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Vigilance, alertness, or sustained attention: physiological basis and measurement

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Abstract

Vigilance is a term with varied definitions but the most common usage is sustained attention or tonic alertness. This usage of vigilance implies both the degree of arousal on the sleep–wake axis and the level of cognitive performance. There are many interacting neural and neurotransmitter systems that affect vigilance. Most studies of vigilance have relied on states where the sleep–wake state is altered, e.g. drowsiness, sleep-deprivation, and CNS-active drugs, but there are factors ranging from psychophysics to motivation that may impact vigilance. While EEG is the most commonly studied physiologic measure of vigilance, various measures of eye movement and of autonomic nervous system activity have also been used. This review paper discusses the underlying neural basis of vigilance and its assessment using physiologic tools. Since, assessment of vigilance requires assessment of cognitive function this aspect is also discussed.

Keywords

Arousal; Attention; Sleep deprivation; EEG; Evoked potentials; Cognition; Vigilance

1. Introduction

There are activation states of cerebral cortex that impact the ability to process information where the activation itself contains no specific information. These activation states can be tonic or phasic and may be relatively global or more localized. Terms that have been used to describe these states include arousal, alertness, vigilance, and attention. Unfortunately, no terms are ideal to describe these states of cortical activation since most terms are in broad use with varied associations and there are not perfect physiological markers. The term *vigilance*, in particular, has unfortunately been used in different ways by different groups of scientists. Psychologists and cognitive neuroscientists use the term to describe an ability to sustain attention to a task for a period of time (Davies and Parasuraman, 1982; Parasuraman, 1998). They often specifically refer to a vigilance decrement, the decline in attention-requiring performance over an extended period of time (Mackworth, 1964). Animal behavior scientists and psychiatric clinicians use the term vigilance similarly but more specifically referring to attention to potential threats or dangers, with hypervigilance being one of the symptoms of post-traumatic stress disorder (American Psychiatric Association, 1994). This usage of *vigilance* is probably closest to the common lay usage and to the English dictionary primary definitions of vigilance,

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e.g. ‘state of being alertly watchful, especially to avoid danger’ (Merriam-Webster [online], 2005). A third group of scientists are clinical neurophysiologists who sometimes use the term vigilance level to refer more narrowly to arousal level on the sleep–wake spectrum without any mention of cognition or behavioral responsiveness. This is partly related to the EEG’s exquisite sensitivity to the activity of the corticothalamic networks underlying the sleep–wake dimension (Steriade, 1999). It also may relate to the lack of lay usage of the term vigilance in languages other than English, the translation of the English word arousal into a more medically used term *vigilance* in French and *Vigilanz* in German, and to a less common English definition of the term vigilance. Most would consider arousal or wakefulness an aspect of vigilance (Parasuraman et al., 1998) and in many cases the two are very closely related, e.g. with sleep-deprivation. For this discussion, *vigilance* will mean sustained attention, the most common scientific usage.

Arousal is another term that is used differently by different groups of scientists but more consistently refers to non-specific activation of cerebral cortex in relation to sleep–wake states. While *vigilance* as we have defined it is conceptually distinct from arousal, most research on vigilance has, in fact, studied alterations in arousal through the use of subjects who are sleep-deprived, have sleep disorders, or are taking sedative medications. This problem is compounded by the fact that relative sleep-deprivation is common in the overtly healthy population (Bonnet and Arand, 1995b; Levine et al., 1988) contributing to healthy subjects becoming drowsy during performance of a prolonged, often tedious task. Thus, the aspect of vigilance distinct from arousal that requires a normally awake person to attend to a task for a prolonged period has not been as well-studied physiologicially. Attention usually refers to a more focused activation of cerebral cortex that enhances information processing (Mesulam, 1990; Mountcastle, 1978; Parasuraman, 1998; Posner and Petersen, 1990) but one aspect, sustained attention, is used synonymously with the most common usage of vigilance (Parasuraman, 1998b). While focused attention, divided attention, and shifting of attention, as well as executive control of attention, are all important, sustained attention is the aspect closely related to the alertness systems and the only attentional aspect that will be discussed in detail. *Alertness* is another term that overlaps with arousal but more specifically includes some cognitive processing. Some researchers use the terms phasic and tonic alertness (Nebes and Brady, 1993; Posner and Petersen, 1990). Phasic alertness relates to the orienting response (Sokolov, 1963) and tonic alertness will be used synonymously to vigilance and sustained attention.

This review paper of the biologic bases and physiologic correlates of vigilance, perhaps better referred to as tonic alertness or sustained attention, encompasses an extremely large field. The paper focuses on the basic underlying mechanisms including animal studies and on physiologic measurements that have been related to these states, including EEG, event-related potentials, eye movements, and measures of autonomic nervous system activity. The human electrophysiology section focuses on just several conditions associated with altered alertness: the normal wake–sleep transition, sleep-deprivation and sleep fragmentation, as well as declines on sustained continuous performance tasks. Some relevant topics such as drug effects were omitted in the interest of space. Additionally, only a subset of excellent papers could be cited.

2. Underlying mechanisms and physiology

Alertness and sustained attention to the environment have multiple underlying brain processes and related psychological constructs. A very important aspect already referred to is the sleep–wake state, dependent on multiple brain-stem–thalamo–cortical pathways. There are also many modulatory systems that impact the sleep–wake state and alertness. These neural-based systems include the suprachiasmatic nucleus–circadian rhythm (Dijk and Czeisler, 1995), the

hypothalamo–pituitary–adrenal axis, and limbic system (including amygdala and nucleus accumbens). Also, alertness may be modulated by metabolic systems and substrates such as thyroid, glucose, oxygen and electrolytes. Additionally, to sustain attention there needs to be motivation and cognitive processing.

2.1. Sleep–wake systems

The sleep–wake aspect is probably the most studied component of alertness and sustained attention in terms of underlying mechanisms and physiological correlates and thus is the focus of much of this discussion. The multiple brain structures and neurotransmitter systems responsible for the sleep–wake state are highly interconnected and usually interact in predictable ways, but may become dissociated in pathologic states. Even during the awake state a person may be more or less engaged in processing or responding to environmental stimuli. In catatonia there is intact wakefulness but a significantly reduced ability to interact with the environment. Cataplexy is associated with conscious wakefulness but atonia related to partial intrusions of REM sleep. Fatal familial insomnia (FFI) associated with thalamic pathology produces marked decreases in total sleep and REM time with the awake state characterized by increased slowing, decreased alpha and deficits in attention and vigilance (Lugaresi, 1992; Sforza et al., 1995). In persistent vegetative state, severe dementia, or minimally conscious states, there may be some preservation of sleep–wake cycles. However, even though awake in some sense, i.e. EEG state change with eyes open, the alertness or cognition of the person in a persistent vegetative state is essentially absent.

The brain systems underlying the sleep–wake state include both wakefulness-promoting and sleep-promoting components which are interconnected and mutually inhibitory. The relevant systems include: the hypothalamus (tuberomamillary histaminergic projections and preoptic nuclei); the serotonin projection system from the raphe nuclei; the norepinephrine projection system from the locus coeruleus; the cholinergic system including both thalamic projections from the midbrain and cortical projections from basal forebrain regions; and several thalamic nuclei. While a detailed understanding of the brain systems contributing sleep is well beyond the scope of this paper, the systems are important for normal alertness and sustained attention and are affected by pathologic states and medications altering alertness and sustained attention.

