Metabolic implications of the Lifewave X39 Patch

Melinda H. Connor, D.D., Ph.D., AMP, FAM
Caitlin A. Connor, MAcOM, DAOM
Naran Gombosuren, Ph.D.
Jens Eickhoff, Ph.D.

Introduction

This study explores the metabolic implications and physiologic results of wearing the Lifewave X39 patch over a one week period of time. Measures were taken at baseline/Day 1, Day 2 and at 1 Week of wearing the patch. 15 subjects were selected to participate in this study using a sample of convenience. This was made up of both men and women aged 40-65.

Background

The Lifewave X39 patch focuses on stimulating the copper tripeptide GHK- Cu. "Copper tripeptide-1(GHK-Cu) is a small protein composed of the three amino acids (protein building blocks) glycine, histidine, and lysine combined in a specific geometric configuration with the physiologically beneficial mineral (copper)" (DeHaven, C., 2014). This tripeptide was first discovered by Dr. Loren Pickart in 1973, when he isolated it from human plasma albumin. Pickart, noticed differences in the levels of fibrinogen based on age. He additionally noticed that these differences stopped when the older liver cells were incubated in blood from younger individuals. "In 1977, David Schlesinger of the Harvard University Chemistry Department confirmed that the growth modulating peptide isolated by Pickart was a glycyl-L-histidyl-L-lysine peptide." It is interesting to note that this peptide has also been found in saliva, urine, and collagen. Later research

also established that GHK has two forms, GHK alone and GHK-CU, in which the GHK peptide has bound with copper due to the strong affinity the GHK peptide has for it. It is also of note that none of the research around GHK has ever found it to cause a negative side effect. (DeHaven, C., 2014)

The "copper tripeptide-1 belongs to a group of emergency response molecules which are released during injury and come to the body's aid..." (DeHaven, C., 2014) It is naturally released by the body when there is any type of injury to tissue. Research has identified that the peptide is used to signal the beginning of the natural repair process. This benefit has specifically been documented through research for post-laser or surgical wounds, ischemic, burns, skin or hair transplants, and diabetic ulcers. "Diabetic wounds healed three times faster in the presence of Copper tripeptide-1. Time to re-epithelialization is shortened." (DeHaven, C., 2014) The "copper tripeptide-1 has been suggested to have a potential therapeutic role in age-related neurodegeneration and cognitive decline. It improves axon survival and maintenance of nerves." (DeHaven, C., 2014)

The tripeptide has also been shown to improve skin repair. "It increases keratinocyte proliferation and normal collagen synthesis, improves skin thickness, skin elasticity and firmness, improves wrinkles, photodamage and uneven pigmentation, improves skin clarity, and tightens protective barrier proteins." (DeHaven, C., 2014) This has an impact on both scars and other effects of damage to the skin, and natural aging processes. The effects of tissue remodeling also appear to have an impact on cancerous cells. "The fact that GHK was able to suppress 70% of genes involved in the development of an aggressive metastatic form of colon cancer indicates that GHK is

capable of the regulation of various biochemical pathways on a gene level and it seems to be resetting the gene activity back to health, which leads to the improvement of tissue repair." (Pickart, L., 2015)

GHK-Cu also has a demonstrated impact on other organs in the body after they have been damaged. "A collaborative study conducted by scientists from Boston University, University of Groningen, University of British Columbia, and University of Pennsylvania established that the GHK peptide reverses the gene expression signature of COPD, which is manifested by emphysema, inflammation, lung tissue destruction, and significant reduction of lung capacity." (Pickart, L., 2015) It is also important to note that "…the level of GHK is about 200 ng/mL(10−7M) at age 20, but declines to 80 ng/mL by age 60." (Pickart, L., 2015) This likely explains the increasing effects of aging. It would also suggest that increased levels over time of GHK-Cu would have a positive effect on both life expectancy and aging.

Non-transdermal Patch

The X39 patches are sealed so that nothing in the patch will penetrate the skin. This produces consistent promotion of the light flow throughout the time the patch is worn. In this study the initial baseline readings were taken, and then the X39 patch was applied. The participant was asked to wear the patch 12 hours each day. The participant removed the patch at night and a fresh patch was applied each morning prior to 8 am. The patch was worn for a minimum of 1 hour before the additional data measures were taken. Patches were worn for a total of 7 days. Data taking with the patch applied was done on day one, day two and day seven.

Phototherapy

Phototherapy has been defined as “the use of ultraviolet (UV) light for its healing effects.” (Kakimoto, C., 2017) Supported by normal electro-dermal skin conductance (Becker, (1985), Flick, (2004)), the human body gives off a number of materials biochemically including particulate release, gas emission, ultraviolet light, near infrared light, and visible spectrum light. The Lifewave patches have been specifically developed to reflect this light back onto the skin where the patch has been placed. This then stimulates the area of skin, producing improved physiological effects. Variations on phototherapy have been used for at least 100 years. In that time there has not been much evidence of negative side effects, though there is a concern about a potential increase in cancer rates. It is currently largely theoretical, and “there was no significant association found with basal cell carcinoma, squamous cell carcinoma or melanoma.” (Kakimoto, C., 2017) This suggests that phototherapy represents a relatively unexplored option for healing with reasonably few risks.

Meridian Implications and Patch placement

Specific meridian points are chosen for the placement of the Lifewave patches to maximize effectiveness. The Chinese meridian system is over 3000 years old, with current information mapping the meridian system to parts of the lymphatic system. Two points were specifically chosen for the X39 patch. The first is GV14, Du-14, or Tao Dao , which is a point on the back, and the second is CV-6, Ren 6, or Qi Hai, which is a point on the lower abdomen. (Deadman, P., 2001)

This study focused on the metabolic impact of patch usage, with half the participants using the CV6 point and half using the GV14 point.

Metabolic Suite

For the purposes of this study the Sabre Sciences HPA2 metabolic suite has been selected. The HPA 2 Profile includes both urine and saliva collection. The urine evaluates: 5-HTP, Serotonin, Dopamine, Epinephrine, Norepinephrine, GABA, Glutamate, Histamine, L-DOPA, Normetanephrine, Metanephrine, and 3-Methoxytyramine. The saliva evaluates: Cortisol and DHEA. Several additional measures have been added to the HPA2 suite, Glutathione, and a cysteine to cystine ratio will also be tested using the urine sample. Three measures will be taken: baseline, 24 hours and 7days. (Sabre Sciences Laboratory, http://www.sabresciences.com/):

Metabolic testing consisted of one 10am urine taken at baseline/day one, day two and day seven. Saliva Testing consisted of a six swabs taken in one day at baseline/day one, day two and seven. Subjects self-administered the swab under the supervision of Dr. Connor when in the laboratory, which was then placed back in the shipping container and labeled with the subject number. Samples were kept in the freezer at -20F and were shipped with ice by UPS to the Sabre Science lab in Carlsbad, CA on a daily basis.

Physiology Suite

All study participants had the following physiological testing done at base line, 24 hours and 7 days: Six minute recordings of EKG, pulse, respiration, heart rate variability (HRV), temp, blood volume pulse, galvanic skin response, and 2 EMG (muscle) leads (one on each shoulder area). At baseline testing, participants were checked for any

allergic reactions to the adhesive patches. Allergic reactions to physiological test patches happen at a rate of 1:100,000 and if an allergic reaction was discovered participants would be referred to the local urgent care for treatment and then dropped from the study. No participants in this study had an adverse event of any type. Fresh adhesive patches were used for each person tested. Adhesive patches are disposed of in bio hazard containers after use.

Questionnaires

A series of questionnaires were administered to support the metabolic findings.

Marlowe Crowne

The Marlowe Crowne is a 13 Item true/false short form that is a measure of subjects' tendencies to give answers that they may perceive are desired by the interviewer and/or reflect perceived positive social norms. This variable can produce inaccurate or misleading findings unless properly controlled for in statistical analysis. Estimated completion time 2 minutes. This instrument was normed by Reynolds in 1982.

McGill Pain Scale

This scale is comprised of three sections regarding a subject's pain. Section number one asks, "What Does Your Pain Feel Like?" and then lists 20 descriptive categories that are numerically rated as 1 – 5. Section number two asks, "How Does Your Pain Change with Time?" The first question asks the subject to describe the pattern of their pain; and this is followed by 22 descriptive terms regarding their effects on increasing or decreasing pain. The third section reflects upon the strength of the pain and has six questions that give a context and comparison to the current pain compared to

other types of pain suffered in the past. Again this section is ranked numerically 1-5, with one being mild and five being excruciating. (Melzack, R., 1975)

Pittsburg Sleep Quality Index

This scale is comprised of a mix of quantitative questions and five likert scale questions 0-3. It explores the type and quality of sleep experienced by an individual over the past month. It was normed by Cole et al. (2006).

Arizona Integrative Outcome Scale, Visual Analogue Scale (AIOS-VAS) for Vitality

The AIOS- VAS rates subject's "overall sense of well-being and vitality" over the past 24 hours, using a 100mm one-line visual analogue scale. This instrument was normed by Bell in 2004.

Profile of Mood States (POMS)

The POMS is a 37-item 5 factor scale which is a basic measure of affective state in several dimensions including vigor, mood, anxiety and depression. 8 minutes maximum completion time. It was normed by McNair et al., 1971/1981; Shacham, 1983.

WAS III

A subsection of the WAS III will be used to determine level of short and long term memory and if there is an improvement in memory from baseline to 7 days.

Statistical Analysis

Data from questionnaires were collected on standard answer sheets and scored. Then the data points were entered into an excel spread sheet for statistical evaluation. Standardized tests were scored and reviewed for data trends and significant results. All questionnaires parameters were summarized in terms of means and standard deviation, stratified by assessment time point.

Changes between assessment time points were evaluated using a paired t-test or nonparametric Wilcoxon Signed Rank test. All physiology parameters were summarized in terms of means and standard deviation, stratified and across the 6 study epochs. Changes from pre-to post patch administration were evaluated using a paired t-test. Normal probability plots were examined to verify the distribution assumptions. All reported P-values are two-sided and $P<0.05$ was used to define statistical significance. All metabolic parameters were summarized in terms of means and standard deviation, stratified by assessment time point. Changes from day 1 (pre-patch) to day 2, day 2 to day 7, and day 1 to day 7 were evaluated using a paired t-test or nonparametric Wilcoxon Signed Rank test. Cortisol levels were obtained at 8am, 12pm, 4pm, 8pm and 12am. DHEAS levels were collected at 8am, 8pm and 12am. The area under the curve (AUC) for Cortisol and DHEAS levels over the data collection periods were calculated using the trapezoid rule. AUC levels were summarized in terms of means and standard deviations, stratified by assessment time point. Changes between assessment time points were evaluated using a paired t-test or Wilcoxon signed rank test.

Results

The complete data results of the testing are found in Appendix A. Significant results of the Lifewave X39 patch testing are as follows:

Table 1: Demographics (N=15)

	N (%)
Gender	
Female	10 (67%)
Male	5 (33%)
Age (yrs), means ± SD	61.9 ± 9.3

A sample of convenience of individuals who responded to locally placed flyers consisted of 15 individuals. There were five men and 10 women in the study which had a mean age of 61.9 ± 9.3 years.

Questionnaire Outcomes

- Marlowe-Crowne
- AIOS-VAS
- WAIS III
- Profile of Mood States (POMS)
- Modified Pittsburg Sleep Quality Index
- McGill Pain Instrument

Table 2: Summary of Marlowe-Crowne instrument scores, stratified by day

Day	N	Mean	SD
1	15	16.0	2.1
7	15	15.5	2.4

Table 3: Changes in Marlowe-Crowne instrument scores from day 1 to day 7

	Mean Change	SD	p-value
Change from day 1 to day 7	-0.47	0.2	0.4614

The Marlowe-Crowne looks at social desirability. It is used to measure the reliability of the data. One common confounding variable in research is research subjects telling the researchers the answers they think the researchers want. The middle range that is being shown here suggests that this was not an issue with this particular group. It is also interesting that this group had a non-significant negative mean change, indicating that the responders became more honest.

Table 4: Summary of AIOS-VAS instrument scores, stratified by assessment time point

Time	N	Mean	SD
Consent	15	62.7	22.8
1.2	14	67.1	22.8
2	14	71.1	27.3
6	15	78.0	23.1

Table 5: Changes in AIOS-VAS instrument scores from Consent to 1.2, Consent to day 2, and Consent to day 7 assessments

	Mean Change	SD	p-value
Change from 1.1 to 2	7.6	15.3	0.0877
Change from 1.1 to 7	15.3	20.6	0.0151

The AIOS-VAS looks at the overall wellness of an individual. In this case there was a clear, though not quite significant shift established by the second day of testing. It had increased to significance by day 7 showing clear overall improvement in the feelings of vitality and wellness.

Table 6: Summary of WAISIII instrument scores, stratified by assessment time point

Time	Outcome	N	Mean	SD
Day 1	# Short	15	6.2	1.9
	# Mid	15	5.3	2.3
	# Long	15	5.1	2.3
Day 7	# Short	15	7.3	2.3
	# Mid	15	6.1	2.9
	# Long	15	6.1	3.1

Table7: Changes in WAISIII instrument scores from day 1 to day 7

	Outcome	Mean Change	SD	p-value
Change from Day 1 to Day 7	# Short	1.1	2.4	0.0872
	# Mid	0.8	2.9	0.3008
	# Long	1.1	3.2	0.2170

Memory is a common issue for people above age 45. The WAIS III is a well established intelligence test which includes a standard memory test. There was a clear, though not significant, improvement in short term memory by day 7. It is likely that this would get more significant with a larger group of people and a longer intervention period. It is also interesting that there was improvement in both mid and long term memory as well, though to a much lower degree. Further research should be done in this specific area

as a non-invasive support to memory as one ages has the potential to be of benefit to many individuals.

Table8: Summary of modified PSQI instrument total scores, stratified by assessment time point

Time	N	Mean	SD
Day 1	11	6.7	2.8
Day 2	11	5.2	2.7
Day 7	7	4.6	2.9

Table 9: Changes in modified PSQI instrument scores from day 1 to day 2 and from day 1 to day 7

	Mean Change	SD	p-value
Change from Day 1 to Day 2	-1.0	1.3	0.0676
Change from Day 1 to Day 7	-3.0	2.9	0.0522

The Pittsburg Sleep Quality Index was used to look at sleep, which is also a common issue once people get past 45. This questionnaire showed an immediate strong shift the first night, though it was not quite significant. The shift by day 7 was significant. This is particularly important as sleep strongly effects everything else related to health and wellbeing.

