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Understanding alcohol use disorders with neuroelectrophysiology

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Abstract

Neurocognitive deficits associated with impairments in various brain regions and neural circuitries, particularly involving frontal lobes, have been associated with chronic alcoholism, as well as with a predisposition to develop alcohol use and related disorders (AUDs). AUD is a multifactorial disorder caused by complex interactions between behavioral, genetic, and environmental liabilities. Neuroelectrophysiological techniques are instrumental in understanding brain and behavior relationships and have also proved very useful in evaluating the genetic diathesis of alcoholism. This chapter describes findings from neuroelectrophysiological measures (electroencephalogram, event-related potentials, and event-related oscillations) related to acute and chronic effects of alcohol on the brain and those that reflect underlying deficits related to a predisposition to develop AUDs and related disorders. The utility of these measures as effective endophenotypes to identify and understand genes associated with brain electrophysiology, cognitive networks, and AUDs has also been discussed.

Keywords

Alcoholism; EEG; ERP; oscillations; cognition

INTRODUCTION

The literature is replete with compelling evidence of brain dysfunction in chronic alcoholics as well as their high-risk offspring from neuropsychological, neuroimaging, neuropathological and neurophysiological techniques; in particular frontal lobe changes have been highlighted (Moselhy et al., 2001; Zahr et al., 2010, 2011). Neuroimaging methods, such as structural/functional magnetic resonance imaging (MRI) and positron emission tomography, (PET) have certain advantages that include excellent spatial resolution; yet they offer relatively poor temporal resolution compared to electrophysiological methods that evaluate brain function in the millisecond range (Celesia and Brigell, 1992; Krieger et al., 1995). Neuroelectrophysiological techniques have further advantages of being non-invasive and relatively inexpensive to implement.

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Electrophysiology has provided several excellent measures of acute and chronic effects of alcohol on the brain. While it was assumed that these aberrant characteristics in alcoholics were solely due to the neurotoxic effects of alcohol on the brain, the evidence indicates that some neuroelectrophysiological characteristics reflect predispositions that antecede the development of alcoholism and related disorders.

Alcoholism is a complex neuropsychiatric condition with a multifactorial etiology that warrants the use of diverse neurobiological methods. This disorder not only involves effects of alcohol on brain structures but also subsequent alteration in brain electrophysiology potentiated by the addiction cycle. Alcoholism or alcohol use disorder (AUD) is a common familial disorder with increased risk among biological relatives of alcoholics (Goodwin et al., 1973; Cadoret et al., 1980; Bohman et al., 1987; Prescott, 2001). Family, twin, and adoption studies that highlight genetic contributions to AUDs suggest that both genders are equally vulnerable (Heath et al., 1997; Prescott et al., 1999). Yet AUDs may not be a specific disease but part of a spectrum of co-occurring disinhibitory disorders with overlapping genetic factors and shared underlying risk factors (Krueger et al., 2002; Kendler et al., 2003) and differential expression (Hicks et al., 2004). Thus, these behavioral phenomena – antisocial, impulsive traits, substance use disorders (SUDs), are variable expressions of a disinhibitory complex (Gorenstein and Newman, 1980) with AUD as one possible outcome in this spectrum. Understanding addictive behavior is complex and involves interactions among behavioral, environmental, and genetic factors; neuroelectrophysiological techniques allow dissection of some of these issues and provide hope for finding useful intervention loci.

Ongoing brain activity that comprises action potentials and graded potentials like IPSP (inhibitory post synaptic potentials) and EPSP (excitatory post synaptic potentials) generated by a dynamically regulated collection of synapses on excitatory and inhibitory cells results in an ensemble field of electric activity that can be recorded non-invasively using scalp electrodes. Since the first recorded human electroencephalogram (EEG), pioneered in 1924 by Hans Berger (1873–1941) (Haas, 2003), digitization methods have revolutionized EEG acquisition, generating new methods of analysis. Three general approaches can be used to record and analyze these neuroelectric phenomena: (1) continuous EEG; (2) event-related potentials (ERPs); and (3) event-related oscillations (EROs).

CONTINUOUS ELECTROENCEPHALOGRAM

Continuous EEG records brain activity when the subject is at rest or in relaxed wakefulness. Resting-state EEG is primarily analyzed in the frequency domain, as no specific periodicity can be imposed using fast Fourier transform-based methods. Traditionally, EEG is decomposed into the following frequency bands: delta (0–3 Hz), theta (4–7 Hz), alpha (8–12 Hz), beta (13–28 Hz), and gamma (>29 Hz), and each band reflects different types of brain activity. Variations in relative power of these specific frequency bands can indicate level of consciousness, psychological state, or presence of neurological disorders (Nunez, 1995; Niedermayer and Lopes Da Silva, 1999). Resting theta rhythm has its maximum power in the posterior scalp region but is not prevalent in the normal adult waking EEG. Alpha band is a posterior dominant rhythm that emerges with closing of the eyes and relaxation and

attenuates with eye opening or mental exertion. Hence, it is described as an index of relaxed wakefulness. Alpha is slower in young children (closer to theta frequency) and increases with age into high alpha frequencies and is a key feature of EEG maturation (Niedermayer and Lopes Da Silva, 1999); alpha power is stable throughout adult life. Beta rhythm is present all over the scalp but predominantly at frontocentral loci and is enhanced in response to certain barbiturates, sedatives, and tranquilizers.

EVENT-RELATED POTENTIALS

Event-related potentials (ERPs) are averaged scalp EEG responses time-locked to specific events in a sensory, motor, or cognitive task. The averaged responses or waveforms are composed of characteristic negative and positive deflections (i.e., components). They reflect the summated activity of network ensembles active during the various processes involved in the task (Luck, 2005). Time domain analysis compares the amplitudes and latencies of these sequential peaks and troughs. Early components with a latency of less than 100 milliseconds reflect sensory processes, followed by early components that are associated with attention processes, while later components reflect higher associative processes. See Figure 23.1 (top panel) for illustration of various ERP components. Most early studies used “oddball” paradigms and focused on the P3 or P300 component related to stimulus significance. Amplitude of P3 is taken to reflect central nervous system (CNS) inhibition (the larger the P3, the more the inhibition) (Birbaumer et al., 1990). While the P3 component, particularly in the oddball paradigm, is most widely used to study alcohol, more recent studies have focused on various other ERP components and cognitive tasks. This review is restricted to the examination of those ERP components that have proved most significant in the study of alcoholism and they are described in later sections.

EVENT-RELATED OSCILLATIONS

Event-related oscillations (EROs) are embedded in continuous scalp-recorded EEG activity acquired during cognitive tasks. A substantial literature indicates that some ERP features arise from changes in dynamics of ongoing EEG rhythms/oscillations of different frequency bands that reflect ongoing sensory and/or cognitive processes (see Figure 23.1 (bottom) for illustration of EROs during P3 response to targets in oddball task). While EROs may be partitioned into the same frequency bands as spontaneous resting EEG (e.g., delta, theta, alpha, beta, gamma), they are functionally different from spontaneous rhythms (Klimesch et al., 2007). Specific frequency oscillatory responses have been attributed to underlie various cognitive processes, as follows: delta: signal detection and decision making; theta: conscious awareness, recognition memory, and episodic retrieval; slow alpha: attribution of attentional resources; fast alpha: semantic memory and stimulus processing; beta and gamma: sensory integrative processes (Basar, 1999). Newer time by frequency transformations such as S-transform (Stockwell et al., 1996) or other wavelet-type analyses provide a time-based decomposition of the EEG signal associated with an event (van Vugt et al., 2007), and generate amplitude/power measures and phase information. EROs influence the timing of neural activity and coordinate synchronous activity in groups of active neurons (Fries, 2005). Synchronization of oscillations underlie self-organization of neural networks and are important indices of maturity and efficiency of these networks, providing an energy-efficient

mechanism for coordination of distributed neural activity (Buzsaki and Draguhn, 2004). Phase relationships between signals from different brain regions provide a measure of temporal interactions between transient active cognitive networks; hence phase synchrony can be considered as an index of "crosstalk" or communication in the brain (Sauseng and Klimesch, 2008; Uhlhaas et al., 2010) and aids in the study of functional connectivity. High-frequency (i.e., beta and gamma) EROs are implicated in short-range communication, whereas low-frequency (i.e., delta, theta, and alpha) EROs are involved in longer-range communication between brain areas (von Stein and Sarnthein, 2000).

