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Use of actigraphy to objectively measure motor restlessness in Restless Legs Syndrome

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USE OF ACTIGRAPHY TO OBJECTIVELY MEASURE MOTOR RESTLESSNESS IN RESTLESS LEGS SYNDROME

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ABSTRACT

Restless Legs Syndrome (RLS) is a disorder characterized by disagreeable leg sensations, usually prior to sleep onset, which cause an almost irresistible urge to move the legs. A characteristic feature of this disorder is that the movements are partially or completely relieved with leg motions. Attempts to find the underlying pathology have been unsuccessful. Thus, there are no objective physiological tests to diagnose this condition. Using the Suggested Immobilization Test (SIT), the current study attempted to validate a new and practical method for quantifying the motor symptoms of RLS, actigraphy. To this end, the SIT with actigraphy was evaluated for its usefulness as either a diagnostic or screening tool using indices of sensitivity, specificity, false positive and false negative rates, taking base rates into account. The actigraphic SIT was not found to be an effective diagnostic or screening tool. Further advancements in actigraph technology and future research may eventually provide evidence of an actigraphic SIT being an effective screening or diagnostic tool, despite the findings in the present study. Limitations in actigraph technology were encountered. These limitations are described, as well as the implications for the current study and similar existing research.

INTRODUCTION

Restless Legs Syndrome (RLS) is a disorder characterized by disagreeable leg sensations, usually prior to sleep onset, which cause an almost irresistible urge to move the legs. A characteristic feature of this disorder is that the movements are partially or completely relieved with leg motions. Attempts to find the underlying pathology of RLS have been unsuccessful. Thus, there are no objective pathophysiological assessments to diagnose this condition. The diagnosis of RLS remains a clinical one based on the patient's self-report of symptoms. Identifying any objective means of quantifying RLS symptomatology could be used diagnostically and aid in research of RLS. Objective testing could provide for development of objective screening tests or aid in comparing participant characteristics in research studies.

Ongoing research is attempting to develop objective tests of RLS symptoms. To that end, two tests have been developed to measure the motor restlessness experienced by RLS patients, the Suggested Immobilization Test (SIT) and the Forced Immobilization Test (FIT). The ability to use these tests both clinically and for research purposes is somewhat limited by the specialized equipment and staff time/resources needed to perform these. Thus, the current study aimed to validate a new and more practical method for quantifying the motor symptoms of RLS,

actigraphy. Additionally, whether or not the SIT or the FIT has adequate sensitivity and specificity to discriminate between RLS and normal individuals has proved debatable. To this end, the current study aimed to evaluate the SIT with actigraphy using indices of positive and negative predictive values, taking base rates into account.

First, characteristics of RLS identified in research and clinical samples will be described in detail and related to current diagnostic criteria. Features and conditions associated with RLS will be described. Then, actigraphy will be discussed, with particular emphasis on how this methodology is applicable to the assessment of RLS symptoms. Next, specific research findings pertinent to the current study will be described. Last, the methodology and findings from the current study are detailed.

REVIEW OF LITERATURE

Clinical Features

Restless Legs Syndrome (RLS), as defined by the ASDA (ASDA, 1990), is a disorder characterized by disagreeable leg sensations, usually prior to sleep onset, that cause an almost irresistible urge to move the legs. The ASDA delineates six diagnostic criteria for RLS, the first three of which are necessary for a diagnosis. The criteria are: (1) a complaint of an unpleasant sensation in the legs at night or difficulty in initiating sleep; (2) disagreeable sensations of "creeping" inside the calves often associated with general aches and pains in the legs; (3) the discomfort is relieved by movement of the legs; (4) polysomnographic monitoring demonstrates leg movements at sleep onset; (5) no evidence of any medical or psychiatric disorders that account for the leg movements; (6) other sleep disorders may be present but do not account for the symptom.

The ASDA categorizes severity into three categories. Mild refers to symptoms that occur episodically with no more than a mild disruption of sleep onset that does not cause the patient significant distress. Moderate RLS refers to symptoms that occur less than twice a week, with a significant delay of sleep onset, moderate disruption of sleep and mild impairment of daytime function. In severe RLS, the symptoms occur three or more times a week, with severe disruption of nighttime sleep

patterns and marked daytime symptoms. Also, duration criteria are delineated: acute (two weeks or less), subacute (more than two weeks but less than three months) and chronic (three months or longer).

RLS patients often have difficulty describing the nature of the uncomfortable sensations. Some terms most often used by patients to describe the sensations include “creeping”, “crawling”, “itching”, “tingling”, “prickling”, or “pins and needles” (ASDA, 1990; Ekbom, 1960; Walters & Hening, 1987). Researchers often use the term paresthesias or dysesthesias, which simply imply abnormal sensations. These uncomfortable sensations develop or are exacerbated during periods of motor inactivity and are relieved by agitated motor activity. For many RLS patients, sleep onset is particularly difficult to attain due to the increase in symptoms and symptom severity associated with lying still in bed, such that they may have to get out of bed and walk to relieve their discomfort. Pelletier, Lorraine and Montplaisir (1992) studied whether the motor movements exhibited were a direct consequence of the uncomfortable sensory events by examining the temporal relationship between these events. These researchers found that while almost all of the sensory events were associated with leg movements, determined by a sensory event occurring either 5 seconds before or after the leg movement, there were some

sensory events without motor events. Additionally, only half (49%) of the motor symptoms were associated with sensory events, indicating that some were not in an effort to relieve discomfort. Thus, the authors concluded that the sensory and motor events in RLS represent independent manifestations of a common neural dysfunction.

RLS symptoms have been found to be worse in the evening or at night, and worse when lying or sitting during the day or the night (Ekbomb, 1946; Ekbomb, 1960). Part of this worsening appears to be due to the fact that people tend to sit and lie down more in the evening hours than during the day. However, there is also evidence for an independent circadian factor contributing to the nighttime worsening (Montplaisir, Boucher, Gosselin, Gaetan, & LaVigne, 1995; Trenkwalder, et al., 1995). Research examining this feature of RLS is discussed later in the current paper.

Another characteristic of RLS relevant to the current study is the degree of lateralization of symptoms. Historically, most patients have been reported as having bilateral sensory and movement symptoms. Montplaiser et al. (1997) found that forty-two percent of patients reported at least some lateralization of sensory and motor symptoms to either the right or the left leg. Additionally, Montplaiser et al. (1998) found that movements were predominantly bilateral (mean index of bilateral

movements=52/hour), though there were a number of movements exhibited exclusively on the right leg only (mean index=14/hour) or on the left leg only (mean index=10/hour). Of the sixteen RLS patients who participated in their study, there was one RLS patient for whom the movements were predominantly or exclusively exhibited on the right and one whose movements were such on the left. Thus, the above findings confirm that many patients have predominantly bilateral movements; however, some patients do have some lateralized movements and some patients have predominantly lateralized movements.

Associated Features and Conditions

Prevalence. Ekbom (1945) first estimated the prevalence of RLS in the normal population as being 5%. Across studies, the prevalence of RLS in the general population has been estimated to be from 2-15%; however, definitive data are not available (ASDA, 1990). Much of the variability in the rates described is due to vast differences in methodology employed, from face-to-face interviewing performed by trained professionals (Rothdach, Trenkwalder, Haberstock, Keil, Berger, 2000) to a single RLS question added to a survey of multiple phenomena (Phillips et al., 2000). Most studies have found rates of approximately five percent.

Age of Onset. To date there have been no longitudinal studies performed to definitively identify the typical age or age range

in which RLS develops. Thus, most studies reporting age of onset in RLS are based on retrospective self-report. Not surprisingly, vast differences reported in the literature concerning the age of onset of RLS have been largely due to methodological differences. RLS has typically been considered to be a disorder of the middle to older age population. However, some studies have suggested that this is inaccurate. RLS patients in a study by Ondo and Jankovic (1996) reported an average age of onset of 34 years, though there was a high degree of variability (standard deviation of 20.3). In another study (Walters et al., 1996), more than one third of the RLS patients reported experiencing their first symptoms before the age of 10, and 43% had their first symptoms before the age of 20. These findings suggest that RLS may not be predominantly a disorder of middle age, but a condition that has a much earlier onset than previously identified. One hypothesis suggested for this discrepancy is that young persons with the RLS symptoms are initially misdiagnosed as experiencing "growing pains" or the symptoms were thought to by psychogenic (Walters et al., 1996). Additionally, given that the symptoms have often been found to increase in severity with age for many individuals, it is possible that RLS is present, but not diagnosed, in younger individuals who may not present for treatment until the symptoms become severe.

Clinical Course. RLS symptoms can have a varied course, with some patients reporting that the symptoms increase over time and others reporting a constant degree of symptom severity. Many patients report that symptoms remit occasionally. In a questionnaire study of 138 patients with RLS (Walters et al., 1996), 15% of the patients reported a previous total remission of symptoms of a month or more. Thus, the symptoms may have a waxing and waning course, though there have been no findings to explain this information.

Associated Conditions. Attempts to find biological markers have yet to be successful. Although there have been abnormalities identified in some subsets of persons with RLS, the sensitivity and the specificity of these has not been sufficient for their usefulness as diagnostic markers. RLS has been found to exist at higher than normal rates in a number of medical conditions: 11% of pregnant women, 15-20% of uremic patients, and up to 30% of patients with rheumatoid arthritis (ASDA, 1990). RLS has often been associated with another, related condition, namely periodic limb movement disorder (PLMD). In one study, approximately 80% of RLS patients had co-morbid PLMD (Montplaisir et al., 1997). Individuals for whom there is no identifiable medical cause of this symptom are referred to as having primary or idiopathic RLS. Individuals reporting symptoms of RLS, but with an identified cause are

generally referred to as having secondary RLS. There do not appear to be any differences in symptom presentation between the primary and secondary forms of the disorder (Walters, 1995).

