Metabolic implications
of the
Lifewave X39 Patch

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Introduction

This study explores the metabolic implications and physiologic results of wearing the Lifewave X39 patch over the period of one week. Measures were taken at baseline, 24 hours and at 7 days of wearing the patch. A sample of convenience of 15 subjects made up of both men and women aged 40-65 were selected to participate in this study.

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 isolated from human plasma albumin in 1973 by Dr. Loren Pickart. 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. Additional research has established the strong affinity the GHK peptide has for copper, and exists in two forms,

as this was not covered in the initial experiment. These two forms are GHK and GHK-Cu. It is also important to mention that none of the research around GHK has ever found it to cause an issue. (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-epitheliazation 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 demonstrated to improve tissue remodeling. "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($10-7$M) 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

All X39 patches are sealed so that none of the substances in the patch actually penetrate the skin. This allows for consistent patch promotion of the light flow through out the time the patch is worn. In this study the initial baseline readings were taken, then the X39 patch was applied. The participant will be 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 been little evidence of negative side effects. There is a theoretical concern about an increase in cancer rates, but "there was no significant association found with basal cell carcinoma, squamous cell carcinoma or melanoma." (Kakimoto, C., 2017) This suggests that this is a relatively untapped option for healing with relatively few risks.

Meridian Implications and Patch placement

The Lifewave patches are placed on specific meridian points to maximize effectiveness. 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" 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).

There are two options for patch placement which have been defined for the X39 patch. The first is a point on the back, also known as GV14, Du-14, or Tao Dao, which

may create a few relevant effects. It is a meeting point of the Governing vessel with all of the Yang meridians. It is also the Point of the Sea of Qi. All of these mean that point would have a direct impact on the Yang meridians of the body, and both generally Qi and Yang in the body. It specifically expels wind and firms the exterior, which will help prevent illness and reduce shaking. It also clears heat, which would include inflammation and redness, which is a common sign of tissue damage. It also works specifically on malaria, as well as building any bodily substance that is depleted and pacifies wind. (Deadman, P., 2001)

The second, is a point on the lower abdomen, also known as CV-6, or Qi Hai. This point works in a slightly different direction. It fosters Original Qi, builds Qi overall, supports the Kidneys and fortifies Yang, rescues collapsed Yang, regulates Qi, and harmonizes blood. This means that it helps congenital problems or the general effects of aging. It also helps with genital issues, such as impotence, prolapse of the uterus, and infertility. It also helps with pain or masses in the abdomen. Between these two points most, if not all, of the previously noted impacts of the X39 patch are supported. (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

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 Carlesbad, 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 participats 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 Renyolds 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.

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 2003.

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

Important Questionnaire Outcomes
- Marlowe-Crowne consistent
- AIOS-VAS
- WAIS III
- Profile of Mood States (POMS) No change
- Modified PSQI
- McGill Pain Instrument No change

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

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

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

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

There were no significant changes in the POMs and the McGill pain scores from the baseline (pre-patch) assessment.

Important 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
Ala	Day 1 to Day 2	-20.17	36.89	0.0526
Cys	Day 2 to Day 7	-16.07	23.86	0.0206
E	Day 1 to Day 2	-2.09	3.08	0.0197
E	Day 2 to Day 7	1.59	2.94	0.0552
GABA	Day 1 to Day 7	-0.73	1.50	0.0818
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
HCys2	Day 1 to Day 2	0.35	0.55	0.0296
His	Day 1 to Day 2	-46.32	75.35	0.0320
His	Day 1 to Day 7	-46.64	49.35	0.0026
Hist	Day 1 to Day 2	-9.24	20.20	0.0981
Hlys	Day 1 to Day 7	-0.80	1.75	0.0992
Leu	Day 1 to Day 2	-4.84	7.84	0.0313
NorM	Day 2 to Day 7	-13.06	23.32	0.0479
PEA	Day 1 to Day 7	-0.59	1.12	0.0589
Phe	Day 2 to Day 7	6.33	10.94	0.0418
Ratio	Day 1 to Day 2	-0.71	1.40	0.0700
Trp	Day 2 to Day 7	-10.81	18.55	0.0406
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

Important 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
A_EKG	SDNN	2	-42.89	82.71	0.06430

B_BVP	HF	5	-1085.13	2038.55	0.05830
B_BVP	NN50	1	-3.13	5.34	0.03950
B_BVP	NN50	2	-2.13	4.12	0.06470
B_BVP	NN50	3	-1.73	2.89	0.03580
B_BVP	NN50	5	-2.73	3.03	0.00360
B_BVP	PNN50	1	-0.05	0.08	0.03820
B_BVP	PNN50	2	-0.03	0.07	0.06880
B_BVP	PNN50	3	-0.03	0.04	0.04290
B_BVP	PNN50	5	-0.04	0.04	0.00360
B_BVP	RMSSD	5	-21.13	36.49	0.04160
B_BVP	SDNN	5	-19.42	27.08	0.01480
B_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
A_EKG	HF	-1115.01	28492.47	0.7113
A_EKG	LF	14424.43	104293.22	0.1929
A_EKG	LF/HF	0.28	1.31	0.0487
B_BVP	HF	-786.72	3852.92	0.0559
B_BVP	LF	205.48	4414.61	0.6599
B_BVP	LF/HF	-0.08	5.93	0.9004
B_BVP	NN50	-1.96	3.80	<.0001
B_BVP	PNN50	-0.03	0.06	<.0001
B_BVP	RMSSD	-21.78	76.48	0.0083
B_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
BVP_HR	1:Average	2	4.51	7.83	0.0426
BVP_HR_Max_Min	1:Average	5	-2.23	3.13	0.0153
BVP_HR_Max_Min	2:Mode	1	-1.18	2.17	0.0533
BVP_HR_Max_Min	2:Mode	2	-0.73	1.57	0.0917
EKG_HR_Max_Min	2:Mode	6	-33.34	67.42	0.0871
Resp_Rate	2: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
BVP_HR	1:Average	2.54	8.31	0.0047
BVP_HR	2:Mode	2.31	9.60	0.0249
BVP_HR_Max_Min	1:Average	-1.67	5.50	0.0049
C_EMG	1:Average	-39.44	124.62	0.0035
C_EMG	2:Mode	-38.45	128.72	0.0057
C_EMG	3:Area	-2366.63	7477.30	0.0035

Discussion

It is important to recognize that this was both a sample of convience and a short-term study with a small sample size. However,

Summary

This study, as designed, is fairly comprehensive in nature, exploring the metabolic and physiologic aspects of the Lifewave X39 patch. In addition the questionnaires which were administered 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 Phase III patch daily.