There were no significant changes in the Profile of Mood States and the McGill Pain scores from the baseline (pre-patch) assessment to close of study.

Metabolic Outcomes

Table 10: Change from day 1 (pre-patch) to day 2, day 2 to day 7, and day 1 (pre-patch) to day 7

Marker	**Change**	**Mean Change**	**SD**	**p-value**
Alanine	Day 1 to Day 2	-20.17	36.89	0.0526
Cystine	Day 2 to Day 7	-16.07	23.86	0.0206
Epinephrine	Day 1 to Day 2	-2.09	3.08	0.0197
Epinephrine	Day 2 to Day 7	1.59	2.94	0.0552
GABA	Day 1 to Day 7	-0.73	1.50	0.0818
Glutathione	Day 2 to Day 7	-3.82	6.73	0.0453
Glutathione	Day 1 to Day 7	-5.82	10.37	0.0475
Glycine	Day 1 to Day 2	-72.54	117.73	0.0317
HCys2	Day 1 to Day 2	0.35	0.55	0.0296

Histamine	Day 1 to Day 2	-46.32	75.35	0.0320
Histamine	Day 1 to Day 7	-46.64	49.35	0.0026
Histamine (free)	Day 1 to Day 2	-9.24	20.20	0.0981
Hydroxylysine	Day 1 to Day 7	-0.80	1.75	0.0992
Leucine	Day 1 to Day 2	-4.84	7.84	0.0313
Normetanephrine	Day 2 to Day 7	-13.06	23.32	0.0479
PEA Phenylethylamine	Day 1 to Day 7	-0.59	1.12	0.0589
Phenylalanine	Day 2 to Day 7	6.33	10.94	0.0418
Tryptophan	Day 2 to Day 7	-10.81	18.55	0.0406
Alpha-aminobutyric acid	Day 1 to Day 7	-8.90	13.79	0.0256
Alpha-aminobutyric acid	Day 2 to Day 7	-5.29	7.79	0.0198

Amino acids and neurotransmitters play a critical role in the health and wellbeing of individuals. If an individual's amino acid and neurotransmitter production is broken, the individual cannot maintain body health for long. The number of statistically significant changes demonstrated in this study shows the powerful impact which can be created by the use of phototherapy products and the clear positive changes produced by the application of this specific non-transdermal Lifewave product X-39. Key findings are Glutamate and Histamine as they show a distinct anti-inflammatory trend produced by the patch.

Of note the amino acids Glycine and Glutamate, which are used in the process to form Glutathione in a transsulfuration pathway, both showed a drop off at a level of significance. This is very important. Gluthione is part of the body system which supports reduction of inflammation pathways in a unique aspect. It specifically acts from the liver to detoxify the blood. So for example, it clears heavy metals from the body rather than acting as an anti-inflammatory agent directly. A decrease in the materials that produce the glutathione as the result of patch usage means that more glutathione is being made. This

results in higher availability of the glutathione in the blood and allows the body to clear more damaging material faster. This supports the overall reduction in inflammation which was demonstrated in the data results.

Physiology Outcomes

Table 11: Change from pre-patch to last-patch (day 7) of HF, LF/HF NN50, PNN50, Power, RMSSD, and VLF, stratified by Epoch (1-6)

Source	Outcome	Epoch	Mean Change	SD	p-value
EKG	SDNN	2	-42.89	82.71	0.06430
BVP	HF	5	-1085.13	2038.55	0.05830
BVP	NN50	1	-3.13	5.34	0.03950
BVP	NN50	2	-2.13	4.12	0.06470
BVP	NN50	3	-1.73	2.89	0.03580
BVP	NN50	5	-2.73	3.03	0.00360
BVP	PNN50	1	-0.05	0.08	0.03820
BVP	PNN50	2	-0.03	0.07	0.06880
BVP	PNN50	3	-0.03	0.04	0.04290
BVP	PNN50	5	-0.04	0.04	0.00360
BVP	RMSSD	5	-21.13	36.49	0.04160
BVP	SDNN	5	-19.42	27.08	0.01480
BVP	VLF	5	-382.47	426.65	0.00370

Table 12: Change from pre-patch to last-patch (day 7) of HF, LF/HF NN50, PNN50, Power, RMSSD, and VLF, across all 6 Epochs

Source	Outcome	Mean Change	SD	p-value
EKG	HF	-1115.01	28492.47	0.7113
EKG	LF	14424.43	104293.22	0.1929
EKG	LF/HF	0.28	1.31	0.0487
BVP	HF	-786.72	3852.92	0.0559
BVP	LF	205.48	4414.61	0.6599
BVP	LF/HF	-0.08	5.93	0.9004
BVP	NN50	-1.96	3.80	<.0001
BVP	PNN50	-0.03	0.06	<.0001
BVP	RMSSD	-21.78	76.48	0.0083
BVP	SDNN	-18.60	63.27	0.0065

Table 13: Change from pre-patch to last-patch (day 7) of BVP-HR, EMG, Skin-Condition, Temperature and Respiratory Rate for Average, Mode, and Area, stratified by Epoch (1-6)

Source	Outcome	Epoch	Mean Change	SD	p-value
BVPHR	Average	2	4.51	7.83	0.0426
BVPHRMaxMin	Average	5	-2.23	3.13	0.0153
BVPHRMaxMin	Mode	1	-1.18	2.17	0.0533
BVPHRMaxMin	Mode	2	-0.73	1.57	0.0917
EKGHRMaxMin	Mode	6	-33.34	67.42	0.0871
RespRate	Mode	1	1.92	4.03	0.0868

Table 14: Change from pre-patch to last-patch (day 7) of BVP-HR, EMG, Skin-Condition, Temperature and Respiratory Rate for Average, Mode, and Area, across all 6 Epochs

Source	Outcome	Mean Change	SD	p-value
BVPHR	Average	2.54	8.31	0.0047
BVPHR	Mode	2.31	9.60	0.0249
BVPHRMaxMin	Average	-1.67	5.50	0.0049
EMG	Average	-39.44	124.62	0.0035
EMG	Mode	-38.45	128.72	0.0057
EMG	Area	-2366.63	7477.30	0.0035

Reduction in blood pressure and improved muscle relaxation are consistent changes which are present in the physiology data. Greater flexibility in HRV in the over age 60 population is an important finding.

Discussion

It should be remembered that this was both a sample of convenience and a 1 week study with a sample size of 15 subjects. However, there are several areas that showed significant change, as well as a few that showed a clear tendency to change, though not quite to the level of significance. It should also be noted that the shift in sleep is

especially interesting given that the research subjects sleep was being interrupted every four hours for the saliva testing on the days those questionnaires were administered. This means that the results may have been stronger without the confounding variable. The lack of shift in POM, which looks at overall mood, is also interesting. The patch itself was not expected to shift the research subjects' mood, but there was a possibility of it being a secondary effect. Improved sleep and energy often improve people's mood.

There are several key pieces of information in this data. The first is the improvement in blood pressure. For a non-invasive process like photo-therapy in comparison with the challenging side-effects caused by most blood pressure medications and a more vulnerable population with those who are aging, further exploration of this parameter should be a priority.

The second is the impact of the metabolic changes shown in amino acid production. While amino acid production and metabolism changes on a daily basis and is strongly impacted by what foods we eat and our daily activities, the data taken over several days gives a snap-shot of change. Key findings are Glutathione and Histamine results as they show a distinct anti-inflammatory trend produced by the patch. This is further confirmed when looking at Glycine and Glutamate in combination. They are used in the metabolic processes to form Glutathione through the transsulfuration pathway. Since both showed a drop off at a level of significance it shows that they are being used for the purpose of the production of Glutathione. This is very important. Gluthione is part of the body system which supports reduction of inflammation pathways in a unique aspect. It specifically acts from the liver to detoxify the blood.

In addition, the third finding shows that flexibility in the gut systems may be able to be restored. As one ages there is often less flexibility in all the body systems. Flexibility is key in human survival. We must be able to adapt moment to moment in order to survive. This patch triggers change in the gut and what may be determined in studies of longer duration to be restoring fitness and adaptability to change. It is important to note as the fourth finding that changes were in most of the types of amino acids and not limited to a single type of amino acid. We saw changes in essential, non-essential, branched chain essential, aromatic and non- proteinogenic amino acids instead of a single amino acid or area of amino acid production.

The fifth interesting finding is the almost as significant (0.08) improved short term memory within a week. Memory loss in aging is a significant issue around the world. Longer studies of larger size which explore the impact of this phototherapy product should be explored.

Summary

This study explored the metabolic and physiologic aspects of the Lifewave X39 patch. In addition, questionnaires which were administered concurrently cover a range of previously reported experiences with the X39 patches. These include quality of sleep improvement, memory improvement, feelings of vitality, reduction of pain and inflammation, and an overall sense of well-being. This study provides a short term picture of the lived experience of participants who are wearing the Lifewave X39 patch.

The data results of improvement in blood pressure, 17 statistically significant amino acid changes over the 7 days, significant improvement in anti-inflammatory response, improvement in sleep levels, reduction in blood pressure, improvement in short

term memory, improvement in reported feelings of vitality and consistency in reporting across the study suggest that further research with a larger sample size be done and confirm the previously reported anecdotal responses in the testing of earlier subjects.

Since this study was done on an aging population it is also important to note that the patch appears to support the movement back toward fitness of the gut system and improved adaptability to change. The human body must live on the edge of chaos so that it can adapt and respond to change moment to moment in order to survive. One of the first areas of the body that shows a lack of adequate responsiveness to change as we age is the gut. While this is only a one week period, the oscillatory effect shown in the data over the three samples taken during that period on each subject, show improved response promoting fitness and adaptability to change. If one can change in response to the environment, one can survive longer. Combined with the anti-inflammatory response shown in this data, there is a potential for impact on longevity. Further longitudinal studies need to be undertaken to determine if these effects are maintained or improved over time.

The Lifewave X39 patch shows clear, significant metabolic, blood pressure, memory improvement, sleep and other changes over the course of one week which should be explored over longer periods of time in future studies so that a better understanding of the comprehensive nature and effects of the phototherapy produced by this patch may be demonstrated.

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Appendix A: Complete Statistical Results

Statistical Analysis Report

GHK- CU Study – Questionnaire Data

Study Design: Single arm study with 2 – 4 assessment time points.

Sample Size: N=15

Statistical Methods: All physiology suite parameters were summarized in terms of means and standard deviation, stratified by assessment time point. Changes between assessment time points were evaluated using a paired t-test or nonparametric Wilcoxon Signed Rank test.

Questionnaire Outcomes

- Marlowe-Crowne
- AIOS-VAS
- WAIS III
- Profile of Mood States (POMS)
- Pittsburgh Sleep Quality Index (PSQI)
- Modified PSQI
- McGill Pain Instrument

Table 4: Demographics (N=15)

	N (%)
Gender	
Female	10 (67%)
Male	5 (33%)
Age (yrs), means ± SD	61.9 ± 9.3

Table 5: Summary of Marlowe-Crowne instrument scores, stratified by day

Day	N	Mean	SD
1	15	16.0	2.1
7	15	15.5	2.4

Table 6: Changes in Marlowe-Crowne instrument scores from day 1 to day 7

	Mean Change	SD	p-value
Change from day 1 to day 7	-0.47	0.2	0.4614

Table 7: Summary of POMS instrument scores, stratified by assessment time point

Time	N	Mean	SD
1.1	15	28.4	19.3
1.2	14	29.3	20.6
2	13	30.6	20.0
7	14	27.2	19.2

Table 8: Changes in POMS instrument scores from 1.1 to 1.2, 1.1 to 2, and 1.1 to 7 assessment time points

	Mean Change	SD	p-value
Change from 1.1 to 1.2	4.4	11.2	0.1622
Change from 1.1 to 2	4.4	16.2	0.3490
Change from 1.1 to 7	1.2	19.2	0.8162

Table 9: Summary of AIOS-VAS instrument scores, stratified by assessment time point

Time	N	Mean	SD
Consent	15	62.7	22.8
1.2	14	67.1	22.8
2	14	71.1	27.3
7	15	78.0	23.1

Table 10: Changes in AIOS-VAS instrument scores from Consent to 1.2, Consent to 2, and Consent to day 7 assessments

	Mean Change	SD	p-value
Change from 1.1 to 1.2	2.6	12.8	0.3146
Change from 1.1 to 2	7.6	15.3	0.0877
Change from 1.1 to 7	15.3	20.6	0.0151

Table 11: Summary of WAISIII instrument scores, stratified by assessment time point

Time	Outcome	N	Mean	SD
Day 1	# Short	15	6.2	1.9
	# Mid	15	5.3	2.3
	# Long	15	5.1	2.3
Day 7	# Short	15	7.3	2.3
	# Mid	15	6.1	2.9
	# Long	15	6.1	3.1

Table 12: Changes in WAISIII instrument scores from day 1 to day 7

	Outcome	Mean Change	SD	p-value
Change from Day 1 to Day 7	# Short	1.1	2.4	0.0872
	# Mid	0.8	2.9	0.3008
	# Long	1.1	3.2	0.2170

Table 13: Summary of PSQI instrument total scores, stratified by assessment time point

Time	N	Mean	SD
Day 1	14	6.3	2.8
Day 7	11	5.3	2.5

Table 14: Changes in PSQI instrument scores from day 1 to day 7

	Mean Change	SD	p-value
Change from Day 1 to Day 7	-0.4	1.6	0.5152

Table 15: Summary of modified PSQI instrument total scores, stratified by assessment time point

Time	N	Mean	SD
Day 1	11	6.7	2.8
Day 2	11	5.2	2.7
Day 7	7	4.6	2.9

Table 16: Changes in modified PSQI instrument scores from day 1 to day 2 and from day 1 to day 7

	Mean Change	SD	p-value
Change from day 1 to day 2	-1.0	1.3	0.0676
Change from day 1 to day 7	-3.0	2.9	0.0522

Table 17: Summary of modified McGill total pain scores, stratified by assessment time point

Time	N	Mean	SD
Day 1.1	15	6.2	6.7
Day 1.2	15	9.2	16.1
Day 2	15	5.9	9.8
Day 7	15	6.1	9.0

Table 18: Changes in modified McGill total pain scores from day 1 to day 2 and from day 1 to day 7

	Mean Change	SD	p-value
Change from Day 1.1 to Day 1.2	3.0	16.9	0.8867
Change from Day 1.1 to Day 2	-0.3	9.5	0.7480
Change from Day 1.1 to Day 7	-0.1	7.7	0.6328

There are no changes in the McGill pain scores from the baseline (pre-patch) assessment.