Periodicity of Movements while Awake

One difficulty often encountered in the literature on RLS is that the ASDA criteria do not adequately describe the motor symptoms of this disorder. The lack of adequate descriptive criteria has led to inconsistent usage of the diagnosis. For example, some researchers have utilized the term RLS as if it were a symptom or form of PLMD. This stems from previous beliefs that RLS always occurred in conjunction with PLMD, and that a diagnosis of PLMD would support a diagnosis of RLS; a PLMS index greater than five or ten has been previously used by some as an "objective diagnostic criterion" of RLS (Walters, Picchietti, Ehrenberg, Wagner, 1994). Given the frequency this association occurs in the RLS literature, a brief review of the clinical characteristics of PLMD is warranted to highlight the similarities and differences in these overlapping disorders and patient populations.

Some researchers have used the terms PLMD interchangeably with periodic limb movements of sleep (PLMS). Other researchers have used PLMD to refer exclusively to patients meeting the diagnostic criteria set forth by the ASDA, and used PLMS to refer to the repetitive limb movements that occur during sleep

in some individuals without necessarily meeting the diagnostic criteria. For the purposes of this paper, PLMD will refer only to those individuals meeting diagnostic criteria for the disorder and PLMS will refer to any movements occurring during sleep that conform to scoring criteria for periodic limb movements (i.e., as opposed to non-periodic movement activity), both of which are described in greater detail below.

PLMD is characterized by periodic episodes of repetitive and highly stereotyped movements that occur during sleep at a rate of five per hour or greater (i.e., PLMS). In PLMD, the movements do not occur during the day and persons with PLMD may or may not experience any daytime symptoms, such as hypersomnolence. Coleman's criteria (Coleman, 1982) have become standard for defining and scoring PLMS. The criteria allow for scoring a limb movement as a PLMS when it occurs as a part of a series of at least four consecutive movements that are separated by at least 4, but not more than 90 seconds. Additionally, the duration of the movement must be between 0.5 and 5.0 seconds. A PLMS index refers to the average number of PLMS per hour of sleep, with an index of more than 5 per hour being pathological and qualifying for a PLMD diagnosis.

Researchers and clinicians, who have conceptualized RLS as being a symptom or form of PLMD, postulate that not all persons with PLMD have RLS, but that all RLS patients have PLMD.

However, research in these populations has documented that while many patients with RLS do indeed have PLMS, many do not show evidence of PLMD or do not have sufficient PLMS to warrant a diagnosis of PLMD (ASDA, 1990). For example, Montplaiser et al. (1997) found that of 133 patients diagnosed with RLS, 20% had PLMS index lower than 5 (i.e., PLMS index in the normal range). Thus, the PLMS index alone would not be either necessary or sufficient to diagnose RLS in patients complaining of sensory and motor symptoms associated with periods of inactivity. PLMD represents a nosological and clinical entity that can be differentiated from RLS; though these conditions are often overlapping, RLS is primarily a problem experienced during wakefulness just prior to sleep onset, while PLMD is primarily a phenomenon occurring during sleep.

As described, the predominant symptoms in RLS occur during wakefulness. Involuntary movements similar to PLMS have been reported to exist during wakefulness in RLS patients (Brodeur, Montplaisir, Godbout, Marinier, 1988; Montplaisir, Godbout, Boghen, De Champlain, Young, 1985; Montplaisir & Godbout, 1989; Pelliter, Lorrain, & Montplaisir, 1992). The movements seen in PLMD are highly stereotyped movements. One similarity between PLMS and the involuntary movements seen in RLS patients is that they are similar in appearance. Specifically, the movements are typically dorsiflexions of the big toe with fanning of the small

toes, accompanied by flexions of the ankles, knees and thighs. PLMS are, by definition, periodic, but the movements exhibited by RLS patients may be either periodic (Pollmacher & Schulz, 1993; Walters et al., 1988) or aperiodic (Walters, 1995). The involuntary movements while awake occur almost exclusively at rest and cease with activity. Moreover, PLMS are rarely rapid enough to be considered myoclonic, while the involuntary movements seen in waking RLS patients can be myoclonic, though they are often more sustained than PLMS (ASDA, 1990). Last, many of the movements in RLS are voluntary movements intended to alleviate paresthesias. Thus, the movements in RLS both during wakefulness seem to be both voluntary and involuntary.

Relevant Research Findings

In response to an evident inconsistency in the definition of RLS, a large international study group was formed and identified essential criteria for the diagnosis of RLS. The study group noted that the ASDA criteria do not adequately characterize the motor restlessness in RLS or the involuntary motor movements evidenced in RLS patients during periods of wakefulness (Walters, 1995). The group delineated four minimal clinical characteristics necessary for the diagnosis: (1) a desire to move the limbs, usually associated with paresthesia/dysesthesias; (2) motor restlessness (i.e., use of various motor activities to relieve the discomfort); (3)

symptoms that are worse or exclusively present at rest (e.g., lying, sitting) with at least partial and temporary relief by activity; (4) symptoms that are worse in the evening or at night. Several other clinical features were identified that are commonly seen in RLS patients, though they are not necessary for the diagnosis: (1) sleep disturbances and its consequences; (2) involuntary movements which could refer to periodic limb or leg movements in sleep or involuntary leg movements while awake and at rest; (3) no neurological abnormalities in the primary form, though these may be present in the secondary form; (4) the clinical course is variable, but most of the more severely affected patients are middle to older age, and the condition is progressive; (5) a familial pattern may be present.

Researchers (Brodeur et al., 1988; Pelletier, Lorrain, Montplaisir, 1992) attempting to quantify the motor symptoms in RLS designed two tests, the Forced Immobilization Test (FIT) and the Suggested Immobilization Test (SIT). For the SIT test, patients sit or lie motionless on a bed with their legs outstretched and eyes closed while electromyogram recordings of the anterior tibialis muscles are recorded bilaterally. This test was first employed in 1988 to measure the therapeutic effects of L-dopa in RLS patients (Brodeur et al., 1988). The FIT employs greater leg immobilization, where the patient sits on a stretcher with both legs immobilized in the extended

position. The stretcher prevents movement of the legs and limits the movement of the ankle and the foot.

Montplaisir et al. (1998) examined the sensitivity and specificity of the SIT and the FIT in differentiating sixteen RLS patients from sixteen age- and sex- matched control subjects. RLS patients had three times more leg movements during the SIT than did normal controls, with a mean of 76 for RLS patient versus 27 for controls. Additionally, both RLS patients and controls evidenced more movements during the second half of the hour-long test, but the difference was significant only in the RLS patients. On the FIT, RLS patients did have more movements than controls, but the difference was statistically significant only when comparing each group on the second half of the test; the differences between the two groups on the first half of the test and on the entire test were not statistically significant. Using receiver-operator characteristic curves to obtain cutoff scores, Dawson-Saunders & Trapp (1994) suggested that a cutoff of 40 movements per hour on the SIT or of 25 movements on the FIT resulted in the highest overall sensitivity and specificity of the two tests. The SIT proved to differentiate between the RLS patients and the controls better than the FIT, with a sensitivity of 81% and a specificity of 81%, compared to 69% and 56%, respectively, for the FIT. The authors posit that the movements exhibited during

the SIT may represent combinations of different types of movements, both involuntary periodic leg movements and voluntary movements to relieve discomfort, and that during the FIT the voluntary movements are decreased due to external leg restraints; also, the decreased movement may not have allowed for as much relief from discomfort and that the patients may have not moved as much as a result. However, they provide no evidence to support this claim.

Two explanations of the finding that RLS symptoms are worse in the evening and at night are that either a circadian factor modulating these symptoms exists, or that people tend to lay down more in the evening and night time hours, or a combination of the two. To examine these hypotheses, Montplaiser et al. (1995) conducted a study to examine sensory symptoms and motor symptoms in the morning and evening in RLS patients. The researchers utilized the SIT to measure motor symptoms, and required the patients to press a button each time they experienced a paresthesia in their legs similar to those experienced at home, to assess subjective sensory symptoms. The SITs were performed once in the morning and again in the evening, with the evening SIT being lengthened from thirty minutes to an hour to examine the role that immobility duration plays in the severity of motor and sensory symptoms. The results indicated that the duration of the immobility did result

in a statistically significant exacerbation of both motor and sensory symptoms. However, neither the sensory nor motor symptoms were statistically greater during the evening than the morning SIT. The data suggest that time of day effects may not be important in differentiating RLS patients from normal controls in relation to motor restlessness, but that it would be useful to increase the duration of the SIT recording from 30 to 60 minutes.

Researchers utilizing the SIT to measure daytime motor restlessness in RLS patients have often used Coleman's PLMS criteria to score movements. One alteration often employed in daytime SIT recording is extending the upper duration limit of the movement to 10 seconds because a large number of movements during wakefulness exceed 5 seconds (Montplaisir et al., 1998). However, it is unclear how appropriate this methodology is given that not all movements by RLS patients are involuntary or periodic. Further, it is unknown how the use of PLM criteria to score movements affects the sensitivity and specificity of the SIT.