The data results of improvement in blood pressure, 17 statistically significant amino acid changes over the 7 days, improvement in sleep levels, improvement in short term memory, improvement in reported feelings of vitality and consistancy in reporting across the study suggest that further research with a larger sample size be done and confirm the previously reported annecdotal responses in the testing of earlier subjects. The Lifewave X39 patch shows clear, significant metabolic 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 physio 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 – Physio Data

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

Sample Size: N=15

Statistical Methods: All physio 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)

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

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

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

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

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

B_BVP	NN50	4	-0.67	3.60	0.48490
B_BVP	NN50	5	-2.73	3.03	0.00360
B_BVP	NN50	6	-1.14	3.37	0.22680
B_BVP	PNN50	1	-0.05	0.08	0.03820
B_BVP	PNN50	2	-0.03	0.07	0.06880
B_BVP	PNN50	3	-0.03	0.04	0.04290
B_BVP	PNN50	4	-0.01	0.06	0.43010
B_BVP	PNN50	5	-0.04	0.04	0.00360
B_BVP	PNN50	6	-0.02	0.05	0.17910
B_BVP	Power	1	545.78	2280.01	0.36960
B_BVP	Power	2	-8328.21	31202.70	0.31880
B_BVP	Power	3	-214.30	1871.40	0.66420
B_BVP	Power	4	307.79	3957.22	0.76770
B_BVP	Power	5	-1009.99	3912.89	0.33440
B_BVP	Power	6	159.57	8096.33	0.94230
B_BVP	RMSSD	1	-17.35	78.45	0.40610
B_BVP	RMSSD	2	-45.31	139.63	0.22940
B_BVP	RMSSD	3	-20.12	53.66	0.16840
B_BVP	RMSSD	4	-3.70	40.78	0.73050
B_BVP	RMSSD	5	-21.13	36.49	0.04160
B_BVP	RMSSD	6	-16.81	66.48	0.36130
B_BVP	SDNN	1	-14.88	51.26	0.27970
B_BVP	SDNN	2	-36.68	127.28	0.28320
B_BVP	SDNN	3	-14.89	36.20	0.13350
B_BVP	SDNN	4	-5.96	38.00	0.55320
B_BVP	SDNN	5	-19.42	27.08	0.01480
B_BVP	SDNN	6	-15.82	50.23	0.25970
B_BVP	VLF	1	103.55	547.35	0.47580
B_BVP	VLF	2	-4649.04	16958.99	0.30630
B_BVP	VLF	3	-57.67	573.83	0.70290
B_BVP	VLF	4	-137.63	741.02	0.48380
B_BVP	VLF	5	-382.47	426.65	0.00370
B_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
A_EKG	HF	23893.77	18487.28	22778.77	24740.27
A_EKG	LF	17020.81	39992.04	31445.25	96188.86
A_EKG	LF/HF	0.65	0.74	0.92	1.08
A_EKG	NN50	38.32	5.43	39.16	5.93
A_EKG	PNN50	0.44	0.03	0.44	0.03
A_EKG	Power	47640.73	67916.09	70076.42	166485.72
A_EKG	RMSSD	546.19	166.44	527.98	201.30
A_EKG	SDNN	372.10	112.67	361.59	148.66
A_EKG	VLF	6726.15	19705.90	15852.41	63648.29
B_BVP	HF	2006.26	5250.16	1219.54	3722.92
B_BVP	LF	1212.62	3001.00	1418.10	4216.50
B_BVP	LF/HF	3.71	5.33	3.64	3.27
B_BVP	NN50	4.86	5.79	2.90	4.04
B_BVP	PNN50	0.07	0.09	0.04	0.05
B_BVP	Power	4346.12	13669.71	2919.37	7809.44
B_BVP	RMSSD	75.74	94.85	53.97	81.91
B_BVP	SDNN	70.89	71.80	52.28	63.04
B_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
A_EKG	HF	-1115.01	28492.47	0.7113
A_EKG	LF	14424.43	104293.22	0.1929
A_EKG	LF/HF	0.28	1.31	0.0487
A_EKG	NN50	0.83	6.31	0.2133
A_EKG	PNN50	0.00	0.04	0.3994
A_EKG	Power	22435.68	177642.61	0.2340
A_EKG	RMSSD	-18.22	214.87	0.4234
A_EKG	SDNN	-10.50	160.20	0.5356
A_EKG	VLF	9126.26	67230.39	0.2012
B_BVP	HF	-786.72	3852.92	0.0559
B_BVP	LF	205.48	4414.61	0.6599
B_BVP	LF/HF	-0.08	5.93	0.9004
B_BVP	NN50	-1.96	3.80	<.0001
B_BVP	PNN50	-0.03	0.06	<.0001
B_BVP	Power	-1426.75	13373.42	0.3142