The first observation of a wake-related structure was that intact brain-stem structures above the midpons were critical to maintaining arousal as evidenced by EEG recording in cats (Moruzzi and Magoun, 1949). Originally termed the ascending reticular activating system, critical constituents of this are thalamic projections from the upper brain-stem: the cholinergic pedunculopontine and laterodorsal tegmental nuclei. Other components are the monoaminergic systems projecting from the brain-stem. In addition, there are two wakefulness promoting systems in the hypothalamus: the histamine projections from the tuberomammillary nucleus and the hypocretin (orexin) projection system. The hypocretin neurons have widespread projections to major nuclei related to sleep–wake state in brain-stem and thalamus and are associated with neuroexcitatory activity (de Lecea et al., 1998). The declines in alertness and increased sleep propensity that occur in narcolepsy are associated with hypocretin deficiency (Mignot et al., 2002; Nishino et al., 2000).

In addition to systems to promote wakefulness there is at least one hypnogenic or sleep-promoting system. Following the description by von Economo of persistent insomnia following hypothalamic lesions (von Economo, 1930) it has become established that the preoptic area of the hypothalamus is critical in inducing sleep, with lesions of the ventrolateral preoptic nucleus region producing as much as a 50% sustained decrease in sleep (Lu et al., 2000; McGinty and Szymusiak, 2001; Saper et al., 2001). Failure to sleep also occurs with the thalamic lesions seen with fatal familial insomnia (Lugaresi, 1992). This disorder produces significant neuropsychological deficits often centering around attentional deficits (Gallassi et al., 1992).

Two distinct thalamocortical activity states related to alertness and attention are associated with specific states of thalamic projection neurons: burst and tonic. The burst state results from relative hyperpolarization and the tonic state from relative depolarization of the resting membrane potential (McCormick and Bal, 1997; Steriade et al., 1993). During EEG synchronized sleep when the thalamic neurons are hyperpolarized and in burst mode, there is a diminished responsiveness of thalamic sensory neurons to stimuli within their receptive fields with lowered signal-to-noise ratio (Livingstone and Hubel, 1981; McCormick and Feeser, 1990). The thalamic burst and tonic activity states are seen in thalamocortical relay and thalamic reticular nucleus neurons. Sleep transition is associated with hyperpolarization of thalamo-cortical neurons and disinhibition of thalamic reticular neurons. These changes alter transmission of signals conveying information from external environment and help generate sleep spindles (Steriade, 1999). During slow wave sleep, the thalamocortical activity consists of synchronous rhythmic activity (EEG delta waves and sleep spindles) associated with burst states in thalamic projection neurons (McCarley et al., 1983). During the awake state there is some sort of cortical activation, presumably related to partial neuronal depolarization bringing neurons closer to firing levels (Steriade, 2000). The tonic state produced during the awake and REM sleep states, produces less rhythmic, less synchronous, lower amplitude thalamocortical activity (McCormick and Bal, 1997; Steriade, 2000).

2.2. Neurotransmitter systems

There are several neurotransmitter systems that are relatively non-specific in that they do not carry specific motor or sensory information but they modulate thalamic and cortical activation (Robbins, 1997). The locus coeruleus– norepinephrine, raphe–serotonin, and tuberomamillary– histamine systems are active while awake, decrease during slow wave sleep and are decreased further during REM sleep. The cholinergic system is active while awake, less active in non-REM sleep and increases during REM sleep to a similar level as awake. Thus, the monoaminergic differences between the awake and REM state suggests that the norepinephrine and other monoaminergic systems are necessary to direct attention or weight of cortical processing to external sensory stimuli. This is in contrast to REM sleep where there is significant cortical activation and even awareness to some degree (of dreams) but little processing of external sensory stimuli. Changes in these neurotransmitter systems are critical to state changes as further evidenced by firing rate changes in cholinergic and norepinephrine neurons preceding state transitions as assessed by EEG or behavior (Aston-Jones and Bloom, 1981a; Steriade et al., 1982). All the systems related to alertness, including the neutortransmitter specific systems, are highly interconnected with direct projections between many of the relevant nuclei. This presumably contributes to the redundancy and compensatory responses such that fairly extensive bilateral lesions of LC are necessary in animals before there is background EEG slowing (Berridge et al., 1993). Additional neurotransmitters impacting alertness via the sleep–wake state but not discussed further include glutamate, gamma aminobutyric acid, nitric oxide, endorphins, and adenosine (Pace-Schott and Hobson, 2002).

2.2.1. Locus coeruleus–norepinephrine—The Locus coeruleus–norepinephrine (LC–NE) system highlights the tonic and phasic aspects of alertness and attention. The concept that NE output is modulatory is consistent with LC neurons being activated synchronously and non-specifically via electronic coupling. In addition to the tonic sleep–wake state dependent LC changes, there is phasic activation of the LC during the awake state (Aston-Jones and Bloom, 1981b; Berridge and Waterhouse, 2003). This phasic activation improves network wide enhancement of sensory processing of salient environmental stimuli and is thought to occur through improvement of signal to noise ratios in neurons or altering receptor field properties such that there is a decreased threshold for response (Berridge and Waterhouse, 2003). The P3-like event-related potentials in monkeys are attenuated by lesions of the LC (Pineda et al.,

1989) even though the mean latency of the LC neuronal responses to the infrequent target stimuli in this paradigm is 90 ms, which is much less than the latency of the P3-like potential. The latency to LC response is correlated with behavioral performance such that LC responses are longer during epochs with poor performance or lowered vigilance (Aston-Jones et al., 1994).

2.2.2. Cholinergic systems—Brain-stem and basal forebrain cholinergic activity are critical for sleep–wake state determination and the basal forebrain cholinergic projections to cortex are important for modulation of cognitive function, with attention being an important aspect (Everitt and Robbins, 1997; Szymusiak, 1995). There is some conflicting data on whether there is a significant cholinergic effect on sustained attention (Dalley et al., 2004; Gill et al., 2000; Grottick et al., 2003). The cholinergic system has a direct impact on EEG, with cholinergic activity in cortex being related to wakefulness and desynchronization of the EEG (Celesia and Jasper, 1966; Vanderwolf and Robinson, 1981). Nicotine increases some measures of EEG alertness (Griesar et al., 2002) but its mechanism is not solely cholinergic because nicotine acts presynaptically on neurons utilizing different neurotransmitters. Nicotine has produced similar effects to hypocretin on sustained attention in rats (Lambe et al., 2005).

2.3. Other factors impacting sustained attention

In addition to the impact of overt sleep–wake systems, there are other brain systems that are necessary for sustained attention to environmental stimuli. The attentional systems overlap in part with some of the sleep–wake systems but there are differences. As already noted, the LC–NE system is important for sleep–wake state changes but it is also phasically active for attention to environmental stimuli while awake. To further consider the other brain systems, it is helpful to recognize awake states where well-rested subjects may have low vigilance. Examples include catatonia, apathy, and attention deficit disorder.