GHK- CU Study – Physiology Suite Data

Study Design: Pre-post study comparing physiology suite outcome measures before patch vs. last (day 7) patch administration.

Sample Size: N=15

Statistical Methods: All physiology suite parameters were summarized in terms of means and standard deviation, stratified and across the 6 study epochs. Changes from pre-to post patch administration were evaluated using a paired t-test. Normal probability plots were examined to verify the distribution assumptions. All reported P-values are two-sided and P<0.05 was used to define statistical significance.

Table 19: Summary statistics for pre- vs. Last patch (day 7) of HF, LF/HF NN50, PNN50, Power, RMSSD, and VLF, stratified by Epoch (1-6)

			Pre-Patch		Last-Patch (Day 7)	
Source	**Outcome**	**Epoch**	**Mean**	**SD**	**Mean**	**SD**
EKG	HF	1	14818.66	9397.29	17973.25	27036.86
EKG	HF	2	19618.35	13617.93	15433.62	16379.32
EKG	HF	3	18536.86	14170.61	24555.99	37015.79
EKG	HF	4	22390.90	16673.95	25806.19	21887.15
EKG	HF	5	29227.28	18814.59	24136.17	20423.67
EKG	HF	6	40386.93	25806.00	28767.37	22120.55
EKG	LF	1	13122.89	14872.21	56825.53	186770.11
EKG	LF	2	19743.73	32193.75	22908.82	49147.72
EKG	LF	3	8202.70	6462.20	17442.07	33209.36
EKG	LF	4	10094.09	10374.86	38185.46	103669.27
EKG	LF	5	9950.67	8720.13	13949.08	22320.38
EKG	LF	6	43733.30	91322.00	39360.51	88028.98
EKG	LF/HF	1	0.81	0.61	1.31	1.57
EKG	LF/HF	2	0.79	0.70	1.01	0.90
EKG	LF/HF	3	0.52	0.38	0.62	0.28
EKG	LF/HF	4	0.52	0.36	1.06	1.54
EKG	LF/HF	5	0.32	0.14	0.47	0.37
EKG	LF/HF	6	0.98	1.46	1.08	1.02
EKG	NN50	1	43.07	5.18	41.20	6.66
EKG	NN50	2	40.00	3.78	42.40	5.62
EKG	NN50	3	39.73	4.95	39.60	5.96
EKG	NN50	4	36.87	5.26	38.73	6.17
EKG	NN50	5	36.27	4.73	38.27	4.51
EKG	NN50	6	33.50	3.55	34.73	4.01
EKG	PNN50	1	0.43	0.03	0.42	0.03

EKG	PNN50	2	0.42	0.03	0.43	0.03
EKG	PNN50	3	0.44	0.04	0.44	0.03
EKG	PNN50	4	0.44	0.03	0.45	0.04
EKG	PNN50	5	0.45	0.03	0.45	0.03
EKG	PNN50	6	0.45	0.03	0.44	0.04
EKG	Power	1	34860.17	32520.80	86493.20	248715.39
EKG	Power	2	46274.43	55655.64	44593.55	74597.54
EKG	Power	3	29563.30	19470.34	50064.10	89856.45
EKG	Power	4	34334.22	26054.82	96776.73	225900.85
EKG	Power	5	44102.87	30199.38	41466.28	43405.32
EKG	Power	6	102250.40	144643.37	101064.63	209062.72
EKG	RMSSD	1	437.24	133.90	461.26	271.09
EKG	RMSSD	2	475.06	123.75	427.67	145.70
EKG	RMSSD	3	510.85	157.72	528.37	234.82
EKG	RMSSD	4	562.71	162.39	564.50	170.37
EKG	RMSSD	5	619.63	144.43	555.78	167.73
EKG	RMSSD	6	684.76	166.62	630.29	146.81
EKG	SDNN	1	301.56	92.65	329.64	218.09
EKG	SDNN	2	332.29	83.30	289.39	99.00
EKG	SDNN	3	339.39	98.53	360.14	177.10
EKG	SDNN	4	376.69	108.60	382.27	129.24
EKG	SDNN	5	410.20	94.19	377.77	117.90
EKG	SDNN	6	481.73	118.18	430.35	93.09
EKG	VLF	1	6918.61	16050.31	11694.41	36194.08
EKG	VLF	2	6912.34	12947.88	6251.11	13237.60
EKG	VLF	3	2823.74	2898.34	8066.03	20471.14
EKG	VLF	4	1849.23	1976.73	32785.09	109783.63
EKG	VLF	5	4924.92	5852.22	3381.04	4844.60
EKG	VLF	6	18130.17	44250.75	32936.76	103944.26
BVP	HF	1	1597.97	5153.98	1478.97	4384.89
BVP	HF	2	3709.23	7997.67	963.81	2638.35
BVP	HF	3	1213.70	3841.98	817.30	2292.51
BVP	HF	4	1191.28	3220.91	1731.82	5853.33
BVP	HF	5	1788.10	4174.04	702.97	2473.38
BVP	HF	6	2699.85	6288.95	1622.39	3902.76
BVP	LF	1	586.06	1059.94	1147.30	3098.88
BVP	LF	2	2868.95	6006.49	1935.19	6356.28
BVP	LF	3	1046.10	3120.94	1285.88	3993.02
BVP	LF	4	885.25	1525.61	790.12	2046.57
BVP	LF	5	969.28	1348.37	1426.88	4933.93
BVP	LF	6	953.94	1637.05	1923.23	4178.71

BVP	LF/HF	1	1.93	2.34	2.74	2.83
BVP	LF/HF	2	4.50	8.23	4.21	3.17
BVP	LF/HF	3	3.37	3.92	4.08	4.33
BVP	LF/HF	4	5.20	6.14	4.15	4.06
BVP	LF/HF	5	3.88	4.17	3.30	2.54
BVP	LF/HF	6	3.52	5.70	3.33	2.49
BVP	NN50	1	6.27	6.98	3.13	4.22
BVP	NN50	2	5.20	6.55	3.07	4.04
BVP	NN50	3	4.60	5.41	2.87	3.83
BVP	NN50	4	3.67	5.52	3.00	4.55
BVP	NN50	5	5.20	5.54	2.47	4.16
BVP	NN50	6	4.07	5.28	2.87	4.09
BVP	PNN50	1	0.09	0.11	0.04	0.06
BVP	PNN50	2	0.08	0.10	0.04	0.06
BVP	PNN50	3	0.06	0.08	0.04	0.05
BVP	PNN50	4	0.05	0.08	0.04	0.06
BVP	PNN50	5	0.07	0.08	0.03	0.05
BVP	PNN50	6	0.06	0.08	0.04	0.05
BVP	Power	1	2382.37	6155.15	2928.16	7928.99
BVP	Power	2	11457.90	30247.47	3129.69	8971.19
BVP	Power	3	2584.70	7538.66	2370.40	6454.10
BVP	Power	4	2478.29	4909.61	2786.08	8202.62
BVP	Power	5	3199.89	5488.39	2189.90	7450.55
BVP	Power	6	4197.62	7790.39	4112.00	8798.95
BVP	RMSSD	1	79.97	88.94	62.61	86.83
BVP	RMSSD	2	100.03	147.13	54.72	90.07
BVP	RMSSD	3	70.34	77.13	50.22	76.08
BVP	RMSSD	4	56.02	77.65	52.32	87.82
BVP	RMSSD	5	67.67	76.84	46.55	79.93
BVP	RMSSD	6	76.44	94.67	57.40	83.28
BVP	SDNN	1	68.99	63.28	54.11	64.74
BVP	SDNN	2	91.37	124.34	54.69	69.80
BVP	SDNN	3	65.83	51.38	50.94	57.78
BVP	SDNN	4	60.53	54.55	54.57	68.48
BVP	SDNN	5	64.02	53.42	44.60	60.89
BVP	SDNN	6	71.61	66.03	54.82	66.16
BVP	VLF	1	198.34	159.61	301.89	532.47
BVP	VLF	2	4879.73	16900.51	230.69	438.64
BVP	VLF	3	324.89	614.07	267.22	326.91
BVP	VLF	4	401.77	684.71	264.15	350.31
BVP	VLF	5	442.51	464.44	60.05	60.14

BVP	VLF	6	543.83	621.41	566.39	1499.95

Table 20: Change from pre-patch to last-patch (day 7) of HF, LF/HF NN50, PNN50, Power, RMSSD, and VLF, stratified by Epoch (1-6)

Source	Outcome	Epoch	Mean Change	SD	p-value
EKG	HF	1	3154.59	29005.20	0.68000
EKG	HF	2	-4184.73	12598.21	0.21910
EKG	HF	3	6019.14	41214.98	0.58060
EKG	HF	4	3415.29	23353.35	0.58010
EKG	HF	5	-5091.11	28409.00	0.49900
EKG	HF	6	-10669.64	31051.54	0.22100
EKG	LF	1	43702.64	188421.31	0.38420
EKG	LF	2	3165.08	51770.52	0.81630
EKG	LF	3	9239.37	35358.13	0.32870
EKG	LF	4	28091.37	104765.04	0.31660
EKG	LF	5	3998.41	22850.85	0.50900
EKG	LF	6	-2024.20	133453.31	0.95560
EKG	LF/HF	1	0.50	1.81	0.30510
EKG	LF/HF	2	0.22	1.11	0.45440
EKG	LF/HF	3	0.09	0.47	0.44920
EKG	LF/HF	4	0.55	1.70	0.23440
EKG	LF/HF	5	0.15	0.36	0.11820
EKG	LF/HF	6	0.14	1.80	0.77260
EKG	NN50	1	-1.87	4.50	0.13060
EKG	NN50	2	2.40	5.78	0.13010
EKG	NN50	3	-0.13	8.13	0.95030
EKG	NN50	4	1.87	6.82	0.30730
EKG	NN50	5	2.00	5.96	0.21500
EKG	NN50	6	1.14	6.09	0.49480
EKG	PNN50	1	-0.01	0.04	0.22480
EKG	PNN50	2	0.01	0.03	0.44660
EKG	PNN50	3	0.00	0.03	0.95160
EKG	PNN50	4	0.00	0.05	0.71980
EKG	PNN50	5	-0.01	0.05	0.51460
EKG	PNN50	6	-0.01	0.04	0.34490
EKG	Power	1	51633.02	253690.12	0.44370
EKG	Power	2	-1680.88	72944.30	0.93020
EKG	Power	3	20500.80	95031.26	0.41750
EKG	Power	4	62442.52	221196.63	0.29270

EKG	Power	5	-2636.59	48451.54	0.83610
EKG	Power	6	4442.72	267301.28	0.95140
EKG	RMSSD	1	24.02	241.70	0.70620
EKG	RMSSD	2	-47.39	118.28	0.14300
EKG	RMSSD	3	17.51	294.04	0.82090
EKG	RMSSD	4	1.79	198.97	0.97270
EKG	RMSSD	5	-63.85	214.48	0.26820
EKG	RMSSD	6	-42.95	211.64	0.46120
EKG	SDNN	1	28.08	208.21	0.60960
EKG	SDNN	2	-42.89	82.71	0.06430
EKG	SDNN	3	20.75	209.31	0.70680
EKG	SDNN	4	5.58	147.42	0.88550
EKG	SDNN	5	-32.43	145.93	0.40390
EKG	SDNN	6	-43.01	148.53	0.29830
EKG	VLF	1	4775.80	41081.08	0.65940
EKG	VLF	2	-661.23	17028.51	0.88260
EKG	VLF	3	5242.29	21025.80	0.35060
EKG	VLF	4	30935.86	109560.83	0.29260
EKG	VLF	5	-1543.89	3669.04	0.12540
EKG	VLF	6	17136.56	120381.27	0.60330
BVP	HF	1	-119.00	1129.86	0.68950
BVP	HF	2	-2745.42	7692.69	0.18860
BVP	HF	3	-396.41	1771.01	0.40060
BVP	HF	4	540.54	2849.49	0.47470
BVP	HF	5	-1085.13	2038.55	0.05830
BVP	HF	6	-969.55	3551.06	0.32560
BVP	LF	1	561.24	2192.12	0.33820
BVP	LF	2	-933.75	8693.08	0.68370
BVP	LF	3	239.78	1035.47	0.38500
BVP	LF	4	-95.13	948.78	0.70360
BVP	LF	5	457.61	4474.31	0.69800
BVP	LF	6	1071.09	4533.33	0.39270
BVP	LF/HF	1	0.82	4.23	0.46800
BVP	LF/HF	2	-0.29	8.11	0.89130
BVP	LF/HF	3	0.71	6.18	0.66280
BVP	LF/HF	4	-1.06	8.15	0.62380
BVP	LF/HF	5	-0.58	3.98	0.57940
BVP	LF/HF	6	-0.27	4.10	0.80980
BVP	NN50	1	-3.13	5.34	0.03950
BVP	NN50	2	-2.13	4.12	0.06470
BVP	NN50	3	-1.73	2.89	0.03580