Sleep laboratories rely on a patient's self-report of symptoms to diagnose RLS. Currently, the only objective measures of motor symptoms experienced by persons with RLS are the SIT and the FIT. Prior research on the sensitivity and specificity indicates that the SIT has greater promise as an

objective means of differentiating normal subjects from individuals with RLS. However, the SIT tests require considerable staff time to perform and analyze results. The latter problem also impedes the ability of researchers to explore ways to increase the sensitivity and specificity of the SIT. Thus, there is a need for an objective measure of RLS that could be completed with minimal staff involvement and/or without the use of specialized staff. The current study attempted to evaluate the appropriateness of using actigraphy instead of a polygraph to complete a SIT test and examined factors potentially related to the ability of the SIT to objectively differentiate RLS patients from control subjects (i.e., persons without RLS or other movement disorders). This novel method for examining RLS, if validated, could allow for long-term night-to-night quantification of RLS symptomatology, a task that is not feasible with standard polysomnography.

Actigraphy

The current study proposed to validate the use of actigraphy to examine RLS motor symptoms. Actigraphs are small, portable devices that detect physical motion, generate an internal signal each time they are moved, and store that information. They are typically used to measure general or random motor restlessness in order to evaluate rest-activity cycles. Actigraph recordings integrate the amplitude values of

an actigraphic signal over a defined time period, usually 10, 30 or 60 seconds, and algorithms can be used to estimate the sleep architecture of an individual. The user can set the frequency desired for integrating the amplitude values of the signal to produce output from every 2 to every 60 seconds.

In the area of sleep and sleep disorders, actigraphy is typically used to estimate sleep onset and duration based on the relative lack of movement activity during sleep. Actigraphy has been shown to best estimate sleep duration, sleep efficiency and waking after sleep onset; it is less accurate at estimating sleep onset latency (ASDA Report, 1995). Research evaluating the usefulness and validity of actigraphy in RLS and PLMD patients, other movement disorders, or insomnia indicates that actigraphy provides a poor estimate of sleep parameters. In all of the latter conditions, the patient may be having movements while asleep, or may be still while lying awake for a prolonged period of time, thereby inaccurately estimating sleep. However, while actigraphy is poor in evaluating the sleep of these patient populations, it is not poor at detecting movement.

Actigraphy provides a measure of general motor activity, and may not accurately measure short, distinctive movements like PLMS. In 1995, Kazenwadel et al. studied the reliability and validity of using actigraphy to measure periodic limb movements. The results showed that there was a high correlation (.91)

between the EMG recording and the actigraph recordings, but actigraphy did underestimate the number of PLMS, with the actigraph recording 30% fewer movements than were identified by EMG recordings. However, one difference between these two methodologies may explain the underestimation of PLM activity by actigraphy: Recordings of tibialis electromyogram monitor movements made by either leg independently or by both legs simultaneously, but the study employed the use of one actigraph placed on one leg, which is the methodology typically employed in actigraphy. The underestimation of PLM activity by the actigraphs may have been due to the use of one actigraph on one leg, which may not have been detected unilateral movements on the leg opposite the actigraph. Therefore, this investigation did not adequately assess the sensitivity of actigraphy as a measure of PLMS. No investigation to date has attempted to evaluate actigraphy as a measure of RLS movements.

Study Objectives

The goals and implications for the current study were as follows. First, validate the use of actigraphy to objectively quantify motor restlessness in RLS, using the actigraphy and the polygraph simultaneously. Second, determine whether or not using PLM criteria to score movements results in significant differences in the number of movements identified during the SIT. Third, determine whether or not it would be advantageous

to use bilateral actigraphs rather than unilateral to approximate polygraph recordings of leg movements. Fourth, evaluate the ability of the SIT to differentiate between normal subjects and persons with RLS. It was hoped that the results from the above analyses would provide support for an actigraphic SIT test to identify persons with RLS.

If the actigraphic SIT test was capable of differentiating between RLS and normal subjects, this methodology could be used as a large-scale screening tool and as a means of longitudinal follow-up in sleep medicine research and in clinical sleep medicine. Serial SIT tests would be useful for objectively assessing symptom variability across time in the RLS population, which is currently not feasible with the use of polygraphic SIT tests. In the following section, the methodology and statistics that were used to test these experimental questions are described.

METHODS

Participants

Fifteen subjects for each group, RLS and controls, were recruited to participate, for a total of thirty subjects. RLS subjects were volunteers recruited through the Ochsner Clinic of Baton Rouge Sleep Disorders Center, through contacts with the Restless Legs Foundation and a local support group leader. RLS subjects were not excluded if they had another sleep disorder, given that having another sleep pathology would not affect a daytime recording or motor activity. Any RLS subjects being treated for RLS or PLMD with medications would have been asked to abstain from taking any medications related to their RLS on the day of the study; however, none of the participants were taking medications at the time of the study. Since there is no difference in the symptom presentation of primary and secondary RLS, conditions known to cause RLS were not ruled out. The latter differentiation would be more important in determining the appropriate treatment, rather than integral in identifying individuals with symptomatology consistent with RLS.

The control group subjects were selected such that they would not be significantly different in age from the RLS group, to control for possible age-related effects. An ANOVA comparing the average age of the participants in the RLS group versus the control group showed that the two groups were not significantly

different in age (F [1,28] =.001, p = .971). See Table 1 for descriptive statistics by group.

Table 1. Age of Participants by Group

	Mean (years)	*Standard Deviation*
RLS	51.73	14.76
Controls	51.93	14.99

Control subjects were recruited from older undergraduate students at Louisiana State University, family members of younger undergraduates enrolled in psychology classes, and from age-similar associates of RLS group subjects. Students who recruited a participant received extra credit towards psychology classes for their participation, but other subjects were not directly compensated for their participation.

Basic demographic data was collected. Tables 2-8 provide the results of information obtained from the questionnaire (shown in Appendix C) completed by the participants.

The genders were equally distributed in the RLS group, with males accounting for 47% of the participant and females accounting for 53% of the participants. The majority of the participants in the control group were female (87%). As a whole, the participants were largely female (70%). The majority of the RLS participants (80%) did not report any lateralization of symptoms (see Table 3). Three RLS participants (20%)

reported that their symptoms were worse on the right side of their body.

Table 2. Gender of Participants by Group

	Male		Female	
	Frequency	*Percent*	*Frequency*	*Percent*
RLS	7	47%	8	53%
Controls	2	13%	13	87%
Total	9	30%	21	70%

Table 3. Lateralization of Symptoms

Activity	*Frequency*	*Percent*
No lateralization	12	80%
Symptoms worse on the left side	0	--
Symptoms worse on the right side	3	20%

The majority of the RLS participants indicated that the following activities provide relief from their symptoms: moving the legs (93%), getting up and walking around (87%), stretching the legs (80%), rubbing or massaging the legs (73%). Few people reported obtaining relief from either using a heating pad/taking a warm bath (27%) or from applying anything cold to the legs (17%). The reported location of the sensations was consistent with clinical descriptions. Specifically, the majority of RLS participants experience symptoms in the legs (87%) and/or their thighs (87%). For a detailed listing of the locations of symptomatology reported, see Table 5.

Table 4. Proportion of RLS Subjects Indicating the Specified Activity Provides Relief

Activity	*Frequency*	*Percent*
Rubbing or massaging the legs	11	73%
Moving the legs	14	93%
Using a heating pad or taking a warm bath	4	27%
Applying anything cold to the legs	2	13%
Stretching the legs	12	80%
Getting up and walking around	13	87%

Table 5. Location of Sensations

Activity	*Frequency*	*Percent*
Feet	10	67%
Lower legs (between the ankle and the knees)	13	87%
Thighs	13	87%
Groin	2	13%
Trunk	2	13%
Shoulders or neck	7	47%
Upper arms	4	27%
Forearms	2	13%
Hands or fingers	4	27%

Results of questions pertaining to freq uency of sensations over the past 6 months illustrated the range of symptom severity in the RLS participants (see Table 6 and 7). Four of the participants (27%) indicated experiencing their symptoms exclusively at night. Only one participant (7%) reported having symptoms every day and one (7%) having symptoms every night.

Table 6. Frequency of Sensations in Legs at Night Over the Past 6 Months

Activity	*Frequency*	*Percent*
One or two nights a week	3	20%
Three or four nights a week	7	47%
Five or six nights a week	4	27%
Every night of the week	1	7%

Table 7. Frequency of Sensations in Legs During the Daytime Over the Past 6 Months

Activity	*Frequency*	*Percent*
One or two days a week	4	36%
Three or four days a week	5	46%
Five or six days a week	1	9%
Every day of the week	1	9%

All of the RLS participants reported that physical activity relieves their symptoms and that their symptoms get worse in the evening. Table 8 shows that the majority (80%) of RLS participants have difficulty falling asleep because of their symptoms. Some of the participants indicated performing a physical regimen prior to attempting sleep to keep from having sleep onset difficulties. Half (53%) of the participants reported that their symptoms are worse when they are under stress. Only five of the participants (33%) had previously sought treatment for their symptoms. Of those who had sought treatment, only one was properly diagnosed with RLS. Half of the participants (53%) had been evaluated by a sleep center prior to participation in the current study.

