Correspondence

Commentary on Kayumov L, Pandi-Perumal SR, Federoff P, Shapiro CM. Diagnostic values of polysomnograph in forensic medicine. J Forensic Sci 2000 Jan;45(1):191–4.

Sir:

We take issue with several crucial comments and call attention to pertinent omissions in the report in question (1), based on current research findings on sleepwalking (SW) and other parasomnias (viz. sleep behavior disorders) in adults, and their forensic implications. The report concerned a 26 year-old man who was accused of murdering a two year-old girl, and the possibility that the crime was committed during an act of SW was investigated by the defense. This diagnostic possibility was considered untenable after two consecutive polysomnographic (PSG) studies, with video monitoring, did not detect any parasomnia behavior, nor any of the allegedly characteristic PSG features of SW, a "disorder of arousal" from nonREM (NREM) sleep. For example, the authors state (without citation) that "in NREM parasomnias all night polysomnography recording traces frequently display EEG slow waves with high amplitude just before the onset of movement." They also state that the EEG "hypersynchronicity . . . persists even after the parasomnia event has begun and the subject is moving." The reference (#13) the authors cite with this assertion contains no data, but rather anecdotal observations. Although these observations possibly hold true in childhood SW, they have been disproven in adult SW by systematically-gathered research published in 1998 (2).

In our study (2), we examined the PSG events surrounding 252 slow-wave sleep arousals (including 89 arousals with parasomnia behaviors) in 38 adults with chronic, injurious SW and sleep terrors. A notable finding was that the "hypersynchronous delta" EEG activity (viz. multichannel, high-voltage delta activity) was detected in $<2\%$ of the 252 slow-wave sleep arousals. Also, EEG "hypersynchronicity" was not detected in the analysis of the post-arousal EEG; instead, three other patterns were detected.

It is unfortunate that the report in question (1) did not contain any information on whether the accused had a past or current history of SW, other parasomnia, or any other sleep disturbance. In fact, no sleep history was provided, and it appears that a clinical evaluation by an experienced sleep specialist was not conducted. Rather, the referral by the forensic psychiatrist was for PSG investigation, which was conducted in a sub-optimal manner for the evaluation of sleep violence, since a portable system was used, which contained minimal EEG and electromyographic (EMG) montages, thus compromising the process of rigorously investigating the various causes of sleep-related violence.

A negative PSG study for SW does not rule out SW, since SW occurs intermittently, and since SW does not have specific, diagnostic EEG findings in the absence of a SW episode captured during PSG monitoring. A compelling clinical history of SW should therefore carry more forensic "weight" than a negative PSG study. We contend that the primary reason for PSG monitoring in forensic parasomnia cases should be to "rule-out" other possible causes of sleep-related violence (3). For example, REM sleep behavior disorder and obstructive sleep apnea have characteristic PSG findings (apart from behavioral manifestations) that are present every night. Nocturnal seizures and nocturnal (psychogenic) dissociative disorders also have characteristic EEG features, although they are intermittent phenomena that may not be recorded during a given PSG study.

In the opening paragraph of the report in question (1), the authors make the inaccurate statement that patients with REM sleep behavior disorder (RBD) are amnestic for their parasomnia behaviors. In fact, patients with RBD usually recall quite vividly their episodes of dream-enacting behaviors (4). Furthermore, adults with SW and ST at times can recall their episodes and can recall dreaming during their episodes (5), which is in contrast to childhood SW/ST. Therefore, the EEG and clinical findings in adult vs. childhood SW may diverge, and this must be recognized in the forensic arena.

In conclusion, the diagnostic values of polysomnography in forensic medicine must be embedded in a proper protocol for evaluating parasomnias and sleep violence (involving a clinical evaluation with an experienced sleep specialist, and extensive PSG monitoring with expanded EEG/EMG montages) (3), and also must be anchored in systematically-gathered data published in peer-reviewed medical journals. Finally, the documentation of a parasomnia during PSG monitoring does not necessarily mean that it was responsible for the crime an individual is alleged to have committed. As information about parasomnias becomes more widely disseminated to the general public by media reports, the risk will increase for using the "parasomnia defense" for a willfully planned and executed crime.