BVP	NN50	4	-0.67	3.60	0.48490
BVP	NN50	5	-2.73	3.03	0.00360
BVP	NN50	6	-1.14	3.37	0.22680
BVP	PNN50	1	-0.05	0.08	0.03820
BVP	PNN50	2	-0.03	0.07	0.06880
BVP	PNN50	3	-0.03	0.04	0.04290
BVP	PNN50	4	-0.01	0.06	0.43010
BVP	PNN50	5	-0.04	0.04	0.00360
BVP	PNN50	6	-0.02	0.05	0.17910
BVP	Power	1	545.78	2280.01	0.36960
BVP	Power	2	-8328.21	31202.70	0.31880
BVP	Power	3	-214.30	1871.40	0.66420
BVP	Power	4	307.79	3957.22	0.76770
BVP	Power	5	-1009.99	3912.89	0.33440
BVP	Power	6	159.57	8096.33	0.94230
BVP	RMSSD	1	-17.35	78.45	0.40610
BVP	RMSSD	2	-45.31	139.63	0.22940
BVP	RMSSD	3	-20.12	53.66	0.16840
BVP	RMSSD	4	-3.70	40.78	0.73050
BVP	RMSSD	5	-21.13	36.49	0.04160
BVP	RMSSD	6	-16.81	66.48	0.36130
BVP	SDNN	1	-14.88	51.26	0.27970
BVP	SDNN	2	-36.68	127.28	0.28320
BVP	SDNN	3	-14.89	36.20	0.13350
BVP	SDNN	4	-5.96	38.00	0.55320
BVP	SDNN	5	-19.42	27.08	0.01480
BVP	SDNN	6	-15.82	50.23	0.25970
BVP	VLF	1	103.55	547.35	0.47580
BVP	VLF	2	-4649.04	16958.99	0.30630
BVP	VLF	3	-57.67	573.83	0.70290
BVP	VLF	4	-137.63	741.02	0.48380
BVP	VLF	5	-382.47	426.65	0.00370
BVP	VLF	6	58.02	1755.00	0.90340

Table 21: Summary statistics for pre- vs. Last patch (day 7) of HF, LF/HF NN50, PNN50, Power, RMSSD, and VLF, across all 6 Epochs

		Pre-patch		Last-patch (Day 7)	
Source	**Outcome**	**Mean**	**SD**	**Mean**	**SD**
EKG	HF	23893.77	18487.28	22778.77	24740.27
EKG	LF	17020.81	39992.04	31445.25	96188.86
EKG	LF/HF	0.65	0.74	0.92	1.08
EKG	NN50	38.32	5.43	39.16	5.93
EKG	PNN50	0.44	0.03	0.44	0.03
EKG	Power	47640.73	67916.09	70076.42	166485.72
EKG	RMSSD	546.19	166.44	527.98	201.30
EKG	SDNN	372.10	112.67	361.59	148.66
EKG	VLF	6726.15	19705.90	15852.41	63648.29
BVP	HF	2006.26	5250.16	1219.54	3722.92
BVP	LF	1212.62	3001.00	1418.10	4216.50
BVP	LF/HF	3.71	5.33	3.64	3.27
BVP	NN50	4.86	5.79	2.90	4.04
BVP	PNN50	0.07	0.09	0.04	0.05
BVP	Power	4346.12	13669.71	2919.37	7809.44
BVP	RMSSD	75.74	94.85	53.97	81.91
BVP	SDNN	70.89	71.80	52.28	63.04
BVP	VLF	1127.24	6929.44	281.73	698.56

Table 22: Change from pre-patch to last-patch (day 7) of HF, LF/HF NN50, PNN50, Power, RMSSD, and VLF, across all 6 Epochs

Source	**Outcome**	**Mean Change**	**SD**	**p-value**
EKG	HF	-1115.01	28492.47	0.7113
EKG	LF	14424.43	104293.22	0.1929
EKG	LF/HF	0.28	1.31	0.0487
EKG	NN50	0.83	6.31	0.2133
EKG	PNN50	0.00	0.04	0.3994
EKG	Power	22435.68	177642.61	0.2340
EKG	RMSSD	-18.22	214.87	0.4234
EKG	SDNN	-10.50	160.20	0.5356
EKG	VLF	9126.26	67230.39	0.2012
BVP	HF	-786.72	3852.92	0.0559
BVP	LF	205.48	4414.61	0.6599
BVP	LF/HF	-0.08	5.93	0.9004

BVP	NN50	-1.96	3.80	<.0001
BVP	PNN50	-0.03	0.06	<.0001
BVP	Power	-1426.75	13373.42	0.3142
BVP	RMSSD	-21.78	76.48	0.0083
BVP	SDNN	-18.60	63.27	0.0065
BVP	VLF	-845.51	6989.71	0.2542

Table 23: Summary statistics for pre- vs. Last patch (day 7) of BVP-HR, EMG, Skin-Condition, Temperature and Respiratory Rate for all distribution characteristics outcomes, stratified by Epoch (1-6)

			Pre-patch		Last-patch (day 7)	
Source	**Outcome**	**Epoch**	**Mean**	**SD**	**Mean**	**SD**
BVPHR	Average	1	75.99	12.00	79.45	13.01
BVPHR	Average	2	75.38	10.23	79.89	12.91
BVPHR	Average	3	77.08	12.44	80.32	12.58
BVPHR	Average	4	78.22	12.40	79.91	14.13
BVPHR	Average	5	79.37	12.55	79.85	13.40
BVPHR	Average	6	78.22	12.22	79.95	13.35
BVPHR	Mode	1	76.27	14.47	78.57	12.18
BVPHR	Mode	2	77.70	12.81	80.04	14.03
BVPHR	Mode	3	77.26	13.21	80.53	13.90
BVPHR	Mode	4	79.69	13.43	81.49	15.08
BVPHR	Mode	5	79.33	13.43	80.63	12.79
BVPHR	Mode	6	78.50	13.00	80.71	13.42
BVPHR	STD	1	5.51	4.65	4.50	4.18
BVPHR	STD	2	6.45	7.38	4.27	3.93
BVPHR	STD	3	5.10	3.47	4.49	3.83
BVPHR	STD	4	5.18	3.87	4.56	4.12
BVPHR	STD	5	5.70	4.42	3.71	3.60
BVPHR	STD	6	5.72	4.61	4.25	3.63
BVPHR	Minimum	1	59.46	15.13	66.60	18.60
BVPHR	Minimum	2	58.19	14.63	69.53	17.78
BVPHR	Minimum	3	58.87	14.55	68.21	15.42
BVPHR	Minimum	4	64.41	13.91	68.17	17.42
BVPHR	Minimum	5	62.90	17.58	69.68	16.71
BVPHR	Minimum	6	61.42	16.43	65.95	18.28
BVPHR	Maximum	1	94.49	27.71	89.97	17.16
BVPHR	Maximum	2	90.18	27.03	87.47	12.96
BVPHR	Maximum	3	86.36	13.21	92.06	17.68

BVPHR	Maximum	4	90.52	17.51	88.19	14.42
BVPHR	Maximum	5	93.50	19.71	86.78	13.82
BVPHR	Maximum	6	87.79	13.16	87.53	14.14
BVPHRMaxMin	Average	1	9.64	9.75	9.10	10.49
BVPHRMaxMin	Average	2	11.32	12.49	8.03	9.49
BVPHRMaxMin	Average	3	9.37	8.36	8.04	8.21
BVPHRMaxMin	Average	4	8.97	8.17	8.34	9.25
BVPHRMaxMin	Average	5	9.21	8.51	6.98	6.97
BVPHRMaxMin	Average	6	10.00	10.85	8.16	8.97
BVPHRMaxMin	Mode	1	7.27	11.25	6.09	11.16
BVPHRMaxMin	Mode	2	7.52	11.82	6.79	11.22
BVPHRMaxMin	Mode	3	4.98	3.55	6.87	10.80
BVPHRMaxMin	Mode	4	7.08	11.08	7.25	11.03
BVPHRMaxMin	Mode	5	7.64	11.65	6.58	10.58
BVPHRMaxMin	Mode	6	7.53	12.04	6.49	10.57
BVPHRMaxMin	STD	1	7.26	6.74	5.98	7.28
BVPHRMaxMin	STD	2	7.90	11.18	4.26	4.46
BVPHRMaxMin	STD	3	6.65	6.04	5.53	6.42
BVPHRMaxMin	STD	4	6.01	6.82	4.43	5.02
BVPHRMaxMin	STD	5	6.96	6.55	4.32	5.47
BVPHRMaxMin	STD	6	6.04	6.01	4.81	5.32
BVPHRMaxMin	Minimum	1	2.64	1.92	2.08	2.34
BVPHRMaxMin	Minimum	2	2.54	2.81	1.87	0.92
BVPHRMaxMin	Minimum	3	2.48	2.65	2.05	1.63
BVPHRMaxMin	Minimum	4	3.01	2.30	2.36	2.20
BVPHRMaxMin	Minimum	5	2.23	1.47	1.87	1.65
BVPHRMaxMin	Minimum	6	2.80	2.05	2.08	2.61
BVPHRMaxMin	Maximum	1	26.71	23.26	20.79	22.32
BVPHRMaxMin	Maximum	2	26.85	32.23	14.99	12.29
BVPHRMaxMin	Maximum	3	23.55	15.58	19.43	20.18
BVPHRMaxMin	Maximum	4	21.30	19.80	15.63	13.79
BVPHRMaxMin	Maximum	5	24.39	21.09	14.86	14.52
BVPHRMaxMin	Maximum	6	22.54	16.95	17.73	16.94
EMG	Average	1	73.73	147.15	26.37	38.59
EMG	Average	2	62.98	136.67	21.32	26.87
EMG	Average	3	53.38	130.88	20.44	26.37
EMG	Average	4	54.91	138.45	17.39	24.66
EMG	Average	5	54.77	133.63	19.50	30.49
EMG	Average	6	56.37	116.57	13.53	17.62
EMG	Mode	1	88.48	192.35	16.98	26.42
EMG	Mode	2	53.96	136.32	22.29	28.61

EMG	Mode	3	54.69	138.62	17.93	24.91
EMG	Mode	4	52.50	130.22	15.97	23.43
EMG	Mode	5	51.44	127.80	19.13	31.35
EMG	Mode	6	34.90	62.74	13.34	18.16
EMG	Area	1	4423.89	8828.48	1581.98	2315.16
EMG	Area	2	3778.68	8200.12	1278.93	1612.16
EMG	Area	3	3203.01	7853.07	1226.24	1582.10
EMG	Area	4	3294.39	8306.75	1043.60	1479.42
EMG	Area	5	3286.20	8017.55	1170.05	1829.65
EMG	Area	6	3382.44	6993.89	811.79	1057.38
EMG	STD	1	13.00	20.72	14.54	43.83
EMG	STD	2	15.68	41.10	3.76	6.59
EMG	STD	3	4.53	6.93	4.98	10.52
EMG	STD	4	3.71	6.56	3.58	5.68
EMG	STD	5	6.89	9.77	3.77	8.27
EMG	STD	6	20.60	47.69	2.00	1.79
EMG	Minimum	1	15.56	18.27	12.55	21.69
EMG	Minimum	2	28.80	73.99	14.71	23.93
EMG	Minimum	3	42.99	111.72	14.22	22.04
EMG	Minimum	4	47.15	122.87	12.08	20.81
EMG	Minimum	5	43.12	114.12	9.31	17.09
EMG	Minimum	6	24.77	44.54	9.94	15.24
EMG	Maximum	1	192.25	244.06	103.39	172.63
EMG	Maximum	2	155.35	237.25	63.62	82.52
EMG	Maximum	3	99.71	164.04	74.06	155.55
EMG	Maximum	4	92.75	161.73	87.60	144.18
EMG	Maximum	5	128.73	188.45	73.03	155.09
EMG	Maximum	6	123.22	212.92	41.55	36.64
EMG	Average	1	28.81	55.86	41.70	93.73
EMG	Average	2	44.06	99.54	35.15	70.91
EMG	Average	3	30.77	68.94	20.33	30.85
EMG	Average	4	24.10	56.73	25.32	53.58
EMG	Average	5	25.06	64.03	25.62	55.95
EMG	Average	6	33.05	92.75	30.84	69.95
EMG	Mode	1	19.34	33.17	38.98	99.90
EMG	Mode	2	32.81	80.55	15.36	22.12
EMG	Mode	3	32.48	74.52	20.35	34.43
EMG	Mode	4	23.25	57.01	19.20	36.53
EMG	Mode	5	24.23	64.31	22.08	46.41
EMG	Mode	6	32.19	94.53	32.10	76.54
EMG	Area	1	1728.66	3351.40	2501.91	5623.55

EMG	Area	2	2643.37	5972.58	2108.70	4254.80
EMG	Area	3	1846.15	4136.32	1219.72	1850.73
EMG	Area	4	1446.25	3403.70	1518.91	3214.78
EMG	Area	5	1503.30	3842.00	1537.14	3357.02
EMG	Area	6	1983.18	5564.93	1850.20	4197.23
EMG	STD	1	16.20	29.48	12.88	32.89
EMG	STD	2	15.59	26.52	20.35	44.28
EMG	STD	3	7.36	14.41	8.05	16.97
EMG	STD	4	4.56	6.66	11.63	35.16
EMG	STD	5	5.49	8.41	6.50	17.55
EMG	STD	6	7.30	11.31	3.43	5.83
EMG	Minimum	1	11.57	25.03	23.23	57.11
EMG	Minimum	2	23.17	65.59	4.87	6.08
EMG	Minimum	3	8.47	21.57	7.63	12.84
EMG	Minimum	4	17.45	47.49	8.75	21.38
EMG	Minimum	5	17.38	50.10	8.74	21.37
EMG	Minimum	6	20.08	60.38	16.09	32.52
EMG	Maximum	1	171.84	224.33	115.20	187.23
EMG	Maximum	2	157.74	240.03	105.02	206.16
EMG	Maximum	3	109.99	178.37	83.18	141.87
EMG	Maximum	4	78.68	80.34	107.54	164.96
EMG	Maximum	5	91.00	135.09	69.77	109.58
EMG	Maximum	6	122.45	188.78	58.92	95.51
EKGHR	Average	2	119.69	12.76	120.06	11.49
EKGHR	Average	3	114.91	8.81	115.04	13.02
EKGHR	Average	4	109.02	7.64	110.87	10.38
EKGHR	Average	5	106.36	9.83	111.51	7.89
EKGHR	Average	6	101.74	10.59	105.43	8.69
EKGHR	Mode	2	80.68	27.74	79.53	29.02
EKGHR	Mode	3	64.20	20.10	63.70	27.99
EKGHR	Mode	4	51.06	11.28	60.64	22.16
EKGHR	Mode	5	52.27	17.00	55.37	14.84
EKGHR	Mode	6	47.46	21.83	54.49	22.47
EKGHR	STD	2	56.89	4.98	55.93	7.50
EKGHR	STD	3	61.09	7.70	58.93	8.71
EKGHR	STD	4	61.57	8.85	57.66	6.93
EKGHR	STD	5	62.12	4.81	62.13	5.65
EKGHR	STD	6	61.74	9.36	63.22	6.44
EKGHR	Minimum	2	35.08	10.57	38.26	11.55
EKGHR	Minimum	3	38.33	7.02	36.63	10.92
EKGHR	Minimum	4	36.34	5.77	36.06	13.51

