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Quantum Physics and Polysomnography: Can We Prevent the Act of Measuring Sleep from Changing Sleep?

Commentary on: Lettieri CJ; Eliasson AH; Andrada T et al. Does Zolpidem enhance the yield of polysomnography? J Clin Sleep Med 2005;1(2):129-131

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German physicist Werner Heisenberg is credited with founding the discipline of quantum physics in 1927 when he stated (with respect to a given particle of matter) that, "The more precisely the position is determined, the less precisely the momentum is known in this instant, and vice versa."[1] As time has passed, his now-famous "Uncertainty Principle" has been widely misquoted and miss-applied outside of the realm of quantum physics. Particularly with respect to other fields of scientific endeavor, the Uncertainty Principle has taken on an alternate meaning, to wit: measuring a thing is apt to change the thing's value. As applied to polysomnography, one might argue that the act of measuring various physiological parameters during sleep could alter the data collected. This is likely to occur since sleep, although defined behaviorally as "a perceptual disengagement from and unresponsiveness to the environment,"[2] is actually so only relative to wakefulness and not in absolute terms. It is well known that the presumed emotional and physical discomfort of polysomnographic monitoring alters the architecture, and perhaps other attributes, of the patient's night of sleep. Reports of this so-called "first-night effect" (FNE) first appeared in the 1960s, shortly after the birth of sleep medicine and polysomnographic technology.[3-5] In some individuals, the FNE may provoke reduced sleep efficiency, prolonged sleep latency, increased wakefulness, more frequent arousals, reduced REM%, and prolonged REM latency.[4] More recent reports using EEG spectral analysis also found reduced delta and theta power density during the first of three nightly polysomnograms in depressed inpatients,[6] although the opposite was just reported in a group of healthy individuals.[7] However, FNE is not invariably present in normals,[8] may occur to a lesser extent in some patient groups than others,[9] and a so-called "reverse" FNE may even occur in patients with psychophysiological insomnia such that sleep is actually better the first night compared with subsequent nights.[10]

Presumably, polysomnographic testing for suspected sleep-disordered breathing in a patient afflicted with particularly severe FNE may not conclude successfully. Those of us directing busy sleep laboratories are doubtless familiar with the late-night call from our polysomnographic technologist asking whether they can send home the patient who is unable to sleep. This is a fairly infrequent occurrence, in my experience, and the outcome is known: no diagnosis is made, and the relatively scarce resource of one night's sleep laboratory bed is wasted. Somewhat more ambiguous is the effect that a less-than-ideal night's sleep (a more typical degree of FNE) might have on respiratory parameters. Consequently, the possibility that FNE or other factors might compromise the accuracy of a single night of polysomnography when performed in the patient suspected of sleep apnea has been the subject of a number of published investigations. The earliest (in 1984) by Wittig and colleagues analyzed the apnea indices from two sequential polysomnograms performed on 243 patients with suspected sleep apnea.[11] They found no difference in apnea index between nights when severe sleep-disordered breathing was present (>100 apneas/night), but in mild-moderate disease the second night tended to yield lower apnea indices than the first. Conversely, Dean and Chaudhary reported nine patients (out of 241 patients with duplicate studies) suspected of having sleep apnea but with no significant sleep-disordered breathing on initial polysomnography; all had positive second sleep studies up to 50 months later.[12] These individuals generally had mild-moderate sleep apnea on the second study and shorter total sleep time (TST) and less REM% on the first polysomnogram. Aber and coworkers performed two consecutive nights of polysomnography in 14 elderly men, and identified five patients whose classification as to presence or absence of sleep apnea changed between nights using a threshold apnea-hypopnea index (AHI) of 5: two subjects with initially negative and three with initially positive studies.[13] Mendelson published data on 50 patients with clinically suspected sleep apnea who underwent two consecutive nights of polysomnography.[14] Using a diagnostic criterion of AHI = 5 to determine presence of obstructive sleep apnea, three patients would have been classified differently from one night to the next (changing from negative to positive), while using AHI = 10 only one patient went from positive to negative and four subjects were negative the first night but positive the second.