Since many persons with RLS report an increase in symptoms in the evening, attempts were made to have subjects participate in the late afternoon or early evening hours. The late afternoon/evening time was preferred because of the probable increase in symptom severity in the evening, which could increase the probability of differentiating between

Table 8. Other Descriptive Questions

Question	Yes		No	
	Frequency	*Percent*	*Frequency*	*Percent*
Do your symptoms get worse in the evening or night?	15	100%	0	--
Does physical activity decrease or relieve your symptoms?	15	100%	0	--
Are your symptoms worse when you are under stress?	8	53%	7	47%
Do you have difficulty falling asleep because of your symptoms?	12	80%	3	20%
Have you ever sought treatment for your symptoms of restless legs?	5	33%	10	66%
Have you ever had a sleep study?	8	53%	7	47%

controls and RLS subjects. It also controls for possible circadian factors. Attempts were made to have equal numbers of subjects from both groups participate in the same time periods. The number of subjects from each group who participated anytime before noon versus afternoon/evening is detailed in Table 9.

Table 9. Participation Times of Participants by Group

	A.M.		*P.M.*	
	Frequency	*Percent*	*Frequency*	*Percent*
RLS	4	13%	11	37%
Controls	7	23%	8	27%
Total	11	37%	19	63%

Measuring Movement Activity

The SIT tests were conducted at the Sleep Laboratory, Department of Psychology, Louisiana State University. Subjects were instructed to stay awake, sit on a bed with their legs outstretched, and to keep their eyes open while attempting to remain completely still for 60 minutes. Movement activity during the SITs was recorded on a Bio-Logic Systems Sleepscan computerized polysomnograph, which recorded anterior tibialis electromyogram (EMG) activity from both legs. The EMG was recorded using Grass Instruments 10 mm gold-cup electrodes and conformed to standard electrode site placement (ASDA Atlas Task Force, 1993).

Two ActiTrac actigraphs were used for each subject, with one being placed on the ankle of each leg. Both recordings occurred simultaneously for 60 minutes. The ActiTrac monitor contains a piezoelectric sensor to record physical motion. The acceleration signal produced by body motion is sampled at a rate of 40 times per second and is digitally integrated to measure movement activity. This activity is converted to data counts and is accumulated for each time epoch and stored in memory.

Experimental Hypotheses

The following experimental hypotheses were tested:

1. It was hypothesized that the actigraph could validly identify and quantify leg motor activity, as defined by anterior tibialis EMG.
2. It was hypothesized that RLS subjects would have significantly more leg movements than control subjects on the SIT, as defined by both anterior tibialis EMG and actigraphy.
3. It was hypothesized that the actigraphic SIT is a valid and effective test (as defined by Gouvier, Hayes, Smiroldo, 1998 discussed in Part II of the Test of Experimental Hypotheses section) of RLS above base rates.

RESULTS

Preliminary Analyses

Pilot Testing of Actigraph Reliability. To test the reliability of the actigraph recordings, a one-hour pilot testing recording was conducted on a single subject using three actigraphs simultaneously. Two actigraphs were placed on the left ankle and one actigraph on the right ankle. Three Kappa correlations were performed to examine the exact agreement between the actigraphs. The results are shown in Table 10. All Kappa statistics were significant, indicating that the actitracs were reliably recording the same movements. The pilot test was conducted with a single subject; as such, the findings may be subject to bias. Had additional subjects been employed, a wider range of movements may have tested the acitgraphs further and led to earlier identification of the recording delay discussed later.

Table 10. Kappa Statistics for Pilot Actitrac Recordings

	Kappa	*Sig.*
Left Actitrac 1: Left Actitrac 2	.844	<.001
Left Actitrac 1: Right Actitrac	.770	<.001
Left Actitrac 2: Right Actitrac	.858	<.001

Evaluating the Utility of Using PLM Criteria to Score Movement Activity. Researchers have been inconsistent in whether or not PLM criteria were used to score movements during the SIT. Clinical descriptions of RLS and RLS research indicate that the

leg movements experienced by RLS patients during the day are both voluntary (i.e., movements deliberately initiated by the patient to alleviate sensory events) and involuntary. Both kinds of movements have shown some evidence of periodicity. It is possible that given the uncomfortable sensations commonly experience by those with RLS, that they would also perform a greater number of voluntary movements to relieve the discomfort than controls who do not experience this added discomfort. Thus, quantifying all movements may provide for larger differences between groups, and therefore better discrimination, as opposed to only using those movements meeting PLM criteria. To examine this, a paired sample t-test was computed to compare the number of movements that conform to PLM criteria versus the total number of movements for both groups of subjects based on tibialis EMG. Table 11 shows the average number of movements identified by type. Analyses showed that significantly more movements were identified when all movements were counted ($t[29] = 6.62$, $p<.001$); however, it was observed in the current study that the ratio of movement activity between the groups was greater for PLM movements than for total movements. In other words, while the average total movements for the RLS participants (37 movements/hour) was about three times greater than the average for the controls (13 movements/hour), the average PLMs for the RLS participants (17 PLMs/hour) was about

six times greater than the average for the controls (3 PLMs/hour). Thus, it is possible that using only the PLMs could in fact prove a better discriminator, and therefore a better classification measure, than using all movement activity. Analyses reported later highlight that there is actually no benefit, or deficiency as initially suspected, in the practice of counting only PLM activity. As it made no difference which outcome measure was chosen, subsequent analyses are based on the more comprehensive measure (i.e., all movement activity), regardless of periodicity.

Table 11. Average Number of Movements by Group*

	Number of PLMs		Other Movements		All Movements	
	Mean	*s.d.*	*Mean*	*s.d.*	*Mean*	*s.d.*
RLS	16.7	24.9	20.0	14.5	36.7	37.4
Control	3.0	4.9	9.7	6.6	12.7	10.4
Total	9.8	18.9	14.8	12.3	24.7	29.6

*Based on EMG Recording

Comparing the Use of One Actigraph versus Two. For the three RLS subjects reporting either some or predominantly lateralized symptoms, scoring of movement based on a single actigraph utilized the data collected on the side the individual reported as the source of the greatest degree of symptomatology. For all control subjects and RLS participants not reporting symptom lateralization, single actigraph scoring of movement was based on the recording from the left leg. To score the number of

movements identified on both actigraphs, a movement was counted if it occurred on either leg or both legs.

The recording interval or epoch length (i.e., the amount of time represented by a data point) can be set to increments ranging from 2-seconds to 30-second epochs. Thus, while the actigraph samples 40 times per second, the most frequent recording epoch is 2-seconds. The 2-second epoch was utilized in the current study. Additionally, the output from the actigraph can be viewed as a bar graph (as illustrated in Figure 1) or can be exported to a Microsoft Excel worksheet (see partial sample output in Table 12). A zero would indicate no movement activity and any number other than zero would indicate that movement occurred in the specified time period. This approach was taken simply to make computing frequency counts possible. If the raw numbers were employed, computing frequency counts in SPSS would have been meaningless, as all numbers would have been treated as a unique entity and become categories of activity that would be counted as often that specific number occurred. Thus, to compute frequency counts, all output was dichotomized, with zeros indicating no movement activity and all other numbers being converted to ones to indicate movement activity. To allow for comparisons in the current study, all actigraph results were first exported to a Microsoft Excel worksheet.

It was hypothesized that if some movements in the Kazenwadel et al. study were missed due to the use of a single actigraph, the use of two actigraphs might have more closely approximated the polygraph recordings of leg movements. In the

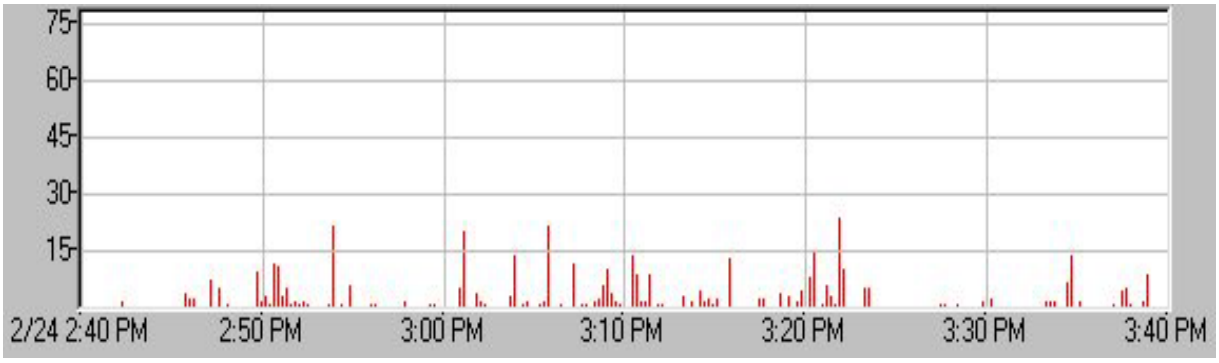

Figure 1. Sample Actitrac Bar Graph Output

present study, the total number of 2-second epochs with movement recorded during the SIT for each group was computed, using the results from one actigraph compared to results from both actigraphs. A paired sample t-test was conducted. The analyses indicated that significantly more movements were identified by the use of two actigraphs than one actigraph ($t[29] = -3.7$, $p = .001$). However, in examining the data closely, these results were found to be misleading.

The actigraphs did appear to be capturing the same movement activity, though not at *exactly* the same time. Table 12 shows one example of the raw output from the left and right leg

recording from one of the subjects. Table 13 provides sample recoded output obtained from the left and right ActiTrac from a subject that had two movements, and illustrates the coding of activity based on both actigraphs. Both the left and the right actigraphs recorded four 2-second epochs with movement activity, with each movement represented by two 2-second epochs. However, in the example shown, the right actigraph is clearly "delayed" in logging the movement compared to the left actigraph. Thus, while both actigraphs were properly logging movement activity, they were not logging the same movement at the exact same point in time according to the output. This lack of synchronization in timing results in overestimating movement activity when recoding the information to quantify activity from both actitracs.