EKGHR	Minimum	5	34.99	6.41	38.06	9.84
EKGHR	Minimum	6	30.61	9.41	31.98	8.99
EKGHR	Maximum	2	289.75	12.26	287.79	11.22
EKGHR	Maximum	3	292.72	9.34	289.50	11.15
EKGHR	Maximum	4	288.53	13.01	286.77	16.66
EKGHR	Maximum	5	286.46	17.62	288.23	10.54
EKGHR	Maximum	6	278.81	19.88	294.45	4.15
EKGHRMaxMin	Average	2	149.43	21.62	145.76	22.80
EKGHRMaxMin	Average	3	155.05	13.59	149.86	13.95
EKGHRMaxMin	Average	4	152.38	24.86	143.01	23.95
EKGHRMaxMin	Average	5	154.93	21.73	153.72	19.80
EKGHRMaxMin	Average	6	143.16	28.85	147.05	15.49
EKGHRMaxMin	Mode	2	77.04	53.27	94.10	64.44
EKGHRMaxMin	Mode	3	95.38	68.18	65.49	53.18
EKGHRMaxMin	Mode	4	64.18	29.38	70.20	64.86
EKGHRMaxMin	Mode	5	89.36	66.60	86.20	44.44
EKGHRMaxMin	Mode	6	81.64	67.36	50.42	32.38
EKGHRMaxMin	STD	2	59.35	8.66	56.69	13.89
EKGHRMaxMin	STD	3	62.24	9.62	61.67	14.11
EKGHRMaxMin	STD	4	61.38	8.95	60.50	10.86
EKGHRMaxMin	STD	5	60.83	11.90	61.78	14.01
EKGHRMaxMin	STD	6	62.13	12.79	69.43	8.42
EKGHRMaxMin	Minimum	2	55.38	32.74	58.32	37.28
EKGHRMaxMin	Minimum	3	52.16	18.12	47.72	25.92
EKGHRMaxMin	Minimum	4	53.76	27.95	48.74	34.97
EKGHRMaxMin	Minimum	5	59.60	33.62	63.48	35.49
EKGHRMaxMin	Minimum	6	58.48	41.86	44.07	26.02
EKGHRMaxMin	Maximum	2	239.95	17.21	232.74	23.85
EKGHRMaxMin	Maximum	3	243.42	15.10	240.36	21.29
EKGHRMaxMin	Maximum	4	241.38	18.73	240.92	25.28
EKGHRMaxMin	Maximum	5	242.32	18.77	242.68	17.09
EKGHRMaxMin	Maximum	6	242.12	21.17	251.81	10.15
SkinCond	Average	1	1.03	0.92	1.12	0.83
SkinCond	Average	2	1.06	0.96	1.15	0.92
SkinCond	Average	3	1.16	1.08	1.18	0.95
SkinCond	Average	4	1.25	1.19	1.21	1.02
SkinCond	Average	5	1.32	1.45	1.28	1.13
SkinCond	Average	6	1.39	1.41	1.31	1.22
SkinCond	Mode	1	0.96	0.71	1.09	0.81
SkinCond	Mode	2	1.02	0.83	1.15	0.93
SkinCond	Mode	3	1.11	1.00	1.17	0.93

SkinCond	Mode	4	1.23	1.16	1.19	0.99
SkinCond	Mode	5	1.24	1.22	1.27	1.11
SkinCond	Mode	6	1.38	1.39	1.30	1.20
SkinCond	Area	1	61.83	55.14	67.10	49.90
SkinCond	Area	2	63.86	57.53	69.22	55.39
SkinCond	Area	3	69.53	64.95	71.02	57.26
SkinCond	Area	4	74.99	71.21	72.60	61.01
SkinCond	Area	5	79.32	87.27	76.62	67.99
SkinCond	Area	6	83.64	84.39	78.81	73.39
SkinCond	STD	1	0.09	0.21	0.06	0.06
SkinCond	STD	2	0.06	0.10	0.05	0.05
SkinCond	STD	3	0.08	0.09	0.05	0.07
SkinCond	STD	4	0.06	0.07	0.05	0.07
SkinCond	STD	5	0.10	0.23	0.05	0.08
SkinCond	STD	6	0.05	0.06	0.05	0.06
SkinCond	Minimum	1	0.90	0.65	1.02	0.75
SkinCond	Minimum	2	0.97	0.82	1.07	0.85
SkinCond	Minimum	3	1.05	0.97	1.09	0.86
SkinCond	Minimum	4	1.16	1.08	1.12	0.94
SkinCond	Minimum	5	1.18	1.16	1.19	1.02
SkinCond	Minimum	6	1.31	1.33	1.24	1.12
SkinCond	Maximum	1	1.23	1.36	1.28	0.98
SkinCond	Maximum	2	1.22	1.25	1.27	1.03
SkinCond	Maximum	3	1.35	1.36	1.32	1.12
SkinCond	Maximum	4	1.40	1.39	1.34	1.16
SkinCond	Maximum	5	1.54	1.92	1.41	1.34
SkinCond	Maximum	6	1.54	1.59	1.44	1.39
Temp	Average	1	33.71	1.49	33.45	1.55
Temp	Average	2	33.71	1.47	33.54	1.60
Temp	Average	3	33.78	1.54	33.58	1.66
Temp	Average	4	33.80	1.56	33.65	1.66
Temp	Average	5	33.78	1.56	33.72	1.62
Temp	Average	6	33.60	1.56	33.75	1.66
Temp	Mode	1	33.67	1.49	33.48	1.55
Temp	Mode	2	33.71	1.48	33.53	1.61
Temp	Mode	3	33.78	1.55	33.59	1.67
Temp	Mode	4	33.81	1.56	33.64	1.70
Temp	Mode	5	33.78	1.57	33.73	1.62
Temp	Mode	6	33.61	1.56	33.72	1.64
Temp	Area	1	2022.30	89.43	2007.15	93.01
Temp	Area	2	2022.78	87.93	2012.27	96.14

Temp	Area	3	2027.00	92.48	2014.61	99.75
Temp	Area	4	2028.09	93.68	2019.13	99.63
Temp	Area	5	2026.95	93.80	2023.50	96.96
Temp	Area	6	2015.76	93.77	2025.01	99.85
Temp	STD	1	0.10	0.09	0.10	0.06
Temp	STD	2	0.08	0.05	0.07	0.03
Temp	STD	3	0.09	0.06	0.07	0.03
Temp	STD	4	0.08	0.04	0.09	0.06
Temp	STD	5	0.08	0.05	0.08	0.06
Temp	STD	6	0.08	0.04	0.09	0.05
Temp	Minimum	1	33.52	1.47	33.28	1.58
Temp	Minimum	2	33.58	1.46	33.41	1.64
Temp	Minimum	3	33.63	1.56	33.45	1.67
Temp	Minimum	4	33.65	1.58	33.50	1.68
Temp	Minimum	5	33.65	1.55	33.58	1.66
Temp	Minimum	6	33.45	1.56	33.59	1.68
Temp	Maximum	1	33.88	1.47	33.62	1.53
Temp	Maximum	2	33.86	1.47	33.67	1.56
Temp	Maximum	3	33.94	1.51	33.71	1.64
Temp	Maximum	4	33.94	1.56	33.82	1.59
Temp	Maximum	5	33.93	1.56	33.88	1.53
Temp	Maximum	6	33.73	1.57	33.89	1.65
RespRate	Average	1	13.82	2.26	14.27	1.88
RespRate	Average	2	13.79	2.40	14.06	1.80
RespRate	Average	3	13.60	2.27	13.72	1.69
RespRate	Average	4	13.65	3.05	13.45	2.05
RespRate	Average	5	13.43	2.61	13.59	2.31
RespRate	Average	6	13.72	2.72	13.65	1.88
RespRate	Mode	1	12.27	4.17	14.18	4.87
RespRate	Mode	2	13.10	5.09	13.55	4.59
RespRate	Mode	3	13.32	4.29	13.41	4.65
RespRate	Mode	4	12.92	5.45	13.20	4.18
RespRate	Mode	5	14.03	4.37	13.01	4.38
RespRate	Mode	6	14.85	4.47	14.68	3.95
RespRate	STD	1	3.29	0.73	3.60	0.94
RespRate	STD	2	3.48	0.81	3.47	0.74
RespRate	STD	3	3.75	0.95	3.53	0.58
RespRate	STD	4	3.27	1.19	3.48	0.62
RespRate	STD	5	3.39	1.20	3.08	0.92
RespRate	STD	6	3.41	1.11	3.32	0.85
RespRate	Minimum	1	8.98	1.63	8.69	2.15

RespRate	Minimum	2	8.40	1.95	8.47	1.57
RespRate	Minimum	3	7.58	2.58	8.39	1.54
RespRate	Minimum	4	8.34	3.16	7.57	1.70
RespRate	Minimum	5	7.85	1.74	8.18	2.40
RespRate	Minimum	6	8.31	2.87	8.35	2.16
RespRate	Maximum	1	19.06	1.35	19.35	1.25
RespRate	Maximum	2	19.04	2.24	19.11	1.66
RespRate	Maximum	3	18.88	1.77	19.48	1.24
RespRate	Maximum	4	18.37	2.50	19.38	1.15
RespRate	Maximum	5	18.03	3.02	18.30	2.08
RespRate	Maximum	6	18.92	2.45	18.69	1.59

Table 24: Change from pre-patch to last patch (day 7) of BVP-HR, EMG, Skin-Condition, Temperature and Respiratory Rate for Average, Mode, and Area, stratified by Epoch (1-6)

Source	Outcome	Epoch	Mean Change	SD	p-value
BVPHR	Average	1	3.47	8.57	0.1393
BVPHR	Average	2	4.51	7.83	0.0426
BVPHR	Average	3	3.23	7.87	0.1338
BVPHR	Average	4	1.69	9.18	0.4866
BVPHR	Average	5	0.48	8.92	0.8378
BVPHR	Average	6	2.69	7.87	0.2231
BVPHR	Mode	1	2.29	9.69	0.3754
BVPHR	Mode	2	2.35	10.46	0.3998
BVPHR	Mode	3	3.26	9.99	0.2261
BVPHR	Mode	4	1.80	11.77	0.5641
BVPHR	Mode	5	1.30	9.01	0.5847
BVPHR	Mode	6	3.34	7.79	0.1329
BVPHRMaxMin	Average	1	-0.54	4.61	0.6583
BVPHRMaxMin	Average	2	-3.29	10.09	0.2272
BVPHRMaxMin	Average	3	-1.33	2.98	0.1047
BVPHRMaxMin	Average	4	-0.63	4.94	0.6286
BVPHRMaxMin	Average	5	-2.23	3.13	0.0153
BVPHRMaxMin	Average	6	-1.73	4.52	0.1763
BVPHRMaxMin	Mode	1	-1.18	2.17	0.0533
BVPHRMaxMin	Mode	2	-0.73	1.57	0.0917
BVPHRMaxMin	Mode	3	1.89	10.29	0.4894
BVPHRMaxMin	Mode	4	0.17	2.56	0.8021
BVPHRMaxMin	Mode	5	-1.06	2.63	0.1390

BVPHRMaxMin	Mode	6	-0.77	2.13	0.2016
EMG	Average	1	-47.37	156.16	0.2597
EMG	Average	2	-41.66	134.35	0.2497
EMG	Average	3	-32.95	120.86	0.3090
EMG	Average	4	-37.51	128.11	0.2758
EMG	Average	5	-35.27	112.16	0.2434
EMG	Average	6	-42.30	116.23	0.1964
EMG	Mode	1	-71.50	198.24	0.1842
EMG	Mode	2	-31.67	128.86	0.3573
EMG	Mode	3	-36.76	133.32	0.3036
EMG	Mode	4	-36.54	123.10	0.2696
EMG	Mode	5	-32.31	105.53	0.2554
EMG	Mode	6	-21.01	63.91	0.2405
EMG	Area	1	-2841.91	9369.34	0.2597
EMG	Area	2	-2499.75	8061.27	0.2497
EMG	Area	3	-1976.78	7251.87	0.3090
EMG	Area	4	-2250.79	7686.36	0.2758
EMG	Area	5	-2116.15	6729.75	0.2434
EMG	Area	6	-2538.04	6974.02	0.1964
EMG	Average	1	12.89	105.67	0.6440
EMG	Average	2	-8.91	100.16	0.7356
EMG	Average	3	-10.44	74.71	0.5969
EMG	Average	4	1.21	82.31	0.9553
EMG	Average	5	0.56	90.21	0.9810
EMG	Average	6	-2.70	121.61	0.9351
EMG	Mode	1	19.63	99.86	0.4590
EMG	Mode	2	-17.45	78.42	0.4033
EMG	Mode	3	-12.13	83.13	0.5810
EMG	Mode	4	-4.05	71.81	0.8302
EMG	Mode	5	-2.15	83.96	0.9225
EMG	Mode	6	-0.54	127.42	0.9876
EMG	Area	1	773.25	6340.13	0.6440
EMG	Area	2	-534.67	6009.89	0.7355
EMG	Area	3	-626.43	4482.69	0.5969
EMG	Area	4	72.67	4938.74	0.9554
EMG	Area	5	33.84	5412.35	0.9810
EMG	Area	6	-161.92	7296.73	0.9351
EKGHR	Average	2	0.37	13.68	0.8827
EKGHR	Average	3	0.13	14.53	0.9736
EKGHR	Average	4	1.85	13.49	0.6037
EKGHR	Average	5	5.15	11.79	0.1130