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Mendelson found only a modest FNE. Most recently, Le Bon and coworkers retrospectively reviewed 169 pairs of consecutive nocturnal polysomnograms in predominantly male (n=113) middle-aged adults.[15] There was a robust FNE with respect to sleep architecture encompassing the classically-described variables; also, when patients were sorted into categories of AHI severity (each category spanning 5 points of AHI), 62 subjects moved into higher AHI categories between night one and night two, while only 32 moved into lower categories. Using Bland-Altman plots, these systematic differences were more striking for patients with lower values of AHI averaged over the two nights. Surprisingly given the distinct FNE observed, changes in sleep variables did not seem to account for the shifts in AHI between nights.

In many laboratories, patients unable to sleep during the first night of polysomnography may simply be scheduled for a second night of testing; others institutions resort to administering a hypnotic medication. The patient with a lesser degree of FNE, if initial polysomnography is negative but clinical suspicion is high, could also simply be scheduled for a second night. Alternatively, some laboratories customarily or by protocol allow for hypnotic medication in these situations as well, but whether such a practice aids or impedes the diagnostic process has never been systematically studied. Finally, none of the foregoing applies to the situation in which positive pressure titration is being attempted, wherein the trials and tribulations of FNE are replaced by the overt disruptions of intrusive therapy.

The report by Lettieri and colleagues, appearing in this issue of the Journal of Clinical Sleep Medicine, now provides some of the information necessary to judge the efficacy of hypnotic medication for ameliorating both FNE and relative degrees of positive pressure therapy intolerance. In this retrospective study of 200 consecutive patients referred for the evaluation of sleep-disordered breathing, 54 (27%) were found to have been administered zolpidem 10 mg prior to polysomnography by order of the referring physician. The authors defined a "poor quality study" as one that needed to be repeated for reasons of too little sleep time for diagnosis, inadequate continuous positive airway pressure (CPAP) titration, or complete CPAP intolerance. Comparisons between the groups receiving and not receiving zolpidem were performed with respect to the proportion rated as being of poor quality, and also for sleep latency, sleep efficiency, and AHI. Not surprisingly, sleep latency and sleep efficiency were significantly better with zolpidem pretreatment, although the mean differences may not be clinically significant (changes of about 14 minutes and 11%, respectively). More important, only 7.4% of the studies done on zolpidem required repeating, while this was true of 33.6% of the studies done without medication. Furthermore, 21 of the studies deemed of poor quality without zolpidem were repeated with zolpidem, and none of these repeat studies were judged as poor quality recordings.

Zolpidem is seemingly an ideal hypnotic for the purpose of facilitating polysomnography, since it usually does not alter sleep architecture nor cause next-day psychomotor impairment,[16,17] although little is known of the latter property in patients with sleep apnea. Fortunately, some data are available concerning zolpidem's potential for worsening sleep-disordered breathing, an important issue when used during diagnostic polysomnography in patients suspected of having sleep apnea. A few studies do suggest that zolpidem could worsen mild obstructive sleep apnea,[18-20] thus raising the specter of causing false-positive sleep studies in some patients. Unfortunately, the retrospective, uncontrolled study design employed by Lettieri and associates does not allow us to judge whether zolpidem had this effect, notwithstanding the fact that mean AHI's in medicated and un-medicated patients were similar. Other questions raised by their findings also need to be addressed: Are the authors advocating the general use of zolpidem in all patients being tested for sleep-disordered breathing? If not, what criteria were used to choose patients that would be medicated for their sleep study? If so, have they considered the cost of administering zolpidem routinely to patients undergoing polysomnography? (Using a recent estimate of 1,170,000 yearly polysomnograms in the United States[21] and a retail cost of $2.73 per 10 mg tablet,[22] such pre-medication would total more than $3 million per year.) Finally, Lettieri and associates report that fully one-third of the polysomnograms performed without zolpidem were scored as of poor quality based on their stated criteria, a troubling assertion that seems inconsistent with more than 40 years of polysomnographic research reports.

In the final analysis, the study by Lettieri and colleagues does little more than bring what may be a fairly common practice (the use of zolpidem or other hypnotics to facilitate polysomnographic studies) out into the open for careful evaluation. Unlike the situation in quantum physics, where the blurring of a particle's attributes by attempting their precise simultaneous measurement is a fundamental property of nature, polysomnography may well yield results suitable for clinical or scientific uses with or without resorting to the pharmacological armamentarium. This subject clearly deserves further study using the techniques of modern, evidence-based medicine.

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