B_BVP	RMSSD	-21.78	76.48	0.0083
B_BVP	SDNN	-18.60	63.27	0.0065
B_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**
BVP_HR	1:Average	1	75.99	12.00	79.45	13.01
BVP_HR	1:Average	2	75.38	10.23	79.89	12.91
BVP_HR	1:Average	3	77.08	12.44	80.32	12.58
BVP_HR	1:Average	4	78.22	12.40	79.91	14.13
BVP_HR	1:Average	5	79.37	12.55	79.85	13.40
BVP_HR	1:Average	6	78.22	12.22	79.95	13.35
BVP_HR	2:Mode	1	76.27	14.47	78.57	12.18
BVP_HR	2:Mode	2	77.70	12.81	80.04	14.03
BVP_HR	2:Mode	3	77.26	13.21	80.53	13.90
BVP_HR	2:Mode	4	79.69	13.43	81.49	15.08
BVP_HR	2:Mode	5	79.33	13.43	80.63	12.79
BVP_HR	2:Mode	6	78.50	13.00	80.71	13.42
BVP_HR	4:STD	1	5.51	4.65	4.50	4.18
BVP_HR	4:STD	2	6.45	7.38	4.27	3.93
BVP_HR	4:STD	3	5.10	3.47	4.49	3.83
BVP_HR	4:STD	4	5.18	3.87	4.56	4.12
BVP_HR	4:STD	5	5.70	4.42	3.71	3.60
BVP_HR	4:STD	6	5.72	4.61	4.25	3.63
BVP_HR	5:Minimum	1	59.46	15.13	66.60	18.60
BVP_HR	5:Minimum	2	58.19	14.63	69.53	17.78
BVP_HR	5:Minimum	3	58.87	14.55	68.21	15.42
BVP_HR	5:Minimum	4	64.41	13.91	68.17	17.42
BVP_HR	5:Minimum	5	62.90	17.58	69.68	16.71
BVP_HR	5:Minimum	6	61.42	16.43	65.95	18.28
BVP_HR	6:Maximum	1	94.49	27.71	89.97	17.16
BVP_HR	6:Maximum	2	90.18	27.03	87.47	12.96
BVP_HR	6:Maximum	3	86.36	13.21	92.06	17.68
BVP_HR	6:Maximum	4	90.52	17.51	88.19	14.42
BVP_HR	6:Maximum	5	93.50	19.71	86.78	13.82
BVP_HR	6:Maximum	6	87.79	13.16	87.53	14.14

BVP_HR_Max_Min	1:Average	1	9.64	9.75	9.10	10.49
BVP_HR_Max_Min	1:Average	2	11.32	12.49	8.03	9.49
BVP_HR_Max_Min	1:Average	3	9.37	8.36	8.04	8.21
BVP_HR_Max_Min	1:Average	4	8.97	8.17	8.34	9.25
BVP_HR_Max_Min	1:Average	5	9.21	8.51	6.98	6.97
BVP_HR_Max_Min	1:Average	6	10.00	10.85	8.16	8.97
BVP_HR_Max_Min	2:Mode	1	7.27	11.25	6.09	11.16
BVP_HR_Max_Min	2:Mode	2	7.52	11.82	6.79	11.22
BVP_HR_Max_Min	2:Mode	3	4.98	3.55	6.87	10.80
BVP_HR_Max_Min	2:Mode	4	7.08	11.08	7.25	11.03
BVP_HR_Max_Min	2:Mode	5	7.64	11.65	6.58	10.58
BVP_HR_Max_Min	2:Mode	6	7.53	12.04	6.49	10.57
BVP_HR_Max_Min	4:STD	1	7.26	6.74	5.98	7.28
BVP_HR_Max_Min	4:STD	2	7.90	11.18	4.26	4.46
BVP_HR_Max_Min	4:STD	3	6.65	6.04	5.53	6.42
BVP_HR_Max_Min	4:STD	4	6.01	6.82	4.43	5.02
BVP_HR_Max_Min	4:STD	5	6.96	6.55	4.32	5.47
BVP_HR_Max_Min	4:STD	6	6.04	6.01	4.81	5.32
BVP_HR_Max_Min	5:Minimum	1	2.64	1.92	2.08	2.34
BVP_HR_Max_Min	5:Minimum	2	2.54	2.81	1.87	0.92
BVP_HR_Max_Min	5:Minimum	3	2.48	2.65	2.05	1.63
BVP_HR_Max_Min	5:Minimum	4	3.01	2.30	2.36	2.20
BVP_HR_Max_Min	5:Minimum	5	2.23	1.47	1.87	1.65
BVP_HR_Max_Min	5:Minimum	6	2.80	2.05	2.08	2.61
BVP_HR_Max_Min	6:Maximum	1	26.71	23.26	20.79	22.32
BVP_HR_Max_Min	6:Maximum	2	26.85	32.23	14.99	12.29
BVP_HR_Max_Min	6:Maximum	3	23.55	15.58	19.43	20.18
BVP_HR_Max_Min	6:Maximum	4	21.30	19.80	15.63	13.79
BVP_HR_Max_Min	6:Maximum	5	24.39	21.09	14.86	14.52
BVP_HR_Max_Min	6:Maximum	6	22.54	16.95	17.73	16.94
C_EMG	1:Average	1	73.73	147.15	26.37	38.59
C_EMG	1:Average	2	62.98	136.67	21.32	26.87
C_EMG	1:Average	3	53.38	130.88	20.44	26.37
C_EMG	1:Average	4	54.91	138.45	17.39	24.66
C_EMG	1:Average	5	54.77	133.63	19.50	30.49
C_EMG	1:Average	6	56.37	116.57	13.53	17.62
C_EMG	2:Mode	1	88.48	192.35	16.98	26.42
C_EMG	2:Mode	2	53.96	136.32	22.29	28.61
C_EMG	2:Mode	3	54.69	138.62	17.93	24.91
C_EMG	2:Mode	4	52.50	130.22	15.97	23.43
C_EMG	2:Mode	5	51.44	127.80	19.13	31.35