Advances in analytical techniques that adapt new mathematical methods have aided the study of complex cognitive processes and neural communication in normal (Hummel and Gerloff, 2005; Chen et al., 2008b; Chorlian et al., 2009) as well as pathological conditions (Uhlhaas and Singer, 2006). Important state-of-the-art analysis tools based on mathematical approaches include: (1) phase synchrony in oscillations (Varela et al., 2001); and (2) methods of source localization (e.g., sLORETA (low-resolution brain electromagnetic tomography) which solves the "inverse problem" to generate anatomically constrained solutions of active sources within the brain that underlie the event-related scalp activity (Pascual-Marqui, 2002). The ERP and ERO analyses are supplemented by source localization techniques to infer anatomical substrates and have been successfully used to study several psychiatric disorders including AUDs (Coutin-Churchman and Moreno, 2008; Holmes and Pizzagalli, 2008; Kamarajan et al., 2010; Itoh et al., 2011; Pandey et al., 2012). Hence, these tools are instrumental in translating and comparing findings from electrophysiological studies with those from imaging methodologies, or using them in conjunction with each other, to create a multimodal approach.

This review will focus on the effects of alcohol on brain function using non-invasive electrophysiological techniques described above (EEG, ERP, ERO), and will be restricted to measures that have proved most significant for the study of AUDs; it will be divided into four main sections: The first will examine the effects of acute doses of alcohol on brain function in social drinkers, and will include studies comparing those with a family history of alcoholism to those without a family history. The second section will address the newer studies dealing with the effects of binge drinking on brain function. The third section will review studies on chronic effects of alcohol on brain function, and will try and tease apart electrophysiological indices of brain dysfunction that antecede the development of AUDs from those that are a consequence of AUDs. The fourth section will discuss the use of these electrophysiological measures as endophenotypes for the development of AUDs and will review results with specific genes that have been identified with these methods.

ACUTE EFFECTS OF ALCOHOL ON THE BRAIN IN SOCIAL DRINKERS

The focus of alcohol challenge studies has been to investigate the effects of alcohol on normal brain function, as assessed by various electrophysiological measures obtained at rest, and while engaged in sensory or cognitive tasks. These studies have also been very useful in examining whether naïve offspring of alcoholics who are at high risk (HR) respond differently to alcohol than offspring of non-alcoholics at low risk (LR), revealing an underlying neural liability with exposure to alcohol. No differences have been reported

between HR and LR subjects in the uptake and clearance of alcohol in the blood on the blood alcohol curve (Newlin and Thomson, 1990). Past and current longitudinal studies have shown that a low level of response to alcohol predicted later heavier drinking and mediated a disposition for developing AUDs (Schuckit, 1994; Volavka et al., 1996; Trim et al., 2009). A meta-analysis suggests that a diminished response to alcohol is more frequently seen in family history-positive (FHP)/HR compared with family history-negative (FHN)/LR subjects (Pollock, 1992), but not all studies concur (see Newlin and Thomson, 1990, for review).

Acute effects of alcohol on EEG

The prominent effects of low doses of alcohol include increases in slow alpha activity or lowering of alpha peak frequency, while moderate doses show increases in slow alpha and theta bands (Ehlers et al., 2004). The effects of alcohol on beta band are more equivocal. Decreases in beta peak frequency (Ehlers et al., 1989) and increases in beta power have been reported (Ehlers and Schuckit, 1990; Stenberg et al., 1994); increased beta is also associated with moderate drinking (Ehlers and Schuckit, 1990). While changes in these frequency bands were marked at both posterior and frontal scalp loci, the alpha increase was very prominent in anterior regions (Ehlers et al., 1989). It has been proposed that acute ethanol administration disrupts the nonlinear structure of EEG oscillations, thus increasing randomness (Ehlers et al., 1998b). The effects of alcohol on the EEG of subjects at risk for developing alcoholism as determined by spectral analysis methods are well known (Table 23.1). FHP individuals have shown greater increases than FHN in alpha (Pollock et al., 1983; Cohen et al., 1993a) and greater decreases of fast alpha after alcohol administration (Pollock et al., 1983). Alpha activity has also been positively associated with desire to drink in FHP before and after consumption (Kaplan et al., 1988), and beta power increases are also prominent (Ehlers and Schuckit, 1990).

Differences in EEG response to alcohol may have ethnic variations; Hispanic FHP young adults had decreased fast alpha while non-Hispanic adults showed an increase in the same band. Fast alpha (9–12 Hz) power at baseline was also found to be negatively associated with level of response to alcohol, with increased EEG alpha power at baseline being predictive of a less intense response to alcohol (Ehlers et al., 2004). An early prospective study (Volavka et al., 1996) showed that, in high-risk men, a diminished alpha-frequency EEG response to alcohol was related to the development of alcohol dependence 10 years later.

Newer studies using a multimodal approach, transcranial magnetic stimulation along with EEG, have shown a strong effect of ethanol on cortical connectivity especially over right frontal and also on left parietal areas (Kahkonen et al., 2001). In a recent interesting experiment that measured alcohol effects in real-world situations – a cocktail party and being in a driving simulator – an equation combining the beta and theta power was shown to be very successful in classifying alcohol and placebo, and the EEG score was significantly related to breath alcohol content (Gevins et al., 2012).

In summary, alcohol challenge studies in HR and LR subjects uncover a reactive alpha system. A tendency of slowing of peak frequency within reactive bands and reduced

nonlinearity of EEG postethanol is suggestive of a widespread synchronization of neuronal substrates, especially since low frequencies are proposed to be involved in long-range synchronizations in the brain (von Stein and Sarnthein, 2000). Both slow (theta and slow alpha) and fast (beta) frequencies appear to be affected postethanol and this is indicative of a modulation in thalamocortical networks. In their model, Llinas and colleagues (1999) have proposed that the enhanced low-frequency (theta) oscillations in the thalamocortical module can affect the lateral inhibitory drive in the cortex and eventually result in high-frequency coherent activation of cortical modules. Stenberg et al. (1994) also observed that a possible harmonic relationship may exist between the theta and beta bands affected in their study and speculated the presence of related or even same oscillators underlying the ethanol effect on EEG. Hence, these findings provide a strong lead for examining the neurophysiologic and neurochemical bases of vulnerability to acute alcohol.

Acute effects of alcohol on ERPs

ERPs were the earliest tools used to study the effects of alcohol on the brain and more recently this has been supplemented by the ERO approach (see next subsection). The early studies were also interested in understanding the modulatory influence of family history and risk on ERPs (Porjesz and Begleiter, 1983). Primarily using auditory oddball tasks and male participants, changes in P3b characteristics after administration of alcohol have been observed in several studies (Table 23.2). Alcohol administration has the general effect of slowing latencies and reducing amplitudes of the P3b peak with both auditory and visual stimuli; a number of studies indicate that HR/FHP subjects manifest less P3b reduction and have a faster recovery of ERP features to baseline levels (Elmasian et al., 1982; Schuckit et al., 1988; Porjesz and Begleiter, 1990). Three-stimulus oddball tasks also generate more anterior P3a components to unattended rare non-target stimuli, which index orienting to novelty (Courchesne et al., 1975; Squires et al., 1975; Knight and Scabini, 1998). Decremental effects of alcohol on P3a amplitudes have also been significant (Campbell and Lowick, 1987; Ehlers et al., 1998a; Jaaskelainen et al., 1999; Marinkovic et al., 2001), suggesting an effect of alcohol on attention processes.

One fundamental question related to low-voltage P3 in HR offspring concerns the potential effect of alcohol in subjects with low P3 at baseline, the subjects who are presumably at risk. Ehlers et al. (1998a) noted that low P3 during a placebo condition was predictive of low level of change or an actual increase in P3 amplitude after alcohol challenge. However, the influence of variables such as ethnicity (Ehlers et al., 1998a) and gender has not been thoroughly explored. Taken together, these findings suggest that, while some electrophysiological differences between HR and LR individuals are apparent without an alcohol challenge, others are seen only in response to ethanol challenges, possibly representing sensitization and tolerance in the HR subjects that may be innate.

