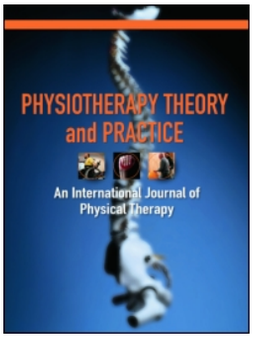

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RESEARCH REPORT

Using near infrared light to manage symptoms associated with restless legs syndrome

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ABSTRACT

The purpose of this study was to determine whether the application of near infrared (NIR) light could positively modulate symptoms associated with restless legs syndrome (RLS). Twenty-one subjects with RLS were treated with NIR three times weekly for four weeks. Baseline measures of: (1) international restless legs syndrome rating scale (IRLSRS) score; (2) Semmes Weinstein monofilament (SWM) test; (3) visual analog pain scale (VAS); (4) ankle-brachial index (ABI); and (5) sonographic imaging of the popliteal and posterior tibial arteries were compared to post-treatment values. NIR (850 nm) was delivered transcutaneously at 8 J/cm^2 to four locations on each leg and the plantar surface of each foot. A pre-test–post-test one group design was employed. Baseline and post-treatment measures were compared using either a dependent *t*-test when data were normal or the Wilcoxon signed rank test in the absence of normality. A significant improvement in IRLSRS scores was observed. Sensation improved from less than protective in 16.6% of sites tested at the baseline to 13.4% post-intervention. There was a significant improvement in ABI scores. VAS and sonographic imaging measures other than ABI remained unchanged. The use of NIR to modulate symptoms associated with RLS was supported by the data.

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Introduction

Restless legs syndrome (RLS) is a chronic condition that is characterized by a strong urge to move during times of rest or inactivity. This urge to move is accompanied by unpleasant sensations most often occurring in the lower limbs, but has also been reported to occur in the upper limbs and even axial segments (Michaud, Chabli, Lavigne, and Montplaisir, 2000; Perez-Diaz, Iranzo, Rye, and Santamaria, 2011; Trenkwalder, Paulus, and Walters, 2005). Common terms used to describe these unrelenting sensations are: “crawling”; “tingling”; “restless”; “cramping”; “creeping”; “pulling”; “painful”; “electric”; “tension”; “discomfort”; and “itching” (Ondo and Jankovic, 1996). Relief from these uncomfortable sensations may be achieved by active movement or position change. Symptoms tend to worsen as the day progresses, peaking during the nighttime hours, and frequently leading to sleep disturbances (Kushida, Allen, Atkinson, 2004).

The diagnosis of RLS is essentially clinical. No specific diagnostic biological markers have been identified. No laboratory test exists to confirm the diagnosis of RLS (Allen et al, 2003; Walters, 1995). Clinically, RLS is defined by the presence of four criteria: (Michaud, Chabli, Lavigne, and Montplaisir, 2000) an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations; (Perez-Diaz, Iranzo, Rye, and Santamaria, 2011) the urge to move and/or the experience of unpleasant sensations begin or worsen during periods of rest or inactivity; (Trenkwalder, Paulus, and Walters, 2005) the urge to move or unpleasant sensations are partially or totally relieved by movement, at least as long as the movement continues; and (Ondo and Jankovic, 1996) the urge to move or unpleasant sensations are worse in the evening or night or only occur in the evening or night (Allen et al, 2003).

RLS is thought to have both genetic (primary) components and secondary causes. Among the patients who fit the clinical criteria for diagnosis of this condition, 18.5–59.6% have a positive family history of RLS (Montplaisir et al, 1997; Winkelmann et al, 2000). Correlations have been found between the presence of RLS and conditions such as: iron deficiencies; obesity; pregnancy; cardiovascular disease; diabetes, peripheral neuropathy; Parkinson’s disease; multiple sclerosis;

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renal disease; and rheumatic diseases. RLS may be linked to the use of certain medications including: antihistamines; dopamine antagonists; antidepressants; and serotonergic reuptake inhibitors (Ekbom, 1945; Leschziner and Gringras, 2012; O'Keeffe, Gavin, and Lavan, 1994; Ondo, 2005; Taylor-Gjevre, Gjevre, Skomro, and Nair, 2009; Winkelmann, Stautner, Samtleben, and Trenkwalder, 2002).

Currently, there are few treatment options for RLS. A pharmaceutical approach has been the most effective option to date (Oertel et al, 2007). Compounds such as dopaminergic agents; opioids; antiepileptic drugs; alpha-2 delta blockers; benzodiazepines; and iron supplements have been prescribed. Dopaminergic agents are currently considered the drugs of choice (Ferini-Strambi et al, 2008; Ondo, 2009). In 2005 the Food and Drug Administration (FDA) approved two dopaminergic agents to specifically treat RLS. The pharmaceutical approach has provided temporary symptom relief, but not a cure (Ondo, 2009). Drugs used to treat RLS are frequently accompanied by adverse effects such as vomiting, dizziness, somnolence, and most commonly, nausea (Ferini-Strambi et al, 2008). Long-term use of the approved dopaminergic agents may result in drug tolerance and augmentation of symptoms (Winkelman and Johnston, 2004).

