STUDY TITLE: Hormonal, Amino Acid, Neurotransmitter, GDV and Physiological Testing of the LifeWave Silent Nights Patches

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LifeWave Protocol: SN2011-001

I have read this report and confirm to the best of my knowledge it accurately describes the conduct and results of the study.

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Date

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Connor, M. and Eickhoff, J.

Abstract

Objective: This was a pilot study of 5 healthy subjects who all wore the active patch aged 21 and above, to assess physiological changes of the sealed FDA registered homeopathic *Silent Nights* patch made by the Lifewave Corporation.

Procedure: Subjects were consented and then the first baseline neuro-transmitter, amino acid and hormonal samples were collected for hormonal testing. Additional tests were done on day 2, 6 and 7. Gas Discharge Visualization device and Thought Technology ProCom with BioGraph Infinity and CardioPro software's physiology suite and HRV testing were taken as a baseline and then day 2, 6 and 7 of the test week.

The Telegen Absorption scale, Marlowe-Crowne Social Desirability scale, Profile of Mood States, Restorative Sleep Questionnaire, the Sleep Scale, Global Mode Scale and Hassles and Uplift scales, sVAS for sleep and a daily sleep and food diary were all utilized during the study.

Participants: Participants were recruited by flyer and email. All participants were healthy, with no chronic conditions and over the age of 21.

Results:

Neurotransmitters, Amino Acids and Hormonal tests:

Two of the participants showed a 202% increase in melatonin over the seven days. Serotonin was significant in all five subjects for all time points over seven days $p=0.0030$ on day 6 and $p=0.0097$ on day seven. Serotonin is the precursor necessary to make melatonin. Significant changes were detected for most neurotransmitter parameters for all times points.

Exception to neurotransmitter significance were for Mtyramine (from day 1 to day 6 and day 7), Glutamate (from baseline to day 6), LDOPA (from day 1 to day 7), NAD/ADR (from day 1 to day 6), Normetane (from day 1 to Day 7), and Theanine (from day 1 to day 2, day 6, and day7), where no significant changes were observed.

There were no significant differences detected for the changes from the baseline to last treatment day assessment between arms for estradial, progesterone, or testosterone.

Physiological Measures:

No significant changes from day 1 to day 2, 3, or 4 were detected for Average HRV/EMG parameters, except for Temperature (F) from Day 1 to Day 4 (epoch 1) (-8.5+/-4.43, $p=0.0313$) and Temperature (F) from Day 1 to Day 4 (epoch 2) (-8.82+/-5.45, $p=0.0479$). No significant changes from day 1 to day 2, 3, or 4 were detected for Mode

HRV/EMG parameters, except for Temperature (F) from Day 1 to Day 4 (epoch 1) (-7.78+/-4.04, p=0.0313). No significant changes from day 1 to day 2, 3, or 4 were detected for Area HRV/EMG parameters, except for Temperature (F) from Day 1 to Day 4 (epoch 2) (-529.04+/-326.74, p=0.0479).

GDV:
A significant decrease in fractality dimension is observed (-0.04+/-0.03, P=0.0376) is observed from baseline to Day +6 at the "3 –Left" finger assessment. A marginally significant decrease was observed for fractality form coefficient from baseline to Day +7 (-7.37+/-7.16, P=0.0828) at the "4 Right" finger assessment.

Questionnaires:
A significant decrease (-4.0+/-2.92, p=0.0373) in Global Mood Scale –Negative Affect from day 1 to day 5 was detected. Significant decreases in the POMS score from Day 1 to Day 6 (-9.2+/-4.02, p=0.0069) and from Day 1 to Day 7 (-12.6+/-2.61, P=0.0004) were observed. Marlowe-Crowne Scale showed that four of the five participants presented in the normal range for social correctness and desirability. One individual leaned toward politically correct answers.

No significant changes were detected for both the Visual Analogue Scale for Sleep, the Hassle and Uplift scale, Telegen Absorption Scale, the Restorative Sleep Questionnaire and the Sleep Scale.

Conclusion:
The significant change in most of the neurotransmitters tested, in all participants, in a study with a sample size this small and with data taken for only a week is relevant. Rapid and consistent change in neurotransmitters to this degree over this period of time is unusual in the literature. Further, while there was no overall significance in Melatonin production in this trial because of the age differential of participants and small sample size, the 202% increase in melatonin in subjects who were under the age of 30 should be explored. It will be important to include age stratification, as Melatonin production is known to decline as one ages.

The additional significance of the change in the temperature parameter in HRV recordings supports an over all down regulation of stress parameters which while not fully reflected in the data because of the small sample size, would reflect an overall down regulation of the stress parameters. Additional study should be done to determine if the significance of the temperature change in a larger sample size with a longer data taking period does in fact demonstrate a reduction in stress parameters.

The GDV data supports the down regulation of stress parameters with significance in the areas of hypothalamus, nervous system and thoracic area of the polyvagal system.

While there was no direct significance in the changes in the sleep questionnaires, the change in the Global Mood Scale and Profile of Mood States showed that there was a significant reduction in negative affect as a result of an increased feeling of wellbeing.

Recommendations: A larger trial should be done to determine if significance of neurotransmitter responses are consistent in a larger sample size and should be done over a longer period of time to determine if the longer period taking the data allows for the significant increase in serotonin in all subjects to create an increase in melatonin in all subjects as serotonin is the precursor to melatonin.

Key Words: Homeopathy, Energy Medicine, Serotonin, Melatonin, Neurotransmitters HRV, EMG, Lifewave, Acrylic Patch

Hormonal, Amino Acid, Neurotransmitter, GDV and Physiological Testing of the Lifewave Silent Nights Patches

Connor, M. and Eickhoff, J.

Introduction

This study attempted to discover if there are specific physiological changes produced by the application of the LifeWave *Silent Nights* patch. Anecdotal reports and early research support users falling asleep faster and staying asleep longer as the result of wearing the patch. This is a sealed non-transdermal patch and is a FDA registered homeopathic product. The patches in this study are consistent with the commercial LifeWave product. The study design was a pilot single arm, longitudinal study with baseline, daily and post-treatment follow-up assessments with N=5 participants with data taken over seven days. Baseline data was taken and all participants wore the LifeWave *Silent Nights* patch for 6 nights for a minimum of 8 hours. Patches were placed at the CV6 point. The placement of the patch at a specific acupuncture point supports changes in the electro-dermal skin conductance of that acupuncture point. It is possible that there is a signal strengthening effect produced by the patch.

Homeopathy

There has been significant misinformation and misunderstanding over the last 100 years as to the mechanisms through which homeopathy works on and with the human body. Various possible mechanisms have been proposed which include changes in cell membrane permeability to water, energy effects and stimulation of the autoimmune system.

Altering molecular properties of water.

Research performed at the Penn State Materials Science Laboratory by Roy et al. (2005) demonstrated that there were clear specific molecular changes in the structure of the water in homeopathic remedies. Research done by Chaplin, (2007) showed specific molecular clustering in water which was significantly different from the standard chemical understanding of H_2O. In addition, Chaplin, (2007[2]) showed that water may retain a level of memory related to epitaxy or the ability of a substance to form into the shape of its container. In this case we are considering the human body as the container. The work by Chaplin continues earlier work done by Del Giudice (1994) which demonstrated that water has unique characteristics among physical materials and might have the ability to retain a level of memory of a substance with which it had been in contact. Research done by Rao et al. (2007) using Raman Spectroscopy, showed that there were discrete differences between the molecular structures of water clusters at different homeopathic potencies.

Research done using TEMS microscopy Chikramane et al. (2010) demonstrated that in the case of homeopathic remedies containing metals, nanoparticles of the metals were

imbedded in the molecular structure of the water even in ultra-high dilutions. This appears to be an exception to the earlier findings that with greater dilutions there are no particles of the original substance present. TEMS microscopy is a new way of examining the molecular structure of homeopathic products. This is one of the first studies using this technology.

The law of similars

Homeopathy is classically thought to work from the "law of similar." It suggests that loading the body with a reactant which produces a similar physical result to the current illness will "wake the body up" to the fact that there is a problem and trigger a system wide response. In the non-linear dynamical theory of homeopathy introduced by Bell et al. (2004, 2006, 2010) and further characterized by Koithan at al. (2007) and Menk et al. (2010), it is suggested that a healthy body lives on the edge of chaos and is thus able to respond rapidly to changes in environmental stimuli. Disease is produced by the individual becoming stuck in one order and thus not being able to respond appropriately to stimuli. This theory is consistent with heart rate variability being significantly greater in healthy, relaxed people, than in those who are emotionally stressed (Task Force of The European Society of Cardiology, 1996). As a result, individuals with healthy body systems should produce oscillations in their responses to stimuli and when a homeopathic remedy is introduced into a "stuck" system it should produce a more significant stimulation and the resulting pattern of oscillation should disrupt the stuck system, eventually returning the individual to health.

LifeWave Silent Nights patch has the following formulary: Aconitum Napellus (Monkshood), Arsenicum Album (Arsenious Acid), Avena Sativa (Common Oat), Belladonna (Deadly Nightshade), Camphora (Camphor), Cinchona Officinalis (Peruvian Bark), Coffea Cruda (Unroasted Coffee), Cypripedium Pubescens (Yellow Lady's Slipper), Hyoscyamus Niger (Henbane), Passiflora Incarnata (Passion flower), Pulsatilla (Wind Flower), and Valeriana Officinalis (Valerian). Each ingredient is in equal volumes of either 10x, 30x, and LM1 potencies in a pure water base.

Gas Discharge Visualization (GDV)

The GDV device was developed in the mid 1990's by Dr. Konstantin G. Korotkov, a Russian professor of Physics at the St. Petersburg Technical University in Russia. The device was developed as a way of photographing and measuring the spectrum of gas emission from the fingertips and the potential biophoton emission. When using the GDV device, the fingertip of the subject is placed on a dielectric plate. The image generated and captured by the camera results from the movement of electrons across the dielectric plate (assuming the finger has a positive potential) and the subsequent collision and ionization of the gas molecules surrounding the finger. The camera takes an image of this emission, which often appears as a corona or branch-like pattern around the finger. Each image takes 1 second to generate, and is stored in a computer for later analysis. Images are taken from each finger on both hands.

Computer software analyzes the spectrum, density and fractal patterns of the discharge from each finger-tip. Additional analysis can be done by specific sections of the finger tips which have been mapped to specific organs of the body. (See Appendix A: GDV development bibliography.

Approved in Russia for clinical use after recommendation of the Russian Academy of Science, the device was approved by the Russian Health Authority for general clinical use without limitations in 1999. Though the device is still considered an experimental device in the US, it is in use in 20 countries and is considered a diagnostic and clinical treatment device in most of them. The largest area of conflict in the acceptance of the device in the US appears to be that the display and analysis programs are centered on the acupuncture meridian system which is in standard use in Russia and Asia, rather than on the organ system standard used in the United States. The GDV software standard display and analysis suite was done looking at specific regional data by finger-tip which is related to specific organs.

The Meridian System

The theory of balancing the body based on the Chinese meridian system is over 3000 years old. Current information now maps the meridian system to parts of the lymphatic system. The concept of the release of "Qi" or correlated with static electric overcharge, though not established as representing a bioelectrical phenomenon, on an area of the lymphatic system is consistent with the evidence that the body has a variety of electrical-dermal potentials across its surface (Becker & Selden, 1985, Flick, 2004) and that acupuncture points are (at least in part) strategic conductors of electromagnetic signals (Feinstein, 2010).

The National Institute of Health in the US performed a detailed review of acupuncture research and published a Consensus Statement on Acupuncture:

> Acupuncture as a therapeutic intervention is widely practiced in the United States. While there have been many studies of its potential usefulness, many of these studies provide equivocal results because of design, sample size, and other factors. The issue is further complicated by inherent difficulties in the use of appropriate controls, such as placebos and sham acupuncture groups. However, promising results have emerged, for example, showing efficacy of acupuncture in adult postoperative and chemotherapy nausea and vomiting and in postoperative dental pain. There are other situations such as addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, low back pain, carpal tunnel syndrome, and asthma, in which acupuncture may be useful as an adjunct treatment or an acceptable alternative or be included in a comprehensive management program. Further research is likely to uncover additional areas where acupuncture interventions will be useful.