C_EMG	2:Mode	6	34.90	62.74	13.34	18.16
C_EMG	3:Area	1	4423.89	8828.48	1581.98	2315.16
C_EMG	3:Area	2	3778.68	8200.12	1278.93	1612.16
C_EMG	3:Area	3	3203.01	7853.07	1226.24	1582.10
C_EMG	3:Area	4	3294.39	8306.75	1043.60	1479.42
C_EMG	3:Area	5	3286.20	8017.55	1170.05	1829.65
C_EMG	3:Area	6	3382.44	6993.89	811.79	1057.38
C_EMG	4:STD	1	13.00	20.72	14.54	43.83
C_EMG	4:STD	2	15.68	41.10	3.76	6.59
C_EMG	4:STD	3	4.53	6.93	4.98	10.52
C_EMG	4:STD	4	3.71	6.56	3.58	5.68
C_EMG	4:STD	5	6.89	9.77	3.77	8.27
C_EMG	4:STD	6	20.60	47.69	2.00	1.79
C_EMG	5:Minimum	1	15.56	18.27	12.55	21.69
C_EMG	5:Minimum	2	28.80	73.99	14.71	23.93
C_EMG	5:Minimum	3	42.99	111.72	14.22	22.04
C_EMG	5:Minimum	4	47.15	122.87	12.08	20.81
C_EMG	5:Minimum	5	43.12	114.12	9.31	17.09
C_EMG	5:Minimum	6	24.77	44.54	9.94	15.24
C_EMG	6:Maximum	1	192.25	244.06	103.39	172.63
C_EMG	6:Maximum	2	155.35	237.25	63.62	82.52
C_EMG	6:Maximum	3	99.71	164.04	74.06	155.55
C_EMG	6:Maximum	4	92.75	161.73	87.60	144.18
C_EMG	6:Maximum	5	128.73	188.45	73.03	155.09
C_EMG	6:Maximum	6	123.22	212.92	41.55	36.64
D_EMG	1:Average	1	28.81	55.86	41.70	93.73
D_EMG	1:Average	2	44.06	99.54	35.15	70.91
D_EMG	1:Average	3	30.77	68.94	20.33	30.85
D_EMG	1:Average	4	24.10	56.73	25.32	53.58
D_EMG	1:Average	5	25.06	64.03	25.62	55.95
D_EMG	1:Average	6	33.05	92.75	30.84	69.95
D_EMG	2:Mode	1	19.34	33.17	38.98	99.90
D_EMG	2:Mode	2	32.81	80.55	15.36	22.12
D_EMG	2:Mode	3	32.48	74.52	20.35	34.43
D_EMG	2:Mode	4	23.25	57.01	19.20	36.53
D_EMG	2:Mode	5	24.23	64.31	22.08	46.41
D_EMG	2:Mode	6	32.19	94.53	32.10	76.54
D_EMG	3:Area	1	1728.66	3351.40	2501.91	5623.55
D_EMG	3:Area	2	2643.37	5972.58	2108.70	4254.80
D_EMG	3:Area	3	1846.15	4136.32	1219.72	1850.73
D_EMG	3:Area	4	1446.25	3403.70	1518.91	3214.78

D_EMG	3:Area	5	1503.30	3842.00	1537.14	3357.02
D_EMG	3:Area	6	1983.18	5564.93	1850.20	4197.23
D_EMG	4:STD	1	16.20	29.48	12.88	32.89
D_EMG	4:STD	2	15.59	26.52	20.35	44.28
D_EMG	4:STD	3	7.36	14.41	8.05	16.97
D_EMG	4:STD	4	4.56	6.66	11.63	35.16
D_EMG	4:STD	5	5.49	8.41	6.50	17.55
D_EMG	4:STD	6	7.30	11.31	3.43	5.83
D_EMG	5:Minimum	1	11.57	25.03	23.23	57.11
D_EMG	5:Minimum	2	23.17	65.59	4.87	6.08
D_EMG	5:Minimum	3	8.47	21.57	7.63	12.84
D_EMG	5:Minimum	4	17.45	47.49	8.75	21.38
D_EMG	5:Minimum	5	17.38	50.10	8.74	21.37
D_EMG	5:Minimum	6	20.08	60.38	16.09	32.52
D_EMG	6:Maximum	1	171.84	224.33	115.20	187.23
D_EMG	6:Maximum	2	157.74	240.03	105.02	206.16
D_EMG	6:Maximum	3	109.99	178.37	83.18	141.87
D_EMG	6:Maximum	4	78.68	80.34	107.54	164.96
D_EMG	6:Maximum	5	91.00	135.09	69.77	109.58
D_EMG	6:Maximum	6	122.45	188.78	58.92	95.51
EKG_HR	1:Average	2	119.69	12.76	120.06	11.49
EKG_HR	1:Average	3	114.91	8.81	115.04	13.02
EKG_HR	1:Average	4	109.02	7.64	110.87	10.38
EKG_HR	1:Average	5	106.36	9.83	111.51	7.89
EKG_HR	1:Average	6	101.74	10.59	105.43	8.69
EKG_HR	2:Mode	2	80.68	27.74	79.53	29.02
EKG_HR	2:Mode	3	64.20	20.10	63.70	27.99
EKG_HR	2:Mode	4	51.06	11.28	60.64	22.16
EKG_HR	2:Mode	5	52.27	17.00	55.37	14.84
EKG_HR	2:Mode	6	47.46	21.83	54.49	22.47
EKG_HR	4:STD	2	56.89	4.98	55.93	7.50
EKG_HR	4:STD	3	61.09	7.70	58.93	8.71
EKG_HR	4:STD	4	61.57	8.85	57.66	6.93
EKG_HR	4:STD	5	62.12	4.81	62.13	5.65
EKG_HR	4:STD	6	61.74	9.36	63.22	6.44
EKG_HR	5:Minimum	2	35.08	10.57	38.26	11.55
EKG_HR	5:Minimum	3	38.33	7.02	36.63	10.92
EKG_HR	5:Minimum	4	36.34	5.77	36.06	13.51
EKG_HR	5:Minimum	5	34.99	6.41	38.06	9.84
EKG_HR	5:Minimum	6	30.61	9.41	31.98	8.99
EKG_HR	6:Maximum	2	289.75	12.26	287.79	11.22