References

1. Kayumov L, Pandi-Perumal SR, Fedoroff P, Shapiro CM. Diagnostic values of polysomnography in forensic medicine. J Forensic Sci 2000;45:191–4.
2. Schenck CH, Pareja JA, Patterson AL, Mahowald MW. Analysis of polysomnographic events surrounding 252 slow-wave sleep arousals in thirty-eight adults with injurious sleepwalking and sleep terrors. J Clin Neurophysiol 1998;15:159–66.
3. Mahowald MW, Schenck CH. Parasomnias: sleepwalking and the law. Sleep Medicine Reviews (in press).
4. Schenck CH, Hurwitz TD, Mahowald MW. REM sleep behavior disorder: an update on a series of 96 patients and a review of the world literature. J Sleep Res 1993;2:224–31.
5. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Mahowald MW. A polysomnographic and clinical report on sleep-related injury in 100 adult patients. Amer J Psychiatry 1989;146:1166–73.

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Authors' Response

We welcome this opportunity to comment on Schenck and Mahowald's commentary about our paper.

In their opening paragraph, Schenck and Mahowald castigate the most widely accepted textbook in the field of sleep medicine by chastizing the authors' use of a chapter in this definitive book as citing only anecdotal observations (1). The authors Schenck and Mahowald would realize that in any science one only knows what is currently known and not what might be known in the future. It should have been easy to calculate that at the time at which the patient in our report was evaluated was prior to their paper in 1998. We distinctly state in the last paragraph of our paper that "one and a half years later . . . ." As experienced scientists (witness the reference list Schenck and Mahowald cite), they would know that the process of publication takes some time bringing us to a point prior to the publication of their paper concerning polysomnographic events surrounding slow wave sleep arousals (2). The authors would also be well aware that a single case study is important but not usually sufficient to definitively conclude that the received wisdom as cited in the textbook by Keefauver and Guilleminault (1994) (1) reference is incorrect.

Their second paragraph is an elaboration of the last point in the first paragraph and provides some details and teases the readers concerning the "three other patterns" that were detected (2).

In the third paragraph, the authors imply that no detailed assessment was carried out, but this is, in fact, inaccurate. Dr. Kayumov who is a Diplomate of the *American Board of Sleep Medicine* interviewed the patient. We agree that it would have been desirable to explicitly state that no convincing evidence of personal history of parasomnia was obtained, but in two places within the paper (the abstract and in the paragraph prior to the discussion) it is noted that a "full assessment was carried out." It is also noted within the section on relevant past history that the subject had no known medical problems and was not on any medication. We report in the text that the patient was adopted and therefore, one presumes, the authors of the critique would appreciate that a family history about parasomnia was not likely to be forthcoming. There are further limitations that the authors of the critique do not cite such as the fact that a sodium amytal test was done before the first sleep study, which is noted in the second paragraph of the polysomnographic findings, and that he had undergone an interview under hypnosis on the day prior to the second sleep assessment. In the best of all possible worlds, neither of these events would have been scheduled in this way. The third paragraph by Schenck and Mahowald continues to claim that a sub-optimal evaluation was carried out. We are unaware of the facilities available in secure forensic psychiatric facilities that Schenck and Mahowald will be called to, but in our circumstance this was as comprehensive an assessment as was possible (and without financial reimbursement). Since we had to use a portable system with only 12 channels available, we recorded classical EEG leads for the standard nocturnal polysomnography (C3 A2, C4 A1). We are aware that for differentiation between parasomnias and nocturnal seizures we would need extended EEG montage, however, we also had to rule out parasomnia-like behaviors induced by sleep disordered breathing (3). Therefore, we used three respiratory channels and oximetry monitoring. There was no history to suggest epilepsy.

In the fourth paragraph, Schenck and Mahowald note that a sleep history rather than a polysomnographic study should be used to rule out other possible causes of sleep related violence. We do not disagree with this. There is the description of breathing patterns in the information provided about the sleep study. Had there been nocturnal seizures or features of REM behavior disorder then this certainly would have been commented upon. Again the authors tease readers by making reference to characteristic features of nocturnal "psychogenic dissociative disorders" without citing any reference. We think it is unreasonably naive to state "a compelling clinical history of SW (sleepwalking) should therefore carry more forensic 'weight' than a negative PSG study." In a forensic situation where the stakes would be higher, it is not difficult to imagine that very compelling stories of sleepwalking episodes would be concocted in order to ameliorate responsibility or sentencing. We would, therefore, suggest that an assessment in a forensic setting requires both the corroborative history and supportive information from objective tests to the extent that such information is available. Tests in medicine do not typically have 100% sensitivity and specificity and the same would apply with arousals during slow wave sleep in patients with parasomnias generally and sleepwalking in particular. However, the combination of those features together with the history would certainly strengthen the argument.