Saliva Testing for Amino Acids and Hormones

Saliva testing receives mixed reviews in the literature since they produce different results than a blood test. Recent research has shown body tissues use both weakly bound and free forms of hormones at receptor sites. Blood tests only measure the amount of hormone in the blood serum. Saliva testing measures the amount of free or unbound hormone in the saliva, (Dollbaum & Duwe, 1997.) Saliva testing was selected for this study so that a comprehensive measure of the free hormones could be obtained. In addition, saliva testing is much more convenient and is less invasive for subjects.

Subjects will self-administer the swab each day under the supervision of Dr. Connor when in the laboratory, which will then be placed back in the shipping container and labeled with the subject number. Samples were then kept in the freezer at -20F and were be shipped with ice by Federal Express to the Sabre Science lab on a daily basis. Tests include Cortisol, DHEA, Testosterone, Estrogen, Progesterone.

Urine Testing for Neurotransmitters

Standard urine testing for neurotransmitters was done at 10 am on day one, two, six and seven. Tests included: Melatonin, Serotonin, Dopamine, Serotonin/Dopamine ratio, Norepinephrine, Epinephrine, Gaba, Glutamate, and Histamine. Each vial was individually numbered and shipped overnight to Saber Sciences Laboratory for analysis.

Thought Technology ProCom Infiniti Physiology Suite

The physiology suite included testing for EMG, EKG, HRV, temperature, skin conductance, respiration, blood volume pulse and galvanic skin response. The ProCom Infinity is one of the most used biofeedback and portable physiology suites available with 2048 samples per second. It uses the BioGraph and CardioPro software to provide comprehensive data taking and analysis.

Materials

This study utilized *Silent Nights* non-transdermal patch made by the Lifewave Corporation. The Thought Technology ProCom Infiniti Physiology Suite for Heart Rate Variability (HRV) and other physiological measures, a Gas Dicharge Visualization device, saliva testing, urine analysis for neurotransmitters and standardized psychological questionnaires. Specialized software developed by Thought Technologies was used to do the HRV analysis. Specialized software included in the GDV system was used to do the fingertip area and density analysis.

Questionnaires included the Marlowe-Crowne social desirability scale, the Hassels and Uplift scale, the Telegen Absorption scale, the Global Mood Scale, Leeds Sleep Questionnaire, the Profile of Mood scale, the Restorative Sleep Questionnaire, and the sVAS visual analogue scale for sleep. In addition, subjects were asked to keep both sleep and food journals.

Methods

Application for human studies permission was made to the National Foundation for Energy Healing internal review board and the study approved as NFFEH 10-17-11-19.

Study recruitment was begun and subjects were recruited by email announcement, through radio announcements and word of mouth. Flyers were also placed on public access bulletin boards. Interested persons were asked to call in to the study call number.

Inclusion criteria: Any healthy individuals with no chronic conditions who were not pregnant and were over the age of 21 were recruited. At the time individuals called by telephone, their eligibility to participate was reviewed and if they were over the age of 21 and met the inclusion/exclusion criterion they were asked to confirm that they did not have any of the following psychological/physical conditions:
1. A history of psychological disorders
2. A history of drug or alcohol abuse
3. A history of any major medical problems
4. Female subjects who are pregnant were also excluded.

Dr. Connor met with the subjects in person at 8:00am to review the consent form and consented subjects. After consenting the Telegen Absorption scale and the Marlow-Crowne Social Desirability Scale, Global Mood Scale, sVAS and Leeds sleep questionnaire were administered. Baseline Gas Discharge Visualization data and Thought Technology measures were taken.

Schedule of Tests:
Initial Contact: Consenting, demographics and baseline questionnaires. (Minimum score of 5 on the Leeds sleep quality questionnaire.) Baseline GDV and Physiology measures.

Day One: Baseline Saliva Neuro-transmitter test taken at 10am. Saliva hormone and cortisol taken during the next 24 hours. Questionnaires, food and sleep diary. GDV and Physiology measures.

Day Two through Six: Neuro-tramsmitter test taken at 10 am on day two and day six. Patch application at night. Questionnaires (day two and six), food and sleep diaries each day. GDV and Physiology measures.

Day Seven: Neurotransmitter test taken at 10 am. Salivary Hormone and Cortisol testing taken five times during the day. Questionnaires, food and sleep diary. GDV and Physiology measures.

The five subjects had seven days of testing which included GDV, physiological measures (HRV, pulse, respiration, galvanic skin response, EMG, EKG), salivary neurotransmitter testing (Serotonin, Dopamine, Serotonin/Dopamine ratio, Norepinephrine, Epinephrine, Gaba, Glutamate, and Histamine) and salivary cortisol and hormonal testing. Questionnaires, food and sleep diary will be done each day. The questionnaires will include Leeds Sleep Quality Index, Tellegen Absorption Scale, Global Mood Scale, Hassels and Uplift Scale, Marlow-Crowne Social Desirability Scale, Profile of Mood States, and Visual Analogue Scale self-assessment for quality of sleep (sVAS).

Statistical Methods

Descriptive statistics were generated to summarize clinical outcomes. Specifically, all outcome measures were summarized in terms of number of means, standard deviations and 95% confidence intervals (CI), stratified by assessment time point. Absolute changes from baseline to Day 1, 2, 3, 4, 5, 6 and 7 were summarized in terms of means, standard deviations and 95% confidence intervals. Changes from baseline to Day 1, 2, 3, 4, 5, 6, and 7 were evaluated using a paired t-test. Analogously, absolute changes from Day 1 to Day 2, 3, 4, 5, 6 and 7 for neurotransmitter parameters were summarized in terms of means, standard deviations and 95% confidence intervals. Changes from Day 1 to Day 2, 3, 4, 5, 6 and 7 were evaluated using a paired t-test. For melatonin values, the Area under the Curve (AUC) over time (8PM to 8AM following day) was calculated using the trapezoid rule. All p-values are two-sided and $P < 0.05$ was considered statistically significant.

Results

Study Design: Single arm, longitudinal study with baseline and post-treatment follow-up assessments with N=5 participants.

Study Endpoints:

Melatonin
Assessments:
Baseline: 8PM, 12AM, 4AM, 8AM,
Post-test: 8PM, 12AM, 4AM, 8AM,

Neurotransmitter Parameters
Assessments:
Day 1, 2, 6 and 7

Amino Acids
Assessments:
Day 1, 2, 6 and 7

HRV and EMG
Assessments:
Day 1, 2, 6 and 7

GDV
Assessments:
Day 1, 2, 6 and 7

Questionnaires
Assessments:

	Day						
	1	2	3	4	5	6	7

Marlowe Crowne	X						
Restorative Sleep	X	X	X	X	X	X	X
Profile of Mood Scales	X				X	X	X
Global Mood Scale	X	X	X	X	X	X	X
Sleep Scale	X	X					X
Leeds	X	X	X	X	X	X	X
Absorption	X						
Hassle and Uplift	X						X

Melatonin

No significant changes in melatonin values from baseline were detected at all time points. However, when individual participants are reviewed there is a 202% increase in Melatonin for participants under the age of 30. This increase was canceled out by the limited but existing change in Melatonin production in participants over age 65.

Neurotransmitter and Amino Acid Parameters

Significant changes were detected for most neurotransmitter parameters for all time points, except for Mtyramine (from dayl 1 to day 3 and 4), Glutamate (from baseline to day 3), LDOPA (from day 1 to day 4), NAD/ADR (from day 1 to day 3), Normetane (from day 1 to day 4) and Theanine (from day 1 to day 2, day 3 and day 4), where no significant changes were observed. No significant changes were recorded in Amino Acids

Analysis of HRV and EMG Parameters

No significant changes from day 1 to day 2, 3, or 4 were detected for Average HRV/EMG parameters, except for Temperature (F) from Day 1 to Day 4 (epoch 1) (-8.5+/-4.43, p=0.0313) and Temperature (F) from Day 1 to Day 4 (epoch 2) (-8.82+/-5.45, p=0.0479). No significant changes from day 1 to day 2, 3, or 4 were detected for Mode HRV/EMG parameters, except for Temperature (F) from Day 1 to Day 4 (epoch 1) (-7.78+/-4.04, p=0.0313). No significant changes from day 1 to day 2, 3, or 4 were detected for Area HRV/EMG parameters, except for Temperature (F) from Day 1 to Day 4 (epoch 2) (-529.04+/-326.74, p=0.0479).

GDV

A significant decrease in fractality dimension is observed (-0.04+/-0.03, P=0.0376) is observed from baseline to Day +6 at the "3 –Left" finger assessment. A marginally significant decrease was observed for fractality form coefficient from baseline to Day +7 (-7.37+/-7.16, P=0.0828) at the "4 Right" finger assessment.

Questionnaires

A significant decrease (-4.0+/-2.92, p=0.0373) in Global Mood Scale –Negative Affect from day 1 to day 5 was detected. Significant decreases in the POMS score from Day 1 to Day 6 (-9.2+/-4.02, p=0.0069) and from Day 1 to Day 7 (-12.6+/-2.61, P=0.0004) were

observed. Marlowe-Crowne Scale showed that four of the five participants presented in the normal range for social correctness and desirability. One individual leaned toward politically correct answers.

No significant changes were detected for both the Visual Analogue Scale for Sleep, the Hassle and Uplift scale, Telegen Absorption Scale, the Restorative Sleep Questionnaire and the Sleep Scale.

Discussion

This study suffered from the very small sample size. In addition, the study data is reflective of the significant age difference between individuals recruited for the study. While overall significance was not demonstrated in Melatonin production in the study largely because of inclusion of individuals over the age of 65 who have age dependant Melatonin production differences from individuals in their 20's, a larger sample size that is organized into age groups should clarify the question of significance particularly in the age 21-40 age grouping.

It is interesting that in such a small study, which included such substantial age differentials, significance was achieved in the production of most neurotransmitters and in data which is consistent with the beginnings of the down regulation of stress parameters. The GDV data which supports changes in the polyvagal response is also consistent with these early markers of change. An increase in the total period during which data is taken on the next study should help determine the overall depth and consistency of change.

There was no significant difference in the Marlowe-Crowne Social Desirability Scale total scores or the Telegen Absorption Scale Total scores detected between arms. The lack of significance in the Marlowe-Crowne would suggest that both groups were consistent in providing correct answers rather than providing answers which were motivated by a need to perform on the tests in a particular way. The lack of significance in the Telegen Absorption Scale would suggest that the results of the study were not based on the subjects being susceptible to hypnosis.

Conclusion

The significant change in most of the neurotransmitters tested, in all participants, in a study with a sample size this small and with data taken for only a week is relevant. Rapid and consistent change in neurotransmitters to this degree over this period of time is unusual in the literature. Further, while there was no overall significance in Melatonin production in this trial because of the age differential of participants and small sample size, the 202% increase in melatonin in subjects who were under the age of 30 should be explored. It will be important to include age stratification, as Melatonin production is known to decline as one ages.

The additional significance of the change in the temperature parameter in HRV recordings supports an over all down regulation of stress parameters which while not fully reflected in the data because of the small sample size, would reflect the beginnings of a down regulation of and reduction in stress parameters. Additional study should be done to determine if the significance of the temperature change in a larger sample size with a longer data taking period does in fact demonstrate a reduction in stress parameters.

The GDV data supports the down regulation of stress parameters with significance in the areas of hypothalamus, nervous system and thoracic area of the polyvagel system.

While there was no direct significance in the changes in the sleep questionnaires, the change in the Global Mood Scale and Profile of Mood States showed that there was a significant reduction in negative affect as a result of an increased feeling of wellbeing.

Recommendations: A larger trial should be done to determine if significance of neurotransmitter responses are consistent in a larger sample size and should be done over a longer period of time to determine if the longer period taking the data allows for the significant increase in serotonin in all subjects to create an increase in melatonin in all subjects as serotonin is the precursor to melatonin.