EKG_HR	6:Maximum	3	292.72	9.34	289.50	11.15
EKG_HR	6:Maximum	4	288.53	13.01	286.77	16.66
EKG_HR	6:Maximum	5	286.46	17.62	288.23	10.54
EKG_HR	6:Maximum	6	278.81	19.88	294.45	4.15
EKG_HR_Max_Min	1:Average	2	149.43	21.62	145.76	22.80
EKG_HR_Max_Min	1:Average	3	155.05	13.59	149.86	13.95
EKG_HR_Max_Min	1:Average	4	152.38	24.86	143.01	23.95
EKG_HR_Max_Min	1:Average	5	154.93	21.73	153.72	19.80
EKG_HR_Max_Min	1:Average	6	143.16	28.85	147.05	15.49
EKG_HR_Max_Min	2:Mode	2	77.04	53.27	94.10	64.44
EKG_HR_Max_Min	2:Mode	3	95.38	68.18	65.49	53.18
EKG_HR_Max_Min	2:Mode	4	64.18	29.38	70.20	64.86
EKG_HR_Max_Min	2:Mode	5	89.36	66.60	86.20	44.44
EKG_HR_Max_Min	2:Mode	6	81.64	67.36	50.42	32.38
EKG_HR_Max_Min	4:STD	2	59.35	8.66	56.69	13.89
EKG_HR_Max_Min	4:STD	3	62.24	9.62	61.67	14.11
EKG_HR_Max_Min	4:STD	4	61.38	8.95	60.50	10.86
EKG_HR_Max_Min	4:STD	5	60.83	11.90	61.78	14.01
EKG_HR_Max_Min	4:STD	6	62.13	12.79	69.43	8.42
EKG_HR_Max_Min	5:Minimum	2	55.38	32.74	58.32	37.28
EKG_HR_Max_Min	5:Minimum	3	52.16	18.12	47.72	25.92
EKG_HR_Max_Min	5:Minimum	4	53.76	27.95	48.74	34.97
EKG_HR_Max_Min	5:Minimum	5	59.60	33.62	63.48	35.49
EKG_HR_Max_Min	5:Minimum	6	58.48	41.86	44.07	26.02
EKG_HR_Max_Min	6:Maximum	2	239.95	17.21	232.74	23.85
EKG_HR_Max_Min	6:Maximum	3	243.42	15.10	240.36	21.29
EKG_HR_Max_Min	6:Maximum	4	241.38	18.73	240.92	25.28
EKG_HR_Max_Min	6:Maximum	5	242.32	18.77	242.68	17.09
EKG_HR_Max_Min	6:Maximum	6	242.12	21.17	251.81	10.15
E_Skin_Cond	1:Average	1	1.03	0.92	1.12	0.83
E_Skin_Cond	1:Average	2	1.06	0.96	1.15	0.92
E_Skin_Cond	1:Average	3	1.16	1.08	1.18	0.95
E_Skin_Cond	1:Average	4	1.25	1.19	1.21	1.02
E_Skin_Cond	1:Average	5	1.32	1.45	1.28	1.13
E_Skin_Cond	1:Average	6	1.39	1.41	1.31	1.22
E_Skin_Cond	2:Mode	1	0.96	0.71	1.09	0.81
E_Skin_Cond	2:Mode	2	1.02	0.83	1.15	0.93
E_Skin_Cond	2:Mode	3	1.11	1.00	1.17	0.93
E_Skin_Cond	2:Mode	4	1.23	1.16	1.19	0.99
E_Skin_Cond	2:Mode	5	1.24	1.22	1.27	1.11
E_Skin_Cond	2:Mode	6	1.38	1.39	1.30	1.20

E_Skin_Cond	3:Area	1	61.83	55.14	67.10	49.90
E_Skin_Cond	3:Area	2	63.86	57.53	69.22	55.39
E_Skin_Cond	3:Area	3	69.53	64.95	71.02	57.26
E_Skin_Cond	3:Area	4	74.99	71.21	72.60	61.01
E_Skin_Cond	3:Area	5	79.32	87.27	76.62	67.99
E_Skin_Cond	3:Area	6	83.64	84.39	78.81	73.39
E_Skin_Cond	4:STD	1	0.09	0.21	0.06	0.06
E_Skin_Cond	4:STD	2	0.06	0.10	0.05	0.05
E_Skin_Cond	4:STD	3	0.08	0.09	0.05	0.07
E_Skin_Cond	4:STD	4	0.06	0.07	0.05	0.07
E_Skin_Cond	4:STD	5	0.10	0.23	0.05	0.08
E_Skin_Cond	4:STD	6	0.05	0.06	0.05	0.06
E_Skin_Cond	5:Minimum	1	0.90	0.65	1.02	0.75
E_Skin_Cond	5:Minimum	2	0.97	0.82	1.07	0.85
E_Skin_Cond	5:Minimum	3	1.05	0.97	1.09	0.86
E_Skin_Cond	5:Minimum	4	1.16	1.08	1.12	0.94
E_Skin_Cond	5:Minimum	5	1.18	1.16	1.19	1.02
E_Skin_Cond	5:Minimum	6	1.31	1.33	1.24	1.12
E_Skin_Cond	6:Maximum	1	1.23	1.36	1.28	0.98
E_Skin_Cond	6:Maximum	2	1.22	1.25	1.27	1.03
E_Skin_Cond	6:Maximum	3	1.35	1.36	1.32	1.12
E_Skin_Cond	6:Maximum	4	1.40	1.39	1.34	1.16
E_Skin_Cond	6:Maximum	5	1.54	1.92	1.41	1.34
E_Skin_Cond	6:Maximum	6	1.54	1.59	1.44	1.39
F_Temp	1:Average	1	33.71	1.49	33.45	1.55
F_Temp	1:Average	2	33.71	1.47	33.54	1.60
F_Temp	1:Average	3	33.78	1.54	33.58	1.66
F_Temp	1:Average	4	33.80	1.56	33.65	1.66
F_Temp	1:Average	5	33.78	1.56	33.72	1.62
F_Temp	1:Average	6	33.60	1.56	33.75	1.66
F_Temp	2:Mode	1	33.67	1.49	33.48	1.55
F_Temp	2:Mode	2	33.71	1.48	33.53	1.61
F_Temp	2:Mode	3	33.78	1.55	33.59	1.67
F_Temp	2:Mode	4	33.81	1.56	33.64	1.70
F_Temp	2:Mode	5	33.78	1.57	33.73	1.62
F_Temp	2:Mode	6	33.61	1.56	33.72	1.64
F_Temp	3:Area	1	2022.30	89.43	2007.15	93.01
F_Temp	3:Area	2	2022.78	87.93	2012.27	96.14
F_Temp	3:Area	3	2027.00	92.48	2014.61	99.75
F_Temp	3:Area	4	2028.09	93.68	2019.13	99.63
F_Temp	3:Area	5	2026.95	93.80	2023.50	96.96