Non-pharmaceutical treatment options for RLS are highly sought. Because the symptoms are usually relieved by movement, Aukerman et al (2006) examined the effects of exercise on RLS. Participants experienced decreased severity of symptoms, but no explanation of the mechanism associated with this outcome was provided. More recently, Mitchell, Myrer, Johnson, and Hilton (2011) conducted a randomized control trial in which near infrared (NIR) light was used to treat subjects with RLS. The NIR treatment significantly improved the symptoms. Unlike in the Aukerman et al (2006) study, an explanation of the treatment's specific mechanism was suggested. This mechanism suggested relates to the production and liberation of nitric oxide, leading to vasodilation.

Our study further explores NIR treatment option for RLS. We examined the effects of the application of NIR in the treatment of RLS while building upon the work of Mitchell, Myrer, Johnson, and Hilton (2011). In this study, we attempted to confirm the work of Mitchell, Myrer, Johnson, and Hilton (2011) as well as to add measures of sensation and vascular status. It was our hope that through the application of NIR, along with multi-variable data collection, we might demonstrate/confirm an effective non-pharmaceutical treatment option for RLS and contribute to the understanding of the mechanisms behind the intervention's effectiveness.

Methods

Design

We employed a one group pre-test–post-test (quasi-experimental) design for this data collection. Each of the dependent variables explained below were measured before and after four weeks of intervention using NIR light. Because no comparison group was used in this study, time served as the independent variable and it existed at two levels (pre and post). This research protocol was approved by the Institutional Review Board (IRB) for Human Subjects at Arkansas State University.

Inclusion/exclusion criteria

After providing informed consent to participate, subjects were screened for inclusion criteria. Inclusion criteria included the existence of each of the following symptoms: (Michaud, Chabli, Lavigne, and Montplaisir, 2000) an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs; (Perez-Diaz, Iranzo, Rye, and Santamaria, 2011) the urge to move or unpleasant sensations that began or worsened during periods of rest or inactivity such as lying or sitting; (Trenkwalder, Paulus, and Walters, 2005) the urge to move or the unpleasant sensations were partially or totally relieved by movement, such as walking or stretching for at least as long as the activity continued; and (Ondo and Jankovic, 1996) the urge to move or unpleasant sensations were worse in the evening or night than during the day or only occurred in the evening or night. Each included subject scored in the moderate-to-severe range on the international restless legs syndrome rating scale (IRLSRS). The IRSLRS is a 10 question, self-completed subjective scale addressing intensity and frequency of symptoms, including sleep dysfunction. The scale has a total possible score of 40 points derived from adding a Lickert scale (0–4; 0 being no symptoms; and 4 being very severe symptoms) score from each of the 10 questions. For subjects to be included in the study, a score of at least 11 was required (moderate). Subjects were excluded from the subject pool if they were less than 18 years of age. Additionally, potential subjects not exhibiting all symptoms in the four-point list above and/or who scored less than a moderate level (less than a score of 11) on the IRLSRS were excluded. Initially, 27 potential subjects respond to our call. Three were eliminated based on the inclusion/exclusion criteria.

The study began with 24 subjects. Two subjects withdrew early on due to scheduling conflicts. One

subject dropped out mid-study after being hospitalized for a musculoskeletal injury brought on by an accident at home. Twenty-one subjects completed the entire study protocol.

Outcome measures

Five outcome measures were used to evaluate the effectiveness of the treatment delivered: (Michaud, Chabli, Lavigne, and Montplaisir, 2000) IRLSRS; (Perez-Diaz, Iranzo, Rye, and Santamaria, 2011) Semmes Weinstein monofilament (SWM) test; (Trenkwalder, Paulus, and Walters, 2005) visual analog pain scale (VAS); (Ondo and Jankovic, 1996) ankle-brachial index (ABI) test; and (Kushida, Allen, Atkinson, 2004) sonographic imaging of popliteal and posterior tibial arteries. Baseline data were obtained from each subject prior to the initial treatment.

These data were again collected within 3–5 days following each subject's last treatment session. The IRLSRS and VAS measures were administered to each subject in print. Subjects completed these scales based on their symptomatic experiences over the past 7 days.