2.3.1. Motivation—One psychological construct with its underlying brain systems impacting sustained attention is motivation. Based on animal as well as human lesion studies, the motivational system includes portions of the frontal lobes (e.g. anterior cingulate) as well as limbic and subcortical structures (striatum, nucleus accumbens, amygdala) and much of the dopamine system (Robbins and Everitt, 1996). The dopamine system may be related to reward but can also be thought of as relating to a stimulus' predictive value of reward (Schultz, 2002). Subjects who are uninterested in the environment or apathetic will not be as vigilant as those with high motivation. Performing a task with a high financial reward for performance will engage the attentional system stronger and with longer duration than performing the same task with no overt reward for performance. The P3 amplitude is increased with financial incentives for performance (Begleiter et al., 1983; Hömberg et al., 1981). Conceptually, effort (Kahneman, 1973) and motivation are related. The extensive literature on physiologic correlates of mental effort generally does not encompass sustained attention. One physiologic measure, frontal midline theta, has correlated with mental effort on working memory tasks and may reflect activity of anterior cingulate cortex (Gevins et al., 1997; Ishii et al., 1999; Jensen and Tesche, 2002; Onton et al., 1995). However, it is not clear if frontal midline theta represents an activation or deactivation of anterior cingulate (Mizuhara et al., 2004).

2.3.2. Stress—Stress (or stressor) describes an event or condition that elicits a certain pattern of physiologic and behavioral responses (McEwen, 2000), with chronic and acute stress producing different responses. Stress has an impact on sustained attention task performance (Hancock and Warm, 2003). The most studied physiologic responses to stress are activation of the hypothalamic–pituitary–adrenal (HPA) axis and the LC–NE-sympathetic nervous system pathway. The amygdala and parasympathetic system also interact with this latter pathway (Bernston et al., 1991). The function of the amygdala impacts vigilance and is thought

to be affected by post-traumatic stress disorder which is associated with hypervigilance, difficulty concentrating, and sensitization of the startle response (Davis and Whalen, 2001). Some of the interaction between stress and alertness is presumably mediated via the amygdala and its corticotrophin-releasing factor inputs to the LC (Valentino et al., 1992). A mild physiologic stress such as exercise may delay EEG measured sleep onset (Bonnet and Arand, 1998). Markers for stress and autonomic nervous system activity have included EEG (various measures of percent alpha or slow wave frequencies), skin temperature, electrodermal activity, heart rate and heart rate variability, breathing (rate, depth, pCO_2 and pO_2), and blood pressure. Certain levels of stress may improve cognitive function, suggesting a U-shaped curve relationship (see Section 2.4).

2.3.3. Cognitive aspects and habituation—Vigilance is affected by some cognitive aspects of the stimuli in addition to the overt rewarding or motivational values. For example, psychophysical variables of external stimuli that affect vigilance include signal modality, intensity, duration, background, event rate, signal probability, and regularity (Parasuraman, 1998b). Executive attention as measured by working memory load or cognitive control are other psychological parameters critical to the vigilance decrement (Caggiano and Parasuraman, 2004; Fisk and Schneider, 1981; Parasuraman, 1979). Decision-making response criteria may also be impacted by vigilance tasks (Loeb and Alluisi, 1984; Parasuraman, 1979).

The brain has a network of changes in response to novel stimuli (Ranganath and Rainer, 2003). Novel stimuli elicit an orienting response as well as the novelty P3 or P3a (Oken, 1997; Squires et al., 1975). Novel stimuli may automatically engage the attentional system and thereby produce improvements in sustained attention compared with more repetitive tasks. Repeated presentations of the same stimuli often produce decreased responses especially of the orienting response (Rockstroh et al., 1987). Many physiological measures including skin conductance, event-related EEG desynchronization, and P3 show some degree of habituation and the speed of habituation may relate to the vigilance decrement (Siddle, 1972). Most studies of vigilance use tasks that involve significant repetition where there will be habituation to the stimulus and decreased orienting.

One can presumably have intact sustained attention without an overt motor response but given the usual experimental designs, the relationship of vigilance to motor systems may also be important. Physiological measurements of motor fatigue have been evaluated, mostly using some EMG measures with repetitive activity (Lou et al., 2003; Vollestad, 1997). However, these have not been specifically evaluated in relationship to sustained attention. Mental fatigue is presumably identical or very closely related to sustained attention and vigilance as defined in this paper.

2.4. Physiologic correlates

Often there is a U-shaped curve relating performance to these various factors impacting cortical activation, such that performance is maximal at arousal states that are neither very low nor very high. This was first described almost 100 years ago with the use of mice that best learned a task with intermediate levels of electric shock; mice receiving negligible or very high level electric shock did not learn as well (Yerkes and Dodson, 1908). This U-shaped curve continues to be relevant for many aspects of alertness and attention. In general, the phasic alerting and attentional systems may be most critical when stimuli are near threshold (Reynolds et al., 2000).

There are many physiologic signals that have been utilized to assess alertness and sustained attention, only some of which are mentioned in this section. Overall there is increased slow frequency activity on the EEG and decreased amplitude of event-related potentials with decreasing vigilance. Additionally, during maximal attention, some awake frequencies, e.g.

alpha, are attenuated. This was initially described as event-related desynchronization (Pfurtscheller and Aranibar, 1977). However, event-related attenuation may be a better term because synchrony was often not directly measured and it has become clearer that the maximally alert state is associated with synchronous activity recorded from cortex, just at faster frequencies, e.g. gamma frequencies (Kaiser and Lutzenberger, 2004; Steriade et al., 1996). These gamma frequencies are difficult to reliably discern in scalp EEG because the skull acts as a low pass filter and EMG artifact contains much activity in the gamma frequencies.

There are several EEG measures used to relate activity in two locations. Neuronal synchrony is a recently developed technique derived from the decomposition of the oscillatory EEG signals in a defined frequency band into amplitude and phase (Lachaux et al., 1999). Large-scale neuronal synchrony has been proposed as a functional link between separate brain regions (Varela et al., 2001). The observation that event-related potentials may dynamically arise from partial phase resetting rather than from amplitude responses in an otherwise silent system (Makeig et al., 2002, 2004) underscores the functional significance of neuronal phase synchrony. This method of obtaining EEG synchrony information differs from the related measure, coherence. While coherence is calculated using fast Fourier transformation, synchrony is usually calculated using wavelet transformations (Le Van Quyen et al., 2001). A significant advantage of synchrony over coherence for the study of attentional phenomena is that by using wavelet analysis, synchrony can be calculated with higher temporal resolution than FFT methods that require several seconds or more of EEG data to calculate coherence. Using magneto-EEG to investigate the attentional blink phenomenon, neuronal synchrony in the beta band locations was increased during successful detection (non-blink) and decreased during missed letters (attentional blink) (Gross et al., 2004). Event-related covariance is another measure of relationship between different locations and decreases in event-related covariance have been related to performance decrements on sustained attention tasks (Gevins et al., 1987).

3. Conditions associated with changes in alertness and sustained attention

To further understand the alertness and sustained attention systems, the physiology associated with altered attentional conditions will next be discussed: the usual awake–sleep transition and sleep deprivation. Due to space limitations of this review, declines in vigilance associated with other conditions will not be discussed further, including attention-deficit hyperactivity disorder (Barkley et al., 1992), sleep apnea (Engleman and Martin, 1994; Verstraeten and Cluydts, 2004) and narcolepsy (Valley and Broughton, 1983).