In the fifth paragraph, Schenck and Mahowald have misread or misunderstood the English in our opening paragraph. We have not stated that REM sleep behavior disorder patients are amnestic for their parasomnia behavior. The sentence in our original paper reads "this complex set of clinical entities (somnambulism, night terrors, REM behavior disorder) characterized by automatic, stereotypic, and amnestic behaviour can result in self-injury . . ." We have gathered together three examples of parasomnia and mentioned three features that do occur. This is not, by any manner, trying to give a detailed description of all three parasomnias! In the second paragraph of our discussion, we actually specifically mention that "violent behavior related to dream enactment" has been reported in REM behavior disorder and cite a reference by Mahowald and Schenck in the aforementioned textbook referred to in the opening paragraph.

The first half of the concluding paragraph we certainly agree with. The final sentence of their criticism is, in fact, exactly the reason that we published our case. Schenck and Mahowald share our view as they state that as "information about parasomnias becomes more widely disseminated to the general public . . . , the risk will increase for using the parasomnia defense . . . ." It is for this reason that we wanted to draw attention to the role of assessment including polysomnography in supporting a negative finding. A careful integration of the different sources of evidence will need to be made. As we conclude in our original description, it should be reassuring that every time an attempt to use "the parasomnia defense" will not lead to acquittal. Describing positive cases has been of more interest and in some ways, more exciting. For exactly that reason we wanted to highlight this negative case.

References

1. Keefauver SP, Guilleminault C. Sleep terrors and sleep walking. In: Kryger MH, Roth T, Dement WC, editors. Principles and Practice of Sleep Medicine. Philadelphia: WB Saunders, 1994;567–73.
2. Shenck CH, Pareja JA, Patterson AL, Mahowald MW. Analysis of polysomnographic events surrounding 252 slow wave sleep arousals in thirty-eight adults with injurious sleepwalking and sleep terrors. J Clin Neurophysiology 1998;15:159–66.
3. International Classification of Sleep Disorders: Diagnostic and Coding Manual. Rochester, MN: American Sleep Disorders Association 1997; 146.
4. Mahowald MW, Schenck CH. REM sleep behaviour disorder. In: Kryger MH, Roth T, Dement WC, editors. Principles and Practice of Sleep Medicine. Philadelphia: WB Saunders, 1994;574–88.

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Phenotypic Differences at the HUMvWA Locus Amplified with Different STR Kits

Sir:

The potential effect on the CODIS databanking program of a mutation in the primer binding site associated with an STR allele was recently encountered in our laboratories. A paternity analysis was performed in two laboratories using different STR kits. The original analysis was performed using a Profiler Plus kit from Perkin Elmer Biosystems (Foster City, CA) while the second lab performed testing for additional systems using the CTTV quadriplex and the Powerplex 1.2 kits available from Promega Corp. (Madison, WI). Additional testing was needed in this case to resolve the questioned paternity. The HUMvWA, D7S820, D13S317, and D5D818 loci were common to kits used in both laboratories and all loci except the HUMvWA system yielded identical phenotypes. The mother's phenotype differed for the HUMvWA locus depending upon the STR typing kit used. The Profiler Plus kit produced a homozygous HUMvWA phenotype for allele #17 whereas the CTTV quadriplex or the Powerplex 1.2 STR kits produced a heterozygous 17,18 phenotype (Fig.1).

The most likely explanation for the discrepant phenotypes is that a single (or limited number) of nucleotides in the primer binding site(s) have been altered through mutation in the #18 allele in the mother's DNA template. Such a mutation could preclude the binding of one or both of the HUMvWA primers in the Profiler Plus kit to the #18 allele in the maternal template thereby resulting in a null allele.