Appendix A
Statistical Analysis Report – Sleep Pilot Study

Statistical Methods:
Descriptive statistics were generated to summarize clinical outcomes. Specifically, all outcome measures were summarized in terms of number of means, standard deviations and 95% confidence intervals (CI), stratified by assessment time point. Absolute changes from baseline to Day 1, 2, 3, 4, 5, 6 and 7 were summarized in terms of means, standard deviations and 95% confidence intervals. Changes from baseline to Day 1, 2, 3, 4, 5, 6, and 7 were evaluated using a paired t-test. Analogously, absolute changes from Day 1 to Day 2, 3, 4, 5, and 6 for neurotransmitter parameters were summarized in terms of means, standard deviations and 95% confidence intervals. Changes from Day 1 to Day 2, 3, 4, 5 and 6 were evaluated using a paired t-test. For melatonin values, the Area under the Curve (AUC) over time (8PM to 8AM following day) was calculated using the trapezoid rule. All p-values are two-sided and $P < 0.05$ was considered statistically significant.

Study Design: Single arm, longitudinal study with baseline and post-treatment follow-up assessments with N=5 participants.

Study Endpoints:

1. **Melatonin**

   Assessments:
   Baseline: 8PM, 12AM, 4AM, 8AM
   Post-test: 8PM, 12AM, 4AM, 8AM

2. **Neurotransmitter Parameters**

   Assessments:
   Day 1, 2, 3, 4, 5, 6

3. **Amino Acids**

   Assessments:
   Run 1, 2, 3 and 4

4. **Questionnaires**

   Assessments:

	Day						
	1	2	3	4	5	6	7

Marlowe Crowne	X						
Restorative Sleep	X	X	X	X	X	X	X
Profile of Mood Scales	X				X	X	X
Global Mood Scale	X	X	X	X	X	X	X
Sleep Scale	X	X					X
Leeds	X	X	X	X	X	X	X
Absorption	X						
Hassle and Uplift	X						X

Results

1. **Melatonin**

Table 1: *Summary statistics of melatonin levels*

Day	Hour	N	Mean	SD	Lower 95% CI	Upper 95% CI
Baseline	8PM	5	6.05	3.50	2.03	10.07
Baseline	12AM	5	11.36	6.91	3.42	19.30
Baseline	4AM	5	5.28	2.33	2.60	7.96
Baseline	8AM	4	4.93	3.76	-0.29	10.15
Baseline	AUC†	5	85.44	49.20	28.88	142.00
Post-test	8PM	5	5.76	5.84	-0.95	12.47
Post-test	12AM	5	8.23	7.41	-0.29	16.75
Post-test	4AM	5	11.15	11.48	-2.05	24.35
Post-test	8AM	4	5.50	5.69	-2.40	13.40
Post-test	AUC†	5	95.21	95.89	-15.03	205.45

† Area under the Curve (AUC) was calculated to characterize the overall kinetics of melatonin over all measurement time points (i.e., 8PM to 8AM following day

Table 2: *Evaluation of changes from baseline in melatonin values*

Hour	N	Mean	SD	Lower 95% CI	Upper 95% CI	p-value^
8PM	5	-0.29	3.36	-4.15	3.57	0.8556
12AM	5	-3.13	5.04	-8.92	2.66	0.2370
4AM	5	5.87	9.27	-4.79	16.53	0.2299
8AM	3	1.24	4.04	-6.18	8.66	0.6478

AUC†	5	9.78	67.38	-67.68	87.24	0.7619

† Area under the Curve (AUC) was calculated to characterize the overall kinetics of melatonin over all measurement time points (i.e., 8PM to 8AM following day

^ p-value for evaluating changes from baseline to post-treatment assessment

Results:
No significant changes in melatonin values from baseline were detected at all time points (8PM, 12AM, 4AM, 8AM) and AUC.

1.1 Melatonin

Table 3: *Summary statistics of melatonin levels*

Age Group	Day	Hour	N	Mean	SD	Lower 95% CI	Upper 95% CI
20-30	1	8PM	3	7.95	2.97	2.49	13.41
20-30	1	12AM	3	16.29	1.46	13.61	18.97
20-30	1	4AM	3	6.66	1.85	3.26	10.06
20-30	1	8AM	3	5.35	4.49	-2.9	13.6
20-30	6	8PM	3	8.55	6.23	-2.9	20
20-30	6	12AM	3	12.7	5.9	1.86	23.54
20-30	6	4AM	3	17.14	11.35	-3.71	37.99
20-30	6	8AM	2	8.45	7.24	-13.58	30.48
>60	1	8PM	2	3.2	2.05	-3.04	9.44
>60	1	12AM	2	3.96	2.02	-2.19	10.11
>60	1	4AM	2	3.2	0.64	1.25	5.15
>60	1	8AM	1	3.67	.	.	.
>60	6	8PM	2	1.58	0.57	-0.15	3.31
>60	6	12AM	2	1.52	0.38	0.36	2.68
>60	6	4AM	2	2.16	0.49	0.67	3.65
>60	6	8AM	2	2.54	3.14	-7.01	12.09

Table 4: *Evaluation of changes from baseline to Day 6 in melatonin values, stratified by age group*

Age	Hour	N	Mean	SD	Lower 95% CI	Upper 95% CI	p-value^
20-30	8PM	3	0.6	4.03	-6.8	8	0.8215
20-30	12AM	3	-3.59	6.97	-16.4	9.22	0.4666
20-30	4AM	3	10.48	9.61	-7.18	28.14	0.1997
20-30	8AM	2	3.54	0.98	0.56	6.52	0.1236
>60	8PM	2	-1.63	2.62	-9.6	6.34	0.542
>60	12AM	2	-2.44	1.64	-7.43	2.55	0.2825
>60	4AM	2	-1.04	0.14	-1.47	-0.61	0.061
>60	8AM	1	-3.35	.	.	.	NA

^ p-value for evaluating changes from baseline to post-treatment assessment

Table 5: P-value for comparison melatonin of change from baseline to Day 6 in melatonin between Age groups

Hour	p-value
8PM	0.5497
12AM	0.8412
4AM	0.2063
8AM	0.1102

2. Neurotransmitter Parameters

Table 6: *Summary of neurotransmitter parameters*

Parameter	Day	N	Mean	SD	Lower 95% CI	Upper 95% CL
ADR	1	5	2.10	0.55	1.47	2.73
ADR	2	5	1.76	0.24	1.48	2.04
ADR	3	5	5.53	3.92	1.02	10.04
ADR	4	5	6.54	4.18	1.73	11.35
Cre	1	5	1.01	0.32	0.64	1.38
Cre	2	5	0.84	0.44	0.33	1.35
Cre	3	5	1.97	1.42	0.34	3.60
Cre	4	5	1.33	0.60	0.64	2.02
DA	1	5	104.59	52.26	44.51	164.67
DA	2	5	118.37	67.64	40.61	196.13

DA	3	5	120.29	43.97	69.74	170.84
DA	4	5	141.34	54.11	79.14	203.54
GABA	1	5	1.68	0.52	1.08	2.28
GABA	2	5	1.88	0.75	1.02	2.74
GABA	3	5	1.61	1.04	0.41	2.81
GABA	4	5	1.89	1.27	0.43	3.35
Glu	1	5	9.03	4.26	4.13	13.93
Glu	2	5	8.93	3.44	4.98	12.88
Glu	3	5	7.53	7.77	-1.40	16.46
Glu	4	5	10.15	7.46	1.57	18.73
Hist	1	5	15.06	10.08	3.47	26.65
Hist	2	5	13.44	9.03	3.06	23.82
Hist	3	5	10.89	3.40	6.98	14.80
Hist	4	5	14.28	2.23	11.72	16.84
LDOPA	1	5	31.65	22.02	6.34	56.96
LDOPA	2	5	40.33	21.73	15.35	65.31
LDOPA	3	5	24.20	16.94	4.73	43.67
LDOPA	4	5	46.25	40.06	0.20	92.30
Melatonin	1	5	136.57	84.44	39.50	233.64
Melatonin	2	5	170.42	92.33	64.28	276.56
Melatonin	3	5	117.74	77.24	28.94	206.54
Melatonin	4	5	124.96	80.33	32.61	217.31
Metaneph	1	5	18.98	2.53	16.07	21.89
Metaneph	2	5	22.14	8.38	12.51	31.77
Metaneph	3	5	20.70	7.69	11.86	29.54
Metaneph	4	5	22.11	10.38	10.18	34.04
Mtyramine	1	5	25.38	29.34	-8.35	59.11
Mtyramine	2	5	37.22	25.11	8.35	66.09
Mtyramine	3	5	28.98	29.97	-5.47	63.43
Mtyramine	4	5	28.29	28.08	-3.99	60.57
NAD	1	5	8.80	1.42	7.17	10.43
NAD	2	5	17.85	8.40	8.19	27.51
NAD	3	5	36.76	30.81	1.34	72.18
NAD	4	5	32.75	20.26	9.46	56.04
NAD/ADR	1	5	4.51	1.63	2.64	6.38
NAD/ADR	2	5	9.93	4.21	5.09	14.77
NAD/ADR	3	5	9.13	8.42	-0.55	18.81

NAD/ADR	4	5	5.88	3.58	1.76	10.00
Normetane	1	5	34.68	19.89	11.81	57.55
Normetane	2	5	92.00	73.87	7.08	176.92
Normetane	3	5	102.89	42.92	53.55	152.23
Normetane	4	5	126.47	108.15	2.14	250.80
Ser	1	5	68.93	36.55	26.91	110.95
Ser	2	5	75.61	54.79	12.62	138.60
Ser	3	5	74.22	25.79	44.57	103.87
Ser	4	5	74.08	35.70	33.04	115.12
SerDA	1	5	0.71	0.21	0.47	0.95
SerDA	2	5	0.69	0.30	0.35	1.03
SerDA	3	5	0.75	0.48	0.20	1.30
SerDA	4	5	0.55	0.26	0.25	0.85
Theanine	1	2	9.47	9.22	-18.58	37.52
Theanine	2	2	4.55	6.21	-14.34	23.44
Theanine	3	2	2.37	2.93	-6.54	11.28
Theanine	4	2	6.03	7.83	-17.79	29.85

Table 7: *Change in neurotransmitter parameters from Day 1 (baseline) to Day 2, 3, and 4*

Source	Change from Day 1 to Day	N	Mean	SD	Lower 95%CL	Upper 95% CL	p-value^
ADR	2	5	-0.34	0.58	-1.01	0.32	<.0001
ADR	3	5	3.43	3.64	-0.75	7.61	0.0342
ADR	4	5	4.43	4.13	-0.31	9.18	0.0249
Cre	2	5	-0.17	0.19	-0.39	0.06	0.0130
Cre	3	5	0.96	1.15	-0.36	2.28	0.0362
Cre	4	5	0.32	0.59	-0.35	0.99	0.0078
DA	2	5	13.78	22.52	-12.11	39.67	0.0174
DA	3	5	15.70	89.42	-87.10	118.50	0.0036
DA	4	5	36.76	55.51	-27.06	100.57	0.0043
GABA	2	5	0.20	0.53	-0.41	0.81	0.0049
GABA	3	5	-0.07	0.61	-0.77	0.62	0.0256
GABA	4	5	0.20	1.05	-1.00	1.41	0.0290
Glu	2	5	-0.10	1.46	-1.78	1.58	0.0044
Glu	3	5	-1.50	4.39	-6.55	3.55	0.0963