3.1. Drowsiness

3.1.1. Awake–sleep transition—When an awake, alert person gradually falls asleep there is a transition from being fully awake to being clearly asleep. This transition is of great importance to understanding clinically relevant changes in alertness and sustained attention and is associated with well-established EEG changes (Dement and Kleitman, 1957; Matousek and Petersen, 1983; Rechtschaffen and Kales, 1968; Santamaria and Chiappa, 1987b). Some EEG changes in stage 1 sleep relate to the alpha rhythm: anteriorization, slowing by 0.5–2.0 Hz, fluctuations in amplitude and, eventually, loss of alpha activity. There is increased slow wave activity more often in the frontal and central regions, brief runs of anterior beta activity and vertex waves. Stage 2 is more clearly defined because of the appearance of sleep spindles and/or K complexes. The transition into stage 1 is particularly difficult to judge from the EEG in subjects with little or no alpha activity. The transition from awake to stage 2 sleep often involves many transitions between awake and stage 1 prior to stage 2 sleep onset. While the more precise EEG criterion of stage 2 sleep is often used to define sleep onset, it is apparent there is actually a sleep onset period beginning while awake and extending to at least stage 2 (Ogilvie, 2001). Some have tried to expand the staging of this sleep onset period by including

up to 9 substages (2 awake, 6 stage 1, 1 stage 2 (Hori et al., 1994)). However the temporal pattern of EEG changes is not uniform across all subjects (Santamaria and Chiappa, 1987b) so this classification based on many patterns is often difficult to implement accurately. In addition to conventional EEG changes, there is decreased amplitude of long-latency evoked potentials (Haider et al., 1964) and of the contingent negative variation (Naitoh et al., 1971; Tecce, 1979).

There are also developmental changes in the EEG during the sleep onset period associated with decreased alertness. The transition from normal waking to sleep in children is associated with runs of high voltage slow waves, also called hypnagogic hypersynchrony (Eeg-Olofsson, 1971). In adolescents and young adults, there may still be rhythmic frontal 5–7 Hz activity during this transition. At the other end of the age spectrum, frontal delta slowing may be seen during drowsiness in elders, although if the amplitude is over 100 micv it may suggest pathology.

3.1.2. Sleep–wake transition—The transition from sleep to awake is similar physiologically to falling asleep although the EEG transition is usually more rapid. Behaviorally, there is a period referred to as sleep inertia following awakening from sleep, during which the EEG reveals awake state but there is decreased cognition and responsiveness to stimuli compared to an awake period compared to what is observed after several more minutes, or even hours, of wakefulness (Simon and Emmons, 1956; Webb and Agnew, 1964). The duration of this decreased performance following arousal on a sustained attention task may last an hour or more (Ferrara et al., 2000; Jewett et al., 1999), but more typically dissipates in 5–35 min (Akerstedt et al., 1989). In fact, sleep inertia is paradoxical because people immediately arising from sleep (when they should be most refreshed) consistently perform more poorly than they did hours earlier, just before going to bed (when they should have been most fatigued). Sleep inertia is not dependent on circadian rhythm (Naitoh et al., 1993) but is partly dependent on the stage of sleep from which one is awakened, e.g. full awakening typically is quicker from stage 1 than slow wave sleep.

3.1.3. Quantitative EEG measures—Using more quantitative measures for alertness, there is an increase in slow frequencies and decrease in fast activities during the sleep onset period, with different investigators advocating using various measures or ratios of theta and delta with beta and alpha (Gevins et al., 1977; Matousek and Petersen, 1983; Merica and Gaillard, 1992). The theta changes are more prominent frontally while the alpha changes may be more generalized (Strijkstra et al., 2003). There are differences between drowsiness with the eyes open and closed, e.g. decreased alertness may be associated with increasing alpha band activity with eyes open but decreasing alpha activity with eyes closed. While reliabilities and sensitivities for the quantitative EEG parameters using visual EEG scoring as the gold standard may approach 90%, the conventional visual scoring of drowsy onsets and offsets varied by more than 5 s in 29% of episodes judged by three scorers (Gevins, 1977). One limitation of the usual quantitative approach is the intersubject variability of key parameters denoting decreased alertness. For example, subjects with low amplitude awake alpha activity have different EEG changes of sleep onset than those with high amplitude alpha. Additionally, conventional EEG frequency analysis does not take advantage of specific patterns, such as vertex waves and sleep spindles. For example, sleep spindle frequencies may overlap with awake alpha frequencies. There is a circadian contribution to the EEG changes during non-REM sleep (Dijk and Czeisler, 1995). Quantitative techniques using within subject parameter provide additional benefit (Penzel and Petzold, 1989).

3.1.3.1. EEG-performance relationship: There is a very large literature concerning the relationship of EEG measures and performance on sustained attention tests including simulated driving as well as more conventional psychological tests. The intersubject correlation between

EEG and performance changes on a sustained attention task is not consistent or large, especially in well-rested subjects (Belyavin and Wright, 1987; Boddy, 1971; Cajochen et al., 1999; Kornfeld and Beatty, 1977; Otmani et al., 2005; Townsend and Johnson, 1979; Valentino et al., 1993; Williams et al., 1962). The two measures that more often correlate with worse performance are increasing theta and decreasing beta. Similar to the univariate EEG measures, multivariate EEG changes do not correlate well with performance on a sustained attention task until performance is markedly diminished, with decreased beta activity being the most useful discriminant (Belyavin and Wright, 1987). This study also observed that the EEG correlated greater with performance on a sustained attention task requiring working memory rather than simply visual discrimination, reinforcing the observations regarding vigilance decrements and working memory described in Section 2.3.3.

Intrasubject analyses have generally yielded better results with more consistent correlations between performance and EEG changes, especially if subjects are drowsy (Makeig and Inlow, 1993; Torsvall and Akerstedt, 1987). While theta and alpha are more consistent markers related to performance, one study reported decreased beta in the seconds prior to stimulus presentation being a better marker than increased theta (Townsend and Johnson, 1979). Makeig and colleagues, using a moving window with higher target presentation rates, observed a consistent within subject correlation between increases in slow activity and decreases in fast activity with performance on a vigilance task, often recording from just a central and a parieto-occipital electrode (Fig. 1) (Jung et al., 1997; Makeig and Inlow, 1993; Makeig and Jung, 1995, 1996). The EEG changes were somewhat different in tasks in which the eyes are open compared with the eyes closed task, perhaps highlighting why alpha frequency activity may not be a very reliable intersubject correlate of performance changes. The decreased performance and EEG changes similar to drowsiness may cycle at lengths on the order of 15 s to many minutes (Conte et al., 1995; Makeig and Inlow, 1993; Makeig and Jung, 1996). Not unsurprisingly, changes in 14 Hz activity (presumably spindles) in the epochs preceding stimulus presentation were associated with performance only when error rates were very high (Jung, 1997; Makeig and Jung, 1996). Using the full EEG power spectrum to predict alertness as measured by reaction time performance was slightly better than simply using EEG at 5 specific frequencies they had previously shown to be sensitive to alertness changes (Jung, 1997).