It should be stated that the delay was clearly not attributable to any true delay in movement activity between one leg and the other leg. In other words, it was not possible that the delay identified was due to a participant moving one leg and later moving the other leg. The identified delays were consistent within a participant's recording. The partial sample output in Table 12 illustrates two successive movements on each leg, with the "movement" on the right leg appearing eight seconds later than the left. If the whole output were shown, one would see that *every* time movement activity occurred on the

Table 12. Sample Actigraph Output in Microsoft Excel

Time	*Left Actigraph*	*Right Actigraph*
6:23:54 PM	10.3	0
6:23:56 PM	1.6	0
6:23:58 PM	0	0
6:24:00 PM	0	0
6:24:02 PM	0	4.7
6:24:04 PM	0	0.9
6:24:06 PM	0	0
6:24:08 PM	0	0
6:24:10 PM	0	0
6:24:12 PM	0	0
6:24:14 PM	0	0
6:24:16 PM	0	0
6:24:18 PM	0	0
6:24:20 PM	0	0
6:24:22 PM	0	0
6:24:24 PM	0	0
6:24:26 PM	3.7	0
6:24:28 PM	0.9	0
6:24:30 PM	0	0
6:24:32 PM	0	0
6:24:34 PM	0	0.3
6:24:36 PM	0	0.3
6:24:38 PM	0	0
6:24:40 PM	0	0

left leg, there would be movement logged on the right actigraph *exactly* eight seconds (or four 2-second epochs) later. The duration of the delay was highly consistent within subjects, but not at all consistent across subjects, ranging from 2 seconds to just over 30 seconds. The duration of delay could not be determined for those participants with almost no movement activity or those with a significant amount of movement activity, because it was not possible to identify a consistent

Table 13. Sample Recoding of Actigraph Output

Time	*Left Actigraph*	*Right Actigraph*	*Both Actigraphs*
6:23:54 PM	1	0	1
6:23:56 PM	1	0	1
6:23:58 PM	0	0	0
6:24:00 PM	0	0	0
6:24:02 PM	0	1	1
6:24:04 PM	0	1	1
6:24:06 PM	0	0	0
6:24:08 PM	0	0	0
6:24:10 PM	0	0	0
6:24:12 PM	0	0	0
6:24:14 PM	0	0	0
6:24:16 PM	0	0	0
6:24:18 PM	0	0	0
6:24:20 PM	0	0	0
6:24:22 PM	0	0	0
6:24:24 PM	0	0	0
6:24:26 PM	1	0	1
6:24:28 PM	1	0	1
6:24:30 PM	0	0	0
6:24:32 PM	0	0	0
6:24:34 PM	0	1	1
6:24:36 PM	0	1	1
6:24:38 PM	0	0	0
6:24:40 PM	0	0	0

trend for the delay. There was no “correction factor” that could be consistently applied either individually or across participants to offset this technical problem

After this delay was identified, the company that developed the ActiTrac monitors was contacted and provided the data. The technical support personnel indicated that there was a flaw with the software used to set the actigraphs to begin recording at the same time. Even when new software was obtained, the

Table 14. Sample Recoding of Pilot Subject Movements

Time	*Left Actigraph*	*Right Actigraph*	*Both Actigraphs*
14:37:02	0	0	0
14:37:04	0	0	0
14:37:06	0	0	0
14:37:08	0	0	0
14:37:10	0	0	0
14:37:12	0	0	0
14:37:14	0	0	0
14:37:16	1	0	1
14:37:18	1	0	1
14:37:20	1	1	1
14:37:22	1	1	1
14:37:24	1	1	1
14:37:26	1	1	1
14:37:28	1	1	1
14:37:30	1	1	1
14:37:32	1	1	1
14:37:34	1	0	1
14:37:36	1	1	1
14:37:38	1	1	1
14:37:40	0	1	1
14:37:42	0	0	0
14:37:44	0	0	0
14:37:46	0	0	0
14:37:48	0	0	0

delay was still apparent. During further communication with the developers of this device, it became clear that the ActiTrac had not been designed to be accurate down to the exact second. Testing after the completion of the study identified the source of the delay and is described in the discussion section.

Because of the inability of the ActiTrac to log movements at the exact point of time that the movement occurs, using the results from both actigraphs would greatly inflate the number of

2-second epochs in which movements were identified. Consequently, subsequent analyses are based on the use of one actigraph.

Because the actigraphs were not logging movements at exactly the same time relative to each other, it could no longer be assumed that the actigraphs were logging movement at the exact same time as the EMG recording. Recordings were taken from both the actigraph and tibialis EMG simultaneously in order to compute exact agreement between these two recording methods. Though the variable recording delay rendered this statistic invalid, and it would have been ideal to perform this calculation, this problem did not represent a major limitation to the current study as long as the actigraphs were still capable of documenting movement activity, as they were. While it was impossible to perform Kappa for exact agreement between these recording methods, it did not interfere with calculating the ability of the actigraphs to distinguish between RLS and control subjects, which is discussed later. Instead of computing Kappa for exact agreement, a Pearson correlation could still be computed between the total number of two-second epochs with movement identified by the EMG recording versus the number of two-second epochs with movement identified by the actigraph recording to provide some documentation of the association

between these recording methods. There was a significant positive correlation ($r=0.7$, $p<.001$) between these two indices.

The original research plan was to perform analyses based on the number of actual discrete movements. The latter proved impossible because the most frequent output from the actigraph is whether or not there was any movement in a given two second period. This is a limitation of the actigraph when compared to the continuous recording of EMG activity. A number of the movements occurred in close proximity, which is easy to distinguish on the EMG recording, but not in the actigraph output. Figure 2 provides an illustration of this finding. Note in the figure that the EMG recording clearly documents multiple, discrete movements. In reviewing the actigraph output, it is impossible to distinguish between multiple movements in close proximity versus one or two long movements. However, there was an important benefit of using two-second epochs as the outcome measure. Counting the number of movements does not take into account the duration of a movement, which is approximately accounted for when counting each 2-second time period with movement activity. Thus, each method has its advantages and limitations, and either one can address the experimental hypotheses of this investigation.

Additionally, one of the proposed advantages of developing an actigraphic method for objectively identifying persons with

RLS was that it would be faster and require less staff time than an EMG evaluation. However, attempting to count discrete

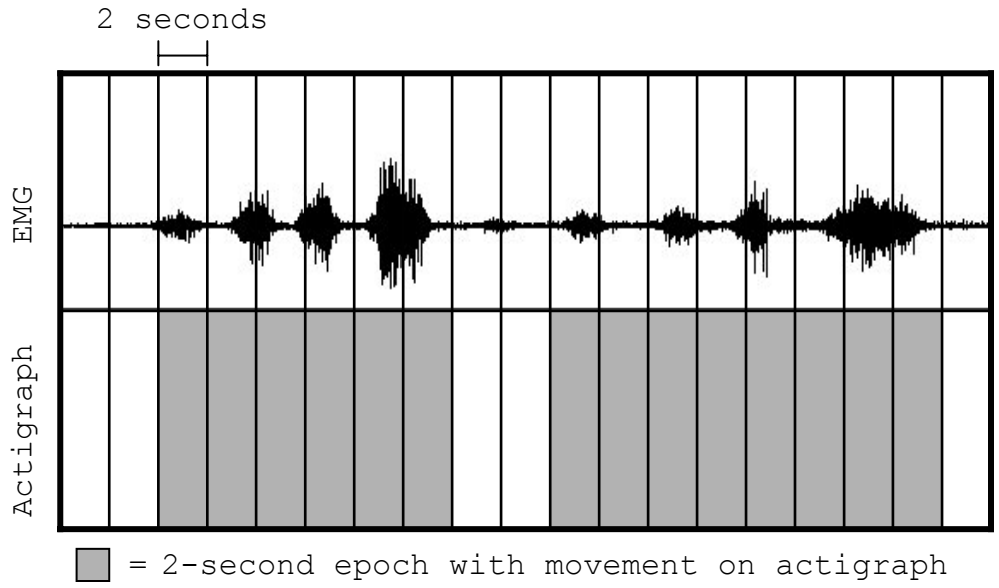

Figure 2. Comparison of EMG and Actigraph Recording using 2-second epochs

movements on the actigraph output as originally planned actually would have required more time than counting movements based on the EMG recording. Fortunately, changing the outcome measure to number of 2-second epochs with movement, as required by the limitations of the ActiTrac, turned out to be significantly faster than examining the EMG recording.

Test of the Experimental Hypothesis

Differentiating RLS from Normal Subjects. To examine the diagnostic utility of a measure such as the SIT, there are a number of statistics that can be computed. The performance of a

test can be quantified in terms of its sensitivity, specificity, positive predictive power, negative predictive power, and the overall correct classification rate. Following is a description of how each of these terms is defined and was calculated for the current study, based on Kessel and Zimmerman (1993). Appendix A provides the computational formulas employed.

Before these statistics were computed, there was an important consideration: What cutoff score should be employed to determine whether an individual's results were consistent with, or diagnostic of, RLS or not? In determining whether or not an individual has a condition or not on the basis of a continuous variable, in this case the number of 2-second epochs with movement activity during the SIT, the sensitivity and specificity of the measure would depend on where the cutoff between a positive and negative test result was set. One method utilized to display the association between sensitivity and specificity for tests that have continuous outcomes is with receiver operator characteristic curves (ROC curves). ROC curves plot the sensitivity against specificity minus 1. ROC curves also provide a useful means of comparing two diagnostic tests.