Glu	4	5	1.12	5.30	-4.97	7.22	0.0384
Hist	2	5	-1.61	1.83	-3.72	0.50	0.0291
Hist	3	5	-4.17	12.05	-18.02	9.69	0.0020
Hist	4	5	-0.78	8.89	-11.00	9.44	0.0001
LDOPA	2	5	8.69	20.72	-15.14	32.51	0.0143
LDOPA	3	5	-7.45	25.33	-36.56	21.67	0.0331
LDOPA	4	5	14.61	23.09	-11.94	41.15	0.0612
Melatonin	2	5	33.85	91.70	-71.57	139.27	0.0145
Melatonin	3	5	-18.82	25.88	-48.57	10.92	0.0271
Melatonin	4	5	-11.61	121.27	-151.02	127.80	0.0254
Metaneph	2	5	3.16	6.45	-4.25	10.58	0.0041
Metaneph	3	5	1.72	6.25	-5.46	8.91	0.0038
Metaneph	4	5	3.13	9.78	-8.12	14.37	0.0089
Mtyramine	2	5	11.83	18.09	-8.96	32.63	0.0295
Mtyramine	3	5	3.60	7.34	-4.84	12.03	0.0967
Mtyramine	4	5	2.91	11.74	-10.59	16.41	0.0873
NAD	2	5	9.05	8.21	-0.39	18.49	0.0090
NAD	3	5	27.96	31.20	-7.91	63.83	0.0559
NAD	4	5	23.95	19.47	1.56	46.33	0.0225
NAD/ADR	2	5	5.42	3.55	1.34	9.51	0.0062
NAD/ADR	3	5	4.62	8.25	-4.86	14.10	0.0724
NAD/ADR	4	5	1.37	2.17	-1.12	3.87	0.0213
Normetane	2	5	57.32	88.61	-44.54	159.19	0.0496
Normetane	3	5	68.21	58.19	1.31	135.11	0.0058
Normetane	4	5	91.79	101.86	-25.31	208.89	0.0591
Ser	2	5	6.68	21.24	-17.74	31.10	0.0367
Ser	3	5	5.29	17.01	-14.27	24.85	0.0030
Ser	4	5	5.15	23.50	-21.86	32.16	0.0097
SerDA	2	5	-0.02	0.16	-0.20	0.16	0.0068
SerDA	3	5	0.04	0.54	-0.58	0.67	0.0258
SerDA	4	5	-0.15	0.22	-0.40	0.10	0.0085
Theanine	2	2	-4.92	3.01	-14.08	4.24	0.4886
Theanine	3	2	-7.11	6.29	-26.23	12.02	0.4585
Theanine	4	2	-3.45	1.39	-7.68	0.79	0.4730

^ p-value for evaluating changes from Day 1 to Day 2, 3, and 4

Results:
Significant changes were detected for most neurotransmitter parameters for all times points, except for Mtyramine (from day 1 to day 3 and day 4), Glutamate (from baseline to day 3), LDOPA (from day 1 to day 4), NAD/ADR (from day 1 to day 3), Normetane (from day 1 to Day 4), and Theanine (from day 1 to day 2, day 3, and day4), where no significant changes were observed.

3. Amino Acids and Hormones

Table 8: *Summary statistics of amino acids values*

Source	Run	Mean	SD	Lower 95% CL	Upper 95% CL
Ala	1	211.32	206.28	-44.81	467.46
Ala	2	190.54	233.20	-99.02	480.09
Ala	3	90.25	108.83	-44.87	225.38
Ala	4	119.99	115.19	-23.03	263.02
Arg	1	5.39	2.64	2.11	8.67
Arg	2	4.41	0.57	3.70	5.12
Arg	3	8.74	5.02	2.50	14.97
Arg	4	9.23	5.70	2.15	16.31
Asn	1	53.83	48.08	-5.87	113.54
Asn	2	62.22	66.23	-20.02	144.46
Asn	3	60.90	56.12	-8.79	130.59
Asn	4	67.05	43.04	13.62	120.49
Asp	1	5.42	4.23	0.16	10.68
Asp	2	7.49	6.42	-0.49	15.46
Asp	3	3.20	2.90	-0.40	6.81
Asp	4	3.28	2.00	0.80	5.77
Bala	1	24.29	36.66	-21.23	69.81
Bala	2	8.06	4.27	2.75	13.36
Bala	3	6.70	7.37	-2.45	15.85
Bala	4	4.49	3.33	0.35	8.62
Car	1	53.03	70.43	-34.42	140.48
Car	2	10.54	6.11	2.95	18.13
Car	3	22.25	17.56	0.45	44.05
Car	4	12.29	8.47	1.77	22.81
Cit	1	3.05	2.39	0.08	6.03
Cit	2	1.76	0.83	0.73	2.79

Cit	3	2.70	1.38	0.99	4.42
Cit	4	3.13	1.36	1.44	4.81
Cys	1	44.21	26.73	11.03	77.40
Cys	2	61.09	44.57	5.75	116.43
Cys	3	37.09	13.44	20.40	53.78
Cys	4	50.69	25.85	18.59	82.79
FiveHTP	1	31.12	12.04	16.17	46.07
FiveHTP	2	28.51	8.69	17.72	39.31
FiveHTP	3	24.00	8.01	14.06	33.94
FiveHTP	4	28.17	11.83	13.48	42.85
Gln	1	203.90	119.98	54.92	352.87
Gln	2	208.06	189.76	-27.55	443.68
Gln	3	139.23	82.72	36.52	241.93
Gln	4	184.50	93.03	68.98	300.01
Glu	1	9.03	4.26	3.74	14.32
Glu	2	8.93	3.44	4.66	13.20
Glu	3	7.53	7.77	-2.12	17.18
Glu	4	10.15	7.46	0.88	19.41
Gly	1	502.84	529.05	-154.06	1160.00
Gly	2	810.29	1132.52	-595.92	2217.00
Gly	3	313.00	430.35	-221.35	847.35
Gly	4	476.45	428.04	-55.04	1008.00
His	1	267.72	138.26	96.04	439.40
His	2	275.69	187.52	42.84	508.53
His	3	233.27	95.39	114.82	351.71
His	4	285.92	148.79	101.17	470.67
Ile	1	8.81	5.64	1.81	15.82
Ile	2	7.56	5.05	1.29	13.82
Ile	3	5.52	3.01	1.78	9.25
Ile	4	7.40	3.02	3.66	11.15
Leu	1	10.17	4.66	4.38	15.95
Leu	2	9.23	4.17	4.05	14.41
Leu	3	6.78	2.66	3.48	10.09
Leu	4	8.93	2.10	6.32	11.53
Lys	1	54.73	41.77	2.87	106.60
Lys	2	37.59	4.51	31.99	43.19
Lys	3	55.10	54.81	-12.96	123.15

Lys	4	58.87	56.44	-11.21	128.94
Met	1	6.83	2.51	3.72	9.95
Met	2	6.83	1.51	4.96	8.70
Met	3	5.01	2.97	1.33	8.70
Met	4	5.85	2.22	3.09	8.61
Orn	1	14.92	9.39	3.26	26.58
Orn	2	11.02	4.08	5.95	16.09
Orn	3	13.43	4.82	7.45	19.42
Orn	4	15.52	3.27	11.47	19.58
Phe	1	112.93	197.56	-132.37	358.22
Phe	2	98.18	164.70	-106.32	302.69
Phe	3	101.25	182.86	-125.81	328.30
Phe	4	57.66	76.19	-36.94	152.26
Pro	1	15.41	23.17	-13.36	44.17
Pro	2	10.07	9.44	-1.65	21.78
Pro	3	2.65	1.51	0.78	4.52
Pro	4	4.51	1.24	2.97	6.05
Ser	1	107.34	64.77	26.92	187.76
Ser	2	90.24	102.05	-36.47	216.94
Ser	3	78.05	61.45	1.75	154.35
Ser	4	119.10	68.69	33.82	204.39
Thr	1	91.75	81.81	-9.82	193.33
Thr	2	98.22	128.65	-61.52	257.96
Thr	3	37.75	58.18	-34.49	109.99
Thr	4	57.88	67.10	-25.44	141.19
Trp	1	40.03	27.88	5.41	74.66
Trp	2	39.40	28.80	3.63	75.16
Trp	3	39.36	24.55	8.88	69.84
Trp	4	40.31	23.45	11.19	69.42
Tyr	1	61.79	42.06	9.56	114.02
Tyr	2	55.80	43.15	2.22	109.38
Tyr	3	51.10	28.48	15.74	86.46
Tyr	4	65.89	42.39	13.26	118.51
Val	1	24.66	23.63	-4.68	54.00
Val	2	18.28	13.06	2.06	34.50
Val	3	11.24	7.04	2.49	19.98
Val	4	16.74	6.42	8.77	24.72

Table 9: Summary statistics for hormone levels

Parameter	Time	Day	N	Mean	SD
Cortisol	4am	1	5	2.056	0.1638
Cortisol	4am	6	5	1.86	0.3576
Cortisol	4pm	1	5	1.368	0.0858
Cortisol	4pm	6	5	1.526	0.3979
Cortisol	8am	1	5	4.154	0.7317
Cortisol	8am	6	5	4.278	0.7299
Cortisol	8pm	1	5	0.69	0.1568
Cortisol	8pm	6	5	1.2	0.5702
Cortisol	midnight	1	5	1.298	0.5672
Cortisol	midnight	6	5	1.282	0.2181
Cortisol	noon	1	5	2.098	0.5522
Cortisol	noon	6	5	2.382	0.4785
DHEA	8am	1	5	4.84	1.9034
DHEA	8am	6	5	4.56	1.324
DHEA	8pm	1	5	3.32	0.531
DHEA	8pm	6	5	3.92	0.8871
DHEA	midnight	1	5	2.8	0.5244
DHEA	midnight	6	5	4.04	1.7111
Estradiol		1	5	1.806	0.8128
Estradiol		6	5	1.704	1.1632
PE_ratio		1	4	51.175	13.0628
PE_ratio		6	5	56	19.6895
Progesterone		1	5	91.6	45.6541
Progesterone		6	5	101.8	93.5505
TE_ratio		1	2	135.4	40.1637
TE_ratio		6	2	140.1	72.1249
TP_ratio		1	2	3.15	0.0707
TP_ratio		6	2	3.85	1.4849
Testosterone		1	5	78.86	70.6347
Testosterone		6	5	80.64	77.4463

Table 10: Hormone values changes from Day 1 to Day 6

Parameter	Time	N	Mean	SD	p-value
Cortisol	4am	5	-0.196	0.4792	0.4122
Cortisol	4pm	5	0.158	0.4456	0.4722
Cortisol	8am	5	0.124	0.8416	0.7583
Cortisol	8pm	5	0.51	0.5917	0.1262
Cortisol	midnight	5	-0.016	0.6511	0.9588
Cortisol	noon	5	0.284	0.9403	0.5365
DHEA	8am	5	-0.28	2.0042	0.7704
DHEA	8pm	5	0.6	0.6325	0.1012
DHEA	midnight	5	1.24	1.2522	0.0912
Estradiol		5	-0.102	0.7952	0.7885
PE_ratio		4	-0.275	13.1976	0.9694
Progesterone		5	10.2	57.4125	0.7115
TE_ratio		2	4.7	31.9612	0.8695
TP_ratio		2	0.7	1.5556	0.6392
Testosterone		5	1.78	11.4842	0.7464

Results: There was no significant change in hormones or amino acids.