3.1.3.2. Responsiveness: During the sleep onset period there is gradually decreased responsiveness to environmental stimuli as assessed by either reaction time or the stimulus intensity needed to elicit a response (Bonnet and Moore, 1982; Ogilvie and Wilkinson, 1984). More recently a standardized measure of behavioral responsiveness to light flashes, the Oxford sleep resistance (OSleR) test, has been used (Bennett et al., 1997) and does correlate strongly with the EEG-based maintenance of wakefulness test (see below) (Krieger et al., 2004). On the OsleR test, sleep onset is considered to occur when a subject fails to press a switch in response to 7 light emitting diode flashes that occur once every 3 s. Since many control subjects have no loss of responsiveness on the time-limited OSleR (Mazza et al., 2005), the lack of behavioral response in a clinical population is considered a marker for sleep onset, rather than simply inattention. Of note, however, there is a significant intersubject difference in terms of relationship of behavioral responsiveness and EEG sleep criteria such that some subjects remain fairly responsive during stage 1 sleep and others do not (Ogilvie et al., 1989).

3.1.3.3. Subjective measures: During the sleep transition, there is increased self-report of sleepiness and increased self-report of being asleep if aroused. Subjective sleepiness has been evaluated with the Stanford sleepiness scale, Profile of Mood States, visual analog scale, Epworth sleepiness scale (Johns, 1991) or Karolinska sleepiness scale (Akerstedt and Gillberg, 1990), with some of the measures geared towards longer assessment time periods.

While there are correlations between the self-rated sleepiness scales and the EEG, self-reports may not relate precisely to CNS state. Subjects are often still able to respond and may, in fact, not report being asleep when awakened from stage 1 or even stage 2 sleep (Ogilvie and Wilkinson, 1984). In one study, 25% of subjects awakened from clear stage 2 sleep reported they had been awake (Hori, 1994) while another study reported the threshold of subjective sleep (50% reporting being asleep) was 2–4 min after stage 2 onset (Bonnet and Moore, 1982). Also, self-reports of sleep may be altered in clinical situations: insomniacs were more likely to report themselves as awake when actually awoken from stage 2 sleep than controls (Moore et al., 1981). In terms of subjective experiences, arousals during this sleep onset period can produce self-reports of sensory experiences that would appear to represent dreaming (Foulkes and Vogel, 1965; Hori, 1994).

3.1.3.4. Conventional EEG measures of sleepiness: The most commonly used clinical EEG measures of sleepiness are the multiple sleep latency test (MSLT) (Carskadon et al., 1986) and the maintenance of wakefulness test (Mitler et al., 1982; Sangal et al., 1992) which both report the mean length of time to sleep onset at multiple time periods. The awake maintenance task is a modification of the maintenance of wakefulness test using only a single 6 min period (Salinsky et al., 1996). These tests are sensitive to alterations in alertness secondary to hypersomnias, sleep-deprivation, circadian rhythm, and drugs (Arand et al., 2005). Of interest, some patients have different results on the two tests simply based on the instructional difference to fall asleep or to stay awake (Sangal, 1992) and these tests and the Epworth sleepiness scale may be assessing different subject characteristics (Johns, 2000). Sleepiness as assessed on these tests correlates with performance on sustained attention tasks (Carskadon and Dement, 1979). However, the correlations are not great (George et al., 1996; Harrison and Horne, 1996), in part related to the lack of ideal definition of sleep onset, varying from a relatively long, 3 consecutive 10-s epochs of stage 1 sleep to an epoch of stage 1 lasting several to 15 s sometimes referred to as a microsleep (Doghramji et al., 1997; Salinsky, 1996; Valley and Broughton, 1983). The lack of a very high correlation between sleepiness and vigilance performance is also because inattention is only partially related to sleepiness (Sangal and Sangal, 2004).

3.1.3.5. Physiological changes other than EEG: The transition from wakefulness to NREM sleep is associated with a number of physiologic changes besides the EEG. One physiologic change associated with state 1 sleep and formally included in staging is the presence of slow lateral eye movements (Dement and Kleitman, 1957; Ogilvie et al., 1988; Rechtschaffen and Kales, 1968). These slow eye movements (SEMs) may be maximal in an EEG defined awake state with alpha still present and may be the first sign of decreased alertness in up to 50% of subjects (Shimazono et al., 1965; Santamaria and Chiappa, 1987b). SEMs have been associated with decreased performance (Torsvall and Akerstedt, 1987). Of note, SEMs decline again during transition into stage 2 sleep (De Gennaro et al., 2000). While awake with eyes closed there are fast eye movements and miniblinks that decrease during transition into state 1 and may precede standard EEG markers for drowsiness (Santamaria and Chiappa, 1987a). Decreased blink rate correlates with decreased performance on a sustained attention task (Van Orden et al., 2000). While this decline in blink rate has not been consistently observed, observed differences may be related to circadian changes in blink rate (Cajochen, 1999) and an increase in blink flurries during sustained attention tasks (Stern et al., 1994) that may even serve as some self-alerting mechanism. There is a decline in blink amplitude and an increase in blink duration during sustained attention tasks that correlate with decreased performance (Morris and Miller, 1996). Declines in eye movements that are presumably associated with refixations are correlated with vigilance decrements during visual task performance (Mackworth et al., 1964; Schroeder and Holland, 1968). Pupil size also decreases during drowsiness (Lowenstein et al., 1963; McLaren et al., 1992; Yoss et al., 1970) and with decreased performance on a sustained attention task (Van Orden, 2000). Frontalis EMG activity does not decrease

significantly during sleep onset (Hauri and Good, 1974) although pharyngeal dilator EMG does decrease (Mezzanotte et al., 1996).

There are physiologic changes affecting respiration and the autonomic nervous system in the awake–sleep transition. There is a decrease in heart rate and this decrease may be seen even prior to onset of stage 1 (Pivik and Busby, 1996) although the heart rate changes during drowsiness are not great (Torsvall and Akerstedt, 1987; Welch and Richardson, 1973). The heart rate decrease during the sleep onset period appears to relate to decreased sympathetic and increased parasympathetic tone (Zemaityte and Varoneckas, 1984). There are also physiologic changes in respiration. While there may be more rhythmic respirations during onset of sleep, there is also a relative fall in abdominal respiration compared to thoracic, a decrease in tidal volume, an increase in pCO_2, a decrease in ventilatory responsiveness to hypercapnia and hypoxia, and an increase in airflow resistance (Colrain et al., 1987; Colrain et al., 1990; Naifeh and Kamiya, 1981; Ogilvie and Wilkinson, 1984; Trinder et al., 1992). The rhythmic deeper respiration during the sleep onset period produces the expected increase in heart rate variability measures secondary to sinus arrhythmia. There is also a decline in core body temperature associated with an increase in peripheral temperature prior to sleep onset (Van Den Heuvel et al., 1998).

Skin potential level and skin potential fluctuations recorded from the palm of the hand, but not the dorsum of the hand, are related to EEG alertness levels and change even prior to onset of stage 1 sleep (Hori, 1982). However, it should be noted that overall there may be changes in spontaneous skin potentials and conductance measures during sleep that do not appear to relate to alertness since there may be high activity even during slow wave sleep (Johnson and Lubin, 1966). The amount of spontaneous skin potentials prior to stimulus presentation may be correlated with performance on a vigilance task (Surwillo and Quilter, 1965), but there is high spontaneous variability.