The SWM test was administered both pre- and post-study by the same examiner, using the same set of monofilaments. The SWM test is a sensory test using a series of graded thickness monofilaments to determine the acuity of a subject's light touch sensory perception. Sensation was tested at nine locations on the plantar surface of each foot (Figure 1). Testing began with a 5.07 monofilament. If the subject could sense the pressure needed to bend this thickness of the monofilament, successively smaller filaments were used until the subject was unable to sense the force needed to bend the monofilament. If the initial 5.07 monofilament was not perceived by the subject, progressively thicker monofilaments were used until sensation was perceived (or until even the thickest monofilament was not perceived). The range of monofilaments used required from 0.001 to 300 grams of force to bend. We used the research set of 20 monofilaments to increase the sensitivity of the measurement. Monofilament sensory testing has been demonstrated as a reliable clinical tool (Shaffer, Harrison, Brown, and Brennan, 2005).

The ABI is a ratio of blood pressure in the lower extremities compared to blood pressure in the upper extremities. This is a standard measure of circulatory status in the lower extremities. Poor ABI scores (>1.4 or <0.8) suggest circulatory compromise in the lower extremities. We included assessment of lower extremity circulatory status as a means to potentially evaluate any circulatory changes that might be associated with the application of the NIR energy. ABIs were measured by utilizing a Unetixs MultiLab Series II system equipped with an 8 MHz transducer. Bilateral ankle pressures were collected from the posterior tibial arteries. Sonographic imaging was performed utilizing Hitachi 8500 and 5500 systems. Grayscale and spectral Doppler images of the popliteal arteries and posterior tibial arteries were obtained bilaterally using a 7.5 MHz

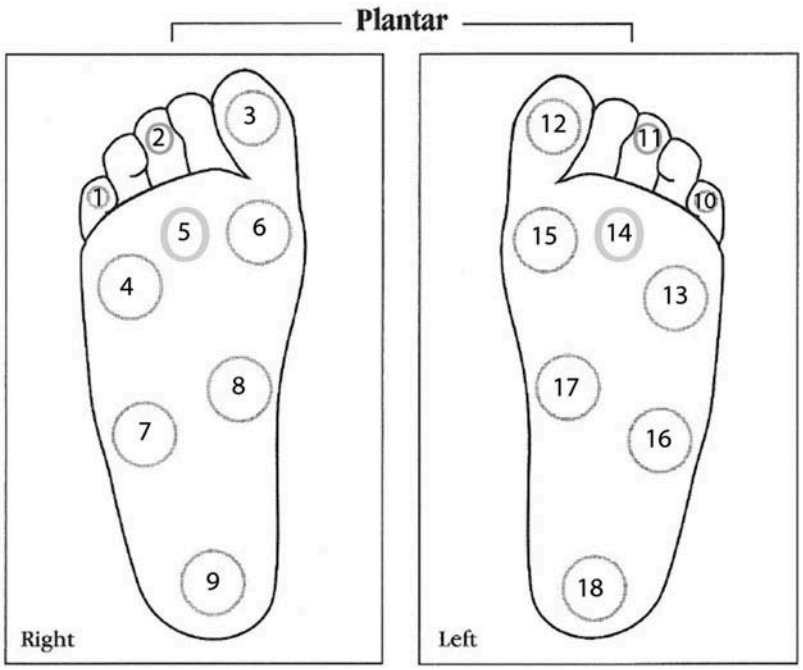

Figure 1. Semmes Weinstein monofilament test sites.

transducer. Interrogation of the popliteal artery occurred just superior to the trifurcation. The posterior tibial arteries were documented just superior to the medial malleolus. Width and height measurements of the vessels were performed in the transverse plane during grayscale imaging. Peak systolic velocity, end-diastolic velocity, resistivity index (RI), and pulsatility index (PI) were measured with spectral Doppler.

The VAS is a self-scored testing technique in which the subject selects a location along a 100 mm line that represents his or her level of pain. The line marked at the left extreme indicating "no pain" and on the right extreme indicating "unbearable pain."

Treatment

Subjects participated in 12 total treatment sessions over a course of 4 weeks. They each received NIR light treatment three times per week for four weeks. Subjects received treatment both in the morning and in the afternoon; however, once a treatment time was established for a given subject that subject consistently received treatment on that "time of day" schedule. Super-luminescent diodes (SLDs) were used to deliver NIR at a wavelength range of 830–870 nm with a dominant wavelength of 850 nm. NIR was delivered transcutaneously at 8 J/cm^2 (58 seconds) with a hand-held probe administered stationary to four locations on each leg (Figure 2), as well as the entire plantar surface of each foot (Choi, Fang, and Longhurst, 2012). Figure 3 displays the handheld probe used in this research. A "bathing" method was used to deliver NIR to the plantar surface of the feet in which the probe was moved along the entirety of the surface for 58 seconds to deliver 8 J/cm^2. The points of energy delivery (acupoints) were chosen because of their supposed contribution to improved circulation and pain modulation. Sandberg, Lindberg, and Gerdle (2004)