4. Analysis of HRV and EMG Parameters

Table 11: *Summary of HRV and EMG parameters – Outcome measure:* ***Average***

Source	Epoch	Day	N	Mean	SD	Lower 95% CL	Upper 95% CL
C_EMG	1	1	5	21.56	21.56	-3.23	46.35
C_EMG	1	2	5	16.75	16.75	-2.51	36.01
C_EMG	1	3	4	14.74	14.74	-5.72	35.2
C_EMG	1	4	4	7.26	7.26	-2.82	17.34
C_EMG	2	1	5	19.98	19.98	-2.99	42.95
C_EMG	2	2	5	13.9	13.9	-2.08	29.88
C_EMG	2	3	4	14.79	14.79	-5.74	35.32
C_EMG	2	4	4	4.18	4.18	-1.62	9.98
C_EMG	3	1	5	26.5	26.5	-3.96	56.96
C_EMG	3	2	5	5.94	5.94	-0.89	12.77

C_EMG	3	3	4	12.93	12.93	-5.02	30.88
C_EMG	3	4	3	5.11	5.11	-4.28	14.5
C_EMG	4	1	5	16.36	16.36	-2.45	35.17
C_EMG	4	2	5	5.36	5.36	-0.8	11.52
C_EMG	4	3	3	5.73	5.73	-4.8	16.26
C_EMG	4	4	2	5.84	5.84	-11.93	23.61
D_EMG	1	1	5	4.47	4.47	-0.67	9.61
D_EMG	1	2	5	6.82	6.82	-1.02	14.66
D_EMG	1	3	4	8.06	8.06	-3.13	19.25
D_EMG	1	4	4	5.57	5.57	-2.16	13.3
D_EMG	2	1	5	4.92	4.92	-0.74	10.58
D_EMG	2	2	5	4.66	4.66	-0.7	10.02
D_EMG	2	3	4	7.38	7.38	-2.87	17.63
D_EMG	2	4	4	2.81	2.81	-1.09	6.71
D_EMG	3	1	5	4.33	4.33	-0.65	9.31
D_EMG	3	2	5	5.06	5.06	-0.76	10.88
D_EMG	3	3	4	5.29	5.29	-2.05	12.63
D_EMG	3	4	3	3.24	3.24	-2.71	9.19
D_EMG	4	1	5	5.09	5.09	-0.76	10.94
D_EMG	4	2	5	3.24	3.24	-0.48	6.96
D_EMG	4	3	3	3.34	3.34	-2.8	9.48
D_EMG	4	4	2	3.58	3.58	-7.31	14.47
E_Skin_Cond	1	1	5	0.44	0.44	-0.07	0.95
E_Skin_Cond	1	2	5	0.25	0.25	-0.04	0.54
E_Skin_Cond	1	3	4	0.39	0.39	-0.15	0.93
E_Skin_Cond	1	4	4	0.33	0.33	-0.13	0.79
E_Skin_Cond	2	1	5	0.45	0.45	-0.07	0.97
E_Skin_Cond	2	2	5	0.32	0.32	-0.05	0.69
E_Skin_Cond	2	3	4	0.41	0.41	-0.16	0.98
E_Skin_Cond	2	4	4	0.34	0.34	-0.13	0.81
E_Skin_Cond	3	1	5	0.45	0.45	-0.07	0.97
E_Skin_Cond	3	2	5	0.41	0.41	-0.06	0.88
E_Skin_Cond	3	3	4	0.37	0.37	-0.14	0.88
E_Skin_Cond	3	4	3	0.44	0.44	-0.37	1.25
E_Skin_Cond	4	1	5	0.49	0.49	-0.07	1.05
E_Skin_Cond	4	2	5	0.36	0.36	-0.05	0.77
E_Skin_Cond	4	3	3	0.41	0.41	-0.34	1.16

E_Skin_Cond	4	4	2	0.14	0.14	-0.29	0.57
F_Temp	1	1	5	86.03	86.03	-12.87	184.93
F_Temp	1	2	5	86	86	-12.87	184.87
F_Temp	1	3	4	88.21	88.21	-34.25	210.67
F_Temp	1	4	4	76.28	76.28	-29.61	182.17
F_Temp	2	1	5	87.09	87.09	-13.03	187.21
F_Temp	2	2	5	86.27	86.27	-12.91	185.45
F_Temp	2	3	4	88.87	88.87	-34.5	212.24
F_Temp	2	4	4	76.84	76.84	-29.83	183.51
F_Temp	3	1	5	87.57	87.57	-13.1	188.24
F_Temp	3	2	5	86.88	86.88	-13	186.76
F_Temp	3	3	4	84.54	84.54	-32.82	201.9
F_Temp	3	4	3	77.84	77.84	-65.18	220.86
F_Temp	4	1	5	88.01	88.01	-13.17	189.19
F_Temp	4	2	5	83.27	83.27	-12.46	179
F_Temp	4	3	3	86.36	86.36	-72.32	245.04
F_Temp	4	4	2	71.66	71.66	-146.36	289.68

Table 12: *Summary of HRV and EMG parameters – Outcome measure:* ***Mode***

Source	Epoch	Day	N	Mean	SD	Lower 95% CL	Upper 95% CL
C_EMG	1	1	5	21.9	30.15	-12.76	56.56
C_EMG	1	2	5	5.1	5.42	-1.13	11.33
C_EMG	1	3	4	13.06	12.46	-4.24	30.36
C_EMG	1	4	4	4.63	3.75	-0.58	9.84
C_EMG	2	1	5	20.74	30.38	-14.18	55.66
C_EMG	2	2	5	5.31	4.77	-0.17	10.79
C_EMG	2	3	4	13.88	12.81	-3.9	31.66
C_EMG	2	4	4	3.93	3.71	-1.22	9.08
C_EMG	3	1	5	27.5	34.23	-11.85	66.85
C_EMG	3	2	5	5.16	4.58	-0.11	10.43
C_EMG	3	3	4	13.25	13.85	-5.98	32.48
C_EMG	3	4	3	4.62	3.74	-2.25	11.49
C_EMG	4	1	5	16.36	30.22	-18.38	51.1
C_EMG	4	2	5	4.74	5.07	-1.09	10.57
C_EMG	4	3	3	4.86	3.01	-0.67	10.39
C_EMG	4	4	2	5.39	3.26	-4.53	15.31

D_EMG	1	1	5	3.46	2.02	1.14	5.78
D_EMG	1	2	5	4.45	2.36	1.74	7.16
D_EMG	1	3	4	6.97	5.51	-0.68	14.62
D_EMG	1	4	4	2.43	1.44	0.43	4.43
D_EMG	2	1	5	3.99	2.74	0.84	7.14
D_EMG	2	2	5	3.39	1.72	1.41	5.37
D_EMG	2	3	4	6.27	4.29	0.31	12.23
D_EMG	2	4	4	1.96	0.78	0.88	3.04
D_EMG	3	1	5	3.49	2.97	0.08	6.9
D_EMG	3	2	5	3.87	1.45	2.2	5.54
D_EMG	3	3	4	3.06	1.56	0.89	5.23
D_EMG	3	4	3	2.42	1.11	0.38	4.46
D_EMG	4	1	5	4.24	3.06	0.72	7.76
D_EMG	4	2	5	2.18	0.84	1.21	3.15
D_EMG	4	3	3	2.8	1.59	-0.12	5.72
D_EMG	4	4	2	2.82	0.94	-0.04	5.68
E_Skin_Cond	1	1	5	0.41	0.35	0.01	0.81
E_Skin_Cond	1	2	5	0.26	0.21	0.02	0.5
E_Skin_Cond	1	3	4	0.38	0.49	-0.3	1.06
E_Skin_Cond	1	4	4	0.32	0.38	-0.21	0.85
E_Skin_Cond	2	1	5	0.45	0.39	0	0.9
E_Skin_Cond	2	2	5	0.31	0.28	-0.01	0.63
E_Skin_Cond	2	3	4	0.41	0.53	-0.33	1.15
E_Skin_Cond	2	4	4	0.35	0.45	-0.27	0.97
E_Skin_Cond	3	1	5	0.45	0.37	0.02	0.88
E_Skin_Cond	3	2	5	0.41	0.27	0.1	0.72
E_Skin_Cond	3	3	4	0.37	0.58	-0.44	1.18
E_Skin_Cond	3	4	3	0.47	0.56	-0.56	1.5
E_Skin_Cond	4	1	5	0.48	0.36	0.07	0.89
E_Skin_Cond	4	2	5	0.36	0.34	-0.03	0.75
E_Skin_Cond	4	3	3	0.4	0.52	-0.56	1.36
E_Skin_Cond	4	4	2	0.13	0.08	-0.11	0.37
F_Temp	1	1	5	85.96	9.55	74.98	96.94
F_Temp	1	2	5	86.22	8.48	76.47	95.97
F_Temp	1	3	4	88.5	8.45	76.77	100.23
F_Temp	1	4	4	76.67	8.63	64.69	88.65
F_Temp	2	1	5	86.82	9.87	75.47	98.17

F_Temp	2	2	5	86.34	8.82	76.2	96.48
F_Temp	2	3	4	88.96	8.6	77.02	100.9
F_Temp	2	4	4	76.73	8.68	64.68	88.78
F_Temp	3	1	5	87.67	10.37	75.75	99.59
F_Temp	3	2	5	86.56	9.23	75.95	97.17
F_Temp	3	3	4	84.52	10.42	70.05	98.99
F_Temp	3	4	3	77.88	11.99	55.85	99.91
F_Temp	4	1	5	88.06	10.57	75.91	100.21
F_Temp	4	2	5	83.26	10.25	71.48	95.04
F_Temp	4	3	3	86.43	8.72	70.41	102.45
F_Temp	4	4	2	71.67	6.81	50.95	92.39

Table 13: *Summary of HRV and EMG parameters – Outcome measure:* ***Area***

Source	Epoch	Day	N	Mean	SD	Lower 95% CL	Upper 95% CL
C_EMG	1	1	5	1293.51	1735.62	-701.76	3288.78
C_EMG	1	2	5	1004.93	1196.98	-371.12	2380.98
C_EMG	1	3	4	884.39	828.11	-265.21	2033.99
C_EMG	1	4	4	435.55	355.17	-57.51	928.61
C_EMG	2	1	5	1198.84	1659.12	-708.48	3106.16
C_EMG	2	2	5	834.21	995.58	-310.31	1978.73
C_EMG	2	3	4	887.47	769.26	-180.43	1955.37
C_EMG	2	4	4	251.07	195.82	-20.77	522.91
C_EMG	3	1	5	1589.94	1902.72	-597.43	3777.31
C_EMG	3	2	5	356.31	232.71	88.79	623.83
C_EMG	3	3	4	775.95	831.27	-378.04	1929.94
C_EMG	3	4	3	306.36	169.99	-5.98	618.70
C_EMG	4	1	5	981.64	1703.27	-976.44	2939.72
C_EMG	4	2	5	321.45	271.76	9.03	633.87
C_EMG	4	3	3	343.68	211.84	-45.55	732.91
C_EMG	4	4	2	350.08	163.43	-147.15	847.31
D_EMG	1	1	5	268.14	78.94	177.39	358.89
D_EMG	1	2	5	409.17	267.43	101.73	716.61
D_EMG	1	3	4	483.86	361.14	-17.48	985.20
D_EMG	1	4	4	334.35	372.67	-183.00	851.70
D_EMG	2	1	5	295.24	155.62	116.34	474.14

D_EMG	2	2	5	279.42	125.21	135.48	423.36
D_EMG	2	3	4	442.91	275.54	60.40	825.42
D_EMG	2	4	4	168.49	55.21	91.85	245.13
D_EMG	3	1	5	260.03	198.62	31.70	488.36
D_EMG	3	2	5	303.87	126.33	158.64	449.10
D_EMG	3	3	4	317.25	246.33	-24.71	659.21
D_EMG	3	4	3	194.20	72.58	60.84	327.56
D_EMG	4	1	5	305.26	188.77	88.25	522.27
D_EMG	4	2	5	194.65	32.18	157.66	231.64
D_EMG	4	3	3	200.25	118.46	-17.41	417.91
D_EMG	4	4	2	214.72	86.63	-48.85	478.29
E_Skin_Cond	1	1	5	26.40	22.43	0.61	52.19
E_Skin_Cond	1	2	5	14.85	13.23	-0.36	30.06
E_Skin_Cond	1	3	4	23.29	30.49	-19.04	65.62
E_Skin_Cond	1	4	4	19.88	23.97	-13.40	53.16
E_Skin_Cond	2	1	5	27.18	23.65	-0.01	54.37
E_Skin_Cond	2	2	5	19.45	16.28	0.73	38.17
E_Skin_Cond	2	3	4	24.68	31.87	-19.56	68.92
E_Skin_Cond	2	4	4	20.45	25.98	-15.62	56.52
E_Skin_Cond	3	1	5	26.94	22.65	0.90	52.98
E_Skin_Cond	3	2	5	24.70	16.65	5.56	43.84
E_Skin_Cond	3	3	4	22.46	35.49	-26.81	71.73
E_Skin_Cond	3	4	3	26.54	31.09	-30.58	83.66
E_Skin_Cond	4	1	5	29.13	22.05	3.78	54.48
E_Skin_Cond	4	2	5	21.51	18.97	-0.30	43.32
E_Skin_Cond	4	3	3	24.66	32.22	-34.54	83.86
E_Skin_Cond	4	4	2	8.10	4.62	-5.96	22.16
F_Temp	1	1	5	5141.66	606.70	4444.20	5839.12
F_Temp	1	2	5	5160.03	506.14	4578.17	5741.89
F_Temp	1	3	4	5292.41	500.63	4597.42	5987.40
F_Temp	1	4	4	4576.55	499.86	3882.63	5270.47
F_Temp	2	1	5	5225.18	598.56	4537.08	5913.28
F_Temp	2	2	5	5176.16	525.47	4572.08	5780.24
F_Temp	2	3	4	5332.32	515.29	4616.98	6047.66
F_Temp	2	4	4	4610.58	538.26	3863.36	5357.80
F_Temp	3	1	5	5254.28	618.61	4543.13	5965.43
F_Temp	3	2	5	5201.01	558.50	4558.96	5843.06

