P300 and the Daytime Consequences of Disturbed Nocturnal Sleep: Easy to Measure but Difficult to Interpret

Comment on Devoto A; Manganelli S; Lucidi F et al. Quality of Sleep and P300 Amplitude in Primary Insomnia: a Preliminary Study. SLEEP; 28(7); 859-863

Ian M. Colrain PhD

Human Sleep Research Program, SRI International, Menlo Park, CA; Department of Psychology, University of Melbourne, Victoria, Australia.

IN 1965, SAM SUTTON PUBLISHED A BRIEF PAPER IN SCIENCE IN WHICH HE DESCRIBED A LATE POSITIVE COMPONENT IN AN AVERAGED AUDITORY evoked potential. 1 Subsequently referred to as P300, this late component has become the most studied EEG phenomenon of the last 40 years. (A recent Medline search produced over 1200 hits for “P300 and EEG” exclusive of articles published in psychology journals not listed in Pubmed and the numerous books and book chapters devoted to its study.) Sleep researchers have conducted relatively few studies of P300, yet there is a small and growing literature attempting to relate P300 during the day to nocturnal sleep or the lack of it. The paper by Devoto and colleagues in this issue is the latest in this growing series. What then is P300, and how can sleep researchers use it?

P300 is an endogenous ERP component; that is, it reflects the higher processing of the psychological meaning of stimuli, rather than their “exogenous” sensory or perceptual properties such as loudness or brightness. It is elicited when subjects attend and discriminate stimulus events that differ from one another on some dimension. Often such discrimination occurs in the context of an “oddball” paradigm, in which P300 is usually elicited to low probability (target), task relevant stimuli. 2 One notable feature of the P300 is that it can be elicited by a variety of stimuli or events from any stimulus modality; the only requirement is that the events have distinct onsets, and that they are classifiable into two or more categories. P300 can also be elicited when only a single stimulus is presented if the stimulus is rare and salient to the subject. 3,4 In addition to standard visual or auditory stimuli, P300 has been produced in response to respiratory, 5 somatosensory, 6 olfactory, 7 and even esophageal stimuli. 8

The classification of P300 is made difficult due to the fact that several late positive components the overlap it. Several studies have reported that a long latency positive wave (labeled P3a) can also be elicited by an unpredictable shift in an ongoing sequence of auditory stimuli under circumstances when no explicit task is given to the subject. Importantly, P3a is considered to be a different brain phenomenon from the classically described P300 (also referred to as P3b), with a shorter latency and fronto-central scalp distribution 9 as compared to the ubiquitous centro-parietal distribution for the P3b. 10 The P3a (or “novelty P3”) also seems to represent psychological events that are quite distinct from those of P3b. It has been linked to processes involved in the involuntary capture of attention by salient events 11 and, in a different context, to the processing associated with the active inhibition of responses in so called “NO GO” paradigms. 12

A number of factors have been suggested to account for the observed variations in P300 amplitude and latency. Amplitude can be independently effected by a number of factors including subjective probability, task complexity, stimulus complexity, stimulus value, expectancy and attention. 13,14,15 P300 amplitude has also been shown to be under some genetic control, 16,17 with a major field of study devoted to the investigation of reduced P300 in the children of alcoholics. 18,19

Studies have generally found that P300 latency increases when there is difficulty in discriminating between stimuli, and is independent of response output processing as indicated by reaction time. 20 This latency increase has been proposed to relate to the longer time for stimulus evaluation required when discriminations are difficult or ambiguous. 21 P300 latency has also been shown to increase in the elderly 22 and with drowsiness preceding sleep onset. 23,24 P300 has been assessed in a variety of clinical populations (see reference 25 for review) and has unfortunately shown a marked lack of clinical specificity, with reduced amplitude and/or increased latency being a common finding in many disorders or syndromes.