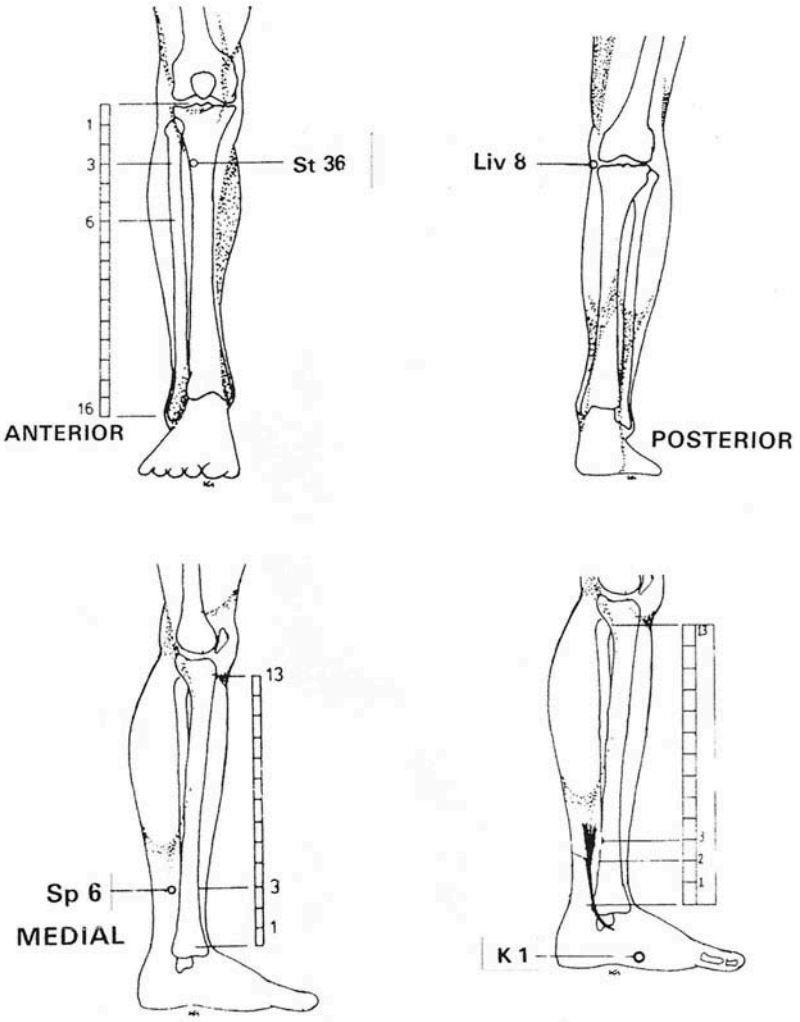

Figure 2. Lower extremity light application sites.

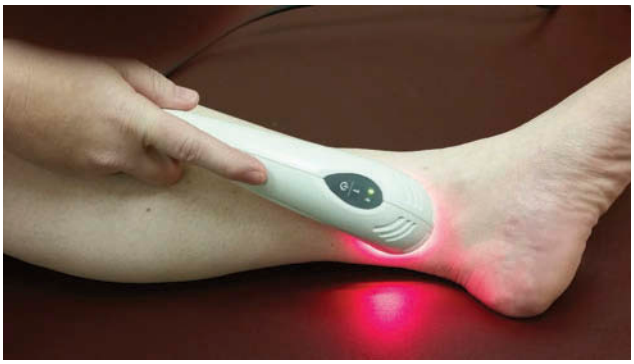

Figure 3. Handheld light probe. Dynatronics Corporation, Salt Lake City, UT.

demonstrated that lower extremity acupoint stimulation increased skin and muscle blood flow. Li et al (2007) also demonstrated improved lower extremity perfusion associated with acupressure applied to selected sites in the lower extremities of patients with peripheral artery occlusive disease. While the mechanism related to these vascular responses to acupoint stimulation is not clearly understood, we attempted to stimulate similar locations to potentially facilitate improved blood flow. The wavelength employed was based on the works of Hamblin (2008) and Karu (1999) related to NIR stimulation of nitric oxide to enhance vascularity and vascular response. No other physical therapy related interventions were used in this study.

Data analysis

Data analysis began by performing tests for normality on each of the datasets associated with the various outcome measures used. Since our sample size was small, the Shapiro–Wilk test was used to explore normality, beginning with the assumption that normality was present and only rejecting this assumption when $p < 0.05$. Based on the outcome of the normality tests, we selected either a parametric or a nonparametric test to compare the pre- and post-intervention scores. The level of data was also considered in the selection of statistical analysis. When normality was demonstrated and the data level was interval or ratio, the dependent *t*-test was employed. When the data were at the ordinal level, the Wilcoxon signed rank test was used.