3.2. Sleep loss

Sleep loss is an extremely common problem that may be caused by sleep deprivation or sleep fragmentation. There is an extensive recent review literature on sleep deprivation (Durmer and Dinges, 2005; Kusida, 2004a,b) so only selected portions of the literature related to topics already mentioned are highlighted.

Insufficient overnight sleep time (average sleep length of < 6.5 h) is estimated to occur in about 1/3 of healthy young adults and a similar percentage have been found to have MSLT values of < 7 min (normal >10 min) (Bonnet and Arand, 1995b, 2005; Levine, 1988). Sleep fragmentation is also part of upper airway resistance syndrome and results in excessive daytime sleepiness (Black et al., 2000; Bonnet and Arand, 2003; Guilleminault et al., 1993). Chronic sleep loss also occurs in nightshift workers, rotating shift workers, and on-call workers, and is compounded by circadian rhythm disturbances (Humphrey et al., 1994; Torsvall and Akerstedt, 1987, 1988a) reviewed in (Akerstedt, 1988). These problems alone or in combination are cumulative for up to a week and beyond (Van Dongen et al., 2003). A ‘sleep debt’ is incurred which results in cognitive and performance deficits, particularly during the overnight and midday circadian peaks of sleep pressure (Mitler et al., 1988).

Sleep loss and drowsiness contribute significantly to accidents and impaired work performance. Drowsiness is known to be a major factor in automobile crashes (Mitler, 1988) reviewed in (George, 2004), with the incidence of crashes over the day being coincident with the expected nadirs in circadian rhythm (Garbarino et al., 2001; Horne and Reyner, 1995; Mitler, 1988). Even minor amounts of sleep deprivation may impair simulated driving performance (Arnedt et al., 2001). Work errors have been related to sleep deprivation and shift work (Akerstedt, 1988; Mitler, 1988; Mitler et al., 1997; Torsvall and Akerstedt, 1987,

1988a). There are documented negative effects of sleep loss and shift work on medical professionals (Cavallo et al., 2002; Friedman, 2004; Steele et al., 1999). Medical house staff experience significant sleep deprivation and it is associated with EEG documented sleepiness during eyes open periods during the night shift (Lockley et al., 2004; Richardson et al., 1996). House staff have a significantly increased risk of motor vehicle accidents following a night shift (Barger et al., 2005; Marcus and Loughlin, 1996; Steele, 1999).

3.2.1. Clinical effects—Overnight and partial night sleep deprivation are consistently associated with excessive daytime sleepiness as measured by both subjective indices and the MSLT (Beaumont et al., 2001; Bonnet and Arand, 1995a, 2003; Carskadon and Dement, 1982; Gillberg et al., 1994; Roehrs et al., 1989; Rosenthal et al., 1993). Sleepiness increases in proportion to the total length of sleep deprivation (Rosenthal, 1993). There may be differential effects based on the sleep stage of deprivation in that REM sleep deprivation does not change MSLT scores (Nykamp et al., 1998). Sleep fragmentation (frequent brief disruptions at regular intervals) similarly increases subjective daytime sleepiness, impairs mood, and decreases MSLT times even when total sleep times are normal based on conventional visual sleep scoring methods, and even if the arousals are subclinical (i.e. based on EEG changes alone) (Bonnet and Arand, 2003; Cote et al., 2003; Kingshott et al., 2000; Levine et al., 1987; Martin et al., 1996; Stepanski, 2002). Sleep interruptions may be as infrequent as every 10 min yet still produce an effect on MSLT scores (Stepanski, 2002). The effects of sleep deprivation are cumulative, up to a week and beyond of partial sleep deprivation (Carskadon, 1981; Dinges et al., 1997; Van Dongen, 2003).

The effects of sleep deprivation on performance tests have been extensively studied, particularly effects on reaction time (RT) and sustained attention tests including driving simulation reviewed in (Dinges, 1992). RT lengthens with even partial sleep deprivation, and there is a progressive lengthening of RT with longer deprivation periods (Beaumont, 2001; Cochran et al., 1992; Dinges, 1997; Doran et al., 2001; Downey and Bonnet, 1987; Gauthier and Gottesmann, 1983; Gillberg, 1994; Humphrey, 1994; Koslowsky and Babkoff, 1992; Lorenzo et al., 1995; Magill et al., 2003; Pilcher and Huffcutt, 1996; Smith et al., 2002; Wesenten et al., 2002; Wilkinson, 1965). Similar findings are seen with classic tests of vigilance using long, repetitive tasks in which there is a signal detection component (Akerstedt, 1988; Gillberg, 1994; Magill, 2003; Strauss et al., 1984; Van Dongen et al., 2001, 2004; Wilkinson, 1965). Vigilance tasks show longer RTs and increased errors of omission at longer time intervals, consistent with the results of the shorter duration RT tests. The effect of sleep deprivation on RT and vigilance tasks represents both an increase in average RT and a lengthening of the right tail of the RT distribution with an increased coefficient of variability (Smith, 2002; Wilkinson, 1965). The latter effect has been thought to represent brief lapses in attention which lead to errors of omission or very long RTs (gaps or lapses), and may be related to brief sleep episodes lasting several to 15 s (microsleeps) (Johnson et al., 1990; Koslowsky and Babkoff, 1992; McCarthy and Waters, 1997; Wilkinson, 1965). Both task duration and length of sleep deprivation have significant effects on performance (Gillberg, 1994; Lorenzo, 1995; Smith, 2002; Steyvers and Gaillard, 1993; Wilkinson, 1965). For example, Lorenzo et al. (1995) demonstrated a linear trend of increased RT and increased omissions (lapses) over a 40 h period of sleep deprivation (Lorenzo, 1995). Also, there is an interaction between the task duration and length of sleep deprivation on performance such that shorter task durations may not be as sensitive to equivalent lengths of sleep deprivation (Caldwell and Ramspott, 1998).

Several factors modify the effects of sleep deprivation on RT and vigilance task performance. Long, simple, low-interest, self-paced RT tests are most affected by sleep loss (Wilkinson, 1965). The effects of sleep deprivation on RT are partially reversed when there is feedback provided, when the task is shorter or more challenging, or when there is a reward used as

incentive for performance, suggesting that increased motivation or interest can at least partially compensate for the effects of sleep deprivation (Steyvers and Gaillard, 1993; Wilkinson, 1965). This motivational effect may be similar to the improvement in vigilance performance that occurs when subjects know they are approaching the end of the task (end-spurt effect) (Bergum and Lehr, 1963). The increase in RT is greater when there is a relatively long interval between a warning signal and the imperative stimulus, less if the interval is short, suggesting that phasic arousal or alertness deteriorates quickly under sleep deprivation (Cochran, 1992). RT performance in overnight sleep deprived subjects is slowed when seated, but normal when standing (Caldwell et al., 2002). The effects of sleep deprivation are complicated by the interaction of diurnal variation (circadian phase) with monotonic effects (length of sleep deprivation), consistent with the two-process model proposed by Borbely (Achermann and Borbely, 2003; Babkoff et al., 1991; Cajochen, 1999). Also, effects of sleep deprivation on performance are not uniform and there is considerable intersubject variability, likely representing individual characteristics (Bonnet and Arand, 2005; Van Dongen, 2004).