F_Temp	3	3	4	5072.30	619.21	4212.70	5931.90
F_Temp	3	4	3	4670.53	714.47	3357.77	5983.29
F_Temp	4	1	5	5280.31	631.29	4554.58	6006.04
F_Temp	4	2	5	4995.99	617.24	4286.41	5705.57
F_Temp	4	3	3	5181.37	519.18	4227.44	6135.30
F_Temp	4	4	2	4299.67	409.99	3052.30	5547.04

Table 14: *Evaluation Change from Day 1 to Day 2, 3, and 4 (for each epoch) – Outcome measure:* ***Average***

Source	Change from Day 1 to Day	Epoch	N	Mean	SD	Lower 95% CL	Upper 95% CL	p-value^
C_EMG	2	1	5	-4.81	30.91	-40.34	30.72	0.7454
C_EMG	3	1	4	-11.45	39.38	-66.13	43.22	0.6017
C_EMG	4	1	4	-18.93	31.28	-62.36	24.50	0.3128
C_EMG	2	2	5	-6.08	29.02	-39.43	27.28	0.6639
C_EMG	3	2	4	-9.46	37.71	-61.82	42.90	0.6504
C_EMG	4	2	4	-20.07	27.05	-57.61	17.48	0.2345
C_EMG	2	3	5	-20.56	29.15	-54.08	12.96	0.1900
C_EMG	3	3	4	-19.42	43.88	-80.33	41.50	0.4413
C_EMG	4	3	3	-20.88	35.00	-85.19	43.42	0.4099
C_EMG	2	4	5	-11.00	23.99	-38.58	16.58	0.3631
C_EMG	3	4	3	-19.46	39.02	-91.14	52.23	0.4787
C_EMG	4	4	2	-31.04	39.93	-152.53	90.45	0.4699
D_EMG	2	1	5	2.35	4.50	-2.82	7.52	0.3076
D_EMG	3	1	4	3.71	6.59	-5.43	12.85	0.3416
D_EMG	4	1	4	1.22	5.68	-6.67	9.11	0.6967
D_EMG	2	2	5	-0.26	3.76	-4.59	4.06	0.8829
D_EMG	3	2	4	2.44	6.07	-5.98	10.86	0.4802
D_EMG	4	2	4	-2.14	2.25	-5.26	0.99	0.1538
D_EMG	2	3	5	0.73	4.85	-4.84	6.30	0.7531
D_EMG	3	3	4	1.10	6.10	-7.37	9.57	0.7423
D_EMG	4	3	3	-1.51	3.28	-7.53	4.51	0.5088
D_EMG	2	4	5	-1.84	2.93	-5.21	1.52	0.2316
D_EMG	3	4	3	-1.38	2.36	-5.71	2.95	0.4166

D_EMG	4	4	2	-2.68	3.37	-12.93	7.57	0.4623
E_Skin_Cond	2	1	5	-0.19	0.27	-0.51	0.12	0.1905
E_Skin_Cond	3	1	4	-0.02	0.48	-0.69	0.64	0.9266
E_Skin_Cond	4	1	4	-0.08	0.34	-0.55	0.39	0.6670
E_Skin_Cond	2	2	5	-0.12	0.34	-0.52	0.27	0.4574
E_Skin_Cond	3	2	4	-0.02	0.53	-0.76	0.71	0.9327
E_Skin_Cond	4	2	4	-0.10	0.40	-0.65	0.46	0.6662
E_Skin_Cond	2	3	5	-0.04	0.37	-0.46	0.39	0.8323
E_Skin_Cond	3	3	4	-0.05	0.49	-0.73	0.62	0.8459
E_Skin_Cond	4	3	3	-0.09	0.46	-0.93	0.75	0.7557
E_Skin_Cond	2	4	5	-0.13	0.39	-0.58	0.33	0.5109
E_Skin_Cond	3	4	3	-0.16	0.55	-1.16	0.85	0.6680
E_Skin_Cond	4	4	2	-0.33	0.56	-2.05	1.39	0.5572
F_Temp	2	1	5	-0.03	1.39	-1.62	1.57	0.9672
F_Temp	3	1	4	3.43	3.15	-0.94	7.81	0.1176
F_Temp	4	1	4	-8.50	4.43	-14.65	-2.34	0.0313
F_Temp	2	2	5	-0.82	1.86	-2.95	1.32	0.3812
F_Temp	3	2	4	3.21	2.47	-0.22	6.65	0.0806
F_Temp	4	2	4	-8.82	5.45	-16.38	-1.26	0.0479
F_Temp	2	3	5	-0.69	2.07	-3.07	1.70	0.4993
F_Temp	3	3	4	-1.59	10.07	-15.57	12.39	0.7731
F_Temp	4	3	3	-6.56	4.81	-15.39	2.27	0.1417
F_Temp	2	4	5	-4.74	7.45	-13.31	3.83	0.2281
F_Temp	3	4	3	1.65	5.50	-8.45	11.75	0.6557
F_Temp	4	4	2	-7.64	6.76	-28.21	12.94	0.3562

^ p-value for evaluating changes from day 1 to day 2, 3 and 4 (for each epoch)

Results: No significant changes from day 1 to day 2, 3, or 4 were detected for **Average HRV/EMG parameters**, except for Temperature (F) from Day 1 to Day 4 (epoch 1) (-8.5+/-4.43, p=0.0313) and Temperature (F) from Day 1 to Day 4 (epoch 2) (-8.82+/-5.45, p=0.0479).

Table 15: *Evaluation Change from Day 1 to Day 2, 3, and 4 (for each epoch) – Outcome measure:* ***Mode***

Source	Change from Day 1 to Day	Epoch	N	Mean	SD	Lower 95% CL	Upper 95% CL	p-value^
C_EMG	2	1	5	-16.80	25.09	-45.65	12.04	0.2086

C_EMG	3	1	4	-13.75	39.03	-67.93	40.44	0.5319
C_EMG	4	1	4	-22.18	29.70	-63.41	19.06	0.2322
C_EMG	2	2	5	-15.43	25.81	-45.09	14.24	0.2523
C_EMG	3	2	4	-11.53	40.03	-67.10	44.04	0.6048
C_EMG	4	2	4	-21.48	29.55	-62.51	19.54	0.2420
C_EMG	2	3	5	-22.34	31.14	-58.14	13.46	0.1839
C_EMG	3	3	4	-20.49	45.81	-84.09	43.10	0.4369
C_EMG	4	3	3	-22.34	37.23	-90.75	46.07	0.4079
C_EMG	2	4	5	-11.62	25.33	-40.74	17.50	0.3630
C_EMG	3	4	3	-21.06	40.62	-95.70	53.58	0.4640
C_EMG	4	4	2	-32.96	41.91	-160.47	94.55	0.4662
D_EMG	2	1	5	0.99	3.94	-3.53	5.52	0.6026
D_EMG	3	1	4	3.63	7.01	-6.10	13.37	0.3761
D_EMG	4	1	4	-0.90	2.68	-4.62	2.82	0.5493
D_EMG	2	2	5	-0.60	3.98	-5.18	3.98	0.7540
D_EMG	3	2	4	2.35	6.26	-6.34	11.05	0.5069
D_EMG	4	2	4	-1.96	2.75	-5.78	1.86	0.2502
D_EMG	2	3	5	0.38	4.04	-4.26	5.02	0.8448
D_EMG	3	3	4	-0.26	2.80	-4.15	3.63	0.8626
D_EMG	4	3	3	-1.40	2.91	-6.73	3.94	0.4930
D_EMG	2	4	5	-2.05	2.81	-5.29	1.18	0.1778
D_EMG	3	4	3	-1.29	2.70	-6.26	3.67	0.4947
D_EMG	4	4	2	-2.83	3.76	-14.27	8.61	0.4804
E_Skin_Cond	2	1	5	-0.15	0.24	-0.44	0.13	0.2312
E_Skin_Cond	3	1	4	0.00	0.43	-0.59	0.59	0.9966
E_Skin_Cond	4	1	4	-0.06	0.28	-0.46	0.33	0.6985
E_Skin_Cond	2	2	5	-0.13	0.33	-0.51	0.24	0.4131
E_Skin_Cond	3	2	4	-0.03	0.51	-0.73	0.68	0.9199
E_Skin_Cond	4	2	4	-0.09	0.39	-0.63	0.44	0.6631
E_Skin_Cond	2	3	5	-0.04	0.36	-0.45	0.37	0.8250
E_Skin_Cond	3	3	4	-0.05	0.47	-0.70	0.60	0.8430
E_Skin_Cond	4	3	3	-0.06	0.48	-0.95	0.82	0.8431
E_Skin_Cond	2	4	5	-0.12	0.39	-0.57	0.33	0.5285
E_Skin_Cond	3	4	3	-0.16	0.52	-1.11	0.80	0.6534
E_Skin_Cond	4	4	2	-0.32	0.54	-1.97	1.33	0.5587
F_Temp	2	1	5	0.27	2.23	-2.30	2.83	0.8034
F_Temp	3	1	4	4.05	3.52	-0.84	8.94	0.1051

F_Temp	4	1	4	-7.78	4.04	-13.40	-2.17	0.0310
F_Temp	2	2	5	-0.48	2.00	-2.78	1.82	0.6183
F_Temp	3	2	4	3.55	2.38	0.24	6.86	0.0587
F_Temp	4	2	4	-8.68	5.15	-15.83	-1.53	0.0434
F_Temp	2	3	5	-1.11	2.37	-3.84	1.61	0.3519
F_Temp	3	3	4	-1.76	10.36	-16.14	12.62	0.7566
F_Temp	4	3	3	-6.59	4.76	-15.33	2.15	0.1385
F_Temp	2	4	5	-4.80	7.51	-13.44	3.84	0.2262
F_Temp	3	4	3	1.73	5.34	-8.09	11.55	0.6309
F_Temp	4	4	2	-7.59	6.74	-28.09	12.90	0.3566

^ p-value for evaluating changes from day 1 to day 2, 3 and 4 (for each epoch)

Results: No significant changes from day 1 to day 2, 3, or 4 were detected for **Mode HRV/EMG parameters**, except for Temperature (F) from Day 1 to Day 4 (epoch 1) (-7.78+/-4.04, p=0.0313).