Results

IRLSRS

Prior to the initiation of any intervention, the subject pool had a mean IRLSRS score of 26.5 ± 5.4 ($\sigma\bar{x}$ = 1.2). After having received NIR treatment three times per week for a total of four weeks, the mean IRLSRS score for the subject pool was 16.1 ± 8.1 ($\sigma\bar{x}$ = 1.8). A lower value on the IRLSRS demonstrates improvement in symptoms. The Shapiro–Wilk Test demonstrated normality in this dataset both pre- and post-intervention ($p = 0.067$ and 0.999 respectively). A dependent *t*-test was conducted to compare the pre- and post-IRLSRS mean values (Table 1). A confidence interval of 95% and alpha-level of 0.05 were used in this process. The dependent *t*-test revealed a statistically significant difference between the mean IRLSRS scores for pre- and post-NIR intervention. The mean change in the IRLSRS score from pre- to post-testing was 9.7 ± 7.7. The minimum clinically important difference (MCID) value for the IRLSRS is three points (Allen, 2013).

While an added total numeric value is computed to express the IRLSRS score, the sub category components are ordinal level values. Rather than completely relying on the *t*-test for analysis, a Wilcoxon signed rank test was performed (Table 2). As Table 2 demonstrates, a significant improvement in symptoms was supported by this analysis as well.

VAS

Fourteen of the twenty-one subjects had lower VAS scores after receiving the NIR treatment, seven subjects had higher scores. The baseline mean VAS value for the subject pool was 11.9 mm ± 19.6 while the post-intervention mean score was 22.1 mm ± 27.6. The MCID for the VAS score is 14 mm (Tashjian, Deloach, Porucznik, and Powell, 2009). These VAS data were examined for normality and the Shapiro–Wilk test revealed that the data were not normally distributed (p = 0.000). Due to the lack of normality in the data, the Wilcoxon signed rank test was used and demonstrated no significant difference in the subject's experience with pain following our intervention protocol ($p = 0.280$). As can be seen from the VAS values, pain was not a significant factor in the subjects' symptom set prior to the intervention.

Table 1. Paired samples' *t*-test for international restless legs syndrome rating scale (IRLSRS) scores.

	Paired differences							
				95% Confidence Interval (CI)				
	Mean	Standard deviation	SEM	Lower	Upper	*t*	*df*	Sig.(2-tailed)
Pre-post (IRLSRS)	9.7	7.7	1.7	6.2	13.2	5.815	20	0.000

SEM, Standard Error of the Mean.

Table 2. Wilcoxon signed rank test for pre- to post-IRLSRS scores (descriptive included).

Ranks

		N	Mean rank	Sum of ranks
Pre-post-IRLSRS	Negative ranks	16	10.50	168.00
	Positive ranks	2	1.50	3.00
	Ties	3		
	Total	21		

Test statistics

	Post-IRLSRS–pre-IRLSRS
Z	−3.596e
Asymp. sig. (2-tailed)	0.000

Descriptive statistics

	N	Minimum	Maximum	Mean	Standard deviation	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Standard error
Pre IRLSRS	21	11.00	34.00	26.5	5.4	−1.116	0.501
Post-IRLSRS	21	0.00	34.00	16.8	8.1	0.044	0.501
Valid *N* (listwise)	21						

Table 3. Wilcoxon signed rank test for ankle-brachial index (ABI) values.

Ranks

Right lower extremity ABI		*N*	Mean rank	Sum of ranks
Post-RABI–Pre-RABI	Negative ranks	3[a]	15.3	46.00
	Positive ranks	18[b]	10.3	185.00
	Ties	0[c]		
	Total	21		

[a] Post-RABI < Pre-RABI.
[b] Post-RABI > Pre-RABI.
[c] Post-RABI = Pre-RABI.

Test statistics[a]

	Post-RABI–Pre-RABI
Z	−2.417[b]
Asymp. sig. (2-tailed)	0.016

[a] Wilcoxon signed rank test.
[b] Based on negative ranks.

Ranks

Left lower extremity ABI		*N*	Mean rank	Sum of ranks
Post-LABI–Pre-LABI	Negative ranks	6[a]	7.3	43.5
	Positive ranks	13[b]	11.3	146.5
	Ties	2[c]		
	Total	21		

[a] Post-LABI < Pre-LABI.
[b] Post-LABI > Pre-LABI.
[c] Post-LABI = Pre-LABI.

Test statistics[a]

	Post-LABI–Pre-LABI
Z	−2.075[b]
Asymp. sig. (2-tailed)	0.038

[a] Wilcoxon signed rank test.
[b] Based on negative ranks.

SWM test

The mean value of the thinnest monofilament sensed in baseline testing for the subject pool was 4.37 on the right foot and 4.32 on the left foot. Post-testing mean monofilament gauges were 4.28 on the right foot and 4.28 on the left. To have normal sensation, one must be able to sense the monofilament thickness of 3.61 (Jeng, Michelson, and Mizel, 2000).