The ROC curve was plotted for the actigraph to determine the cutoff score that would result in the highest combination of sensitivity and specificity that could be used to determine

whether an individual's SIT results were consistent with RLS or not (see Figure 3). The ROC curve test statistic indicated that the cut-off score that should be employed to maximize sensitivity and specificity was 82 two-second epochs with movement/hour. The reference line illustrates a test that is no better than chance. The closer an ROC curve is to the upper left-hand corner of the graph, the more accurate it is, because the sensitivity and specificity approach 100%. Complete detailed explanations of the use and meaning of ROC curves are have been published (e.g., Begg, 1991; Hanley & McNeil, 1982; Hanley & McNeil, 1983; Thompson & Zucchini, 1989).

The corresponding sensitivity, specificity, false-positive rate, false-negative rate, positive predictive value, and negative predictive value calculated given this cut-off score are detailed in Table 15. Sensitivity is the ability of a test to accurately identify individuals who have a condition as having the condition. For the present study, sensitivity was60% and was computed by dividing the number of RLS patients accurately identified by actigraphy (i.e., true-positives) by the total number of RLS patients. Specificity is the ability of a test to accurately identify those who do not have the condition as not having the condition (i.e., true-negatives). Specificity was 73% and was computed by dividing all of the control subjects identified as not having RLS by the total number of controls.

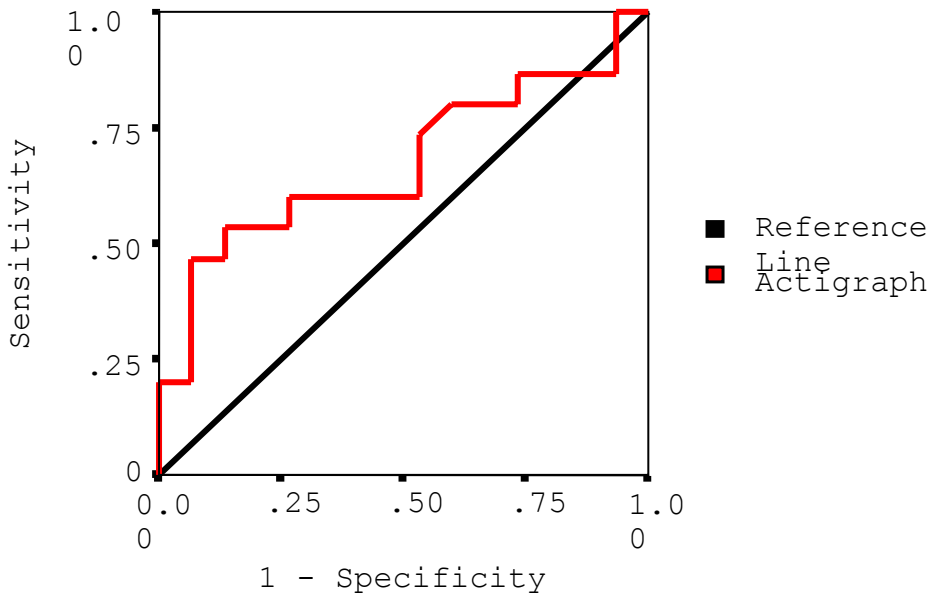

Figure 3. ROC Curve Based on Actigraph

False-negatives are the number of individuals incorrectly identified as not having the condition. In the present study, the false negative rate was 40% and was computed by dividing the number of individuals incorrectly identified as not having RLS by all subjects with a positive test result. The false-positive rate is the number of individuals incorrectly identified by the test as having a condition. There was a 27% false positive rate, which was computed by dividing the number of participants incorrectly identified as having RLS by all of the subjects with positive results.

Table 15. Test Characteristics of the SIT Using Number of 2-Second Epoch with Movement on Actigraph Recording

Test	**Diagnosis**	
	Positive	*Negative*
Positive	9 A	4 B
Negative	6 C	11 D

True Positive/Sensitivity = 60%
True Negative/Specificity = 73%
False Positive = 27%
False Negative = 40%
Positive Predictive Power = 69%
Negative Predictive Power = 65%
Overall Correct Classification = 67%
Valid if (9/4)> (6/11); Actigraphic SIT valid
Test is effective only if base rate is > 33%
-Screening: 5% is not > 33%; Not effective for screening
-Clinical: 9% is not > 33%; Not effective for use in clinical setting

The positive predictive value of a test indicates the probability that an individual will be correctly identified as having a condition, given a positive indication on the test. In the present study, it was computed by dividing all of the true-positives by all individuals with positive test results. The negative predictive value of a test indicates the probability that an individual will be correctly identified as not having a condition, given a negative test result. It was computed in the present study by dividing the number of true-negatives by all subjects with negative results. The positive predictive value and negative predictive value were 69% and 65% respectively.

Last, the overall accuracy, or overall correct classification rate, refers to the proportion of individuals correctly identified as having a condition or not. This was computed by dividing the combined total of true-positives and true-negatives by the total number of tests performed. Two thirds of the participants (67%) were correctly classified using actigraphy.

An additional factor was considered before making a final determination as to the usefulness of the actigraphic SIT to discriminate between those with RLS and controls. Specifically, the base rate of RLS, and how that related to the utility of the SIT as a diagnostic test, was examined. Thorough explanations of the association between base rates the interpretation of a test result has been published (e.g., Gouvier, Hayes, Smiroldo, 1998; Hayes, Hilsabeck, Gouvier, 1999; Pinkston, 1998). Base rates refer to the current population prevalence of a condition, and can be determined by dividing the number of persons with the condition by the number of persons in the population of interest. In other words, base rate is the prior probability that an individual has a specific condition, regardless of the outcome of a test. A test is considered a valid indicator if the sensitivity (60%) divided by the false positive error rate (27%) is greater than the false negative error rate (40%) divided by specificity (73%). The actigraphic SIT was found to

be valid (see Table 15). However, a test is not considered effective unless the classification rate of the test is superior to classification based on base rates alone. In order for a test to be an effective tool for a clinician, the combined error rates of the test (i.e., false positive rate plus false negative rate) should be less than the base rate of the condition. Otherwise, a clinician would be more accurate overall in making judgments using base rates alone. This description applies only when the base rate of the condition is less than 50%, as with the current study; an alternate formula is utilized when the base rate exceeds 50%.

The effectiveness of a test can depend on the base rate employed. For example, if one were interested in using the SIT test as a screening tool to evaluate all persons in the population for RLS, you would use population prevalence as the base rate. Current prevalence studies indicate that RLS exists in approximately 5% of the population. On the other hand, if you want to evaluate effectiveness of the SIT test as a diagnostic test on persons presenting to a sleep laboratory, one would use the prevalence of RLS among those presenting to the sleep laboratory. There are no published data indicating the prevalence of RLS in persons presenting to sleep laboratories. However, a review of 100 sequential referrals to the Baton Rouge General Medical Center Sleep Disorders Center indicated a

prevalence or base rate of 9%. Thus, the effectiveness of the SIT test was computed using both of the identified base rates to evaluate the effectiveness of this test for each purpose. Given the combined error rates for the SIT (33%), the test was not found to be effective for either screening (assuming 5% prevalence) or for use clinically (assuming 9% prevalence).

To examine this possibility, all of the test characteristics were recomputed using number of PLMs as the dependent variable for the SIT. ROC curves were completed, which indicated a cutoff of 2 PLMs/hour provides the greatest combined sensitivity and specificity. The calculated test characteristics are shown in Table 16. There were a few differences when using PLMs rather than the number of 2-second epochs on the actigraph. The specificity declined slightly due to one less control being accurately identified, decreasing the overall correct classification slightly to 63%. Similar to the result using actigraphy recordings, this measure did not prove to be effective for either a screening or a diagnostic tool.

As an additional means of comparing the EMG recording to the actigraph recording, these test characteristics were computed using the total number of movements identified on the EMG recording, using a cutoff score of 17 movements/hour obtained with an ROC curve. The results are shown in Table 17. The sensitivity and specificity improved slightly due to one

Table 16. Test Characteristics of the SIT Using Total PLMs Based on EMG Recording

Test	**Diagnosis**	
	Positive	*Negative*
Positive	9 A	5 B
Negative	6 C	10 D

True Positive/Sensitivity = 60%
True Negative/Specificity = 67%
False Positive = 33%
False Negative = 40%
Positive Predictive Power = 64%
Negative Predictive Power = 63%
Overall Correct Classification = 63%
Valid if (9/5)> (6/10); EMG SIT using PLMs valid
Test is effective only if base rate is > 37%
-Screening: 5% is not > 37%; Not effective for screening
-Clinical: 9% is not > 37%; Not effective for use in clinical setting

additional control and RLS participant being accurately identified, increasing the overall correct classification slightly to 70%. The ROC curves for each of these three possible outcome measures can be visually compared using Figure 4.

Last, the diagnostic classification status indicated by the actigraph versus the EMG recording was compared and the Kappa statistic was calculated to indicate the agreement between these two measures. The Kappa value was moderate, though statistically significant from zero (0.4, $p<.05$).