Table 16: *Evaluation Change from Day 1 to Day 2, 3, and 4 (for each epoch) – Outcome measure:* ***Area***

Source	Change from Day 1 to Day	Epoch	N	Mean	SD	Lower 95% CL	Upper 95% CL	p-value^
C_EMG	2	1	5	-288.58	1854.42	-2420.42	1843.26	0.7454
C_EMG	3	1	4	-687.14	2362.90	-3967.36	2593.09	0.6017
C_EMG	4	1	4	-1135.98	1877.03	-3741.71	1469.75	0.3128
C_EMG	2	2	5	-364.62	1740.94	-2366.01	1636.76	0.6639
C_EMG	3	2	4	-567.55	2262.87	-3708.92	2573.82	0.6504
C_EMG	4	2	4	-1203.95	1622.81	-3456.78	1048.88	0.2345
C_EMG	2	3	5	-1233.63	1749.27	-3244.59	777.34	0.1899
C_EMG	3	3	4	-1164.94	2632.64	-4819.63	2489.76	0.4413
C_EMG	4	3	3	-1253.08	2099.88	-5111.38	2605.21	0.4099
C_EMG	2	4	5	-660.19	1439.50	-2315.04	994.67	0.3631
C_EMG	3	4	3	-1167.50	2340.89	-5468.63	3133.62	0.4787
C_EMG	4	4	2	-1862.44	2395.89	-9151.79	5426.92	0.4699
D_EMG	2	1	5	141.03	269.90	-169.25	451.31	0.3075
D_EMG	3	1	4	222.73	395.11	-325.77	771.23	0.3416
D_EMG	4	1	4	73.22	341.08	-400.28	546.72	0.6967
D_EMG	2	2	5	-15.82	225.59	-275.16	243.52	0.8830

D_EMG	3	2	4	146.33	363.94	-358.90	651.56	0.4801
D_EMG	4	2	4	-128.09	134.92	-315.39	59.21	0.1538
D_EMG	2	3	5	43.83	290.87	-290.55	378.21	0.7531
D_EMG	3	3	4	66.02	366.24	-442.40	574.43	0.7424
D_EMG	4	3	3	-90.60	196.69	-452.00	270.81	0.5087
D_EMG	2	4	5	-110.61	175.52	-312.38	91.16	0.2316
D_EMG	3	4	3	-82.93	141.36	-342.67	176.82	0.4165
D_EMG	4	4	2	-160.97	202.13	-775.93	454.00	0.4623
E_Skin_Cond	2	1	5	-11.54	16.41	-30.40	7.32	0.1908
E_Skin_Cond	3	1	4	-1.44	28.78	-41.39	38.51	0.9264
E_Skin_Cond	4	1	4	-4.85	20.42	-33.21	23.50	0.6670
E_Skin_Cond	2	2	5	-7.73	20.31	-31.08	15.62	0.4429
E_Skin_Cond	3	2	4	-1.76	31.37	-45.32	41.79	0.9176
E_Skin_Cond	4	2	4	-5.99	23.60	-38.75	26.78	0.6468
E_Skin_Cond	2	3	5	-2.24	22.06	-27.60	23.13	0.8319
E_Skin_Cond	3	3	4	-3.09	29.19	-43.61	37.44	0.8460
E_Skin_Cond	4	3	3	-5.65	27.44	-56.07	44.77	0.7556
E_Skin_Cond	2	4	5	-7.62	23.61	-34.76	19.52	0.5103
E_Skin_Cond	3	4	3	-9.45	32.89	-69.88	50.98	0.6681
E_Skin_Cond	4	4	2	-20.04	33.86	-123.06	82.99	0.5564
F_Temp	2	1	5	18.37	112.64	-111.11	147.86	0.7338
F_Temp	3	1	4	230.99	219.88	-74.25	536.23	0.1264
F_Temp	4	1	4	-484.87	308.92	-913.72	-56.02	0.0517
F_Temp	2	2	5	-49.02	111.50	-177.20	79.17	0.3813
F_Temp	3	2	4	192.70	148.45	-13.38	398.78	0.0806
F_Temp	4	2	4	-529.04	326.74	-982.64	-75.45	0.0479
F_Temp	2	3	5	-53.26	145.30	-220.30	113.77	0.4584
F_Temp	3	3	4	-95.31	604.29	-934.20	743.58	0.7731
F_Temp	4	3	3	-393.68	288.30	-923.39	136.04	0.1417
F_Temp	2	4	5	-284.32	447.15	-798.37	229.72	0.2281
F_Temp	3	4	3	98.78	329.77	-507.13	704.69	0.6556
F_Temp	4	4	2	-458.20	405.77	-1692.74	776.33	0.3562

^ p-value for evaluating changes from day 1 to day 2, 3 and 4 (for each epoch)

Results: No significant changes from day 1 to day 2, 3, or 4 were detected for **Area HRV/EMG parameters**, except for Temperature (F) from Day 1 to Day 4 (epoch 2) (-529.04+/-326.74, p=0.0479).

5. 5. Questionnaires

Table 17: *Summary statistics Global Mood Scale (GMS) – Positive Affect (PA)*

Day	N	Mean	SD	Lower 95% CI	Upper 95% CL
1	5	13.20	6.98	5.18	21.22
2	5	13.20	4.87	7.60	18.80
3	5	16.80	5.45	10.53	23.07
4	5	20.60	7.37	12.13	29.07
5	5	12.60	2.41	9.83	15.37

Table 18: *Summary statistics Global Mood Scale (GMS) – Negative Affect (NA)*

Day	N	Mean	SD	Lower 95% CI	Upper 95% CL
1	5	11.00	12.00	-2.80	24.80
2	5	9.60	14.79	-7.40	26.60
3	5	7.80	13.61	-7.85	23.45
4	5	2.60	3.05	-0.91	6.11
5	5	7.00	12.92	-7.85	21.85

Table 19: *Change from Day 1 to Day 2, 3, 4 and Day 5 for Global Mood Scale – Positive Affect (PA)*

Change from Day 1 to Day	N	Mean	SD	Lower 95% CI	Upper 95% CL	p-value^
2	5	0.00	5.74	-6.60	6.60	1.0000
3	5	3.60	5.03	-2.18	9.38	0.1848
4	5	7.40	7.20	-0.88	15.68	0.0830
5	5	-0.60	5.22	-6.60	5.40	0.8100

^ p-value for evaluating changes from Day 1 to Day 2, 3, 4, and 5

Table 20: *Change from Day 1 to Day 2, 3, 4 and Day 5 for Global Mood Scale – Negative Affect (NA)*

Change from Day 1 to Day	N	Mean	SD	Lower 95% CI	Upper 95% CL	p-value^
2	5	-1.40	3.58	-5.52	2.72	0.4310
3	5	-3.20	2.95	-6.59	0.19	0.0723
4	5	-8.40	9.07	-18.83	2.03	0.1072
5	5	-4.0	2.92	-7.36	-0.64	0.0373

^ p-value for evaluating changes from Day 1 to Day 2, 3, 4, and 5

Results:
A significant decrease (-4.0+/-2.92, p=0.0373) in GMS –NA from day 1 to day 5 was detected.

Table 21: *Summary statistics for Marlowe-Crowne Scale*

	N	Mean	SD	Lower 95%	Upper 95% CI
	5	17.20	3.96	12.64	21.76
		N	%		
Categories					
Moderate (9-19)		4	80%		
Severe (>19)		1	20%		

Table 22: *Summary statistics Restorative Sleep Questionnaire (RSQ) IPM*

Day	N	Mean	SD	Lower 95%	Upper 95% CI
1	5	47.78	13.09	32.73	62.83
2	5	42.78	15.04	25.49	60.07
3	5	53.89	12.04	40.05	67.73

4	5	56.67	19.50	34.25	79.09
5	5	70.00	17.94	49.38	90.62
6	5	56.11	15.64	38.13	74.09
7	5	59.44	12.20	45.41	73.47

Table 23: *Change in RSQ IPM scores from Day 1 to Day 2,3,4,5,6, and 7*

Change from Day 1 to Day	N	Mean	SD	Lower 95%	Upper 95% CI	p-value^
2	5	-5.00	22.60	-30.98	20.98	0.6468
3	5	6.11	14.88	-11.00	23.22	0.4104
4	5	8.89	30.26	-25.90	43.68	0.5472
5	5	22.22	18.84	0.56	43.88	0.0577
6	5	8.33	27.71	-23.53	40.19	0.5381
7	5	11.67	23.19	-14.99	33.33	0.3236

^ p-value for evaluating changes form Day 1 to Day 2,3,4,5,6, and 7

Results:
No significant changes from Day 1 to Day 2, 3, 4, 5, 6, or 7 were detected.

Table 24: *Summary statistics Sleep Scale*

Day	N	Mean	SD	Lower 95%	Upper 95% CI
1	5	49.60	22.51	23.72	75.48
2	5	60.00	12.73	45.37	74.63
7	5	68.0	7.69	59.96	77.64

Table 25: *Change from Day 1 to Day 2 and 3 in Sleep Scale*

Change from Day 1 to Day	N	Mean	SD	Lower 95%	Upper 95% CI	p-value^
2	5	10.4	24.92	-18.25	39.05	0.4035
7	5	19.2	27.30	-12.18	50.58	0.1909

^ p-value for evaluating changes form Day 1 to Day 2 and 7

Results:
No significant changes from Day 1 to Day 2 or 7 were detected.

Table 26: *Summary statistics Sleep Visual Analog Scale (sVAS)*

Day	N	Mean	SD	Lower 95%	Upper 95% CI
1	5	61.20	15.91	42.91	79.49
2	5	55.00	23.08	28.47	81.53
3	5	68.40	7.50	59.78	77.02
4	5	64.80	23.16	38.18	91.42
5	5	77.20	12.21	63.16	91.24
6	5	73.20	17.43	53.16	93.24
7	5	83.60	12.22	69.55	97.65

Table 27: *Change in sVAS scores from Day 1 to Day 2,3,4,5,6, and 7*

Change from Day 1 to Day	N	Mean	SD	Lower 95%	Upper 95% CI	p-value^
2	5	-6.20	20.10	-29.31	16.91	0.5284
3	5	7.20	12.77	-7.48	21.88	0.2761
4	5	3.60	33.19	-34.56	41.76	0.8203
5	5	16.00	14.78	-0.99	32.99	0.0727
6	5	12.00	23.15	-14.61	38.61	0.3109

^ p-value for evaluating changes form Day 1 to Day 2,3,4,5,6, and 7

Results: No significant changes from Day 1 to Day 2, 3, 4, 5, 6,

Table 28: *Summary statistics POMS*

Day	N	Mean	SD	Lower 95%	Upper 95% CI
1	5	40.80	15.40	23.10	58.50
5	4	41.50	18.98	15.15	67.85
6	5	31.60	17.71	11.24	51.96
7	5	28.20	14.60	11.42	44.98

Table 29: *Change in POMS scores from Day 1 to Day ,5,6, and 7*

Change from Day 1 to Day	N	Mean	SD	Lower 95%	Upper 95% CI	p-value^
5	4	-1.00	9.56	-14.27	12.27	0.8476
6	5	-9.20	4.02	-13.82	-4.58	0.0069
7	5	-12.60	2.61	-15.60	-9.60	0.0004

^ p-value for evaluating changes form Day 1 to Day 5,6, and 7

Results: Significant decreases in the POMS score from Day 1 to Day 6 (-9.2+/-4.02, p=0.0069) and from Day 1 to Day 7 (-12.6+/-2.61, P=0.0004) were observed.

Table 30: *Summary statistics for Telegen Absorption Scale*

N	Mean	SD	Lower 95%	Upper 95% CI
5	25.0	3.08	21.46	28.54

Table 31: *Summary statistics for Hassle & Uplift Scale*

Scale	Day	N	Mean	SD	Lower 95%	Upper 95% CI

Hassle	1	5	13.80	6.14	6.74	20.86
	7	5	12.00	11.51	-1.23	25.23
Uplift	1	5	30.20	20.75	6.35	54.05
	7	5	32.20	27.22	0.91	63.49

Table 32: *Change in Hassle & Uplift scores from Day 1 to Day 7*

Scale	Change from Day 1 to Day	N	Mean	SD	Lower 95%	Upper 95% CI	p-value^
Hassle	7	5	-1.8	8.17	-11.19	7.59	0.6480
Uplift	7	5	2.0	11.51	-11.23	15.23	0.7174

^ p-value for evaluating changes form Day 1 to Day 7

Results: No significant changes in the Hassle and Uplift scale were observed from Day 1 to Day 7.

