

Actigraphy as applied to clinical assessments in insomnia trials for recording multiple sleep parameters

Overview

In an insomnia study, there are many challenges involved in reliably capturing sleep/wake data:

- How to be certain that the time the subject spends in the sleep lab accurately represents the subject's sleep. A valid screening tool is a polysomnogram (PSG) which can provide a more complete picture of sleep architecture at important clinical end points. But, the PSG alone may not tell enough.
- How to be sure that the subject is being compliant with the sleep schedule in the protocol. A sleep diary is a “gold standard” measure of subjective endpoints, but the sleep diary alone may not tell enough.

In a review of actigraphy validation studies, agreement between actigraphic and PSG measures across most sleep indices is > 90%.^{1,2} In the largest study to date (n=84) – which looked at the validity of Actiwatch and the related Actiware software to record sleep in chronic primary and co-morbid insomniacs – Lichstein et al. demonstrated no significant differences between Actiwatch and PSG in measures of Total Sleep Time (TST), Wake After Sleep Onset (WASO), Sleep Efficiency (SE), and Number of Nocturnal Awakenings (NWAK).³

The value of the Actiwatch actigraphy system in an insomnia clinical trial is supported not only by its validation, but also by the substantial benefits that the Actiwatch brings to a study of insomnia. Actiwatch can deliver high-quality, objective data across all study phases of an insomnia trial by logging continuous, ambulatory sleep/wake activity data in each subject. Actigraphy, periodic PSG data and subjective sleep diaries are appropriate and complementary assessment tools that can be used at different points during clinical trials.

Subject screening

Actiwatch can be used to resolve the issues surrounding the screening and selection of subjects in an insomnia study.

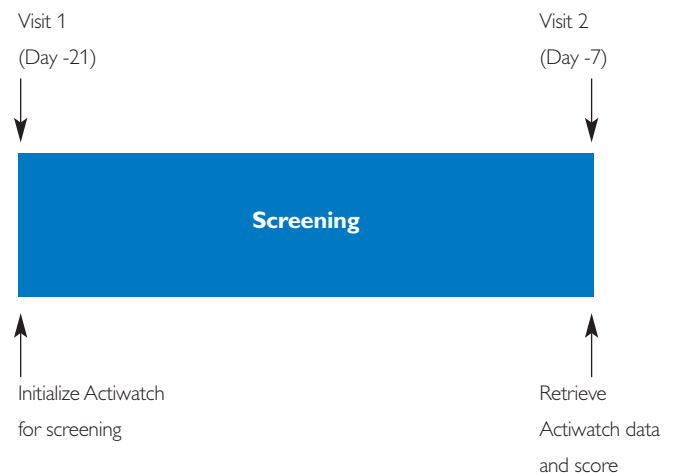
- Multiple articles have asserted that the strength of actigraphy is that it provides a measure of sleep over several nights at home. And, that actigraphic measures are therefore **strong, real-world indices** of subjects' sleep.⁴⁻⁶ Capturing real-world data can be critical to subject selection. In an insomnia study, two-thirds of the subjects slept better at home than in a lab and their **night-by-night variability** was higher at home.⁷
- Actigraphic data helps identify underlying conditions in subjects with a complaint of insomnia. These include **circadian rhythm** disruptions, issues with **poor sleep hygiene** or other irregular sleep/wake behaviors, or the presence of **periodic limb movements** during sleep.¹
- Obtaining actigraphic data before a lab-based PSG provides a **multiple-night record** of a subject's SE and TST. Actigraphy also ensures the validity of a Multiple Sleep Latency Test (MSLT) by providing an objective view of sleep/wake behaviors – such as chronic sleep deprivation – that may not be identified through an MSLT alone.⁸
- Also critical to subject selection is early **identification of noncompliance** in subjects. An actigraphic record bolsters sleep diary inputs by objectively documenting schedule adherence, week after week.^{9,10}

Phase shift (transient insomnia protocols)

Many transient insomnia protocols use a phase shift to induce a disruption in sleep onset and sleep maintenance in normal sleeping subjects. Ensuring that the phase shift has occurred – resulting in the likelihood of the subject exhibiting insomnia symptoms on the following night of PSG testing in the sleep lab – is key to the success of a transient insomnia study.