EKGHR	Average	6	3.93	15.74	0.3666
EKGHR	Mode	2	-1.15	34.63	0.8569
EKGHR	Mode	3	-0.49	30.98	0.9519
EKGHR	Mode	4	9.58	21.99	0.1137
EKGHR	Mode	5	3.09	22.59	0.6041
EKGHR	Mode	6	6.18	33.79	0.5061
EKGHRMaxMin	Average	2	-3.68	29.92	0.5063
EKGHRMaxMin	Average	3	-5.19	20.06	0.3338
EKGHRMaxMin	Average	4	-9.37	35.70	0.3267
EKGHRMaxMin	Average	5	-1.20	16.30	0.7793
EKGHRMaxMin	Average	6	3.92	36.00	0.6905
EKGHRMaxMin	Mode	2	17.06	88.11	0.2976
EKGHRMaxMin	Mode	3	-29.89	80.06	0.1701
EKGHRMaxMin	Mode	4	6.02	77.88	0.7690
EKGHRMaxMin	Mode	5	-3.16	79.37	0.8798
EKGHRMaxMin	Mode	6	-33.34	67.42	0.0871
SkinCond	Average	1	0.09	0.85	0.6960
SkinCond	Average	2	0.09	0.82	0.6779
SkinCond	Average	3	0.02	0.98	0.9231
SkinCond	Average	4	-0.04	0.92	0.8692
SkinCond	Average	5	-0.05	1.03	0.8678
SkinCond	Average	6	-0.03	0.97	0.9008
SkinCond	Mode	1	0.12	0.74	0.5349
SkinCond	Mode	2	0.13	0.77	0.5148
SkinCond	Mode	3	0.07	0.95	0.7922
SkinCond	Mode	4	-0.04	0.92	0.8594
SkinCond	Mode	5	0.03	0.89	0.9042
SkinCond	Mode	6	-0.03	0.97	0.8988
SkinCond	Area	1	5.27	51.27	0.6963
SkinCond	Area	2	5.36	49.02	0.6785
SkinCond	Area	3	1.49	58.64	0.9231
SkinCond	Area	4	-2.39	55.13	0.8691
SkinCond	Area	5	-2.70	61.68	0.8677
SkinCond	Area	6	-1.97	58.15	0.9011
Temp	Average	1	-0.25	1.51	0.5273
Temp	Average	2	-0.18	1.50	0.6576
Temp	Average	3	-0.21	1.48	0.5966
Temp	Average	4	-0.15	1.54	0.7128
Temp	Average	5	-0.06	1.45	0.8797
Temp	Average	6	0.17	1.41	0.6557
Temp	Mode	1	-0.19	1.46	0.6293

Temp	Mode	2	-0.18	1.52	0.6535
Temp	Mode	3	-0.19	1.46	0.6150
Temp	Mode	4	-0.16	1.54	0.6851
Temp	Mode	5	-0.06	1.52	0.8907
Temp	Mode	6	0.12	1.38	0.7519
Temp	Area	1	-15.15	90.55	0.5274
Temp	Area	2	-10.51	89.84	0.6574
Temp	Area	3	-12.39	88.59	0.5966
Temp	Area	4	-8.96	92.41	0.7128
Temp	Area	5	-3.45	86.90	0.8800
Temp	Area	6	10.36	84.89	0.6555
RespRate	Average	1	0.45	1.52	0.2686
RespRate	Average	2	0.26	2.15	0.6419
RespRate	Average	3	0.12	2.22	0.8423
RespRate	Average	4	-0.20	2.83	0.7899
RespRate	Average	5	0.16	1.81	0.7435
RespRate	Average	6	0.10	2.12	0.8571
RespRate	Mode	1	1.92	4.03	0.0868
RespRate	Mode	2	0.45	4.49	0.7032
RespRate	Mode	3	0.08	4.34	0.9409
RespRate	Mode	4	0.28	5.94	0.8556
RespRate	Mode	5	-1.02	3.57	0.2859
RespRate	Mode	6	-0.06	4.32	0.9582

Table 25: Summary statistics for pre- vs. Last patch (day 7) of BVP-HR, EMG, Skin-Condition, Temperature and Respiratory Rate for all distribution characteristics outcomes, across all 6 epochs

		Pre-patch		**Last-patch (Day 7)**	
Source	**Outcome**	**Mean**	**SD**	**Mean**	**SD**
BVPHR	Average	77.35	11.67	79.90	12.87
BVPHR	Mode	78.02	13.04	80.33	13.24
BVPHR	STD	5.71	4.85	4.30	3.79
BVPHR	Minimum	60.70	15.14	68.02	16.96
BVPHR	Maximum	91.06	20.82	88.67	14.81
BVPHRMaxMin	Average	9.78	9.50	8.11	8.73
BVPHRMaxMin	Mode	6.98	10.32	6.68	10.59
BVPHRMaxMin	STD	6.98	7.41	4.89	5.61
BVPHRMaxMin	Minimum	2.61	2.18	2.05	1.92

BVPHRMaxMin	Maximum	24.84	22.28	17.24	16.72
EMG	Average	59.20	130.01	19.76	27.63
EMG	Mode	56.05	133.55	17.61	25.23
EMG	Area	3552.07	7800.39	1185.43	1657.62
EMG	STD	10.59	27.06	5.44	18.98
EMG	Minimum	33.88	87.88	12.14	19.88
EMG	Maximum	135.41	202.29	73.88	131.16
EMG	Average	30.80	72.46	29.82	63.93
EMG	Mode	27.23	67.56	24.68	58.06
EMG	Area	1848.17	4347.81	1789.43	3835.60
EMG	STD	9.35	18.43	10.47	28.32
EMG	Minimum	16.30	46.42	11.55	29.90
EMG	Maximum	120.96	179.72	89.94	152.99
EKGHR	Average	112.05	12.28	113.83	11.66
EKGHR	Mode	62.81	25.24	65.54	26.41
EKGHR	STD	60.11	7.19	58.97	7.58
EKGHR	Minimum	35.18	8.62	36.54	11.13
EKGHR	Maximum	287.79	14.64	289.09	11.44
EKGHRMaxMin	Average	150.88	22.16	147.53	20.04
EKGHRMaxMin	Mode	82.18	58.59	76.75	56.55
EKGHRMaxMin	STD	61.09	10.19	61.13	13.16
EKGHRMaxMin	Minimum	55.50	31.15	53.44	33.24
EKGHRMaxMin	Maximum	241.60	17.62	240.21	21.49
SkinCond	Average	1.19	1.15	1.21	1.00
SkinCond	Mode	1.14	1.05	1.19	0.98
SkinCond	Area	71.52	69.18	72.56	59.72
SkinCond	STD	0.07	0.14	0.05	0.06
SkinCond	Minimum	1.08	1.00	1.12	0.91
SkinCond	Maximum	1.37	1.45	1.34	1.15
Temp	Average	33.75	1.49	33.62	1.58
Temp	Mode	33.75	1.49	33.62	1.59
Temp	Area	2024.94	89.35	2016.94	95.02
Temp	STD	0.08	0.06	0.08	0.05
Temp	Minimum	33.60	1.49	33.47	1.61
Temp	Maximum	33.90	1.48	33.77	1.54
RespRate	Average	13.66	2.48	13.79	1.91
RespRate	Mode	13.37	4.59	13.67	4.36
RespRate	STD	3.43	0.99	3.41	0.78
RespRate	Minimum	8.26	2.35	8.28	1.93
RespRate	Maximum	18.73	2.24	19.05	1.55

Table 26: Change from pre-patch to last patch (day 7) of BVP-HR, EMG, Skin-Condition, Temperature and Respiratory Rate for Average, Mode, and Area, across all 6 Epochs

Source	Outcome	Mean Change	SD	p-value
BVPHR	Average	2.54	8.31	0.0047
BVPHR	Mode	2.31	9.60	0.0249
BVPHRMaxMin	Average	-1.67	5.50	0.0049
BVPHRMaxMin	Mode	-0.31	4.67	0.5361
EMG	Average	-39.44	124.62	0.0035
EMG	Mode	-38.45	128.72	0.0057
EMG	Area	-2366.63	7477.30	0.0035
EMG	Average	-0.98	93.72	0.9213
EMG	Mode	-2.55	89.76	0.7881
EMG	Area	-58.74	5623.21	0.9213
EKGHR	Average	1.78	13.68	0.2212
EKGHR	Mode	2.73	29.70	0.3857
EKGHRMaxMin	Average	-3.36	28.34	0.2641
EKGHRMaxMin	Mode	-5.43	82.06	0.5317
SkinCond	Average	0.02	0.90	0.8557
SkinCond	Mode	0.05	0.85	0.5926
SkinCond	Area	1.04	54.01	0.8560
Temp	Average	-0.13	1.45	0.3849
Temp	Mode	-0.13	1.45	0.3941
Temp	Area	-8.00	86.95	0.3851
RespRate	Average	0.13	2.09	0.5621
RespRate	Mode	0.30	4.44	0.5281

GHK- CU Study – Metabolic Data

Study Design: Single arm study with 3 assessment time points.

Sample Size: N=15

Statistical Methods: All physiology suite parameters were summarized in terms of means and standard deviation, stratified by assessment time point. Changes from day 1 (pre-patch) to day 2, day 2 to day 7, and day 1 to day 7 were evaluated using a paired t-test or nonparametric Wilcoxon Signed Rank test.

Table 27: Summary statistics for metabolic markers, stratified by assessment time point

Marker	N	Assessment Time point	Mean	SD
2-amino	15	Day 1 (pre-patch)	11.82	11.65
2-amino	15	Day 2	13.26	10.88
2-amino	15	Day 7	14.70	12.27
3-MT	15	Day 1 (pre-patch)	64.46	45.27
3-MT	15	Day 2	55.99	39.14
3-MT	15	Day 7	52.33	26.14
5-HT	15	Day 1 (pre-patch)	76.14	37.36
5-HT	15	Day 2	80.52	43.01
5-HT	15	Day 7	82.99	57.52
5-HT/DA	15	Day 1 (pre-patch)	0.87	0.90
5-HT/DA	15	Day 2	0.69	0.62
5-HT/DA	15	Day 7	0.63	0.44
5-HTP	15	Day 1 (pre-patch)	49.21	26.41
5-HTP	15	Day 2	59.70	67.25
5-HTP	15	Day 7	46.89	25.25
Age	15	Day 1 (pre-patch)	61.27	8.65
Age	15	Day 2	61.27	8.65
Age	15	Day 7	61.27	8.65
Ala	15	Day 1 (pre-patch)	117.66	45.05
Ala	15	Day 2	97.49	42.89
Ala	15	Day 7	119.53	74.69
Arg	15	Day 1 (pre-patch)	5.97	1.69
Arg	15	Day 2	5.13	2.79
Arg	15	Day 7	7.36	6.59
Asn	15	Day 1 (pre-patch)	18.09	15.41
Asn	15	Day 2	15.58	10.84
Asn	15	Day 7	16.07	11.14
Asp	15	Day 1 (pre-patch)	4.99	2.86
Asp	15	Day 2	5.29	2.31

Asp	15	Day 7	4.88	2.45
Bala	15	Day 1 (pre-patch)	27.64	26.24
Bala	15	Day 2	16.33	12.97
Bala	15	Day 7	20.52	26.90
C-C	15	Day 1 (pre-patch)	31.37	12.67
C-C	15	Day 2	31.57	12.59
C-C	15	Day 7	35.51	22.37
Car	15	Day 1 (pre-patch)	10.67	13.07
Car	15	Day 2	6.26	4.94
Car	15	Day 7	6.10	6.31
Cit	15	Day 1 (pre-patch)	2.27	1.25
Cit	15	Day 2	2.41	1.40
Cit	15	Day 7	2.51	1.25
Cre	15	Day 1 (pre-patch)	138.07	83.78
Cre	15	Day 2	178.40	108.96
Cre	15	Day 7	172.73	120.95
Cys	15	Day 1 (pre-patch)	57.45	27.87
Cys	15	Day 2	66.58	27.24
Cys	15	Day 7	50.50	11.58
Cys/C-c	15	Day 1 (pre-patch)	2.29	1.82
Cys/C-c	15	Day 2	2.64	1.95
Cys/C-c	15	Day 7	2.21	2.14
Cystathion	15	Day 1 (pre-patch)	9.94	6.25
Cystathion	15	Day 2	10.82	7.78
Cystathion	15	Day 7	9.54	9.63
DA	15	Day 1 (pre-patch)	154.62	71.19
DA	15	Day 2	151.33	53.82
DA	15	Day 7	161.26	58.60
E	15	Day 1 (pre-patch)	5.44	3.27
E	15	Day 2	3.34	1.60
E	15	Day 7	4.93	3.02
GABA	15	Day 1 (pre-patch)	3.79	1.77