6. GDV

2. Fractality parameters:
    2.1 Form Coefficient
    2.2 Fractality Dimension
3. Spectrum parameters
    3.1 Average Brightness
    3.2 Spectrum Width

Study Calendar:

	Baseline	Patch Application	Day+6	Day+7
GDV Outcomes	X	X	X	X

6.1 Summary statistics

Table 33: *Summary statistics of Fractality parameters (form coefficient and fractality dimension)*

		Form Coefficient		Fractality Dimension	
Location	**Time**	**Mean**	**SD**	**Mean**	**SD**
1L	Baseline	22.06	23.61	1.10	0.03
1L	Patch Application	8.73	4.67	1.15	0.10
1L	Day 6	9.56	3.97	1.14	0.04
1L	Day 7	11.86	16.14	1.19	0.09
1R	Baseline	12.42	15.63	1.14	0.11
1R	Patch Application	7.24	4.56	1.14	0.13
1R	Day 6	8.74	6.47	1.12	0.03
1R	Day 7	4.66	3.62	1.16	0.12
2L	Baseline	31.46	55.73	1.19	0.05
2L	Patch Application	24.55	43.24	1.14	0.04
2L	Day 6	10.65	12.23	1.15	0.03
2L	Day 7	4.48	1.76	1.19	0.10
2R	Baseline	16.50	27.40	1.14	0.07
2R	Patch Application	28.05	55.55	1.15	0.03
2R	Day 6	5.11	1.87	1.15	0.06
2R	Day 7	4.07	1.55	1.17	0.07
3L	Baseline	34.80	61.85	1.17	0.04
3L	Patch Application	28.27	42.03	1.12	0.04
3L	Day 6	9.19	9.94	1.13	0.05
3L	Day 7	4.92	2.81	1.15	0.07
3R	Baseline	39.44	74.16	1.17	0.07
3R	Patch Application	96.92	207.60	1.16	0.08
3R	Day 6	7.45	6.86	1.22	0.06
3R	Day 7	3.99	1.99	1.19	0.05
4L	Baseline	9.11	8.44	1.18	0.14
4L	Patch Application	14.89	21.18	1.12	0.05
4L	Day 6	4.84	3.20	1.17	0.04
4L	Day 7	3.83	2.54	1.21	0.05

4R	Baseline	9.56	7.75	1.24	0.08
4R	Patch Application	22.00	31.60	1.14	0.07
4R	Day 6	4.17	2.59	1.21	0.04
4R	Day 7	2.19	0.68	1.16	0.05
5L	Baseline	3.49	2.28	1.21	0.13
5L	Patch Application	3.58	1.54	1.19	0.09
5L	Day 6	2.31	0.59	1.20	0.04
5L	Day 7	1.81	0.38	1.22	0.05
5R	Baseline	6.51	5.22	1.20	0.07
5R	Patch Application	6.29	7.40	1.21	0.08
5R	Day 6	2.38	1.13	1.27	0.07
5R	Day 7	2.75	1.16	1.28	0.10
Overall	Baseline	18.54	27.33	1.18	0.07
Overall	Patch Application	24.05	41.28	1.15	0.05
Overall	Day 6	6.44	4.50	1.18	0.02
Overall	Day 7	4.46	3.06	1.19	0.06

Table 34: *Summary statistics of Spectrum parameters (average brightness and spectrum width)*

		Spectrum Average Brightness		**Spectrum Width**	
Location	**Time**	**Mean**	**SD**	**Mean**	**SD**
1L	Baseline	12.03	7.37	64.10	29.43
1L	Patch Application	8.35	4.21	66.18	28.17
1L	Day 6	10.94	6.03	69.94	22.16
1L	Day 7	8.53	4.85	72.21	32.45
1R	Baseline	18.02	7.64	89.35	33.42
1R	Patch Application	13.34	5.13	88.70	31.14
1R	Day 6	15.14	6.58	82.21	26.98
1R	Day 7	15.10	4.89	103.91	33.25
2L	Baseline	12.75	8.07	64.70	21.91
2L	Patch Application	8.02	3.24	66.90	26.84
2L	Day 6	11.43	5.91	74.09	24.47
2L	Day 7	7.69	2.58	70.58	21.03

2R	Baseline	14.33	7.52	77.88	25.50
2R	Patch Application	10.93	6.55	82.85	33.54
2R	Day 6	11.82	5.48	74.00	21.09
2R	Day 7	11.24	3.45	88.82	32.22
3L	Baseline	12.06	7.69	63.38	23.40
3L	Patch Application	7.10	3.06	59.00	24.09
3L	Day 6	10.79	5.41	76.52	37.31
3L	Day 7	7.69	2.61	72.42	22.47
3R	Baseline	11.85	7.63	60.98	22.62
3R	Patch Application	8.84	4.18	68.13	28.94
3R	Day 6	11.00	6.15	70.88	26.42
3R	Day 7	8.62	2.58	79.97	23.98
4L	Baseline	12.78	7.74	69.83	19.60
4L	Patch Application	7.47	3.29	65.93	25.39
4L	Day 6	11.24	5.22	79.15	23.17
4L	Day 7	7.91	2.67	73.88	22.94
4R	Baseline	11.85	8.10	62.45	25.72
4R	Patch Application	8.57	3.99	69.90	27.99
4R	Day 6	11.34	6.20	75.70	23.32
4R	Day 7	8.34	2.86	81.85	27.53
5L	Baseline	14.03	8.09	80.07	25.11
5L	Patch Application	8.72	3.25	78.93	36.44
5L	Day 6	12.58	4.90	88.27	21.29
5L	Day 7	8.93	2.57	88.09	25.84
5R	Baseline	13.05	8.17	69.75	25.88
5R	Patch Application	8.32	3.40	73.65	28.97
5R	Day 6	12.21	5.87	85.48	22.24
5R	Day 7	8.60	3.00	82.21	28.14
Overall	Baseline	13.27	8.08	70.25	13.11
Overall	Patch Application	8.97	2.85	72.02	22.35
Overall	Day 6	12.63	5.54	81.89	19.29
Overall	Day 7	9.09	1.88	77.65	20.35

6.2 Evaluation of absolute changes from baseline to Patch Application assessment, Day+6, and Day+7 assessment

Table 35: *Evaluation of absolute changes from baseline (pre-treatment) for Fractality parameters (form coefficient and fractality dimension)*

		Fractality Form Coefficient			**Fractality Dimension**		
Location	**Change from Baseline to:**	**Mean**	**SD**	**p-value**	**Mean**	**SD**	**p-value**
1L	Patch Application	-13.32	23.21	0.2686	0.05	0.10	0.3345
1L	Day 6	-12.50	21.70	0.2673	0.04	0.05	0.1451
1L	Day 7	-10.19	14.22	0.1842	0.09	0.09	0.1014
1R	Patch Application	-5.18	12.49	0.4063	0.00	0.14	0.9754
1R	Day 6	-3.68	9.98	0.4554	-0.02	0.12	0.7606
1R	Day 7	-7.76	12.05	0.2232	0.02	0.17	0.7613
2L	Patch Application	-6.91	12.73	0.2915	-0.05	0.06	0.1129
2L	Day 6	-20.81	43.60	0.3459	-0.05	0.08	0.2371
2L	Day 7	-26.98	54.48	0.3302	-0.01	0.11	0.9082
2R	Patch Application	11.56	28.29	0.4127	0.01	0.07	0.7582
2R	Day 6	-11.39	26.27	0.3873	0.01	0.09	0.8909
2R	Day 7	-12.43	26.15	0.3477	0.03	0.13	0.6746
3L	Patch Application	-6.53	23.52	0.5684	-0.05	0.05	0.1202
3L	Day 6	-25.61	51.96	0.3323	-0.04	0.03	0.0376*
3L	Day 7	-29.88	59.49	0.3242	-0.02	0.08	0.6492
3R	Patch Application	57.48	133.56	0.3904	-0.01	0.14	0.8283
3R	Day 6	-32.00	67.57	0.3494	0.05	0.06	0.1585
3R	Day 7	-35.45	72.18	0.3337	0.02	0.09	0.6463
4L	Patch Application	5.78	15.96	0.4631	-0.06	0.18	0.4648
4L	Day 6	-4.27	6.24	0.2010	-0.01	0.12	0.8894
4L	Day 7	-5.28	6.67	0.1516	0.03	0.16	0.7363
4R	Patch Application	12.44	28.86	0.3896	-0.09	0.12	0.1573
4R	Day 6	-5.39	6.48	0.1363	-0.02	0.06	0.4348
4R	Day 7	-7.37	7.16	0.0828^	-0.08	0.08	0.1014
5L	Patch Application	0.09	1.72	0.9087	-0.02	0.15	0.7763
5L	Day 6	-1.18	2.47	0.3456	-0.01	0.13	0.8740
5L	Day 7	-1.68	2.19	0.1614	0.01	0.15	0.8630

5R	Patch Application	-0.22	3.57	0.8979	0.01	0.14	0.8587
5R	Day 6	-4.13	4.36	0.1012	0.07	0.06	0.0640^
5R	Day 7	-3.76	4.24	0.1183	0.08	0.16	0.3508
Overall	Patch Application	5.52	15.28	0.4645	-0.02	0.10	0.6396
Overall	Day 6	-12.10	23.03	0.3053	0.00	0.06	0.9555
Overall	Day 7	-14.08	24.36	0.2658	0.02	0.11	0.7466

* P<0.05

^ P<0.10

A significant decrease in fractality dimension is observed (-0.04+/-0.03, P=0.0376) is observed from baseline to Day +6 at the "3 –Left" finger assessment. A marginally significant decrease was observed for fractality form coefficient from baseline to Day +7 (-7.37+/-7.16, P=0.0828) at the "4 Right" finger assessment.

Table 36: *Evaluation of absolute changes from baseline (pre-treatment) for Spectrum parameters (average brightness and spectrum width)*

		Spectrum Average Brightness			**Spectrum Width**		
Location	**Change from Baseline to:**	**Mean**	**SD**	**p-value**	**Mean**	**SD**	**p-value**
1L	Patch Application	-3.67	9.29	0.4265	2.08	17.97	0.8090
1L	Day 6	-0.24	13.59	0.9703	10.58	29.75	0.4713
1L	Day 7	-3.08	10.70	0.5554	5.45	23.02	0.6246
1R	Patch Application	-4.68	7.37	0.2293	-0.65	35.25	0.9691
1R	Day 6	-1.35	13.11	0.8294	0.70	9.80	0.8809
1R	Day 7	-3.53	10.01	0.4747	7.75	46.02	0.7256
2L	Patch Application	-4.73	8.81	0.2960	2.20	16.05	0.7745
2L	Day 6	0.92	15.68	0.9017	14.98	31.96	0.3540
2L	Day 7	-5.15	8.13	0.2298	0.70	6.69	0.8264
2R	Patch Application	-3.40	8.12	0.4020	4.98	28.30	0.7143
2R	Day 6	-1.59	13.22	0.8015	-0.20	21.40	0.9843
2R	Day 7	-3.72	9.75	0.4412	2.40	41.40	0.9031
3L	Patch Application	-4.95	8.51	0.2632	-4.38	16.82	0.5919
3L	Day 6	-0.77	13.34	0.9036	15.50	27.05	0.2693
3L	Day 7	-4.42	8.54	0.3116	5.48	10.40	0.3042
3R	Patch Application	-3.01	7.54	0.4222	7.15	17.88	0.4218

3R	Day 6	-0.40	13.83	0.9513	18.50	39.57	0.3549
3R	Day 7	-3.72	8.94	0.4048	13.23	17.67	0.1695
4L	Patch Application	-5.31	8.47	0.2337	-3.90	15.97	0.6140
4L	Day 6	-1.33	12.92	0.8290	13.15	28.09	0.3544
4L	Day 7	-4.55	9.21	0.3309	3.73	12.57	0.5438
4R	Patch Application	-3.28	8.60	0.4419	7.45	25.63	0.5512
4R	Day 6	-0.32	14.11	0.9616	18.38	34.50	0.2995
4R	Day 7	-3.68	9.05	0.4141	19.95	20.64	0.0967^
5L	Patch Application	-5.31	9.13	0.2633	-1.14	12.47	0.8476
5L	Day 6	-0.76	13.32	0.9048	11.66	23.46	0.3289
5L	Day 7	-5.35	8.33	0.2241	9.76	18.08	0.2940
5R	Patch Application	-4.73	8.95	0.3030	3.90	20.13	0.6872
5R	Day 6	-0.63	13.69	0.9227	13.20	20.82	0.2293
5R	Day 7	-4.60	9.70	0.3487	5.60	18.26	0.5306
Overall	Patch Application	-4.31	8.10	0.3000	1.77	16.38	0.8212
Overall	Day 6	-0.65	13.54	0.9200	11.64	24.16	0.3419
Overall	Day 7	-4.18	8.82	0.3492	7.40	13.42	0.2850

* P<0.05

^ P<0.10