The effects of sleep deprivation on other cognitive tasks have been less consistent than effects on RT and vigilance tasks. To some extent this lack of consensus is due to different experimental conditions and study designs (length of sleep deprivation, length of testing battery, difficulty of the task, etc.). For example, Stroop performance change was affected by the pattern of sleep deprivation (Beaumont, 2001; Binks et al., 1999; Herscovitch et al., 1980). Variable effects on memory may be related to task difficulty (Cajochen, 1999; Harrison et al., 2000; Humphrey, 1994; Linde and Bergstrom, 1992; McCarthy and Waters, 1997; Smith, 2002). Significant effects have also been demonstrated on the Sternberg working memory task and were correlated with decreased fMRI activation in multiple brain areas, particularly the bilateral parietal cortices (Mu et al., 2005). Sleep deprivation effects on Raven's matrices (Linde and Bergstrom, 1992), verbal fluency (Horne, 1988), Tower of London (non-verbal planning) (Horne, 1988), Paced auditory serial addition test (Martin, 1996), and Trails B (Martin, 1996), have been reported. The effect of sleep fragmentation on cognitive abilities is generally less pronounced than the effects of sleep deprivation, despite similar effects on MSLT scores (Cote, 2003; Kingshott, 2000; Philip et al., 1994; Stepanski, 2002).

Measures of subjective sleepiness (the Karolinska sleepiness scale or the Stanford sleepiness scale) are generally sensitive to decreased alertness and performance decrements during sleep deprivation but are poorly correlated to performance on RT, vigilance and cognitive tasks in individuals (Binks, 1999; Gillberg, 1994; Herscovitch and Broughton, 1981). A meta-analysis emphasized that although motor and cognitive tasks are generally affected by sleep deprivation, subjective mood measures showed the greatest effects (Pilcher and Huffcutt, 1996).

3.2.2. Electrophysiological measures

3.2.2.1. EEG: As already described, the transition from the awake to the sleep state involves several EEG changes including slowing and anteriorization of the dominant posterior rhythm, an increase in fronto- central theta power, a reduction in eye blinks followed by increasing amounts of slow eye movements, and eventually attenuation of the posterior dominant rhythm, and development of vertex sharp waves. These features are also seen with sleep deprivation. During and following sleep deprivation there is a progressive increase in absolute power and in relative theta and delta power in the EEG background, accompanied by an increase in slow eye movements, and correlated with subjective sleepiness (Caldwell, 2002; Cajochen et al., 1995; Lorenzo, 1995; Smith, 2002; Torsvall and Akerstedt, 1988b). This EEG slowing gradually increases until the sleep deprived subject dozes off (Torsvall and Akerstedt, 1988b). This phenomenon has been observed in train drivers on the job, with correlation to subjective sleepiness and driving errors (Torsvall and Akerstedt, 1987). The increase in absolute power is related to slowing of RT and increased errors on a vigilance task (Corsi-

Cabrera, et al. 1996; Lorenzo, 1995). Standing upright attenuates the increase in theta activity seen with sleep deprivation (along with RT changes; see above) (Caldwell, 2002). Awake EEG changes are also seen following sleep fragmentation despite normal total sleep time. A decrease in the alpha:theta ratio was observed following a single night of sleep fragmentation, increased following a second night, and correlated with subjective complaints despite a lack of significant effect on performance measures (Cote, 2003). Although sleep deprivation reliably produces effects on the EEG power spectrum and task performance, there is no effect on task related frontal midline theta activity (Smith, 2002).

The increase in EEG frontal slow wave activity following sleep deprivation appears to be independent of circadian variation (Cajochen, 1999). However, in the same experiment neurobehavioral measures (vigilance RT, short-term memory) showed circadian effects with deterioration following melatonin secretion (after about 16 h of wakefulness). These neurobehavioral changes correlated with an increase in slow eye movements, and changes in the dominant posterior rhythm suggesting that some EEG components are phase locked to the circadian cycle whereas others are not (Cajochen, 1999). Increased frontal slow activity is a prominent feature in the sleep deprived EEG, lending some support to the hypothesis that frontal regions are more susceptible to sleep deprivation effects than other brain regions (Cajochen, 1999; Horne, 1993). During slow wave sleep cerebral blood flow (measured by positron emission tomography) in the orbitofrontal and anterior cingulate cortex is negatively correlated with EEG delta activity (Hofle et al., 1997).

EEG has also been used to study the *dynamics* of the decreased performance associated with sleep deprivation. During an auditory vigilance task, there was a pattern of increased near 4 Hz (low) theta and decreased near 40 Hz gamma during missed targets (lapses) with the opposite pattern during accurate target detections (hits) (Makeig and Jung, 1996). The increase in low theta power with poor performance was subsequently confirmed in a more difficult continuous performance task using subjects studied throughout 42 h of sleep deprivation (Makeig et al., 2000). Both studies revealed a periodicity of about 18 s for both performance and EEG low theta activity during periods of relatively poor performance related to drowsiness, with the two measures correlated to one another (Makeig and Jung, 1996; Makeig, 2000). Following overnight or diurnal sleep there is an increase in interhemispheric correlations as compared to presleep baseline, with the opposite effect seen after a night of sleep deprivation (Corsi-Cabrera et al., 1992). All of these EEG changes are associated with functional impairment and therefore have potential practical applications for monitoring performance (Corsi-Cabrera, 1992; Jung, 1997).

3.2.2.2. Event related potentials

3.2.2.2. Event related potentials: *P3:* Long latency ERPs have primarily been used as a measure of phasic attention. The latency of the P3 potential increases, and the amplitude decreases, progressively during overnight sleep deprivation, suggesting problems with stimulus evaluation and attention (Humphrey, 1994; Lorist et al., 1994; Morris et al., 1992; Smith, 2002). These changes can be seen even in the absence of RT changes (Morris, 1992). However, the largest reductions in P3 amplitude correlated with increased RT, decreased response accuracy, and increased response variability (Smith, 2002). It is unclear whether the decrease in P3 amplitude and increase in latency are manifestations of a decreased magnitude of response or a greater variability in response. Results with sleep fragmentation (preserving total sleep time) are inconsistent, with one study showing a decrease in amplitude without change in latency, and another showing no change in either parameter (Cote, 2003; Kingshott, 2000).

VEP: Overnight sleep deprivation induced a progressive reduction in amplitude and increase in latency of the late components of the visual evoked potential (P180 and beyond) obtained during a visual vigilance task (Corsi-Cabrera et al., 1999). The late component was consistent with the time window for the N2 potential which correlates with the decision process for RT (Ritter et al., 1979). Early components (P100) were unchanged, suggesting that processes affected were for sensory discrimination and target selection. In the course of a 100 min visual vigilance task (light flashes), the amplitude of the N160 potential decreased and its latency progressively increased in correlation with the number of detection failures (Haider, 1964). Averages from the detection failures showed much greater attenuation, the electrophysiologic correlate of behavioral 'lapses' as defined above. In an n-back visual working memory task the N170 was slowed and attenuated by sleep deprivation suggesting an effect on 'selective focusing of attention onto particular stimulus attributes' (Smith, 2002).

AEP (N1, P1): The latencies of the P1 and N1 auditory evoked potentials were increased, and the N1 amplitude reduced, following 48 h of sleep deprivation, suggesting that there is a delay in sensory encoding processes (Cote, 2003; Gauthier and Gottesmann, 1983). N1 amplitude was also mildly reduced after 1 and 2 nights of sleep fragmentation, though P3 was unaffected (Cote, 2003).