GABA	15	Day 2	3.25	1.19
GABA	15	Day 7	3.07	1.13
GSH	15	Day 1 (pre-patch)	1.35	1.40
GSH	15	Day 2	1.58	1.48
GSH	15	Day 7	2.09	1.71
Gln	15	Day 1 (pre-patch)	174.16	97.68
Gln	15	Day 2	149.88	77.00
Gln	15	Day 7	147.20	52.69
Glu	15	Day 1 (pre-patch)	18.22	11.34
Glu	15	Day 2	16.21	8.32
Glu	15	Day 7	12.40	5.45
Gly	15	Day 1 (pre-patch)	272.51	182.74
Gly	15	Day 2	199.97	122.82
Gly	15	Day 7	234.64	155.33
HCys2	15	Day 1 (pre-patch)	0.86	0.49
HCys2	15	Day 2	1.21	0.52
HCys2	15	Day 7	1.13	0.60
HYP	15	Day 1 (pre-patch)	2.55	1.18
HYP	15	Day 2	2.19	0.87
HYP	15	Day 7	2.21	0.65
Hcys	15	Day 1 (pre-patch)	0.91	0.49
Hcys	15	Day 2	0.97	0.63
Hcys	15	Day 7	1.07	0.64
His	15	Day 1 (pre-patch)	182.17	75.01
His	15	Day 2	135.85	60.51
His	15	Day 7	135.53	57.98
Hist	15	Day 1 (pre-patch)	28.77	24.03
Hist	15	Day 2	19.52	12.04
Hist	15	Day 7	24.35	29.92
Hlys	15	Day 1 (pre-patch)	1.23	1.97
Hlys	15	Day 2	0.61	0.67
Hlys	15	Day 7	0.43	0.30
Hser	15	Day 1 (pre-	11.63	8.21

		patch)		
Hser	15	Day 2	8.53	6.01
Hser	15	Day 7	9.12	6.65
Ile	15	Day 1 (pre-patch)	14.10	7.32
Ile	15	Day 2	12.11	4.04
Ile	15	Day 7	11.30	4.75
LDOPA	15	Day 1 (pre-patch)	21.31	13.72
LDOPA	15	Day 2	23.32	10.67
LDOPA	15	Day 7	22.80	12.70
Leu	15	Day 1 (pre-patch)	19.98	8.16
Leu	15	Day 2	15.13	4.94
Leu	15	Day 7	17.10	7.83
Lys	15	Day 1 (pre-patch)	49.09	32.44
Lys	15	Day 2	40.21	29.33
Lys	15	Day 7	41.45	34.56
ME	15	Day 1 (pre-patch)	23.52	16.61
ME	15	Day 2	19.24	8.73
ME	15	Day 7	17.79	7.79
Met	15	Day 1 (pre-patch)	7.08	5.74
Met	15	Day 2	6.65	3.93
Met	15	Day 7	6.36	3.88
NE	15	Day 1 (pre-patch)	26.29	13.51
NE	15	Day 2	25.52	15.95
NE	15	Day 7	36.02	38.37
NE/E	15	Day 1 (pre-patch)	7.44	6.59
NE/E	15	Day 2	10.35	9.99
NE/E	15	Day 7	12.07	13.78
NorM	15	Day 1 (pre-patch)	89.67	52.78
NorM	15	Day 2	89.67	41.19
NorM	15	Day 7	76.61	27.62
Orn	15	Day 1 (pre-patch)	13.57	10.95
Orn	15	Day 2	10.27	7.72
Orn	15	Day 7	11.77	11.33

PEA	15	Day 1 (pre-patch)	2.08	1.92
PEA	15	Day 2	1.91	2.04
PEA	15	Day 7	1.48	1.25
Phe	15	Day 1 (pre-patch)	22.92	14.05
Phe	15	Day 2	18.79	9.87
Phe	15	Day 7	25.11	12.30
Pro	15	Day 1 (pre-patch)	13.00	6.54
Pro	15	Day 2	10.65	4.54
Pro	15	Day 7	10.70	6.17
Ratio	15	Day 1 (pre-patch)	1.60	1.50
Ratio	15	Day 2	0.89	0.47
Ratio	15	Day 7	1.35	1.36
Sar	15	Day 1 (pre-patch)	10.05	5.57
Sar	15	Day 2	9.83	7.58
Sar	15	Day 7	10.04	7.57
Ser	15	Day 1 (pre-patch)	77.68	42.05
Ser	15	Day 2	74.23	45.67
Ser	15	Day 7	68.77	31.37
Thr	15	Day 1 (pre-patch)	68.86	41.99
Thr	15	Day 2	62.84	38.12
Thr	15	Day 7	63.39	40.77
Trp	15	Day 1 (pre-patch)	21.08	11.49
Trp	15	Day 2	27.49	20.64
Trp	15	Day 7	16.69	12.78
Tryp	15	Day 1 (pre-patch)	0.68	0.18
Tryp	15	Day 2	0.66	0.21
Tryp	15	Day 7	0.72	0.24
Tyr	15	Day 1 (pre-patch)	36.35	21.55
Tyr	15	Day 2	39.53	21.00
Tyr	15	Day 7	38.79	21.25
Tyra	15	Day 1 (pre-patch)	5.64	2.76
Tyra	15	Day 2	4.60	1.86

Tyra	15	Day 7	4.97	2.31
Val	15	Day 1 (pre-patch)	45.11	41.02
Val	15	Day 2	34.25	24.67
Val	15	Day 7	41.84	28.03
a-amino	15	Day 1 (pre-patch)	18.79	16.63
a-amino	15	Day 2	15.18	9.86
a-amino	15	Day 7	9.90	5.57
b-aminoiso	15	Day 1 (pre-patch)	80.13	76.39
b-aminoiso	15	Day 2	98.49	178.48
b-aminoiso	15	Day 7	59.81	51.33

Table 28: Change from day 1 (pre-patch) to day 2, day 2 to day 7, and day 1 (pre-patch) to day 7

Marker	Change	Mean Change	SD	p-value
2-amino	Day 1 to Day 2	1.44	11.94	0.6474
2-amino	Day 2 to Day 7	1.44	9.32	0.5585
2-amino	Day 1 to Day 7	2.88	12.91	0.4017
3-MT	Day 1 to Day 2	-8.47	23.61	0.1862
3-MT	Day 2 to Day 7	-3.66	20.89	0.5080
3-MT	Day 1 to Day 7	-12.14	29.06	0.1281
5-HT	Day 1 to Day 2	4.37	37.33	0.6569
5-HT	Day 2 to Day 7	2.47	68.38	0.8908
5-HT	Day 1 to Day 7	6.84	63.59	0.6832
5-HT/DA	Day 1 to Day 2	-0.18	0.83	0.4202
5-HT/DA	Day 2 to Day 7	-0.06	0.68	0.7305
5-HT/DA	Day 1 to Day 7	-0.24	0.89	0.3117
5-HTP	Day 1 to Day 2	10.48	72.69	0.5852
5-HTP	Day 2 to Day 7	-12.80	74.71	0.5176
5-HTP	Day 1 to Day 7	-2.32	31.99	0.7830
Ala	Day 1 to Day 2	-20.17	36.89	0.0526
Ala	Day 2 to Day 7	22.04	55.11	0.1437
Ala	Day 1 to Day 7	1.87	64.03	0.9115
Arg	Day 1 to Day 2	-0.84	2.32	0.1850
Arg	Day 2 to Day 7	2.22	5.27	0.1246
Arg	Day 1 to Day 7	1.39	6.37	0.4138
Asn	Day 1 to Day 2	-2.51	10.74	0.3802

Asn	Day 2 to Day 7	0.49	14.07	0.8942
Asn	Day 1 to Day 7	-2.02	16.81	0.6488
Asp	Day 1 to Day 2	0.30	2.31	0.6174
Asp	Day 2 to Day 7	-0.41	2.88	0.5869
Asp	Day 1 to Day 7	-0.11	2.84	0.8830
Bala	Day 1 to Day 2	-11.31	27.09	0.1283
Bala	Day 2 to Day 7	4.19	21.26	0.4578
Bala	Day 1 to Day 7	-7.12	33.99	0.4309
C-C	Day 1 to Day 2	0.20	8.83	0.9302
C-C	Day 2 to Day 7	3.94	14.15	0.2991
C-C	Day 1 to Day 7	4.14	11.81	0.1958
Car	Day 1 to Day 2	-4.41	14.24	0.2499
Car	Day 2 to Day 7	-0.15	4.45	0.8949
Car	Day 1 to Day 7	-4.57	13.87	0.2228
Cit	Day 1 to Day 2	0.14	1.39	0.6968
Cit	Day 2 to Day 7	0.09	1.29	0.7854
Cit	Day 1 to Day 7	0.24	1.61	0.5800
Cre	Day 1 to Day 2	40.33	110.05	0.1776
Cre	Day 2 to Day 7	-5.67	94.86	0.8204
Cre	Day 1 to Day 7	34.67	107.60	0.2326
Cys	Day 1 to Day 2	9.12	27.62	0.2215
Cys	Day 2 to Day 7	-16.07	23.86	0.0206
Cys	Day 1 to Day 7	-6.95	20.99	0.2205
Cys/C-c	Day 1 to Day 2	0.35	1.58	0.4053
Cys/C-c	Day 2 to Day 7	-0.43	1.77	0.3677
Cys/C-c	Day 1 to Day 7	-0.07	0.80	0.7244
Cystathion	Day 1 to Day 2	0.88	8.71	0.7009
Cystathion	Day 2 to Day 7	-1.28	9.25	0.5989
Cystathion	Day 1 to Day 7	-0.40	8.28	0.8533
DA	Day 1 to Day 2	-3.28	48.13	0.7954
DA	Day 2 to Day 7	9.93	54.17	0.4893
DA	Day 1 to Day 7	6.65	65.22	0.6990
E	Day 1 to Day 2	-2.09	3.08	0.0197
E	Day 2 to Day 7	1.59	2.94	0.0552
E	Day 1 to Day 7	-0.51	3.93	0.6264
GABA	Day 1 to Day 2	-0.54	1.20	0.1034
GABA	Day 2 to Day 7	-0.19	1.20	0.5558
GABA	Day 1 to Day 7	-0.73	1.50	0.0818
GSH	Day 1 to Day 2	0.23	0.71	0.2262
GSH	Day 2 to Day 7	0.51	1.37	0.1737
GSH	Day 1 to Day 7	0.74	1.68	0.1099

Gln	Day 1 to Day 2	-24.29	69.86	0.1996
Gln	Day 2 to Day 7	-2.67	60.13	0.8657
Gln	Day 1 to Day 7	-26.96	86.37	0.2467
Glu	Day 1 to Day 2	-2.00	6.71	0.2674
Glu	Day 2 to Day 7	-3.82	6.73	0.0453
Glu	Day 1 to Day 7	-5.82	10.37	0.0475
Gly	Day 1 to Day 2	-72.54	117.73	0.0317
Gly	Day 2 to Day 7	34.67	107.20	0.2308
Gly	Day 1 to Day 7	-37.87	83.70	0.1016
HCys2	Day 1 to Day 2	0.35	0.55	0.0296
HCys2	Day 2 to Day 7	-0.08	0.55	0.5806
HCys2	Day 1 to Day 7	0.27	0.79	0.2125
HYP	Day 1 to Day 2	-0.37	1.02	0.1856
HYP	Day 2 to Day 7	0.02	0.93	0.9262
HYP	Day 1 to Day 7	-0.34	1.31	0.3281
Hcys	Day 1 to Day 2	0.06	0.68	0.7225
Hcys	Day 2 to Day 7	0.10	0.76	0.6112
Hcys	Day 1 to Day 7	0.17	0.66	0.3446
His	Day 1 to Day 2	-46.32	75.35	0.0320
His	Day 2 to Day 7	-0.33	56.38	0.9824
His	Day 1 to Day 7	-46.64	49.35	0.0026
Hist	Day 1 to Day 2	-9.24	20.20	0.0981
Hist	Day 2 to Day 7	4.82	25.30	0.4724
Hist	Day 1 to Day 7	-4.42	18.90	0.3804
Hlys	Day 1 to Day 2	-0.62	1.36	0.1000
Hlys	Day 2 to Day 7	-0.18	0.43	0.1301
Hlys	Day 1 to Day 7	-0.80	1.75	0.0992
Hser	Day 1 to Day 2	-3.10	8.41	0.1751
Hser	Day 2 to Day 7	0.60	8.42	0.7873
Hser	Day 1 to Day 7	-2.50	9.34	0.3169
Ile	Day 1 to Day 2	-2.00	5.96	0.2157
Ile	Day 2 to Day 7	-0.80	6.14	0.6207
Ile	Day 1 to Day 7	-2.80	8.50	0.2232
LDOPA	Day 1 to Day 2	2.01	11.54	0.5111
LDOPA	Day 2 to Day 7	-0.52	9.83	0.8408
LDOPA	Day 1 to Day 7	1.49	10.18	0.5798
Leu	Day 1 to Day 2	-4.84	7.84	0.0313
Leu	Day 2 to Day 7	1.97	8.21	0.3681
Leu	Day 1 to Day 7	-2.87	11.54	0.3515
Lys	Day 1 to Day 2	-8.88	32.44	0.3070
Lys	Day 2 to Day 7	1.24	30.39	0.8768

Lys	Day 1 to Day 7	-7.64	34.89	0.4106
ME	Day 1 to Day 2	-4.29	14.51	0.2718
ME	Day 2 to Day 7	-1.45	6.17	0.3775
ME	Day 1 to Day 7	-5.74	14.29	0.1421
Met	Day 1 to Day 2	-0.43	4.04	0.6863
Met	Day 2 to Day 7	-0.28	3.88	0.7816
Met	Day 1 to Day 7	-0.71	4.61	0.5582
NE	Day 1 to Day 2	-0.78	16.15	0.8544
NE	Day 2 to Day 7	10.50	44.57	0.3769
NE	Day 1 to Day 7	9.72	40.68	0.3702
NE/E	Day 1 to Day 2	2.92	6.55	0.1064
NE/E	Day 2 to Day 7	1.72	14.81	0.6605
NE/E	Day 1 to Day 7	4.63	13.58	0.2074
NorM	Day 1 to Day 2	0.00	28.16	0.9996
NorM	Day 2 to Day 7	-13.06	23.32	0.0479
NorM	Day 1 to Day 7	-13.06	33.37	0.1519
Orn	Day 1 to Day 2	-3.30	9.38	0.1949
Orn	Day 2 to Day 7	1.50	9.82	0.5632
Orn	Day 1 to Day 7	-1.80	7.13	0.3456
PEA	Day 1 to Day 2	-0.17	1.16	0.5730
PEA	Day 2 to Day 7	-0.42	1.61	0.3262
PEA	Day 1 to Day 7	-0.59	1.12	0.0589
Phe	Day 1 to Day 2	-4.13	9.28	0.1067
Phe	Day 2 to Day 7	6.33	10.94	0.0418
Phe	Day 1 to Day 7	2.19	15.37	0.5889
Pro	Day 1 to Day 2	-2.35	8.45	0.2989
Pro	Day 2 to Day 7	0.05	5.99	0.9747
Pro	Day 1 to Day 7	-2.30	8.15	0.2921
Ratio	Day 1 to Day 2	-0.71	1.40	0.0700
Ratio	Day 2 to Day 7	0.46	1.25	0.1782
Ratio	Day 1 to Day 7	-0.25	1.32	0.4732
Sar	Day 1 to Day 2	-0.22	6.88	0.9038
Sar	Day 2 to Day 7	0.22	3.86	0.8301
Sar	Day 1 to Day 7	0.00	5.17	0.9996
Ser	Day 1 to Day 2	-3.44	49.51	0.7915
Ser	Day 2 to Day 7	-5.47	31.29	0.5096
Ser	Day 1 to Day 7	-8.91	38.25	0.3821
Thr	Day 1 to Day 2	-6.02	41.35	0.5819
Thr	Day 2 to Day 7	0.55	37.91	0.9563
Thr	Day 1 to Day 7	-5.47	29.80	0.4887
Trp	Day 1 to Day 2	6.41	21.61	0.2699

Trp	Day 2 to Day 7	-10.81	18.55	0.0406
Trp	Day 1 to Day 7	-4.40	17.07	0.3355
Tryp	Day 1 to Day 2	-0.03	0.15	0.5022
Tryp	Day 2 to Day 7	0.06	0.20	0.2341
Tryp	Day 1 to Day 7	0.04	0.26	0.5873
Tyr	Day 1 to Day 2	3.19	12.77	0.3503
Tyr	Day 2 to Day 7	-0.75	12.29	0.8175
Tyr	Day 1 to Day 7	2.44	12.23	0.4527
Tyra	Day 1 to Day 2	-1.04	3.18	0.2259
Tyra	Day 2 to Day 7	0.37	2.36	0.5546
Tyra	Day 1 to Day 7	-0.67	2.96	0.3963
Val	Day 1 to Day 2	-10.85	24.39	0.1068
Val	Day 2 to Day 7	7.58	31.90	0.3728
Val	Day 1 to Day 7	-3.27	43.87	0.7772
a-amino	Day 1 to Day 2	-3.61	9.26	0.1534
a-amino	Day 2 to Day 7	-5.29	7.79	0.0198
a-amino	Day 1 to Day 7	-8.90	13.79	0.0256
b-aminoiso	Day 1 to Day 2	18.36	177.75	0.6952
b-aminoiso	Day 2 to Day 7	-38.68	150.08	0.3351
b-aminoiso	Day 1 to Day 7	-20.32	51.24	0.1468

GHK- CU Study – Cortisol and DHEAS

Study Design: Single arm study with 3 assessment time points.