A combined total of 378 locations were tested; 9 locations on the plantar surface of both feet for each subject (18 locations/subject × 21 subjects = 378 locations). Data were combined to compute an average sensory score for each subject. This was done for both the right and the left foot. Data were checked for normality and the normality was not demonstrated. Therefore, the pre- to post-change in the sensory score for each foot was compared using the Wilcoxon signed rank test. Significant improvement in sensation was seen in both feet (p = 0.000 for each foot). Pre-intervention, there were 63 of 378 locations tested where protective sensation was absent. Seven individual subjects were represented by these 63 sensory deficit locations. Post-NIR treatment, testing demonstrated that the number of locations with sensation less than protective had decreased from 63 to 51 and the number of subjects with deficient sensation in at least one tested location had dropped to five. Stated another way, two subjects gained protective sensation in their feet. See the Discussion section of this paper for further comments related to interpreting these data.

ABI

Before any intervention was applied, the ABI values recorded for the majority of subjects were considered within normal limits (≥0.9). The mean values for both right and left limb ABI's were computed pre- and post-testing. The mean ABI values for the right and left limbs at baseline data collection were 1.09 ± 0.17 ($\sigma\bar{x}$ = 0.04) and 1.06 ± 0.21 ($\sigma\bar{x}$ = 0.05). Post-testing mean ABI values were 1.16 ± 0.14 ($\sigma\bar{x}$ = 0.03) for the right limb and 1.13 ± 0.19 ($\sigma\bar{x}$ = 0.04) for the left. Tests for normality revealed that the pre-ABI data lacked normality (p = 0.001). Due to the lack of normality in the ABI data, the Wilcoxon signed rank test was used. The ABI scores for both lower extremities improved significantly pre- to post-intervention (p = 0.016 for the right and 0.038 for the left). A toe/brachial index (TBI) can be used to further evaluate the degree to which peripheral vascular disease (PAD) is present. This additional test is indicated when the ABI exceeds 1.4 or is less than 0.9 (Aboyans et al, 2012). While we had no subjects with excessively high ABI values, we did see subjects with ABI values below 0.9. We did not, however, employ the TBI in our research since our work was not directly related to PAD, but rather to RLS. Figure 4 demonstrates the baseline ABI values for the subjects in the study.

Only one subject had abnormal pre-testing ABI values. This abnormality was present in both lower limbs (right = 0.55, left = 0.41). This subject's post-testing ABI values were significantly improved (right = 0.91, left = 0.87), so much that the right limb (at the end of intervention) was considered to have an ABI value within normal limits while the left limb was near that threshold.

Due to the outlier nature of the one subject's data, we re-calculated the statistic with this subject's data removed. The result of that re-calculation revealed that the pre- to post-change in ABI on the right remained significant (p = 0.027). The pre- to post-ABI change with this subject's data removed for the left resulted in slightly less than a significant difference (p = 0.067).

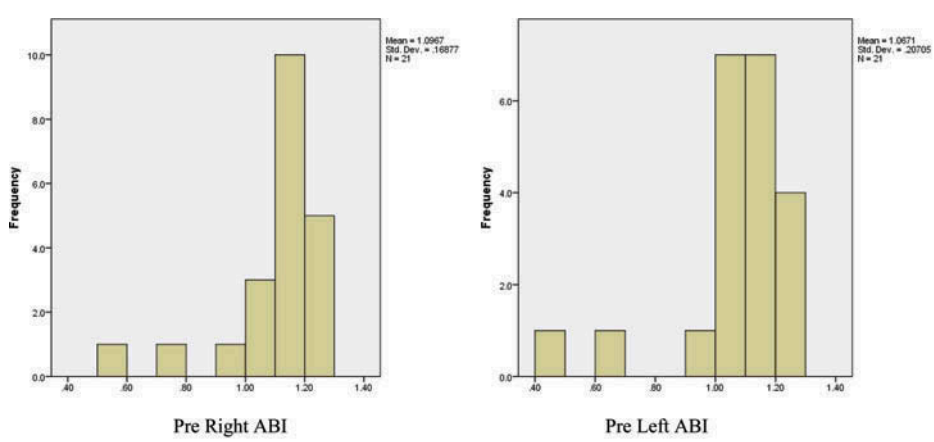

Figure 4. ABI baseline histogram.

Other vascular measures (sonographic)

No change was observed in any of the other vascular measures for which data were collected. Peak systolic velocity, end-diastolic velocity, RI, and PI showed no difference when comparing pre- and post-testing values.

Discussion

We realize that our one group design carries with it threats to internal validity. It is possible that events other than the intervention affected the measured changes. History and maturation effects would be the most likely threats to the internal validity of the study. It is also possible, in the absence of a comparison group, that improvements seen in the IRLSRS were related to a placebo effect. However, the improvements in ABI and sensory scores would not have been facilitated by a placebo effect.

Threats to external validity are present in this study. The lack of probability sampling, random assignment, and a comparison group threaten the degree to which these results can be generalized to the greater population of persons suffering from RLS.