Mutations associated with STR loci typically take the form of small additions or deletions of repeats from the parent allele presumably occurring during meiosis (1,2). More importantly here, null alleles have been observed for a number of STR systems with a mutation rate as high as 0.68% for the CYP19 system (2). A null allele in a parentage analysis can result in a false exclusion of an alleged father or mother when the overwhelming preponderance of other genetic evidence demonstrates the individual to be a true parent of a child. In such cases, statistical analysis of the data can incorporate the possibility of a mutation into the final probability of parenthood. In this particular case, the resulting paternity index calculated for the HUMvWA system was in error by a factor of two when using the Profiler Plus data because of the apparent homozygosity of the mother and its impact on the maternal transmission frequency for the #17 allele used in the calculations. Null alleles can have a more profound effect in forensic matching of an unknown assailant's STR phenotype with entries in a CODIS databank. For example, had the HUMvWA phenotype described here been produced in a crime laboratory using a Promega STR typing kit and then compared with entries in a CODIS databank containing the STR phenotype of the assailant produced using Profiler Plus, the results of the query at face value might be interpreted to exclude the CODIS entry as a possible contributor.

Null alleles have been reported for several of the 13 core loci included in the CODIS databanking program (HUMTPOX, D5S818, D16S539, HUMCSF1P0, and HUMTHO1) (2). The HUMTPOX locus in particular exhibits a reported null allele rate of about 0.6% (2), which is similar to rates reported for more traditional mutations involving the addition or deletion of repeats from the tandem array. With a mutation rate of 0.6%, complications in CODIS matching due to mutations of the type reported here could be somewhat common occurrences. The CODIS matching program was developed in

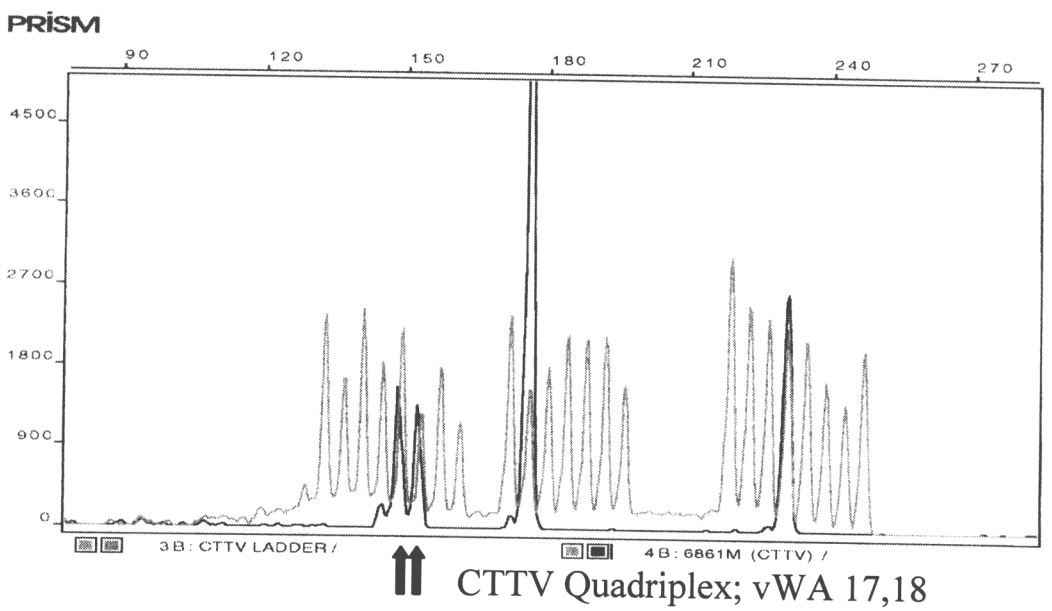

FIG. 1—*Phenotypes for the HUMvWA locus in a sample amplified with STR kits from different manufacturers. A sample of DNA extacted from a buccal swab of the mother in a parentage analysis was subjected to STR typing using kits from Perkin-Elmer or Promega Corp. and the ABI 310 capillary electrophoresis system. The particular STR typing kit used to amplify the DNA and the HUMvWA phenotype are shown below each electropherogram along with vertical arrows denoting the positions of the HUMvWA alleles.*