Studies conducted on obstructive sleep apnea syndrome (OSAS) patients during wakefulness have however reported mixed results, with some evidence for an increased P300 latency to visual 26-28 and auditory stimuli, 28,30,31 although no effect on auditory P300 latency has also been reported. 26,27,28 Some studies have 26,30,31 and some have not 26,28,29 found OSAS patients to have reduced auditory P300 amplitudes, although there is 1 report of significant correlations between P300 amplitude and respiratory disturbance index , % stage 1 sleep and the maintenance of wakefulness test. 33 Likewise improved nocturnal sleep following effective CPAP treatment has, 30,31 and has not, 27,39 been associated with decreased P300 latency relative to that seen prior to treatment. Neither of the studies that have evaluated respiratory somatosensory P300 in OSAS patients found a significant effect on amplitude or latency of the response relative to controls. 32,34

Findings of the impact of experimental sleep fragmentation or deprivation on P300 have also been mixed. Morris et al 45 reported reduced P300 amplitude and increased latency during 18 hours of sleep deprivation. Cote et al 46 found no changes in P300 following two nights of sleep fragmentation, although they did report...
significant decreases in N1 amplitude. Kingshott et al37 found reduced P300 amplitudes following a night of sleep fragmentation at some frontal, central and temporal scalp sites but not over parietal areas where P300 (P3b) is most prominent. In the most recent, and most comprehensive study of evoked potential effects of sleep deprivation, Gosselin et al38 reported decreased target P3b amplitudes at Fz, Cz and Pz and decreased novelty P3a amplitude at Fz following 36 hours of sleep deprivation. P3a and P3b latencies were increased at all sites.

The evoked potential methodology has rarely been used to study insomnia. Regestein et al39 reported increased N1 amplitudes during the day in insomnia patients and interpreted this finding as being supportive of a hyperarousal hypothesis. Szelenberger and Niemieciewicz40 studied current source densities of a variety of ERP components in primary insomniacs and reported that, compared with controls, insomniacs displayed less event related current density in a variety of brain regions in association with N1, N2 and P3 ERP components.

The study published by Devoto et al in this issue investigating P300 in primary insomniacs includes some important design features such as the classification of responses based on the quality of the sleep obtained and the measurement prior to, and following nocturnal sleep. While these data were not separately presented in this preliminary report, presumably this will occur as more data are collected. Additional data will also permit the examination of other variables of potential utility, such as P300 latency and N1 amplitude.

While the small number of subjects and the associated low power and small effect sizes make the data from the Devoto et al study difficult to interpret, they raise some interesting possible future research directions. The findings, indicative of group differences being most prominent at a frontal EEG site, raise the possibility that insomnia may well be associated with elevated P3a amplitude. Future studies should then include a novelty P3 method similar to that used by Gosselin et al or a NOGO task similar to that adapted by Ford et al.41 Such an extended methodology would permit testing of an alternative hypothesis to explain the preliminary finding of Devoto et al. That is that increased frontal P300 amplitude following a poor night of sleep is consistent with P3a amplitude reflecting a strengthened frontally mediated inhibitory process, rather than an elevated arousal level.

As is obvious above, P300 amplitude is influenced by a range of factors with “arousal” being one of the least well supported. Indeed there is strong convergent evidence that the P300 represents the output of a network of cortical and subcortical regions involved in widespread cortical inhibition associated with cognitive closure or termination of mental processes. In this model, P300 amplitude reflects the degree to which responses to irrelevant stimuli are inhibited in order to correctly respond to targets (see reference 43 for review).

A better component to evaluate arousal hypothesis of Devoto et al would be N1. This component has both “exogenous” and “endogenous” properties being influenced by stimulus features as well as attention.42 In the present context however, it is also extremely sensitive to fluctuations in arousal related to sleepiness.43 N1 could be easily extracted from their current data set.

Insomnia is an intriguing disorder, with its unique combination of hyperarousal and sleepiness, and one in which the use of evoked potentials may well provide answers to hitherto inscrutable questions. The preliminary waking evoked potential data presented by Devoto and colleagues should act as an encouragement to them and to others to further pursue this area.

REFERENCES