The P3 results suggest a multifocal influence of alcohol on cognition, which is supported by later ERP studies examining the effect of alcohol on several cognitive domains, including attention and monitoring, leading to effective performance control. These domains are part of the rubric of executive control, and impairment in these processes has a widespread influence on cognition. Alcohol-induced changes have been reported in components related

to visual processing (Colrain et al., 1993; Weschke and Niedeggen, 2012), covert attention (Jaaskelainen et al., 1995; Kenemans et al., 2010), sustained attention (Rohrbaugh et al., 1987), motor preparation (Marinkovic et al., 2000), response inhibition (Easdon et al., 2005), error/action monitoring (Ridderinkhof et al., 2002; Euser et al., 2011), and semantic memory (Marinkovic et al., 2004).

Among the early ERP components, the N100 amplitude is consistently reduced postalcohol, suggesting involvement of early sensory or attention-related process, particularly in auditory paradigms. Reporting on earlier components of the oddball task – N100 and P200 (Fig. 23.1) – greater sensitization of P2 on the ascending limb of the blood alcohol curve and faster recovery to baseline on the descending limb for both N1 and P2 in HR was seen (Cohen et al., 1998), in keeping with the differentiator model of Newlin and Thomson (1990). Some studies using visual stimuli did not report N1 amplitude reduction postalcohol (Rohrbaugh et al., 1987; Colrain et al., 1993). A preattentive component to spatial frequency (SFD80), which appears at 80 ms after the stimulus, was not affected by moderate alcohol (Kenemans et al., 2010). Alcohol was found to decrease the discrimination ability for visual contrast, resulting in reduced visual evoked potential amplitudes, but its effects on motion perception indicated impairment in visuospatial attention (Weschke and Niedeggen, 2012).

Similarly, covert attention is affected by alcohol, as indicated by the reduced mismatch negativity (MMN) amplitudes for both auditory and visual stimuli (Jaaskelainen et al., 1995, 1996; Kenemans et al., 2010). MMN is an automatic neuronal mismatch between a deviant auditory input and a sensory-memory trace representing the standard stimuli; it is a preattentive process engaging covert attention, and provides an objective measure of auditory discrimination and sensory memory (Näätänen, 1990). (See section on attention – N100 and mismatch negativity, below, for studies on MMN and chronic alcoholics.)

Two theoretical models have been proposed to evaluate the effects of alcohol on cognition: Firstly the attention allocation model, which suggests that alcohol enhances the focus and affects shifts of attention, such that only the most salient cues are attended to and other available cues are ignored (Steele and Josephs, 1988, 1990). This is supported by results of studies on overt and covert attention, as described previously (Jaaskelainen et al., 1996). The second related model is the response inhibition model (Fillmore and Vogel-Sprott, 1999, 2000) based on the theory of cognitive control (Logan and Cowan, 1984), where behavioral activation and inhibition are two independent processes. Impaired behavioral inhibition processes underlie deficits of self-control observed postalcohol. The alcohol-related decline in performance may be related to difficulties in maintaining attention on the task at hand and/or deficits in inhibiting a prepotent response.

This has been studied with a “reverse oddball” Go/NoGo task, a paradigm widely used to estimate response inhibition (Jodo and Kayama, 1992; Eimer, 1993; Falkenstein et al., 1999) wherein a subject has to respond to a given stimulus (Go) and withhold it for another stimulus (NoGo). The ERPs to the two stimuli were examined to evaluate the neural correlates of response production and inhibition. Two significant ERP signatures of response inhibition have been found: an enlarged negative frontocentral N2 component (200–300 ms)

on NoGo trials, and an augmented positive-going frontocentral “NoGo P3” (300–600 ms) (Pfefferbaum et al., 1985; Pfefferbaum and Ford, 1988; Eimer, 1993; Filipovic et al., 1999).

Low and moderate doses of alcohol increased the number of errors relative to alcohol-free performance (Easdon et al., 2005). Success in withholding a prepotent response was associated with an early-enhanced stimulus-locked negativity (N170) at inferior parietal sites, which was delayed when participants failed to inhibit the motor command. Moreover, both doses reduced N170 and P3 amplitudes during Go, NoGo, and error trials. In comparison with correct responses, errors generated large response-locked negative (Ne) and positive (Pe) waves at central sites to feedback, components reflecting motivation significance and recognition of error. Both doses of alcohol reduced Ne amplitude, whereas Pe amplitude decreased only after moderate doses. These results indicate that behavioral disinhibition following alcohol consumption involved alcohol-induced deficits in maintaining and allocating attention, thereby affecting the processing of incoming stimuli and the recognition that an errant response has been made.

A frontal negativity in the N2 range [variously named as ERN (Error related negativity), FERN, FMN (Fronto-Medial Negativity), ORN (Outcome related negativity)] has been identified as the ERP correlate of the feedback response (Nieuwenhuis et al., 2004; Hajcak et al., 2006). Moderate alcohol has been shown to increase the detrimental effects of incongruent flankers of a visual target in a response inhibition task (Bartholow et al., 2005), along with increased ERN and decreased P3 amplitudes, suggesting a restructuring of self-monitoring processes postalcohol use. To answer the question if alcohol causes a reduction in the efficiency of control processes in general, a study using the flanker task revealed impairments in both interference control and error detection (Ridderinkhof et al., 2002). The investigators found that the frontocentral ERN was attenuated significantly by alcohol consumption while N2 amplitude was not, indicating that alcohol in moderate doses produced a significant deterioration in detection of erroneous responses (ERN). Another study suggested that later stages of outcome processing were affected by alcohol, as indicated by reduced P300 to loss feedback (Euser et al., 2011). Motor preparation was evaluated using the lateralized readiness potential (LRP) in trials where the response had to be withheld (No-Go); the LRP was significantly higher postalcohol ingestion and the movement-related mu rhythm was also significantly attenuated, suggesting a premature activation of the motor system (Marinkovic et al., 2000). This also provides evidence for enhanced motor impulsivity that may be part of the conceptual framework of the response inhibition model.

Alcohol effects on cognitive domains such as semantic and mnemonic processes have not been studied extensively; however, one study showed that alcohol ingestion attenuated the temporoparietal negative potential (N180), revealing an effect of a moderately low alcohol dose on early prelexical stage of verbal processing (Marinkovic et al., 2004). Alcohol significantly increased the difficulty of semantic access and integration, as reflected in its effect on later potentials – larger N450 amplitude and longer P580 latency. This effect was particularly prominent in arousal-related trials, suggesting that alcohol impairs processes that modulate cognitive functioning related to semantic and integration systems rather than via memory processes.

These studies provide some evidence for both models, suggesting either a multifactorial pathway or a common upstream factor perhaps relating to structural–functional dynamics of the brain networks. Studies in the following section have attempted to explore the latter.

Acute effects of alcohol on EROs

More recently, with the use of EROs, a small number of studies have attempted to parse apart the effects of alcohol on various frequency bands and brain regions involved in aspects of cognitive processing.

Several studies have examined the effects of alcohol on cognitive processing in the auditory modality. The dose-related impact of alcohol on auditory transient evoked 40-Hz responses during a selective attention task was investigated; higher doses of alcohol significantly suppressed the early evoked gamma responses in both attended and non-attended conditions, suggesting cognitive impairment or lack of sensory binding (Jaaskelainen et al., 2000). Administration of alcohol was shown to decrease early synchronization during auditory encoding and increase later desynchronization in theta (4–6 Hz), low alpha (6–8 Hz), and high alpha (8–10 Hz) bands (Krause et al., 2002). This indicates that alcohol has disorganizing effects on the brain's electric oscillatory systems in theta and lower alpha frequency ranges during cognitive processing. Similarly, disorganizing effects of alcohol on phase synchronization of EROs during an auditory oddball task were recently reported in humans and rats (Ehlers et al., 2012). They demonstrated reduced synchrony within and between neuronal networks with ethanol, perhaps by increasing the level of noise in key interactions; reduced alpha-phase synchrony was also correlated with blood alcohol level.