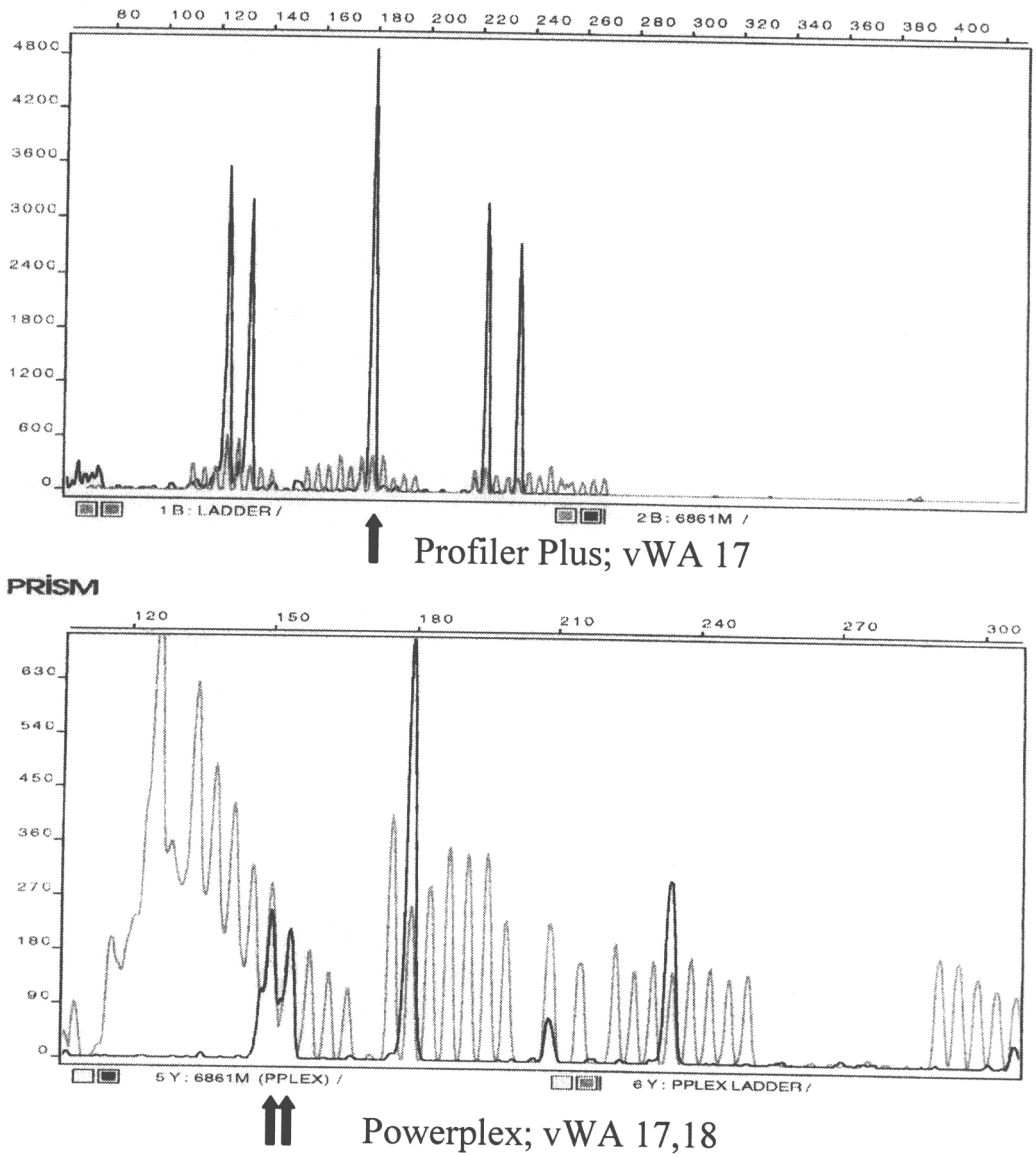

FIG. 1—*(continued)*

a manner that scores as positive "partial matches" between a query and database phenotype that differ for a limited number of alleles. Partial matches can result from errors in assigning a phenotype to a database entry or to a query phenotype. In addition, partial matches can result from a database entry and query that represent phenotypes from related individuals. As shown here, partial matches can also stem from mutations that produce null alleles when amplified using a particular STR typing kit. The key to identifying such mutations is the homozygous nature of one phenotype that matches one of the alleles in a heterozygous phenotype amplified from the same template with a different STR typing kit. When a partial match of this type is obtained, the crime laboratory may easily resolve the apparent discrepancy through repeat typing using an STR kit from a different manufacturer.

References

1. Brinkmann B, Klintschar M, Neuhuber F, Huhne J, Rolf B. Mutation rate in human microsatellites: influence of the structure and length of the tandem repeat. Am J Hum Genet 1998;62:1408–15.
2. Parentage Testing Standards Committee. Annual Report Summary for 1998. Bethesda, MD, American Association of Blood Banks.

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