in all participants. This may be concluded from the consistent similarity in temperature change from one condition to the other. Additionally, effects of the biofeedback-training procedure seem to have persisted for at least three months, as indicated by the informal follow-up.

The most obvious indication of a possible relationship between skin-temperature control and cell proliferation is the fact that both parameters showed changes in the same

direction during the experimental procedure. Careful consideration of the data yields additional, albeit tentative, evidence in support of this position. A small but consistent trend which recurs in reviewing the generalization data (feedback versus no-feedback) suggests that a somewhat greater degree of response specificity occurred in the case of Subject A than with Subject B or C. Inspection of the slopes of the acquisition curves presented in Figure 1 suggests similar training effects in the feedback and no-feedback conditions, especially for Subjects B and C. This trend can be more readily detected upon visual inspection of Figure 2. The data graphically presented in Figure 3, however, illustrate this tendency most clearly. Subject A, in all but the first session, achieved a greater degree of temperature change under the feedback condition than under the no-feedback condition. Conversely, temperature control seems equally effective in either condition for Subjects B and C. When these data are compared to the cell proliferation data of Figure 4, the trend persists--only more obviously.

This line of discussion is not intended to suggest a direct relationship. Such a position would be contrary to the data collected in the present investigation. Subject A's starting temperatures were consistently lower than the other patients' and his training sessions resulted in the greatest amount of temperature reduction. If temperature control were

directly related to cell growth, we would predict a larger reduction in cell proliferation and a lower initial growth rate for Subject A. Instead, the results show Subject B to have attained the most drastic reduction in cell turnover rate--and Subject C, the lowest initial growth rate. Also, a direct relationship would require generalization of training effects from session to session. This was not achieved as shown in Figure 5.

The present findings support the hypothesis that some aspect of the biofeedback training was responsible for the reduction in proliferation of diseased tissue. In the present biofeedback-training procedure, feedback was delivered not only on temperature variations, but (in a more general sense) on degree of success at voluntary control of a physiological process. It is possible that the response of voluntary temperature control requires activation of a more basic psychological process or state, common to voluntary control of certain physiological functions. If this were the case, initiation of this process would be signaled by the resultant temperature changes in the appropriate direction. Having received this signal, a psoriasis patient might begin attending to his/her psoriasis in the same manner that had resulted in successful temperature control. In doing this, he/she would be applying a similar procedure to the psoriatic tissue as had been successful with temperature control previously. The degree of correlation between

temperature change and cell proliferation would thus be determined by the extent to which each participant attended these two functions simultaneously.

There are alternative explanations. For instance, it is possible that psoriasis is susceptible to emotional or attitudinal factors. This position is supported by Graham's (1954) conclusion that in 8 of 10 patients he studied, there was a "clear-cut temporal correlation between the presence of disturbing life situations and onset of flare-up of psoriasis" (p. 379). In 1959, Susskind and McGuire (cited in Baughman & Sobel, 1971) used an interview technique to document a possible temporal relationship between emotionally charged events and onset or relapse of psoriasis in 20 unselected patients. They concluded that such a relationship existed for onset in 40% of the cases and for relapse in 70% of the cases studied. In a 5-year study of 252 psoriasis patients, Baughman and Sobel found stress and severity of psoriasis to be "moderately but significantly positive" (p. 65). La Barba (1970) reviewed several studies which resulted in evidence supporting this hypothesis for cancer as well. Blumberg (1954) showed tumor growth rate to be related to performance on the Minnesota Multiphasic Personality Inventory. Schmale and Iker (1971) concluded that depression affiliated with hopelessness was a predictor of whether or not cancer would be detected in women presenting for cervical bone biopsy.

If emotional or attitudinal factors are involved in psoriasis, biofeedback training may have been effective through the establishment of better emotional control by the patients. It is possible that through training, the patients' attitudes were changed by demonstrating to them that they did, in fact, have some control over the diseased areas.

The present investigation could have been improved in several ways. A necessary aspect of any further study of this kind would be a larger number of participants. A false-feedback condition would have been instrumental in determining the specific effect of biofeedback per se. Additionally, the use of a second thermometer (used exclusively for monitoring the no-feedback condition) would have precluded the necessity of interrupting the training sessions. Steps could have been taken to maximize training effects from session to session by increasing the number of training sessions, reducing the interval between sessions (one per day instead of one per week), or attenuation of feedback by gradually introducing more intermittent schedules.

Visually, the plaques cleared up completely in Subjects B and C, and showed great improvement in Subject A. Consequently, before-and-after pictures of the plaques would have made the results much clearer. If done in some standardized manner, pictorial data would also have allowed for a long pretraining baseline and a formal follow-up. In the present study, changes of a magnitude great enough to yield clear-cut

visual differences in plaque appearance were a complete surprise. It is for this reason that plaque appearance was not recorded via before-and-after photographs.

The significance of the present study include the fact that it was the first to show skin-temperature control of diseased tissue through biofeedback techniques. This indicates that psoriasis patients may be able to learn appropriate vasoconstrictive responses, thereby enabling them to better adapt to ambient temperature changes. There exists the distinct possibility that patients may be able to reduce or eliminate psoriasis in specific areas. This is of therapeutic value especially because current chemotherapy often involves the use of many drugs with dangerous side effects. The results also suggest an area of needed investigation in cancer research. Perhaps the most important aspect of the present study is the indication that control of physiological functions at the cellular level can be affected by biofeedback techniques.

In summary, the exact mechanism by which the results were achieved cannot be ascertained without further investigation. The fact remains, however, that decrease in cellular proliferation did occur and seemed to be in some way related to temperature change achieved during biofeedback training. Furthermore, since this procedure produced dramatic improvement in the diseased state and was in no case detrimental, these data should be of great interest to anyone in the field of behavioral medicine.

Appendix A

Table 1

Summary Table of the Analysis of Variance for
Skin Temperature Changes over Sessions
in Experimental and Control Plaques

Source	DF	Sum of Squares	Mean Square	<u>F</u>	<u>p</u>
Blocks	2	59.389	29.695	35.703	0.000
Treatments	13	17.986			
Experimental					
vs. Control	1	1.375	1.375	1.654	0.210
Sessions	6	16.396	2.733	3.286	0.015
Interaction	6	0.215	0.036	0.043	0.999
Residual	26	21.624	0.832		
Total	41	98.999			

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