There is also evidence to suggest acute effects of alcohol on theta oscillations during various cognitive tasks in the visual modality. Moderate alcohol intoxication modulated event-related theta activity during visual word processing, although alcohol was shown to attenuate theta power overall (Marinkovic et al., 2012). Moderate alcohol consumption was particularly deleterious to semantic retrieval since it reduced theta oscillations for real words but not pseudowords. Event-related theta power was also associated with sources in left-lateralized frontotemporal areas, reflecting lexical-semantic retrieval processes. This finding is in agreement with previous studies that suggest that executive functions are especially vulnerable to alcohol intoxication. Task-related EEG changes were studied during the performance of a mental arithmetic task for low "social" alcohol dosages with the presumption that even social drinking may have detrimental effects. While no detrimental alcohol effect was seen on behavioral indices of task performance, there was an ethanol-induced attenuation of the task-related frontally dominant theta increase; this effect was modest (Boha et al., 2009). Alcohol dose had an activating effect on autonomic measures of heart rate and electrodermal activity, and changes in nonlinear measures – omega complexity and synchronization likelihood – indicate increased synchrony in the theta band corresponding to increased working memory effort (Molnar et al., 2009). Moderate alcohol consumption caused spatiotemporal changes to conflict in both early and late processing stages during a Stroop task, and attenuated total event-related theta power, suggesting that alcohol-induced deficits in cognitive control may result from theta suppression in the executive network (Kovacevic et al., 2012). Slower reaction time was associated with

attenuated theta power that was attributed to anterior cingulate cortex, indicating an impairment in top-down control of motor preparation and execution. Alcohol significantly increased theta activity in subjects who were engaged in performing an attentional motor task of simulated automobile driving. Hence these results suggest that an alcohol-induced impairment of top-down strategic processing may underlie poor self-control, which in turn may affect drinking (Laukka et al., 1995).

Taken together, alcohol studies of EROs during various cognitive tasks indicate reduced-phase synchrony between and within neural networks in alpha and theta bands, and reduced theta oscillations, particularly implicating effects on frontal areas. The impact on the synchrony and generation of oscillations may influence the various cognitive operations leading to deficits in attention and response inhibition.

EFFECTS OF BINGE DRINKING ON ELECTROPHYSIOLOGY

Binge drinking is a relatively new term in the field of alcoholism and involves short periods of excessive drinking alternating with abstinence; it is generally defined as consumption of five or more drinks (four or more in females) during a 2-hour interval (Courtney and Polich, 2009). This behavior is widely prevalent among young adults and is associated with impairments in executive, visuospatial, and other domains (Hermens et al., 2013). Understanding the correlates of binge drinking in the developing brain is instrumental to designing prevention and management protocols. Animal studies have shown more brain damage from binge drinking in adolescent compared to adult animals. Regional damage to frontal association cortex and impaired hippocampal neurogenesis are both greater in adolescent than in adult rats (Crews et al., 2000, 2006). Courtney and Polich (2009) have provided clear recommendations regarding coherent and precise definitions of binge drinking in order to pursue a proper evaluation of brain deficits.

Binge drinking and EEG

Investigations of resting EEG in binge drinkers have emerged in recent years, aided by a clear definition of binge drinking. In earlier studies, moderate drinkers showed greater spectral power and higher peak frequency in the beta (12–20 Hz) band when compared to low/social drinkers, suggesting that beta activity might index quantity and frequency of alcohol consumption (Ehlers et al. 1989, Ehlers and Schuckit, 1990). More recently, Courtney and Polich (2010) examined male and female non-binge drinkers, low-binge drinkers, and high-binge drinkers who had been drinking alcohol at their respective levels for an average of 3 years. The non- and low-binge drinkers exhibited less spectral power than the high-binge drinkers in the delta (0–4 Hz) and fast beta (20–35 Hz) bands. Although the causal relationship between binge drinking and increased fast beta power is unclear, the authors suggest that the alteration of fast beta activity in high-binge drinkers is similar to the EEG spectral pattern seen in alcoholics (Rangaswamy et al., 2002), and may be a biomarker for potential future AUDs, even in the absence of familial alcoholism.

Functional connectivity during eyes-closed EEG was different between light and heavy drinkers in a study on EEG synchronization in heavy-drinking college students, defined as those who consume more than 30 units containing 12 grams of alcohol per week (de Bruin

et al., 2004). Heavy drinkers exhibited abnormally increased synchronization in theta (4–8 Hz) and gamma (30–45 Hz) bands. These frequency bands have been associated with memory formation involving hippocampo-neocortical connections (Buzsaki, 1996). Altered synchronization could reflect structural changes in neural networks involving the hippocampus and cortex, as observed in pathological studies (Harper, 2009). EEG synchronization in six frequency bands (delta, theta, alpha, slow beta, fast beta, and gamma) when compared between low, moderate, and heavy drinkers revealed a loss of lateralization in alpha and slow beta bands in male and female heavy drinkers (de Bruin et al., 2006). In addition, moderately and heavily drinking males had lower fast beta (20–30 Hz) synchronization than light-drinking males; synchronization in alpha and beta frequencies was impaired during rest and mental rehearsal in those drinking in excess of 21 alcoholic drinks per week.

Binge drinking and ERPs

Studies examining the neurophysiological consequences of binge drinking are revealing both early and global effects on cognition as evaluated using event-related activity (Maurage et al., 2012). One of the earliest studies of binge drinking on cognitive changes investigated ERPs in young adult Southwest California Indians with a history of binge drinking during adolescence (Ehlers et al., 2007). Using a facial discrimination task, they found that adolescent binge drinking was associated with lower P450 (like P3b) amplitude and a longer P350 (like P3a) latency, in those with family histories of ethanol dependence.

Another study using a working memory continuous performance task and a principal component analysis approach in analyzing ERPs examined attention and working memory processes (Crego et al., 2009). They reported increased N2 components for matching stimuli in binge drinkers, interpreting these findings as more effortful processing in the performance of the task. They also reported no P3 amplitude differences between the matching and non-matching conditions in binge drinkers, indicating a deficit in differentiating relevant and irrelevant processes. Employing a similar task in a later study, they revealed reduced amplitudes of the late positive complex in binge drinkers when compared to controls (Crego et al., 2010). This was also associated with hypoactivation of right anterior prefrontal cortex, determined using source localization with eLORETA (exact low-resolution brain electromagnetic tomography).

A longitudinal study that compared young adult binge drinkers with age-matched non-drinking controls showed progressive cerebral dysfunction without marked behavioral deficits (Maurage et al., 2009). The baseline assessments showed no differences; however after 9 months, the binge drinkers had significantly delayed latencies for all ERP components (P1, N2, P3b) of emotional auditory processing, reflecting impairments in perceptive as well as decisional processes. However, a more recent visual oddball study reported an opposite result of increased P3b amplitudes in binge drinkers when compared to controls (Crego et al., 2012); participants included only those without a personal or family history of alcoholism, unlike the previously described Ehlers et al. study (2007), which may indicate a differential vulnerability in those with and without family history.

A study that investigated links between response inhibition in a visual Go/NoGo paradigm in social drinkers found that Go and NoGo N2 showed a strong trend of being smaller centrally for heavy drinkers compared to light drinkers, but the Go P3 showed no group differences (Oddy and Barry, 2009). Only the NoGo P3 reduction was correlated with alcohol consumption. A response inhibition longitudinal study from the same laboratory (Lopez-Caneda et al., 2012) also reported increased P3 amplitudes for both Go (at baseline and follow-up) and NoGo (only at follow-up), suggesting a progressing influence of binge drinking on response inhibition. The authors suggested that increased amplitudes of P3 may reflect compensatory mechanisms within the adolescent brain.

An alcohol cue reactivity study (Petit et al., 2012) on binge drinkers reported enhanced P100 amplitude for alcohol-related images versus neutral images. This finding is similar to that seen in adult alcoholics and was not observed in control subjects. The later components (N2 and P3) were not affected, suggesting an early attention bias for alcohol-related cues. Maurage et al. (2012), in a most detailed study on binge drinking and its ERP correlates, used a face detection oddball task to evaluate both early and late cognitive processes, effect of comorbid conditions, and alcohol consumption pattern and amount. The authors reported massive ERP impairments from the early P100/N100, N170/P2, N2b/P3a, and P3b. Alcohol intake amount and specific binge-drinking patterns were also associated with these impairments.

Taken together, these studies suggest an ongoing process of refinement in ascertaining binge drinking, and as this is still in development, a definitive picture of electrophysiological deficits is yet to emerge. Binge drinking appears to be associated with a specific pattern of EEG activity (increased fast beta) in young adults that may reflect the future development of AUDs. The ERP measures are equivocal, particularly in the context of response inhibition; however a few studies do indicate deficits in perceptive as well as decisional processes, as reflected in decrements in early (P1, N1) and late (N2, P3b) ERP components, as well as changes in frontal sources of these activities.