F_Temp	3:Area	6	2015.76	93.77	2025.01	99.85
F_Temp	4:STD	1	0.10	0.09	0.10	0.06
F_Temp	4:STD	2	0.08	0.05	0.07	0.03
F_Temp	4:STD	3	0.09	0.06	0.07	0.03
F_Temp	4:STD	4	0.08	0.04	0.09	0.06
F_Temp	4:STD	5	0.08	0.05	0.08	0.06
F_Temp	4:STD	6	0.08	0.04	0.09	0.05
F_Temp	5:Minimum	1	33.52	1.47	33.28	1.58
F_Temp	5:Minimum	2	33.58	1.46	33.41	1.64
F_Temp	5:Minimum	3	33.63	1.56	33.45	1.67
F_Temp	5:Minimum	4	33.65	1.58	33.50	1.68
F_Temp	5:Minimum	5	33.65	1.55	33.58	1.66
F_Temp	5:Minimum	6	33.45	1.56	33.59	1.68
F_Temp	6:Maximum	1	33.88	1.47	33.62	1.53
F_Temp	6:Maximum	2	33.86	1.47	33.67	1.56
F_Temp	6:Maximum	3	33.94	1.51	33.71	1.64
F_Temp	6:Maximum	4	33.94	1.56	33.82	1.59
F_Temp	6:Maximum	5	33.93	1.56	33.88	1.53
F_Temp	6:Maximum	6	33.73	1.57	33.89	1.65
Resp_Rate	1:Average	1	13.82	2.26	14.27	1.88
Resp_Rate	1:Average	2	13.79	2.40	14.06	1.80
Resp_Rate	1:Average	3	13.60	2.27	13.72	1.69
Resp_Rate	1:Average	4	13.65	3.05	13.45	2.05
Resp_Rate	1:Average	5	13.43	2.61	13.59	2.31
Resp_Rate	1:Average	6	13.72	2.72	13.65	1.88
Resp_Rate	2:Mode	1	12.27	4.17	14.18	4.87
Resp_Rate	2:Mode	2	13.10	5.09	13.55	4.59
Resp_Rate	2:Mode	3	13.32	4.29	13.41	4.65
Resp_Rate	2:Mode	4	12.92	5.45	13.20	4.18
Resp_Rate	2:Mode	5	14.03	4.37	13.01	4.38
Resp_Rate	2:Mode	6	14.85	4.47	14.68	3.95
Resp_Rate	4:STD	1	3.29	0.73	3.60	0.94
Resp_Rate	4:STD	2	3.48	0.81	3.47	0.74
Resp_Rate	4:STD	3	3.75	0.95	3.53	0.58
Resp_Rate	4:STD	4	3.27	1.19	3.48	0.62
Resp_Rate	4:STD	5	3.39	1.20	3.08	0.92
Resp_Rate	4:STD	6	3.41	1.11	3.32	0.85
Resp_Rate	5:Minimum	1	8.98	1.63	8.69	2.15
Resp_Rate	5:Minimum	2	8.40	1.95	8.47	1.57
Resp_Rate	5:Minimum	3	7.58	2.58	8.39	1.54
Resp_Rate	5:Minimum	4	8.34	3.16	7.57	1.70

Resp_Rate	5:Minimum	5	7.85	1.74	8.18	2.40
Resp_Rate	5:Minimum	6	8.31	2.87	8.35	2.16
Resp_Rate	6:Maximum	1	19.06	1.35	19.35	1.25
Resp_Rate	6:Maximum	2	19.04	2.24	19.11	1.66
Resp_Rate	6:Maximum	3	18.88	1.77	19.48	1.24
Resp_Rate	6:Maximum	4	18.37	2.50	19.38	1.15
Resp_Rate	6:Maximum	5	18.03	3.02	18.30	2.08
Resp_Rate	6: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
BVP_HR	1:Average	1	3.47	8.57	0.1393
BVP_HR	1:Average	2	4.51	7.83	0.0426
BVP_HR	1:Average	3	3.23	7.87	0.1338
BVP_HR	1:Average	4	1.69	9.18	0.4866
BVP_HR	1:Average	5	0.48	8.92	0.8378
BVP_HR	1:Average	6	2.69	7.87	0.2231
BVP_HR	2:Mode	1	2.29	9.69	0.3754
BVP_HR	2:Mode	2	2.35	10.46	0.3998
BVP_HR	2:Mode	3	3.26	9.99	0.2261
BVP_HR	2:Mode	4	1.80	11.77	0.5641
BVP_HR	2:Mode	5	1.30	9.01	0.5847
BVP_HR	2:Mode	6	3.34	7.79	0.1329
BVP_HR_Max_Min	1:Average	1	-0.54	4.61	0.6583
BVP_HR_Max_Min	1:Average	2	-3.29	10.09	0.2272
BVP_HR_Max_Min	1:Average	3	-1.33	2.98	0.1047
BVP_HR_Max_Min	1:Average	4	-0.63	4.94	0.6286
BVP_HR_Max_Min	1:Average	5	-2.23	3.13	0.0153
BVP_HR_Max_Min	1:Average	6	-1.73	4.52	0.1763
BVP_HR_Max_Min	2:Mode	1	-1.18	2.17	0.0533
BVP_HR_Max_Min	2:Mode	2	-0.73	1.57	0.0917
BVP_HR_Max_Min	2:Mode	3	1.89	10.29	0.4894
BVP_HR_Max_Min	2:Mode	4	0.17	2.56	0.8021
BVP_HR_Max_Min	2:Mode	5	-1.06	2.63	0.1390
BVP_HR_Max_Min	2:Mode	6	-0.77	2.13	0.2016
C_EMG	1:Average	1	-47.37	156.16	0.2597
C_EMG	1:Average	2	-41.66	134.35	0.2497
C_EMG	1:Average	3	-32.95	120.86	0.3090