Table 17. Test Characteristics of the SIT Using Total Movements Based on EMG Recording

Test	Diagnosis	
	Positive	*Negative*
Positive	10 A	4 B
Negative	5 C	11 D

True Positive/Sensitivity = 67%
True Negative/Specificity = 73%
False Positive = 27%
False Negative = 33%
Positive Predictive Power = 71%
Negative Predictive Power = 69%
Overall Correct Classification = 73%
Valid if (10/4)> (5/11); EMG SIT valid
Test is effective only if base rate is > 27%
-Screening: 5% is not > 27%; Not effective for screening
-Clinical: 9% is not > 27%; Not effective for use in clinical setting

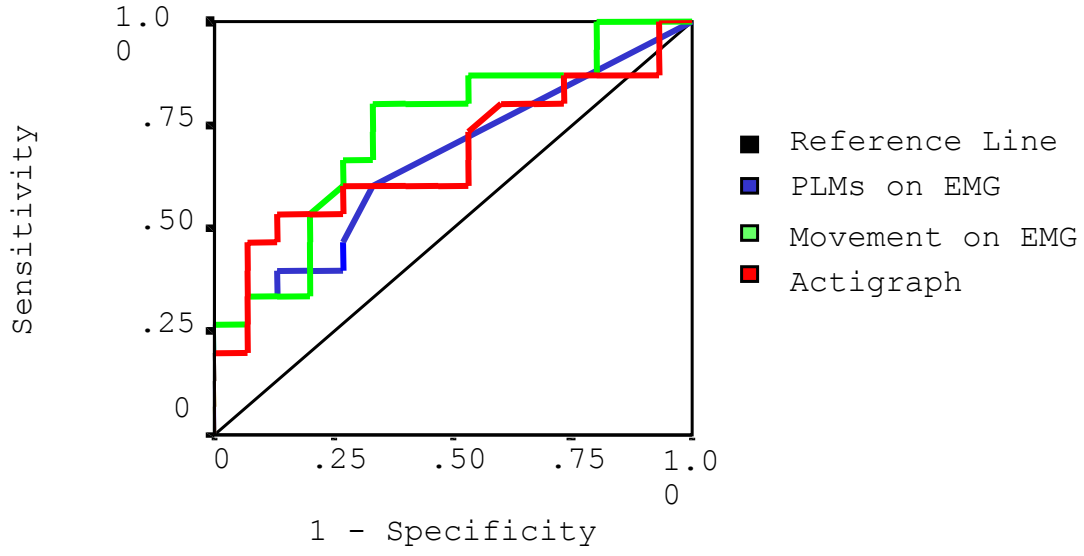

Figure 4. Comparison of ROC Curves

DISCUSSION

Due to unexpected technical limitations of the actigraph recordings, an index of exact agreement (i.e., moment-to-moment, Kappa) between tibialis EMG and actigraphy measures was not possible, though a more general index of agreement (i.e., Pearson) was possible. There was a statistically significant positive correlation between EMG and actigraph measures of movement. The described technical problem, which appeared to be a variable recording initiation lag (across subjects), led to systematic testing of several factors, such as changes in the intensity and duration of movements, as well as changes in the initialization process of the two ActiTracs utilized in the current study, to find any possible explanation for the "delay".

Initializing the actigraph involves plugging a specialized cable provided with the devices (connected to a port in a computer) into the actigraph and starting the device's software program. The program provides the experimenter the opportunity to set the output frequency of the device, delineate a name for the file that will be generated, and to set a delayed recording time if desired. The user's manual for the ActiTracs used in the current study states that after the initialzation process is completed for a unit that has a delayed recording time specified, that the unit "will go to 'sleep' until the specified date and time, at which time it will 'wake up' and begin

recording". Given this information, the experimenter had initialized the ActiTracs to each delay the recording time, but with the same specified future time. For example, if a SIT was to begin at 6:30 p.m., the experimenter initialized the first actigraph with setting a delayed recording time at 6:30 p.m., disconnected the first device, and then initialized the second actigraph with the same delayed recording time (6:30 p.m.). The actigraphs were taped to a small board; the experimenter simulated activity by moving the board. Attempts were made to characteristics about the simulated movements, such as the speed of a simulated movement (e.g., short, slow movements; short, rapid movements; long, fast movements), as well as the interval between the simulated movements.

The test data revealed that the ActiTracs were not properly delaying the beginning of the recording to correspond to the time specified by the user. The ActiTracs were in fact beginning recording at the end of the initialization process, not at the programmed start time. The time of completion of the initialization process was different between the two actigraphs (as only one could be initialized at time), which accounts for the different "delay" across participants. The problem was tested by varying the interval between the completion of the initialization process and the delayed start time, with short periods of activity subsequently simulated on the actigraph, and

the time the actigraph logged those movements noted. For example, on one test trial, the initialization was done at 7:18:44 pm, the start time specified for 7:20:00 p.m., and the first test movement done at 7:20:10 p.m., the ActiTrac logged this movement at 7:21:26 p.m., 1 minute 16 seconds later than it actually occurred. The time between initialization and the actual movement was 1 minute 16 seconds, but the time between the programmed (and actual) start time and the movement was only 10 seconds. The data thus show that the ActiTrac began recording at the time of initialization instead of the programmed time, but labeled that initial epoch as the programmed start time; this means that the data included the time between initialization and the programmed start time (the start of the SIT), when it should have only included data from the programmed start time and the start of the SIT (actually, the same time). Hence the delay. This outcome was repeatedly found over 8 independent test trials on each of the two ActiTracs used in this investigation.

Testing also evaluated if the ActiTracs were logging the duration of movements accurately, if they were properly logging the interval between movements, and what intensity of movement was necessary to be logged. During the 16 test trials (8 for each ActiTrac), movements of duration varying between 1-10 seconds were simulated. Each time a movement was simulated, the

duration and clock time at the start of the simulated movement was noted. The interval between simulated movements was also varied from 10-60 seconds. The notations were then compared to the duration of movements and interval between movements identified on the actigraph output. Testing revealed that the movements were being logged at the accurate time (from the time of initialization), were being logged for the approximate duration consistently, and consistently logged the inter-movement interval. For example, on trials in which a 6 second movement was simulated, the actigraph output consistently showed either three or four two-second epochs with movement (the approximate agreement due to such factors as human reaction time). Also, attempts were made to alter other characteristics about the simulated movements, such as the speed of a simulated movement (e.g., short, slow movements; short, rapid movements; long, fast movements). It proved difficult to simulate a movement that the actigraph would not log. In other words, the actigraphs appeared to be sensitive enough to pick up a wide range of intensity of movements.

The above described technical problems with programming a delayed start support the decision that statistics such as Kappa would not have been appropriate, as the units were truly not beginning to record at the same time, despite the output indicating they were doing so. Obviously there is a flaw in the

software used to initialize the actigraphs. The beginning portion each participants recording time, therefore, corresponds to differences in the time to set up the equipment (i.e., initialize the actigraph). Given the relatively small delays identified (when the delay could be identified) this would unlikely result in significant changes in the current findings. However, clearly future studies such as this should not be undertaken until the true nature of the actigraphy is better tested to ensure it's validity.

There was significantly more movement during the SIT than activity meeting PLM criteria. It initially appeared that previous studies using only PLM activity were too limiting (Brodeur et al., 1988; Pelletier et al., 1992; Montplaisir et al., 1998); evaluation of test characteristics showed that this index was neither too limiting nor additionally beneficial. In other words, using a count of the PLMs during the SIT was no better or worse than using all movement activity. One of the PLM criteria in particular, a maximum duration of 4 seconds, would result in several of the longer voluntary movements not being counted. However, the analyses of subsequent test characteristics did not indicate that an actigraphic SIT would be an effective diagnostic tool for either screening or clinical purposes, either when all movement activity was counted, when

PLM activity only was counted, or when tibialis EMG was used instead of actigraphy.

Surprisingly, many of the persons with RLS who ultimately participated in this study had never heard of this disorder. Only 2 of the 15 RLS participants (13%) knew of RLS prior to participating in the current study, even though 5 of the participants had sought treatment for their symptoms previously and 8 had had a sleep study previously. Only 1 of the 5 participants who sought treatment specifically for symptoms consistent with RLS were properly identified as having RLS. Physicians do not appear to be identifying RLS, which is a significant public health education issue. In addition, inadequate recognition of RLS has significant implications for previously estimated prevalence rates of RLS. Overall, studies examining the prevalence of RLS in the general population have found that the population prevalence of RLS is approximately 5%. Recent studies have indicated that the prevalence may be as high as 15% (Lavigne & Montplaisir, 1994), though some studies have estimated prevalence on the basis of a single telephone survey question. Clearly one isolated question would not provide adequate evidence of whether or not a person has RLS, which to be properly diagnosed requires multiple indicators. As most of the participants had not been identified as having RLS prior to enrolling in the current study, the need for public education is

evident, and the possibility that the 5% rate used in the current study underestimates the actual prevalence rate of RLS must be considered in interpreting the clinical utility of the findings.

The current study does not support the clinical use of an actigraphic SIT using the methodology described. In fact, the sensitivity and specificity found in the current study is somewhat lower than that found by Montplaisir and fellow researchers (1998), who also examined the diagnostic utility of the SIT using polygraph EMG recordings. Many of the initial studies examining the SIT were testing the utility of a particular medication to treat RLS (e.g., Brodeur et al., 1988). Persons with RLS seeking medical treatment are likely in the severe range, though most studies do not report any indicators of symptom severity, such as frequency of symptoms. The current study recruited participants from the entire range of symptom severity. While this sample would better allow for evaluating the SIT as a diagnostic and screening tool, it is also likely the key reason the SIT proved less discriminating than in prior research. The possibility of an actigraphic SIT to objectively measure RLS symptomatology should not be ruled out; changes in SIT procedures and actigraph outcome variables may be all that is needed to attain an effective actigraphic SIT, regardless of symptom severity. Additionally, the current study utilized one

outcome measure to discriminate between RLS and control participant; future studies could examine other objective and subjective variables in combination with SIT outcome would improve on the sensitivity and specificity found in the current study. Also, the cutoff score utilized in the current study did provide for the highest combined sensitivity and specificity. The cutoff score employed could be altered to maximize sensitivity (i.e., accurately identify a larger proportion of RLS persons), if one were willing to accept a higher rate of false positives. For example, this practice could lead to a tiered approach in a screening process in which a larger proportion of persons could be initially identified as possibly having RLS (likely including the majority of people who truly have RLS) by using a lower cutoff score, which could be then followed up by interviewing to exclude higher rate of false positives that would be generated by the use of a lower cutoff score.