CHRONIC ALCOHOLISM AND NEUROELECTROPHYSIOLOGY

Chronic alcoholism is associated with a broad spectrum of brain disturbances ranging from severe symptoms of Wernicke–Korsakoff syndrome to subtle but nonetheless significant cognitive disturbances characteristic of a majority of alcoholic patients. The etiology of alcohol-related brain damage/dysfunction is not entirely known, as there are brain changes during acute and chronic intoxication, as well as during withdrawal; some brain changes recover with prolonged abstinence and some brain anomalies antecede the development of AUDs and may be involved in the predisposition to develop AUDs. This section will focus on EEG, ERP, and ERO measures of brain dysfunction in AUDs in abstinent alcoholics, as well as in HR offspring of alcoholics, to help determine which are consequences of AUDs and which antecede its development. (For earlier reviews of other aspects of alcoholism and electrophysiology (e.g., sensory components), see Porjesz and Begleiter, 1983, 1985, 1993, 1996.)

Chronic alcoholism and resting EEG

Differences in both EEG power and coherence have been reported in alcoholics; some of these are the consequence of chronic alcoholism while others antecede its development. This section will review EEG power and coherence measures in alcoholics and those at risk.

Theta band—Increased resting theta power in alcoholics has been reported in a number of studies in the literature (Propping et al., 1981; Pollock et al., 1992; Rangaswamy et al., 2003); no relationship between the length of abstinence and theta power was found (Pollock et al., 1992). However another study reported a decrease in theta power in female alcoholics (Propping et al., 1981). Elevated resting theta activity observed in the EEG of alcohol-dependent individuals is indicative of a dysfunctional neurophysiological status in these individuals. As suggested previously in this chapter, we can speculate that the increases of theta produced by the acute administration of alcohol in healthy individuals may subsequently evolve into a more pervasive increase in theta in chronic alcoholics following prolonged exposure. No strong evidence of increased resting theta has been reported in offspring of alcoholics, suggesting that this measure may index a state-dependent condition.

Increases of theta rhythm have been seen in altered neurophysiological states of the brain, involving altered cholinergic functioning, such as Alzheimer's disease, aging, and the transition from wakefulness to sleep (Niedermayer and Lopes Da Silva, 1999). Slow EEG activity (theta and delta) has been correlated with cholinergic activity and central cholinergic pathways (Steriade, 1990). Elevated tonic theta power in the EEG may reflect a deficiency in information-processing capacity of the CNS (Klimesch et al., 2001). The theta power increase may be an electrophysiological index of the imbalance in the excitation-inhibition homeostasis in the cortex.

Alpha band—There is extensive literature, dating back to the 1940s, indicating unstable or poor alpha rhythm in alcoholics; alcoholics manifest less prevalent and lower alpha than do non-alcoholics (for reviews, see Begleiter and Platz, 1972; Propping et al., 1981). However some more recent studies did not find the same results (Pollock et al., 1992; Enoch et al., 1999). A pronounced slow alpha decrease is associated with relapse (Saletu-Zyhlarz et al., 2004); there is an increase in slow alpha, a decrease in fast alpha, and a deceleration of the alpha centroid with six months of abstinence. On the other hand, participants who had a family history of alcoholism had significantly higher spectral power in the slow alpha frequencies (7.5–9 Hz) (Ehlers and Phillips, 2003); this was found for males with alcoholic fathers (Ehlers and Schuckit, 1991) and women at high risk for developing alcoholism (Ehlers et al., 1996). While reduced EEG alpha power in male and female offspring of alcoholics has been reported (Finn and Justus, 1999), this was not related to comorbid traits of anxiety or antisocial personality. A distinctive low-voltage alpha variant (LVA), has been reported to be associated with a subtype of alcoholism that is associated with anxiety disorder (Enoch et al., 1999). LVA, which is characterized by an absence or very low-amplitude alpha rhythmicity, is found in 5–10% of individuals (Anokhin et al., 1992; Enoch et al., 1995). Ethnic variations may exist in the prevalence of LVA, EEG variants, and association with alcoholism or risk (Ehlers and Phillips, 2003).

Beta band—Beta frequency rhythms are also known as inhibition-based rhythms. Increased beta power in the EEG of alcoholics, particularly in the resting condition, has been well documented (Propping et al., 1981; Costa and Bauer, 1997; Winterer et al., 1998; Bauer, 2001; Rangaswamy et al., 2002). Increased beta power was observed at all scalp loci in the large Collaborative Study on the Genetics of Alcoholism (COGA) sample, but was most prominent in the central region for slow-medium-frequency beta (12–20 Hz) and over the frontal regions for fast beta (20–28 Hz) (Rangaswamy et al., 2002). Increased beta activity, particularly fast beta (19.5–39.8 Hz), has proved to be an excellent predictor of relapse (Bauer, 2001; Saletu-Zyhlarz et al., 2004). Desynchronized beta activity over frontal areas in relapsers has been suggested as a correlate of functional disturbance of prefrontal cortex (Winterer et al., 1998).

Increased beta power has also been described in the EEG of relatives of alcoholics (Gabrielli et al., 1982; Pollock et al., 1995; Finn and Justus, 1999; Rangaswamy et al., 2004b). However, some studies examining acute effects of alcohol on HR report an absence of pre-ethanol baseline differences in resting EEG between LR and HR subjects (Pollock et al., 1983; Kaplan et al., 1988; Cohen et al., 1991). A positive family history of alcoholism was related to increased beta power in HR (Gabrielli et al., 1982; Pollock et al., 1995; Finn and Justus, 1999), and when present along with a diagnosis of antisocial personality (ASP), it was associated with increased frontal beta power (Bauer and Hesselbrock, 1993). In the COGA study, increased beta power on the resting EEG was demonstrated in a large sample of offspring of alcoholics (Rangaswamy et al., 2004b). Taken together, as the increase in beta power in alcoholics was not related to length of abstinence (Rangaswamy et al., 2002) and was also present in individuals at risk (Rangaswamy et al., 2004b), this suggests that it may not be an effect of alcohol use, but perhaps antecede the development of AUDs.

Most studies reporting beta band differences in alcoholics and HR offspring also underscore the issue of gender in electrophysiologic research. In studies evaluating alcoholics and HR offspring of both genders, beta band changes were more robust in males while females showed either no elevation or only a modest increase (Gabrielli et al., 1982; Pollock et al., 1995; Finn and Justus, 1999; Rangaswamy et al., 2002, 2004b). Gender differences were highlighted in the COGA study, where male HR offspring had elevated slow beta (12–16 Hz), while female HR offspring showed significantly increased faster beta power (16–28 Hz), particularly those with two or more alcoholic first-degree relatives. Existing gender differences in the progression and pathology of alcoholism and spectral properties of EEG highlight the importance of studying risk indicators within the context of gender.

Interhemispheric coherence: EEG in alcoholics also reveals an increased interhemispheric coherence when compared to unaffected individuals (Kaplan et al., 1985; Michael et al., 1993). Bilateral intrahemispheric coherences in alpha and beta frequency bands were increased in both long-term abstinent and non-abstinent alcoholics compared to controls (Winterer et al., 2003a). These findings were strongest for the high alpha (10.5–12 Hz) frequency band, and were most pronounced at temporal, parietal, and occipital regions, particularly when depressiveness was included as a covariate; there was no effect of length of abstinence on these findings.

In summary, studies that have investigated the resting EEG composition indicate beta band increases as a primary characteristic feature in alcoholics and HR subjects, and, less significantly, theta band increases in the alcoholics. This reactivity of beta band has also been observed in studies assessing binge drinkers. The alpha band differences in chronic alcoholism are not conclusive and remain equivocal, although alcohol challenge studies in HR and LR subjects have uncovered a reactive alpha system that tends to shift to slower frequencies (see earlier in this chapter). The evidence of elevated beta power also provides strong support for the excitation-inhibition imbalance model proposed to underlie the predisposition to alcohol dependence (Begleiter and Porjesz, 1999), and future studies are required to clarify gender differences in EEG profiles in alcoholism.