Sample Size: N=15

Statistical Methods: Cortisol levels were obtained at 8am, 12pm, 4pm, 8pm and 12am. DHEAS levels were collected at 8am, 8pm and 12am. The area under the curve (AUC) for Cortisol and DHEAS levels over the data collection periods were calculated using the trapezoid rule. AUC levels were summarized in terms of means and standard deviations, stratified by assessment time point. Changes between assessment time points were evaluated using a paired t-test or Wilcoxon signed rank test.

Table 29: Summary statistics for AUC of Cortisol and DHEAS, stratified by assessment time point

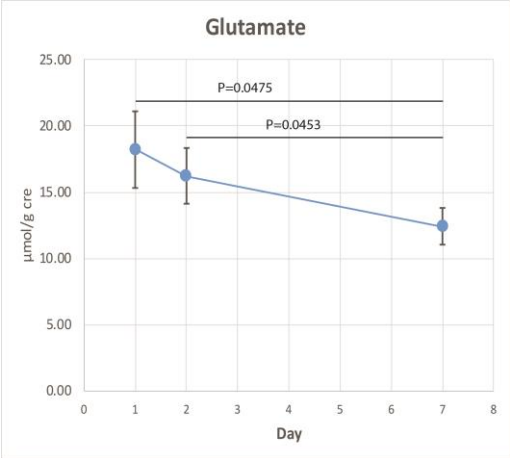
Marker	Assessment Time point	Mean AUC	SD
Cortisol	R1 (pre-patch)	109.1	36.9
Cortisol	R2	120.6	28.4
Cortisol	R3	141.7	76.4
DHEAS	R1 (pre-patch)	178,2	154,5
DHEAS	R2	180.7	117.7
DHEAS	R3	291.0	378.4

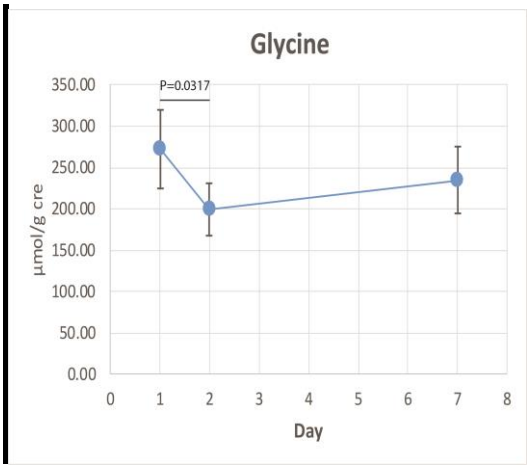
Table 30: Change from R1 to R2, R2 to R3 and R1 to R3

Marker	Change	Mean Change in AUC	SD	p-value
Cortisol	R1 to R2	11.5	41.9	0.7615
	R2 to R3	21.1	90.2	0.9780
	R1 to R3	32.6	87.9	0.2769
DHEAS	R1 to R2	1.2	97.7	0.7148
	R2 to R3	111.6	362.6	0.7609
	R1 to R3	112.8	345.7	0.5016

There are no significant changes in Cortisol or DHEAS levels between assessment time points.

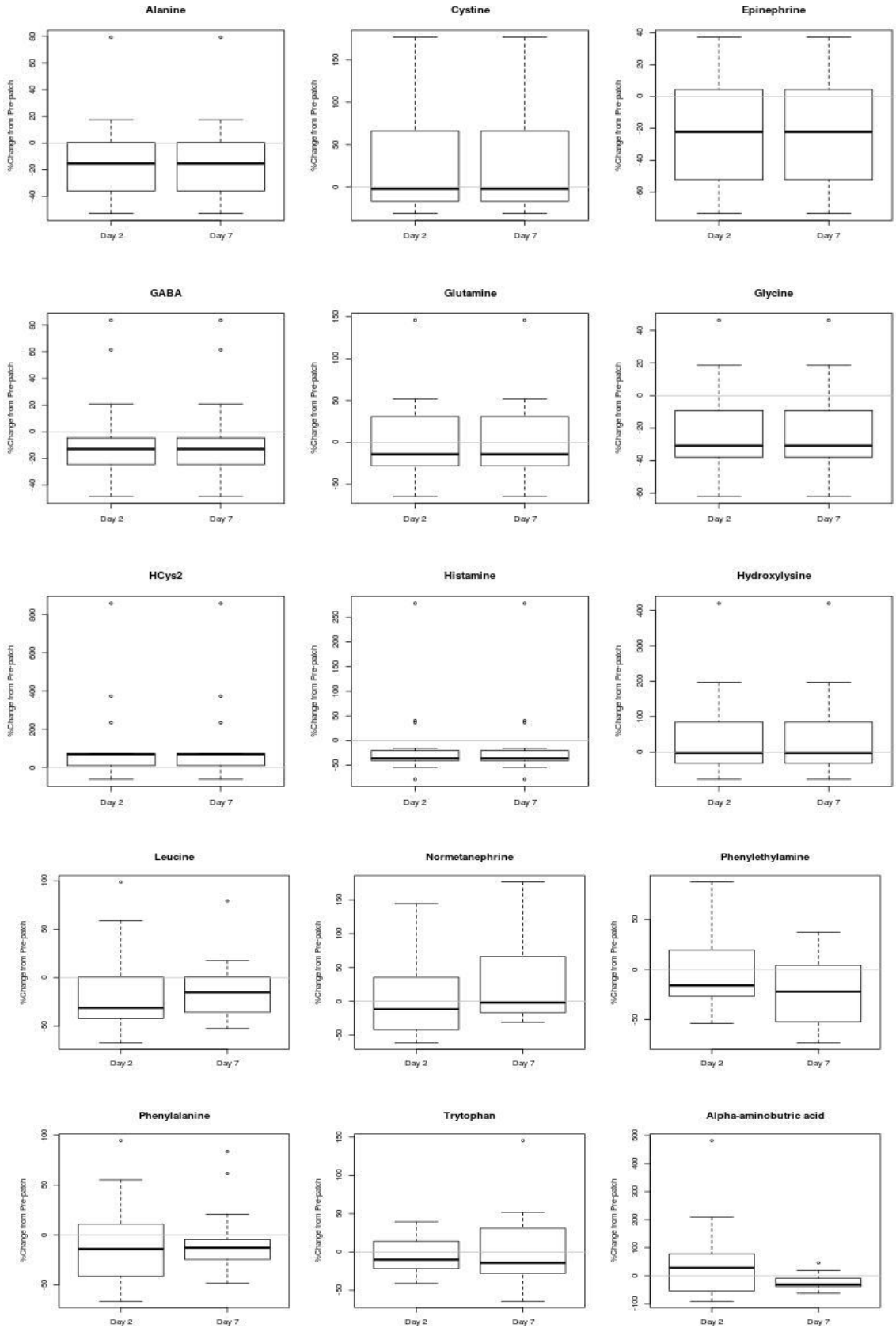
Appendix B: Graphs of Amino Acids Showing Significance





You will note that Glycine and Glutamate which are used in the process to form Glutathione both showed a drop off at a level of significance. Gluthione is part of the reduction of inflammation pathway in a unique aspect. It specifically acts from the liver to detoxify the blood. So for example it clears heavy metals from the body rather than acting as an anti-inflammatory agent directly. A decrease in the materials that produce the glutathione means that more glutathione is being made. This results in higher availability of the glutathione in the blood. This allows the body to clear more material which is damaging to the body faster.

Each of the graphs presented below are Box-Whisker plots for the changes in the various lab parameter values from baseline. The middle line represents the median change; the lower and upper lines of the box represent the 25th and 75th percentiles.


Alanine
Cystine
Epinephrine
GABA
Glutamine
Glycine
HCys2
Histamine
Hydroxylysine
Leucine
Normetanephrine
Phenylethylamine
Phenylalanine
Trytophan
Alpha-aminobutric acid
%Change from Pre-patch
Day 2
Day 7

Appendix C: General Study Protocol

1. IRB submission
2. IRB approval
3. Distribute flyers and email announcements
4. Begin recruiting as people call in for study information
5. Schedule participants that meet inclusion and exclusion criterion
6. Consent a participant and administer baseline questionnaires, metabolic tests and baseline physiology test.
7. Schedule participant for next am and issue one patch for application 8 am.
8. Call participant to confirm patch application.
9. Meet participant at laboratory for initial testing at 9:00 am
    a. First salivary swab
    b. Physiology suite testing
    c. Memory test part 1
    d. 10 am urine
    e. Questionnaires
    f. Memory test part 2
10. Schedule for next day and issue salivary kit and patch for next morning
11. Call and confirm salivary test and patch application 8 am
12. Repeat 9a-f
13. Issue salivary kit and 5 patches and remind participant to freeze salivary samples or bring them in the next morning if local.
14. The 6^{th} night of study period, call and remind participant of appointment. Remind them to bring salivary kit.
15. Repeat 9 a-f. Issue new salivary kit. Receive participant's second salivary kit.
16. Arrange for participant to deliver salivary kit the next day.
17. Ship kits and urines received once a week to Sabre Sciences.
18. Do ongoing data entry of physiology data and questionnaire data to maximize study turn around.
19. When study is complete email spreadsheets to statistics analysis.
20. Receive analysis and submit report.

Appendix D: Study Team

Dr. Melinda H. Connor, D.D., Ph.D., AMP, FAM: PI

Dr. Melinda Connor, has trained as a clinical psychologist, neuropsychologist, and is board certified in alternative medicine and a Fellow of the American Alternative Medicine Association. Dr. Connor holds an A.A. in Humanities from Harvard University, a B.A. in Theatre and English from Wellesley College. Her training includes master's degrees from programs at University of San Francisco and American Public University and a Ph.D. in clinical psychology from California Coast University with a one-year rotation in neuropsychology. As a National Institutes of Health T-32 post-doctoral fellow, Dr. Connor received her training as a research scientist at the University of Arizona under Dr. Andrew Weil and Dr. Iris Bell and was director of the Optimal Healing Research Program at the Laboratory for Advances in Consciousness and Health under Dr. Gary E. Schwartz. Dr. Connor is currently the CEO of Earthsongs Holistic Consulting and holds faculty positions at several universities. Dr. Connor has a research laboratory in Arizona and is the author of ten books.

Dr. Caitlin C. Connor, MAcOM, DAOM: Co-I

Dr. Caitlin Connor holds a bachelors degree from Mount Holyoke College with a dual focus in political science and anthropology, a master's degree in acupuncture and oriental medicine from Arizona School of Acupuncture and Oriental Medicine and a doctorate in Acupuncture and Oriental Medicine from California Institute for Integral Studies/American College of Traditional Chinese Medicine. Dr. Connor's research training began in high school in a special program at the University of Arizona where she was mentored by Dr. Gary Schwartz at the Laboratory for the Advancement in Consciousness and Health in the Department of Psychology. Dr. Connor was the *ISSSEEM 2011* gold medal winner of the *Rustum Roy Emerging Scientist Award* for undergraduates, a 2014 *Bernard Grad Emerging Scientist* silver medal winner for graduate students and a 2018 *Patricia Norris Award* gold medal winner. Dr. Connor is currently doing additional research training at University of Oxford, UK and commuting between countries.

Dr. Naran Gombosuren, Ph.D.: Metabolic Analysis

Dr. Naran Gombosuren, Ph.D., is technical director and lead research scientist at Sabre Sciences Laboratory/EndoSciences in Carlsbad, CA. Originally from Mongolia and trained in Hungary, Dr. Gomobsuren received her Ph.D. from Eotvos University in Budapest. Dr. Gombosuren has worked with such prestigious groups as Scripps Research Institute and Sanford-Burnham Prebys Medical Discovery Institute. A specialist in complex metabolic process Dr. Gombosuren has participated in studies with topics ranging from virology to gut-brain interactions.

Dr. Jens Eickhoff, Ph.D: Statistics

Dr. Jens Eickhoff earned his Ph.D. in 2002 in statistics from Iowa State University. He is a senior scientist in the Department of Biostatistics and Medical Informatics at University of Wisconsin Madison where he teaches Biostatistics. A specialist in complex research statistics he has participated in studies ranging from oncology to endocrinology and published extensively on bio-statistical modeling.