One possible alteration in SIT procedures that could be evaluated in future studies would be whether or not establishing a standardized recording time in the evening would enhance the diagnostic accuracy of the test. The latter would capitalize on the worsening of symptom severity experienced in the evening by most persons with RLS. Additionally, given the variable nature of RLS, these participants may not experience symptoms on the

day a single SIT is performed. It is possible that performing serial SITS would capture at least one or more days of symptom activity, and using the combined information would allow for superior discrimination over controls, who would not be expected to have significant day-to-day changes in SIT outcome.

Advancements in actigraph technology may also correct some of the problems encountered. It would be beneficial if actigraphs were capable of providing output on a frequency greater than every 2 seconds, which would make it easier to identify and count discrete movements and would more closely approximate EMG recording. Last, it would be useful to evaluate changes in the directions for the SIT. Some of the RLS participants did not have much movement activity. During discussion afterwards, some such participants indicated they did not have symptoms during the SIT; however, others reported that they were uncomfortable but were able to exert significant self-control over their movements and thus limited their movement activity despite their discomfort. Changes in the standard instructions could reduce the likelihood that lack of movement is due to the ability of an individual to resist movement even while withstanding significant discomfort.

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APPENDIX A: COMPUTATIONAL FORMULAS FOR EVALUATING TEST CHARACTERISTICS

Test	**Diagnosis**	
	Positive	*Negative*
Positive	A	B
Negative	C	D

True Positive/Sensitivity = A/ (A + C)
True Negative/Specificity = D/ (B + D)
False Positive = B/ (B + D)
False Negative = C/ (A + C)
Positive Predictive Power = A/(A + B)
Negative Predictive Power = D/(C + D)
Overall Correct Classification = (A + D)/N
Valid = (A/B)> (C/D)
Effective if base rate > (B + C)/N

APPENDIX B: CONSENT FORM

1. **Study Title:**
Use of actigraphy in restless legs syndrome

2. **Performance Sites:**
Louisiana State University, Audubon Hall

3. **Contacts:** The following investigators are available for questions at the phone numbers listed below.

Investigators:	Phone Number:	Times Available:
William F. Water	225-578-8745	Monday 10-1; Tuesday 10-5
Tai A. Istre	504-568-3068	Monday-Friday, 9-5

4. **Purpose of the Study:** The goal of the current study is to evaluate whether two different tests can assess leg muscle activity the same. The tests being used in the study may help in diagnosing individuals with a sleep disorder called restless legs syndrome.

5. **Subjects:**

A. Inclusion Criteria: Subjects must be at least 18 years old to participate. In order to be included, participants must meet criteria for restless legs syndrome or must be close in age to a participant who has restless legs syndrome.

B. Exclusion Criteria: Persons younger than 18 years old.

C. Maximum number of subjects: 30

6. **Study Procedures:** All participants will be asked to provide descriptive information such as their age, gender, and symptoms of restless legs syndrome. During the study, participants will be need to stay awake, sit on a bed with their legs outstretched, and to keep their eyes open while attempting to remain completely still for 60 minutes. Each participant will have four electrodes placed on their lower leg, two on each leg, which will measure how much they move their legs. Participants will also have an actigraph (a small device that looks like a wrist watch) placed on each ankle, which will also measure how much they move their legs. The study will take approximately one and a half hours to complete.

7. **Benefits:** The study will not benefit subjects directly. The current study may provide an easy test that would be helpful in diagnosing Restless Legs Syndrome in the future.

8. **Risks/Discomforts:** The risks are very small, and include a small possibility of developing mild skin irritation where recording devices are attached to the skin. Persons with Restless Legs Syndrome who withdraw from medications being used to treat their disorder may have a return of their symptoms the day they abstain from their medication. Participants may experience discomfort while attempting to keep their legs completely still. Though participants will be asked to keep as still as possible, they can move their legs if necessary to help decrease any discomfort.

9. **Measures taken to reduce risk**: Participants who will be abstaining from their medications related to their Restless Legs Syndrome will be doing so under the supervision of their physician.

10. **Right to Refuse:** Participation in the study is voluntary and participants may change their mind and withdraw from the study at any time without penalty.

11. **Privacy:** The results from the study may be published as group data in which no subjects' results are presented individually. The privacy of participating subjects will be protected and the identity of participants will not be revealed. The data collected will not be used for any purpose not approved by the participants and the LSU Institutional Review Board.

12. **Financial Information:** There will be no monetary compensation for participation in the study.

13. **Withdrawal:** Participants may withdrawal from the study at any time by telling the investigator at any time.

14. **Removal:** Restless Legs Syndrome participants who do not abstain from medication prescribed for the treatment of this condition or who do not obtain written permission from their doctors to do so will not be able to participate.

15. **Signatures:** The study has been discussed with me and all my questions have been answered. I may direct additional questions regarding study specifics to the investigators. If I have questions about subjects' rights or other concerns, I can contact Robert c. Mathews, Chairman, LSU Institutional Review Board, (225)578-8692. I agree to participate in the study described above and acknowledge the researchers' obligation to provide me with a copy of this consent form if signed by me.

_____Participant Signature _____ Date

_____Witness Signature _____ Date

_____Investigator Signature _____ Date

The study subject has indicated to me that he/she is unable to read. I certify that I have read this consent form to the subject and explained that by completing the signature line above, the subject has agreed to participate.

_____Signature of Reader _____ Date

APPENDIX C: RESTLESS LEGS SYNRDOME QUESTIONNAIRE

1. Do you ever have uncomfortable sensations in your legs?

☐ Yes
☐ No (if not, skip to question #24)

2. Please describe the sensations in your legs as best you can:

3. At what times do you get the symptoms?

4. Do your symptoms get worse in the evening or night?

☐ Yes
☐ No

5. What do you do when you get the symptoms?

6. Does physical activity decrease or relieve you symptoms?

☐ Yes
☐ No (if not, you make skip to question #8)

7. Which of the following activities are helpful in relieving your symptoms? (check all that apply)

☐ Rubbing or massaging your legs
☐ Moving your legs
☐ Using a heating pad or taking a warm or hot bath
☐ Applying anything cold to the legs
☐ Stretching your legs
☐ Getting up and walking around
☐ Other (please describe):

_____

8. How old were you when you first began to get the symptoms?

_____ years old

9. Have there been periods of time when the symptoms got better or worse or even went away completely? Describe.

10. Are there any things that seem to make your symptoms better or worse? Please describe.

11. Are your symptoms worse when you are under stress?

☐ Yes
☐ No

12. How often have you had the sensations in your legs over the past 6 months?

☐ One or two nights a week
☐ Three or four nights a week
☐ Five or six nights a week
☐ Every night of the week

13. Do you also get the sensations in your legs during the day? If yes, please note how often you have had them over the last 6 months.

☐ One or two days a week
☐ Three or four days a week
☐ Five or six days a week
☐ Every day of the week

14. Please use the list below to indicate where the sensations occur? (check all that apply)

☐ Feet
☐ Lower legs (between the ankle and knee)
☐ Thighs
☐ Groin
☐ Trunk
☐ Shoulders or neck
☐ Upper arms
☐ Forearms
☐ Hands or fingers

15. Are your symptoms worse on one side?

☐ No, it is the same on both side of my body
☐ Yes, the symptoms are worse on the **left** side
☐ Yes, the symptoms are worse on the **right** side

16. Use the rating scale below to indicate how severe your restless legs symptoms usually are:

1	2	3	4	5	6	7
Mild						Severe

17. Do you have difficulty falling asleep because of your symptoms?

☐ Yes
☐ No

18. When you experience symptoms of restless legs, how long does it take you to fall asleep (on average)? _____ min.

19. When you do not experience symptoms of restless legs, how long does it take you to fall asleep (on average)?
_____ minutes

20. Have you ever sought treatment for you symptoms of restless legs?

☐ Yes
☐ No (skip to question #22)

21. What treatment or medication did your doctor prescribe?

22. How effective was the treatment?

23. Have you ever had a sleep study (Polysomnogram) done?

☐ Yes
☐ No

24. What is your date of birth? ☐☐/☐☐/☐☐☐☐

25. Gender:

☐ Male
☐ Female

VITA

Tai Istre was born in Merced, California. After her mother was stationed in Bossier City, Louisiana, she attended Bossier High School. She attended Louisiana State University were she received her Bachelor of Science degree in psychology in May of 1995. In August of 1995, she began her doctoral training in clinical psychology under the supervision of William F. Waters, Ph.D., at Louisiana State University. She obtained her Master of Arts degree in 1998 in psychology. She attended the Louisiana State University Health Sciences Center in New Orleans, Louisiana, where she completed her pre-doctoral internship. She is will receive the degree of Doctor of Philosophy in clinical psychology in December of 2002.