Chronic alcoholism and event-related potentials—This section reviews ERP components reflecting various cognitive functions that are impaired in alcoholics.

Attention – N100 and mismatch negativity (MMN)—Early attention selection processes are affected in both alcohol-dependent and unaffected HR individuals (Steinhauer et al., 1987), as indicated by diminished N100 component. Using a bimodal task (auditory and visual stimuli), a study on abstinent alcoholics, controls, and FHP offspring showed reduced visual N1 amplitude in alcoholics and reduced auditory N1 amplitude in the FHP individuals (Patterson et al., 1987). The dampening of N1 amplitudes to repetitive stimuli may be associated with the refractoriness (Cohen et al., 1996) or may be a reflection of lateral inhibition at the cortical level (Sable et al., 2004); however they were not very effective in differentiating HR from LR individuals.

Larger MMN amplitudes have been reported in recently detoxified alcoholics (Kathmann et al., 1995). The automatic stimulus change detector mechanism associated with MMN generation is impaired in chronic alcoholics over the age of 40, suggesting that the neurotoxic effects of chronic consumption of alcohol are more prone to appear after a critical age (Polo et al., 1999). One study showed no MMN differences between controls and alcoholics who were abstinent for an average of 6 years (Fein et al., 2004), while another (Pekkonen et al., 1998) observed that increasing durations of abstinence reduced the MMN amplitude, perhaps indicating improved efficiency of covert processes upon abstinence. Ahveninen et al. (2000) found significantly enhanced MMN amplitudes to deviant sounds that correlated with reaction time lag caused by deviants, indicating pronounced distractibility and impaired reorienting to the relevant task in alcoholics. The MMN enhancement predicted poorer hit rates in alcoholics and along with reaction time lag it also correlated with an early onset of AUDs. Impairment in neural inhibition of involuntary attention shifting may be more pronounced in early-onset alcoholics. Grau and colleagues (2001) found that, while the MMN component is abolished with more demanding tasks in chronic alcoholics, it is present in normal controls. It has been suggested that the mechanisms to detect auditory differences may be reorganized in the brains of alcoholics, as revealed by lower scalp current densities in left frontal and right temporal areas during MMN in alcoholics (Marco-Pallares et al., 2007). However, no group differences in MMN amplitude have been reported in young HR offspring (van der Stelt et al., 1997; Rodriguez Holguin et al., 1998).

In summary, attention effects seem more associated with state-related aspects and provide a better measure for recovery than a predisposition.

Target detection (oddball tasks)—It is well established that alcoholics manifest reduced amplitudes of P3b to task-relevant target stimuli, particularly over parietal regions; similarly, alcoholics manifest low frontally distributed P3a to rare non-target stimuli in both visual and auditory modalities (for reviews, see Porjesz and Begleiter, 1996; Porjesz et al., 2005). Koskinen et al. (2011) analyzed auditory P3 in a twin study, and lower P3 to novel stimuli (P3a) was consistently associated with alcohol use in adolescence. More recent studies have indicated that low P3b amplitudes are present not only in male alcoholics, but in female alcoholics as well, though not to the same extent as in males (Hill and Steinhauer, 1993; Prabhu et al., 2001; Suresh et al., 2003). The lower P3 amplitude is also significantly associated with increased impulsivity and decreased activity of frontal sources in alcoholics (Chen et al., 2007). However, in an unusual sample of treatment-naive actively drinking adolescents with alcohol dependence, no reduction of P3b amplitude was observed in comparison to matched controls (Cuzen et al., 2013), possibly due to absence of any family history, comorbidity, and short drinking history.

The results for N2 component, especially the amplitude, have been equivocal. Porjesz et al. (1987b) observed longer N2 latency but no changes in amplitude in a visual discrimination oddball task conducted on alcoholics. A multimodal study also reported increased N2 latency and P3 latency in an auditory paradigm (Cadaveira et al., 1991). N2 amplitudes in an auditory oddball task were significantly lower for alcohol-dependent individuals when compared to controls (Realmuto et al., 1993; Cristini et al., 2003) but contrary findings of increased N2 amplitude in alcoholics have also been reported (Olbrich et al., 2000).

Recovery with abstinence: The P3 amplitude in alcoholics did not completely recover with prolonged abstinence (Porjesz and Begleiter, 1985; Glenn et al., 1994) and remained lower when compared to controls. Also, relapse was associated with longer N2 latency and this was not modulated by family history (Glenn et al., 1993). Studies evaluating long-term abstinent alcoholics found that P3b amplitude was reduced even after 3–10 years of abstinence (Porjesz and Begleiter, 1985) and along with increased P3a and P3b latencies after an average abstinence of 6 years (Fein and Chang, 2006).

It has been hypothesized that an underlying CNS disinhibition (i.e., hyperexcitablity) is involved in a predisposition to develop alcoholism (Begleiter and Porjesz, 1999). As described earlier, low-amplitude P3 in alcoholics is also suggestive of reduced CNS inhibition. A collection of studies examining offspring of alcoholics who are at greater risk has helped to understand if the low P3 amplitudes are due to prolonged effects of alcohol on the brain, or if they are antecedent to its development, indicating an underlying predisposition. Young HR sons of alcoholics without prior alcohol exposure had significantly lower P3 voltages compared with matched LR boys from control families without first- or second-degree alcoholic relatives (Begleiter et al., 1984). These findings were replicated in many HR/LR samples (older/younger, male/female) under several experimental conditions (for review, see Porjesz et al., 2005). Furthermore, low P3 amplitude prior to puberty has been found to predict later substance abuse, including alcohol

abuse in adolescence (Berman et al., 1993; Hill et al., 1995b; Iacono et al., 2002, 2003). In addition to P3b results, offspring of alcoholics also manifested low-amplitude P3a components in both visual (Rodriguez Holguin et al., 1999) and auditory paradigms (Hada et al., 2001).

There is evidence that the P3 amplitude is directly related to the number of first-degree alcoholic relatives and not the drinking history of an alcoholic (Pfefferbaum et al., 1991; Cohen et al., 1995) or FHP/HR individual (Benegal et al., 1995). In the COGA study, lower P3 was found in alcoholics and family members from densely affected families compared with those from control families (Porjesz et al., 1998). Family history was significantly and selectively associated with lower P3 amplitudes to alcohol-related stimuli in a group of young adult African American men and women; current use of marijuana and alcohol did not modify P3 amplitudes (Ehlers et al., 2003). In contrast, some studies have failed to find relationships between family history and P3b amplitude (Polich and Bloom, 1987; Ehlers et al., 2001; Houston et al., 2003). Most P3 studies on HR have focused on males; data for female offspring have been less consistent, suggesting a weaker effect (Hill and Steinhauer, 1993; Hill et al., 1995a). Data from the COGA study also showed lower P3 amplitude in female offspring from multiplex alcoholism families, yet to a lesser degree than in males (Porjesz and Begleiter, 1996; Porjesz et al., 1998). In a comprehensive meta-analysis of all published HR versus LR studies at the time, Polich et al. (1994) found that the strongest P3 group differences were obtained in young male offspring with relatively difficult visual tasks and concluded that low-voltage P3 may have predictive value as an index of vulnerability for alcoholism. Thus, the low-voltage P3 component is a robust finding that characterizes individuals at risk for alcoholism, and provides an excellent phenotypic “trait” marker.

Response inhibition (Go/NoGo tasks)—Understanding response inhibition lies at the core of behavioral control, which may be impaired across the spectrum of disinhibitory disorders (Zucker et al., 2011). Alcoholics not only manifest reduced P3 amplitudes to Go stimuli, but reduced P3 to NoGo stimuli as well (Pfefferbaum et al., 1991; Cohen et al., 1997b; Fallgatter et al., 1998; Rodriguez Holguin et al., 1999; Hada et al., 2000). Furthermore, chronic alcoholics manifest less differentiation between their responses to task-relevant target stimuli and task-irrelevant non-target stimuli, suggesting less effective inhibitory processes. Similarly, Cristini et al. (2003) reported reduced N2 in alcoholics in a Go/NoGo task. A recent study reported significantly reduced N2 amplitudes in alcohol-dependent subjects for Go and NoGo trials, particularly for NoGo trials in frontal regions where alcoholics did not show a more frontal distribution (Pandey et al., 2012) (Fig. 23.2); controls had significantly larger frontal amplitudes for NoGo, in line with a frontal generator for N2 (van Veen and Carter, 2002; Nieuwenhuis et al., 2004). The anteriorly distributed NoGo P3 potentials were also markedly reduced in amplitude in alcoholic subjects as well as in high-risk individuals, indicating impaired inhibitory control in these individuals (Cohen et al., 1997a, b; Kamarajan et al., 2005a, b; Colrain et al., 2011).