Twenty-four to thirty-six h of sleep deprivation also produces a mild but significant decrease in the amplitude of auditory mismatch negativity (a potential related to deviant stimuli in a non-attended train), while the N1 potential was preserved (Raz et al., 2001). This suggests that while sensory encoding was intact a later process is affected, possibly one related to the transient (reflexive) capture of attention.

Contingent negative variation. Contingent negative variation was reduced in amplitude and increased in variability following 24–48 h of sleep deprivation (Gauthier and Gottesmann, 1983; Naitoh, 1971). It is unclear whether this is an effect on sleep deprivation on attention or a non-specific effect on arousal (Gauthier and Gottesmann, 1983).

3.2.3. Sleep deprivation summary—In summary, there is extensive behavioral and electro-physiologic evidence that sleep deprivation or fragmentation impairs brain function. The effects are at least partly mediated by decreased arousal (represented by EEG) and increased sleep pressure leading to inconsistent performance (greater response variability with lapses on RT and sustained attention tests). The effects on performance are mirrored by brief intrusions of drowsy features into the waking EEG (microsleeps), eventually building to a more continuous drowsy pattern. There also appears to be a significant effect of sleep deprivation on ERPs. These include effects on initial sensory encoding (auditory N1, in some studies), and more consistent effects on later potentials believed to represent attentional processes involved with stimulus discrimination (N2, N170, P3).

4. Conclusions

There are a number of neural and functional systems relatively directly affecting phasic and tonic alertness. In addition, there are a number of systems that directly modulate these alertness systems, such as the neural systems related to motivation and stress. The multiple constructs and neural systems underlying the relatively non-specific phasic and tonic alertness activation states imply that they are not unidimensional. Thus, one should rarely, if ever, simplify and speak about vigilance or alertness on a unidimensional continuum, When studying these activation states, one should try to experimentally control and report on as many parameters and utilize as many specific physiologic or behavioral measurements as possible. Recruitment strategies and performance incentives should be fully described. While there are discrete state

changes, when studying transitional and pathologic states it is apparent that these activation states function on a continuum.

The field has been hindered by inconsistent or poorly defined terminology. Researchers should be particularly careful about the usage of the term *vigilance*, understanding there are factors contributing to vigilance other than just arousal on the sleep–wake dimension. Avoidance of the term *vigilance* because of its varied definitions would be most helpful. The use of the term *tonic alertness* may be preferable since it does not already have a confusing history. Whatever terms are used should be operationally defined in order to avoid impeding progress in our understanding of these important topics. Future studies should continue to incorporate analysis of finer temporal aspects of physiologic-performance relationships, and not simpy averaging both over many minutes. Other helpful research may include trying to better ascertain the contributions of other neural systems that may impact on vigilance, including stress, motivation, and novelty. It is likely that some of the variability of research results to date relates to inadequate control of these aspects. Neural systems related to stress are important clinically and studying the modulation of alertness and performance by stress may be particularly useful.

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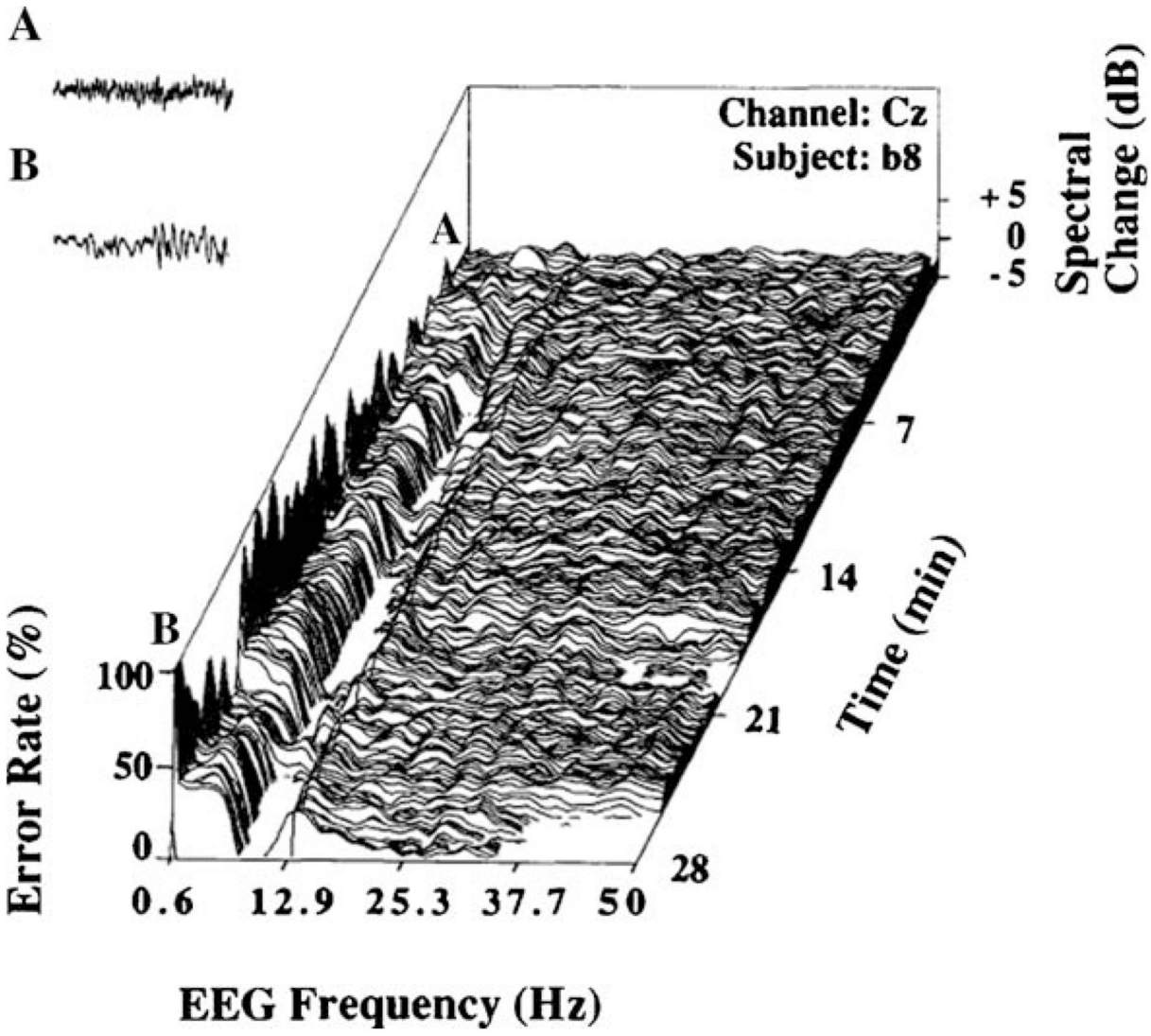

Fig. 1.

Error rate and EEG spectral power for a single subject during a 28-min continuous performance task. The local error rate is plotted to the left of the spectra. Note the relationship between changes in the EEG spectrum (decreases in alpha frequency and increases in theta frequency activity) and increasing error rate over time. From Makeig et al. (1993).