Previous research that included control groups has demonstrated similar changes in response to NIR intervention (Oertel et al, 2007; Mitchell, Myrer, Johnson, and Hilton, 2011). Secondly, the ethics of withholding treatment from any of these volunteer/uncompensated subjects motivated us to choose the one group design.

Despite the over six decades of associated study, the pathophysiology explaining RLS remains unclear. The two most widely accepted pathophysiologic theories are a central nervous system (CNS) dopamine imbalance and iron deficiency (Einollahi and Izadianmehr, 2014). These theories suggest a centrally mediated cause. In contrast, some literature supports the idea that RLS is a peripherally mediated condition. This evidence suggests that RLS may be a neuropathic related condition. Forty-five percent of those suffering from RLS have existing peripheral neuropathies (Polydefkis et al, 2000). RLS has been associated with the latter stages of pregnancy, venous insufficiencies, and peripheral embolisms. Links to these conditions, in combination with the relief of symptoms provided by vasodilator treatment, support a vascular mechanism for RLS (O'Keeffe, 1996). The vascular theory includes the idea of impairment in local circulation leading to ischemic changes or a build-up of toxic metabolites accompanied by microvascular changes in the superficial veins, leading to unpleasant sensory experience (Jones and Derodra, 1997). In an attempt to better understand the physiology of RLS, we chose to include sensory (SWM test) and vascular measures (ABI scores and arterial sonographic imaging), respectively, in addition to the pain (VAS) and functional (IRLSRS) measures that have been utilized in previous studies.

Our subjects, when explaining their past experiences with RLS, frequently expressed feelings of discomfort in their lower extremities throughout the day. Although this discomfort was often quite significant, the subjects did not interpret this experience as pain. The mean pain rating for the subject pool was minimal in baseline testing and changed insignificantly following four weeks of NIR treatment. These findings suggest that pain is not a significant factor in the symptoms associated with RLS. While unpleasant sensations associated with RLS may cause a great amount of discomfort and an unyielding urge to move, the perception in this group of subjects was not pain.

The sensory data collected in this study clearly indicate that some of our subjects had neuropathy. We elected to allow these subjects to be included in the study since it has been demonstrated that RLS is more prevalent among patients with some forms of neuropathy (Hattan, Chalk, and Postuma, 2009). One of our earlier studies (Guffey, Motts, Payne, and Clough, 2014) demonstrated that peripheral neuropathy could be positively affected by NIR light. We believed that it might also be possible to see similar improvements in patient who presented with RLS and peripheral neuropathy. This was one of the primary reasons why sensation testing was included in this design.

SWMs are a useful tool for examining light touch/pressure sensation of the skin. The monofilament thickness is logarithmic in difference from one monofilament to the next. Normal sensation for the plantar surface of the foot is measured by the 3.16 monofilament, requiring 0.4 gram of force to bend. Protective sensation is measured by the 5.07 monofilament, requiring 10 grams of force to bend. The thickest monofilament is 6.65, requiring 300 grams of force to bend. Persons who have protective sensation will sense potential injury if they step on a damaging object, such as a nail or a tack. Persons without protective sensation will not perceive stimulus such as injurious, and will not attempt to off-load the pressure, often leading to tissue damage (Birke and Sims, 1986). One can measure sensation at multiple points; in the case of this study, we measured nine points on the plantar surface of each foot. One way to report these data would be to find the mean sensation for each foot. This is of interest, because in this study, the mean sensation improved toward normal sensation. Clinically, this is of little use. A person can have normal sensation at eight of the nine points and have no protective sensation at one point. Such a person is at risk of a

wound where protective sensation is absent, putting the entire limb at risk. This person's mean sensation could be normal, but the average sensation does not reflect the person's real risk of skin damage at a specific site. Thus, we also reported the total number of points across our subjects where protective sensation was absent. Before intervention, seven subjects lacked protective sensation in at least one point. A total of 63 points lacked protective sensation in these seven subjects. After treatment, two people had improved to the point that they had protective sensation everywhere that we tested. Additionally, the total number of points without protective sensation was reduced to 51. All but one subject who lacked protective sensation showed at least some improvement in sensation.

Mitchell, Myrer, Johnson, and Hilton (2011) were the first to use NIR as intervention in the management of RLS. Similar to our study, Mitchell, Myrer, Johnson, and Hilton (2011) provided each subject in the treatment group a total of 12 treatment sessions over four weeks. Much like the results that we obtained in our study, those who received NIR showed a decrease in symptoms and improvement in function. The mean decrease in IRLSRS scores from pre- to post-testing was 9.7 in our study and 12.7 in the study conducted by Mitchell, Myrer, Johnson, and Hilton (2011) These values are three to four times the MCID value for the IRLSRS and enough to drop the severity level by one full category (e.g. from "moderate" to "mild") (Allen, 2013). This decline in severity is comparable to the effects of the gold standard dopaminergic agonist treatment (Oertel et al, 2007).