Error monitoring and response evaluation—Reward and feedback evaluation as a behavioral process has come under special scrutiny in the context of addictive and impulsive

disorders. Correlates of valence attached to the negative and positive consequences of behavior have been studied using ERPs in alcoholics and those at risk for AUDs. While there have been very few ERP studies examining reward/feedback processing in alcoholics, they provide interesting insights. Probably the first study of this kind was done by Porjesz et al. (1987a), who reported decreased P3 amplitude in response to incentive stimuli in abstinent alcoholics. More recently, using the balloon analogue risk task (BART), which measures risk-taking propensity, Fein and Chang (2008) reported smaller amplitude in feedback negativity in FHP treatment-naive alcoholics compared to controls. Although these findings support the notion that alcoholics have a specific deficiency in reward evaluation, the nature of these deficits is still not clear due to the paucity of such studies in alcoholics. Increased impulsivity and risk taking have been found in alcoholics with reduced components to outcome/feedback stimuli during a gambling task (Kamarajan et al., 2010).

Studies have shown that the feedback/outcome-related negativity (ORN) is localized to medial frontal areas (Gehring and Willoughby, 2002; Nieuwenhuis et al., 2004; Masaki et al., 2006). Source localization in healthy individuals reveals a medial frontal source for ORN for loss, and a medial posterior source for gain (Kamarajan et al., 2009) (Fig. 23.3). Alcoholics had significantly lower ORN amplitude than controls for loss trials (Kamarajan et al., 2010). However, the outcome-related positivity (ORP) was lower for both gain and loss trials, suggesting that the negative and positive components subserve different aspects of outcome monitoring. The feedback/outcome related positivity in gambling paradigms (ORP) is considered to index the subjective evaluation of the magnitude of outcome (Yeung and Sanfey, 2004; Overbeek et al., 2005; Toyomaki and Murohashi, 2005; Kamarajan et al., 2009). Contrary results have been noted in studies that tested alcoholics and matched controls (Schellekens et al., 2010; Padilla et al., 2011); however these studies were conducted on very small samples. Alcoholics generated larger ERN amplitudes than controls following incorrect and correct responses on the Eriksen flanker task (Padilla et al., 2011). Both groups showed evidence of posterror slowing. The amplitudes in the alcoholics were related to longer reaction time in correct trials, suggesting increased effort in alcoholics. Smaller negative amplitudes were associated with length of sobriety, suggesting a normalization of monitoring activity with extended abstinence.

Semantic processing—A negative ERP component, designated as N4 or N400 (300–650 ms) over centroparietal scalp, and initially elicited to semantic incongruency, has been the cornerstone of semantic ERP studies (Kutas and Hillyard, 1980; Bentin, 1989). The N400 varies systematically with the processing of potentially meaningful stimuli, where the amplitude is reduced by a number of factors (Kutas and Federmeier, 2000). Increased latency for N400 response to related/incongruent semantic information has been reported in alcoholics, especially in those with comorbid antisocial personality (ASP) (Ceballos et al., 2003). Ceballos and colleagues (2005) found significantly less negative N4 amplitudes in alcohol-dependent individuals relative to non-dependent controls. Another widely used paradigm is the semantic priming paradigm, in which a word preceded by an unrelated word (unprimed) produces a larger N400 compared to a word preceded by a related word (primed) (Bentin, 1989; McCarthy and Nobre, 1993). Reduced N4 amplitude of the difference waveform between primed and unprimed words has been reported (Nixon et al., 2002).

Similarly, in a recent semantic decision task there was less attenuation of N400 amplitudes to primed words when compared to unprimed words in alcoholics, a phenomenon that was intact in the controls (Porjesz et al., 2002b; Roopesh et al., 2010) (Fig. 23.4). Significant group differences were not seen for latency; however all subjects had slower reaction time for unprimed words compared to primed words, but significantly less reaction time savings between the unprimed and primed condition was noted for alcoholics. This lack of attenuation for the primed word suggests a deficiency of semantic priming process in the alcoholics where the expectancy for the second word of the antonym pair is not adequately generated. Similarly, young adult male HR offspring from alcoholic families manifested a lack of N400 attenuation, indicating deficits in semantic expectancy and post lexical semantic processing which may be present prior to alcohol dependence (Roopesh et al., 2009) (Fig. 23.4). These studies suggest that alcohol-dependent individuals and those at risk suffer from subtle impairments indicative of a reduced efficiency in resource optimization.

In summary, ERP studies reveal a pattern of deficits that affect primarily the domains of attention, response inhibition, and performance monitoring. More complex cognitive processes such as mnemonic, semantic, and lexical processes are also affected; however these may be associated with underlying attention and executive deficits.

Chronic alcoholism and event-related oscillations—Several studies have demonstrated that P3 responses are primarily the outcome of theta and delta oscillations elicited during cognitive processing of stimuli (Basar-Eroglu et al., 1992; Yordanova and Kolev, 1996; Basar, 1999; Karakas et al., 2000a, b), with delta oscillations more concentrated in the posterior region, while theta is more centered in the frontocentral region (Karakas et al., 2000b) (Fig. 23.1). ERO changes in chronic alcoholics reveal a neuronal state with altered excitability. This has also been suggested by some transcranial magnetic stimulation (TMS) studies (Conte et al., 2008; Muralidharan et al., 2008).

In a visual oddball paradigm, alcoholics manifested significantly reduced theta and delta ERO amplitudes while processing the target stimuli (Jones et al., 2006b); theta differences have a frontal focus while delta tends to be more posterior (Fig. 23.1). Adolescent HR offspring also showed similar reductions in delta and theta power when compared to LR adolescents; however, the topography of theta is shifted more posteriorly to vertex and parietal regions, similar to the topography of delta oscillations (Rangaswamy et al., 2007). Interestingly, the EROs were superior to P3 amplitude in differentiating between HR and LR offspring. Similar to the observations from P3 studies, the results suggest that decreased theta and delta ERO to target stimuli may antecede the development of AUDs and represent an excellent trait marker.

These findings were replicated more recently (Andrew and Fein, 2010a) for evoked and total power in delta and theta ERO in long-term abstinent alcoholics; the authors proposed that P300 and ERO measures provide comparable information. Phase locking enhances signal-to-noise ratios; however the increase in non-phase locked (induced) theta oscillations was suggested to be a marker of chronic alcohol abuse on the brain (Gilmore and Fein, 2012). This effect may recover, at least partially, with extended abstinence. The increased induced theta was also a strong predictor of alcoholism status (Andrew and Fein, 2010b).

Oscillatory responses associated with response inhibition were investigated using a Go/NoGo paradigm in abstinent alcoholics (Kamarajan et al., 2004). Decreased power in delta and theta oscillations was observed in alcoholics, particularly during NoGo processing, and prominent frontally. These changes were confirmed in another study that reported reduced delta oscillations for No-Go, which was correlated with white-matter degradation in the cingulate bundles (Colrain et al., 2011). Offspring of alcoholics showed significantly decreased activity in delta (1–3 Hz), theta (4–7 Hz), and alpha1 (8–9 Hz) bands during the NoGo condition, as well as reduced delta and theta activity during the Go condition (Kamarajan et al., 2006). Similar to alcoholics, differences were more prominent in the NoGo than in the Go condition. Thus it seems probable that these oscillatory responses may antecede the development of AUDs.

In a recent study on reward processing in alcoholics during a gambling task, event-related theta band (3.0–7.0 Hz) oscillations were evaluated during the loss/gain feedback (Kamarajan et al., 2012). The alcoholic group showed significantly decreased theta power during reward processing compared to controls, particularly during the evaluation of loss. Current source density maps of alcoholics revealed weaker and diffuse source activity for all conditions and weaker bilateral prefrontal sources during loss while the controls manifested stronger and more focused midline sources. Alcoholics also exhibited increased impulsivity, risk taking (as revealed by behavioral measures), and a strong association between reduced anterior theta power and impulsive task performance. Decreased power in theta oscillations and more diffuse current density may be due to reorganized and inefficient neural reward network in alcoholics.