C_EMG	1:Average	4	-37.51	128.11	0.2758
C_EMG	1:Average	5	-35.27	112.16	0.2434
C_EMG	1:Average	6	-42.30	116.23	0.1964
C_EMG	2:Mode	1	-71.50	198.24	0.1842
C_EMG	2:Mode	2	-31.67	128.86	0.3573
C_EMG	2:Mode	3	-36.76	133.32	0.3036
C_EMG	2:Mode	4	-36.54	123.10	0.2696
C_EMG	2:Mode	5	-32.31	105.53	0.2554
C_EMG	2:Mode	6	-21.01	63.91	0.2405
C_EMG	3:Area	1	-2841.91	9369.34	0.2597
C_EMG	3:Area	2	-2499.75	8061.27	0.2497
C_EMG	3:Area	3	-1976.78	7251.87	0.3090
C_EMG	3:Area	4	-2250.79	7686.36	0.2758
C_EMG	3:Area	5	-2116.15	6729.75	0.2434
C_EMG	3:Area	6	-2538.04	6974.02	0.1964
D_EMG	1:Average	1	12.89	105.67	0.6440
D_EMG	1:Average	2	-8.91	100.16	0.7356
D_EMG	1:Average	3	-10.44	74.71	0.5969
D_EMG	1:Average	4	1.21	82.31	0.9553
D_EMG	1:Average	5	0.56	90.21	0.9810
D_EMG	1:Average	6	-2.70	121.61	0.9351
D_EMG	2:Mode	1	19.63	99.86	0.4590
D_EMG	2:Mode	2	-17.45	78.42	0.4033
D_EMG	2:Mode	3	-12.13	83.13	0.5810
D_EMG	2:Mode	4	-4.05	71.81	0.8302
D_EMG	2:Mode	5	-2.15	83.96	0.9225
D_EMG	2:Mode	6	-0.54	127.42	0.9876
D_EMG	3:Area	1	773.25	6340.13	0.6440
D_EMG	3:Area	2	-534.67	6009.89	0.7355
D_EMG	3:Area	3	-626.43	4482.69	0.5969
D_EMG	3:Area	4	72.67	4938.74	0.9554
D_EMG	3:Area	5	33.84	5412.35	0.9810
D_EMG	3:Area	6	-161.92	7296.73	0.9351
EKG_HR	1:Average	2	0.37	13.68	0.8827
EKG_HR	1:Average	3	0.13	14.53	0.9736
EKG_HR	1:Average	4	1.85	13.49	0.6037
EKG_HR	1:Average	5	5.15	11.79	0.1130
EKG_HR	1:Average	6	3.93	15.74	0.3666
EKG_HR	2:Mode	2	-1.15	34.63	0.8569
EKG_HR	2:Mode	3	-0.49	30.98	0.9519
EKG_HR	2:Mode	4	9.58	21.99	0.1137

EKG_HR	2:Mode	5	3.09	22.59	0.6041
EKG_HR	2:Mode	6	6.18	33.79	0.5061
EKG_HR_Max_Min	1:Average	2	-3.68	29.92	0.5063
EKG_HR_Max_Min	1:Average	3	-5.19	20.06	0.3338
EKG_HR_Max_Min	1:Average	4	-9.37	35.70	0.3267
EKG_HR_Max_Min	1:Average	5	-1.20	16.30	0.7793
EKG_HR_Max_Min	1:Average	6	3.92	36.00	0.6905
EKG_HR_Max_Min	2:Mode	2	17.06	88.11	0.2976
EKG_HR_Max_Min	2:Mode	3	-29.89	80.06	0.1701
EKG_HR_Max_Min	2:Mode	4	6.02	77.88	0.7690
EKG_HR_Max_Min	2:Mode	5	-3.16	79.37	0.8798
EKG_HR_Max_Min	2:Mode	6	-33.34	67.42	0.0871
E_Skin_Cond	1:Average	1	0.09	0.85	0.6960
E_Skin_Cond	1:Average	2	0.09	0.82	0.6779
E_Skin_Cond	1:Average	3	0.02	0.98	0.9231
E_Skin_Cond	1:Average	4	-0.04	0.92	0.8692
E_Skin_Cond	1:Average	5	-0.05	1.03	0.8678
E_Skin_Cond	1:Average	6	-0.03	0.97	0.9008
E_Skin_Cond	2:Mode	1	0.12	0.74	0.5349
E_Skin_Cond	2:Mode	2	0.13	0.77	0.5148
E_Skin_Cond	2:Mode	3	0.07	0.95	0.7922
E_Skin_Cond	2:Mode	4	-0.04	0.92	0.8594
E_Skin_Cond	2:Mode	5	0.03	0.89	0.9042
E_Skin_Cond	2:Mode	6	-0.03	0.97	0.8988
E_Skin_Cond	3:Area	1	5.27	51.27	0.6963
E_Skin_Cond	3:Area	2	5.36	49.02	0.6785
E_Skin_Cond	3:Area	3	1.49	58.64	0.9231
E_Skin_Cond	3:Area	4	-2.39	55.13	0.8691
E_Skin_Cond	3:Area	5	-2.70	61.68	0.8677
E_Skin_Cond	3:Area	6	-1.97	58.15	0.9011
F_Temp	1:Average	1	-0.25	1.51	0.5273
F_Temp	1:Average	2	-0.18	1.50	0.6576
F_Temp	1:Average	3	-0.21	1.48	0.5966
F_Temp	1:Average	4	-0.15	1.54	0.7128
F_Temp	1:Average	5	-0.06	1.45	0.8797
F_Temp	1:Average	6	0.17	1.41	0.6557
F_Temp	2:Mode	1	-0.19	1.46	0.6293
F_Temp	2:Mode	2	-0.18	1.52	0.6535
F_Temp	2:Mode	3	-0.19	1.46	0.6150
F_Temp	2:Mode	4	-0.16	1.54	0.6851
F_Temp	2:Mode	5	-0.06	1.52	0.8907