Mitchell, Myrer, Johnson, and Hilton (2011) proposed that the mechanism behind the success of the NIR treatment could be related to its ability to increase nitric oxide (NO) generation. In a previous study, we conducted examination of the effects of NIR as intervention for peripheral neuropathy, we also proposed NO to be a factor in the successful outcomes that were observed (Guffey, Motts, Payne, and Clough, 2014). NO is a free radical whose production can be stimulated by the application of NIR energy. Two mechanisms of action in stimulating an increase of NO with the use of NIR have been reported. One possible mechanism is that NIR activates NO synthase (NOS-3), an enzyme that catalyzes the degradation of L-arginine to L-citrulline, and NO (Mitchell, Myrer, Johnson, and Hilton, 2011; Buga, Gold, Fukuto, and Ingarro, 1991). The other mechanism is that NIR acts to release stores of NO, which are bound to hemoglobin in the blood. It is suggested that NIR is the key to this unbinding process (Vladimirov et al, 2000). The increased availability of NO is expected to lead to a cascade of events on the cellular level. The result of these events is smooth muscle relaxation within vessels. As these vessels relax, they dilate (vasodilation), thus increasing perfusion and allowing greater nutrient and oxygen delivery to the affected areas (Bode-Böger et al, 1996) NO also acts as a neurotransmitter and can influence neurotransmission and nerve conduction properties (Culotta and Koshland, 1992). The unpleasant symptoms associated with RLS could be secondary to decreased tissue perfusion. This might explain why walking or moving about often relieves these uncomfortable sensations as these activities increase blood flow (Clifford and Hellsten, 2004; Thijssen et al, 2009).

In our previous research (Guffey, Motts, Payne, and Clough, 2014) on improving sensation in those with peripheral neuropathy, we suggested that the improvement in sensation we observed was as a result of increased perfusion. In our current study, we found the delivery of NIR to have a positive effect on the subjects with sensory deficits. The means of the subject pool lacked normal sensation but many had intact protective sensation. Normal sensation is defined as having the ability to sense the pressure of a 3.61 gauge monofilament when it is applied to a select location on the planter surface of the foot (McPoil and Cornwall, 2006; Nurse and Nigg, 1999). More clinically important is one's ability to be able to detect the 5.07 monofilament. Those who cannot sense the pressure of this monofilament are considered to lack protective sensation in the tested location (Jeng, Michelson, and Mizel, 2000; Olmos et al, 1995). While there was a slight improvement in sensation as demonstrated by the post-intervention means of the subject pool, more interesting were the changes in areas that lacked protective sensation. Those areas in baseline testing where the subjects lacked the ability to sense a noxious and harmful stimulus were positively affected by the NIR treatment. A 20% increase in locations with protective sensation was observed following the intervention. This improved sensory ability may serve to help these subjects avoid common conditions associated with impaired protective sensation such as ulcer formations, joint deformities, and even amputation. As in our previous peripheral neuropathy research, (Guffey, Motts, Payne, and Clough, 2014) we again propose that improved circulation could be responsible for such an improvement. If the theory that RLS could be a peripherally mediated condition is correct, then it is possible that addressing circulatory deficits could be an effective intervention.

We attempted to measure the effects of NIR on the circulatory system. Measuring NO directly can be difficult due to its high reactivity and oxidative

properties as well as its very short half-life (Wennmalm, Benthin, and Petersson, 1992). For these reasons, we chose to measure the ABI, systolic and diastolic velocities, RI, and PI of the major vessels in the lower extremities. The ABI was the only -measure in which change from pre- to post-testing was observed. All other vascular measures showed minute to no differences from their baseline values.

While the majority of our subjects had normal ABI values, one subject had a significantly abnormal ABI in baseline testing. This subject's ABI improved dramatically with NIR treatment. We believe that the significant change observed in ABI values was due to NIR administration. While the pathophysiology behind RLS is still unclear, it is becoming more evident that multiple mechanisms are likely involved, each uniquely contributing to the symptoms associated with the condition. Currently, the most accepted explanations seem to be that the condition is one that is centrally mediated. For this reason, treatment for RLS has been limited to pharmaceutical options, often accompanied by various adverse effects. Recent research, however, suggests alternate treatment options for the condition. Some degree of vascular abnormality seems to contribute to the symptoms associated with RLS.

Conclusion

This research suggests that the application of NIR light to the lower extremities of those suffering from RLS may improve the symptoms (as measured by the IRLSRS) associated with the condition. NIR may be an effective non-pharmaceutical treatment option for those suffering from RLS. This research does not explain the mechanisms for this response, but we suggest that benefits achieved may be a result of IR light's relationship with NO. Additional research is needed to establish the exact mechanism of action associated with NIR's therapeutic properties.

Declaration of interest

The authors report no declarations of interest.

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