- A phase-shift protocol requires that subjects adhere to an imposed sleep/wake schedule over five or more days and nights at home. Actigraphy **provides a record of compliance** to the protocol instructions during this important trial period.
- Actigraphy also objectively confirms that an induced phase-shift has been effective before scheduling a subject for an in-lab PSG. With the exception of serum and urinary melatonin sampling or 24-hour core body temperature monitoring, actigraphy is the only tool that can **objectively document the success** of a phase advance. This is because the transition of a subject's internal circadian phase can take multiple days to elicit. A PSG study cannot detect successful phase advances due to the typical single-night nature of the test.¹¹

The study timeline demonstrates how actigraphy is implemented throughout the phases of a typical insomnia trial.



Treatment response

In an insomnia study, the typical methods for measuring ongoing therapeutic response may not provide a robust picture throughout the study period, particularly in capturing the subject's at-home sleep experience **objectively and consistently, night after night.**

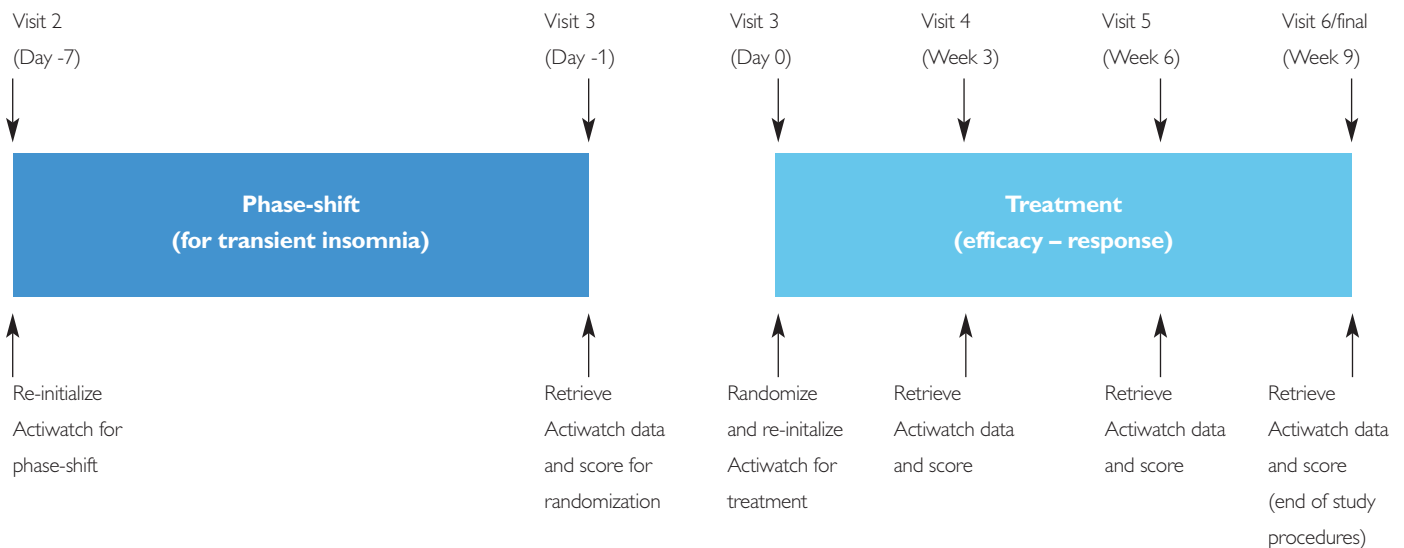
Actiwatch can be used to complement and strengthen the quality of data collected from subjective self-reports (sleep diaries) and PSG.

- Actigraphic data can be used to measure the effects of benzodiazepine and non-benzodiazepine hypnotics, as well as histamine receptor antagonists, in normal healthy subjects. In several studies that **evaluated hypnotic effects**, actigraphy was able to document significant differences in sleep parameters between hypnotic and placebo treatment (agents included midazolam, triazolam, flunitrazepam, flurazepam, temazepam and zolpidem).¹²⁻¹⁷

Other studies in healthy subjects have demonstrated the ability of actigraphy to record treatment **withdrawal effects** and measures of activity related to the **hangover effects** of benzodiazepine hypnotics.^{18,19}

- Actigraphy has been used in combination with sleep diaries and PSG in studies to objectively document changes in sleep parameters in **chronic primary insomnia** and **comorbid insomnia**.²⁰ In a study of elderly subjects with comorbid insomnia, actigraphy assessed significant treatment responses in SE and TST, SOL, Fragmentation Index (FI), NWAK and WASO.²¹ Actigraphy is **particularly suited to elderly subjects**, a population in which collecting consistent self-reporting measures can be a challenge.

- In addition to recording treatment response effects, actigraphy has been used to **assess compliance** to prescribed cognitive behavioral therapy.²²



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