F_Temp	2:Mode	6	0.12	1.38	0.7519
F_Temp	3:Area	1	-15.15	90.55	0.5274
F_Temp	3:Area	2	-10.51	89.84	0.6574
F_Temp	3:Area	3	-12.39	88.59	0.5966
F_Temp	3:Area	4	-8.96	92.41	0.7128
F_Temp	3:Area	5	-3.45	86.90	0.8800
F_Temp	3:Area	6	10.36	84.89	0.6555
Resp_Rate	1:Average	1	0.45	1.52	0.2686
Resp_Rate	1:Average	2	0.26	2.15	0.6419
Resp_Rate	1:Average	3	0.12	2.22	0.8423
Resp_Rate	1:Average	4	-0.20	2.83	0.7899
Resp_Rate	1:Average	5	0.16	1.81	0.7435
Resp_Rate	1:Average	6	0.10	2.12	0.8571
Resp_Rate	2:Mode	1	1.92	4.03	0.0868
Resp_Rate	2:Mode	2	0.45	4.49	0.7032
Resp_Rate	2:Mode	3	0.08	4.34	0.9409
Resp_Rate	2:Mode	4	0.28	5.94	0.8556
Resp_Rate	2:Mode	5	-1.02	3.57	0.2859
Resp_Rate	2: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
BVP_HR	1:Average	77.35	11.67	79.90	12.87
BVP_HR	2:Mode	78.02	13.04	80.33	13.24
BVP_HR	4:STD	5.71	4.85	4.30	3.79
BVP_HR	5:Minimum	60.70	15.14	68.02	16.96
BVP_HR	6:Maximum	91.06	20.82	88.67	14.81
BVP_HR_Max_Min	1:Average	9.78	9.50	8.11	8.73
BVP_HR_Max_Min	2:Mode	6.98	10.32	6.68	10.59
BVP_HR_Max_Min	4:STD	6.98	7.41	4.89	5.61
BVP_HR_Max_Min	5:Minimum	2.61	2.18	2.05	1.92
BVP_HR_Max_Min	6:Maximum	24.84	22.28	17.24	16.72
C_EMG	1:Average	59.20	130.01	19.76	27.63
C_EMG	2:Mode	56.05	133.55	17.61	25.23
C_EMG	3:Area	3552.07	7800.39	1185.43	1657.62

C_EMG	4:STD	10.59	27.06	5.44	18.98
C_EMG	5:Minimum	33.88	87.88	12.14	19.88
C_EMG	6:Maximum	135.41	202.29	73.88	131.16
D_EMG	1:Average	30.80	72.46	29.82	63.93
D_EMG	2:Mode	27.23	67.56	24.68	58.06
D_EMG	3:Area	1848.17	4347.81	1789.43	3835.60
D_EMG	4:STD	9.35	18.43	10.47	28.32
D_EMG	5:Minimum	16.30	46.42	11.55	29.90
D_EMG	6:Maximum	120.96	179.72	89.94	152.99
EKG_HR	1:Average	112.05	12.28	113.83	11.66
EKG_HR	2:Mode	62.81	25.24	65.54	26.41
EKG_HR	4:STD	60.11	7.19	58.97	7.58
EKG_HR	5:Minimum	35.18	8.62	36.54	11.13
EKG_HR	6:Maximum	287.79	14.64	289.09	11.44
EKG_HR_Max_Min	1:Average	150.88	22.16	147.53	20.04
EKG_HR_Max_Min	2:Mode	82.18	58.59	76.75	56.55
EKG_HR_Max_Min	4:STD	61.09	10.19	61.13	13.16
EKG_HR_Max_Min	5:Minimum	55.50	31.15	53.44	33.24
EKG_HR_Max_Min	6:Maximum	241.60	17.62	240.21	21.49
E_Skin_Cond	1:Average	1.19	1.15	1.21	1.00
E_Skin_Cond	2:Mode	1.14	1.05	1.19	0.98
E_Skin_Cond	3:Area	71.52	69.18	72.56	59.72
E_Skin_Cond	4:STD	0.07	0.14	0.05	0.06
E_Skin_Cond	5:Minimum	1.08	1.00	1.12	0.91
E_Skin_Cond	6:Maximum	1.37	1.45	1.34	1.15
F_Temp	1:Average	33.75	1.49	33.62	1.58
F_Temp	2:Mode	33.75	1.49	33.62	1.59
F_Temp	3:Area	2024.94	89.35	2016.94	95.02
F_Temp	4:STD	0.08	0.06	0.08	0.05
F_Temp	5:Minimum	33.60	1.49	33.47	1.61
F_Temp	6:Maximum	33.90	1.48	33.77	1.54
Resp_Rate	1:Average	13.66	2.48	13.79	1.91
Resp_Rate	2:Mode	13.37	4.59	13.67	4.36
Resp_Rate	4:STD	3.43	0.99	3.41	0.78
Resp_Rate	5:Minimum	8.26	2.35	8.28	1.93
Resp_Rate	6: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
BVP_HR	1:Average	2.54	8.31	0.0047
BVP_HR	2:Mode	2.31	9.60	0.0249
BVP_HR_Max_Min	1:Average	-1.67	5.50	0.0049
BVP_HR_Max_Min	2:Mode	-0.31	4.67	0.5361
C_EMG	1:Average	-39.44	124.62	0.0035
C_EMG	2:Mode	-38.45	128.72	0.0057
C_EMG	3:Area	-2366.63	7477.30	0.0035
D_EMG	1:Average	-0.98	93.72	0.9213
D_EMG	2:Mode	-2.55	89.76	0.7881
D_EMG	3:Area	-58.74	5623.21	0.9213
EKG_HR	1:Average	1.78	13.68	0.2212
EKG_HR	2:Mode	2.73	29.70	0.3857
EKG_HR_Max_Min	1:Average	-3.36	28.34	0.2641
EKG_HR_Max_Min	2:Mode	-5.43	82.06	0.5317
E_Skin_Cond	1:Average	0.02	0.90	0.8557
E_Skin_Cond	2:Mode	0.05	0.85	0.5926
E_Skin_Cond	3:Area	1.04	54.01	0.8560
F_Temp	1:Average	-0.13	1.45	0.3849
F_Temp	2:Mode	-0.13	1.45	0.3941
F_Temp	3:Area	-8.00	86.95	0.3851
Resp_Rate	1:Average	0.13	2.09	0.5621
Resp_Rate	2: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 physio 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: 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 test and baseline physio 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. Physio 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 6th 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 physio 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 C: 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 Carlesbad, CA. Originally from Mongolia and trainned in Hungary, Dr. Gomobsuren received her Ph.D. from Eotvos University in Budepest. 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.