Early attention selection impairments have been reported in alcoholics and HR (see section on attention – N100 and mismatch negativity), while some studies report no differences. The underlying reason for the variation in results may arise from an enhanced theta phase resetting in the absence of any N1 amplitude and power changes in alcoholics when compared to controls (Fuentemilla et al., 2009). The phase resetting defines excitability windows of phase-locked neurons, which in turn directs information flow, hence implying a hyperexcited neuronal state in alcoholics. Early phase-locked gamma is an important processing step for the selection/identification of target stimuli, indicative of a top-down mechanism involved in selective attention (Fell et al., 2003); it is larger to attended compared to unattended stimuli, particularly over frontal regions (Basar, 1999; Yordanova et al., 2001). Neuroimaging studies using attentional tasks have implicated the role of frontoparietal networks in this top-down control of selective attention (Corbetta et al., 2000; Giesbrecht et al., 2003). Early gamma (28–45 Hz) band response (1–150 ms) is significantly attenuated in the frontal region for target processing in abstinent alcoholics (Padmanabhapillai et al., 2006a) and children of alcoholics (HR) (7–17 years) (Padmanabhapillai et al., 2006b). Differences were only seen in the parietal region for the target condition in HR individuals. A dysfunctional frontoparietal attentional network may be associated with the impaired gamma band response and a deficient frontal top-down processing mechanism (Rangaswamy et al., 2004a).

ELECTROPHYSIOLOGICAL MEASURES AS ENDOPHENOTYPES

Alcoholism is a common, complex (non-Mendelian) disorder with contributions from both genetic and environmental influences and their interactions. As seen in this review, neuroelectrophysiological measures (e.g., P3, theta ERO, EEG beta) that differentiate between alcoholics and controls, and between HR offspring from densely affected alcoholic families and LR controls, serve as effective endophenotypes (intermediate phenotypes that correlate with diagnosis). These endophenotypes are under genetic control and are highly heritable, and have been successfully used in the search for genes associated with risk for AUDs and related disorders (Porjesz and Rangaswamy, 2007; Rangaswamy and Porjesz, 2008a, b). As the genomic technologies have evolved from linkage scans with microsatellites to candidate gene studies and genomewide association studies (GWAS) these studies have highlighted targets that have proved to be relevant to understanding the pathophysiology of AUDs.

EEG phenotypes

Data on the heritability of EEG frequencies are quite compelling. The largest twin study estimates the heritability of theta and alpha power to be 0.89 and beta to be 0.86 (van Beijsterveldt and Boomsma, 1994; van Beijsterveldt et al., 1996); these heritability estimates are higher than those for AUDs and other psychiatric diagnoses. Heritability estimates for EEG coherence range between 0.5 and 0.7 (Stassen et al., 1988; van Beijsterveldt and Boomsma, 1994; van Baal et al., 1998; van Beijsterveldt et al., 1998; Chorlian et al., 2007).

Using EEG power as an endophenotype, the COGA project reported genetic linkage and linkage disequilibrium between beta and a $GABA_A$ receptor gene (Porjesz et al., 2002a). Beta rhythm is generated in a network of excitatory pyramidal cells and inhibitory interneurons involving $GABA_A$ action as the pacemaker (Whittington et al., 2000). The same $GABA_A$ receptor gene (*GABRA2*) associated with beta EEG was also associated with alcohol dependence (Edenberg et al., 2004), a finding that has been replicated (Covault et al., 2004) and expanded to include other substance dependence in adults and conduct disorder in adolescents (Agrawal et al., 2006; Dick et al., 2006). The involvement of the GABAergic system in AUDs is supported by neuroimaging studies, which indicate deficient GABA benzodiazepine receptors in the brains of alcoholics (Abi-Dargham et al., 1998; Lingford-Hughes et al., 1998) and HR offspring (Volkow et al., 1995). Dysfunction in $GABA_A$ receptor genes may affect neural excitability, or the imbalance between excitation-inhibition (hyperexcitability) reflected in increased beta observed in alcoholics and HR offspring; this in turn may be involved in the predisposition to develop AUDs and related disinhibitory disorders.

A low-voltage alpha (LVA) phenotype, characterized by an absence or very low-amplitude alpha rhythmicity, is found in 5–10% of individuals (Anokhin et al., 1992; Enoch et al., 1995). The exon 7 variant of the $GABA_B$ receptor gene and EEG alpha voltage (LVA or normal) was significantly associated for control but not alcoholic subjects (Winterer et al., 2003b). LVA in females has been associated with a genetic variant resulting in low catechol-*O*-methyltransferase activity, which is involved in the dopaminergic system, yielding low

levels of norepinephrine (Enoch et al., 2003). This may partly explain the association of LVA and anxiety disorders in alcoholic women.

Increased interhemispheric coherence has been a feature of EEG in alcoholism; when associated with increased depressiveness, it has been suggested to involve GABAergic and/or glutamatergic neurotransmission. Winterer et al. (2003c) revealed that three exonic variants of a $GABA_B$ receptor gene influence cortical synchronization (coherence). In the COGA study, significant linkage for theta (6–7 Hz) interhemispheric coherence at parieto-occipital regions led to significant association with several single nucleotide polymorphisms (SNPs) in *GABRA2*. Another significant linkage peak for theta (6–7 Hz) centroparietal coherence was significantly associated with SNPs in *CHRM2*, a cholinergic muscarinic receptor gene (Porjesz and Rangaswamy, 2007; Rangaswamy and Porjesz, 2008b).

EROs as endophenotypes

EROs have proved to be more useful than ERPs in the search for genes involved in AUDs and related disorders in COGA. Theta oscillations to targets have been instrumental in identifying two excellent candidate genes under a significant linkage peak – *CHRM2* and *GRM8*. Both encode subunits of neurotransmitter receptors: *CHRM2* encodes a cholinergic muscarinic receptor M2, whereas *GRM8* encodes the metabotropic glutamate receptor 8 in a family of G-protein-coupled receptors. Significant associations were observed between the frontal theta ERO and SNPs in *CHRM2*, and to parietal delta (Jones et al., 2004, 2006a). Several of the same SNPs were significantly associated with alcohol dependence along with depression, drug dependence and externalizing disorders (DSM-IV) (Wang et al., 2004; Dick et al., 2007), findings that were replicated by other groups (Comings et al., 2002; Luo et al., 2005). Theta oscillations were also significantly associated with several SNPs in *GRM8*, as well as alcohol dependence (Chen et al., 2008a).

Generation of theta and delta oscillations depends on level of activation of M2 muscarinic autoreceptors (Fellous and Sejnowski, 2000; Tiesinga et al., 2001) that inhibit further acetylcholine release by presynaptic cells, leading to inhibition of irrelevant networks. Acetylcholine plays a significant role in stimulus significance (Perry et al., 1999), selective attention (Mitrofanis and Guillery, 1993), P3 generation, and modified memory performance (Hammond et al., 1987; Dierks et al., 1994; Frodl-Bauch et al., 1999; Potter et al., 2000). The GRM8 gene encodes a presynaptic autoreceptor involved in modulating neuronal excitability by inhibiting glutamate release at the synapse (Schoepp, 2001). Hence, these findings implicate *CHRM2* and *GRM8* in the generation and modulation of these oscillations during the P3 response to target stimuli. GABAergic, cholinergic, and glutamatergic system interactions have been proposed to underlie these rhythms and P300 (Frodl-Bauch et al., 1999). Thus, the genetic underpinnings of these oscillations influence the excitability in neural networks.

This is further supported by a recent family GWAS study in COGA with a genomewide significant finding in another neurotransmitter-related gene – *KCNJ6* (a potassium inward rectifier channel, GIRK2) and frontal theta EROs (Kang et al., 2012). These results suggest that *KCNJ6* or its product GIRK2 may account for some of the variations in theta oscillations. GIRK2 receptor activation contributes to slow inhibitory postsynaptic potentials

that modulate neuronal excitability, and therefore influence neuronal networks (Luscher and Slesinger, 2010). Animal models have shown that GIRK channels are directly activated by ethanol and are important effectors in both opioid- and ethanol-induced analgesia and are considered a viable drug target; GIRK2 also modulates opioid effects on analgesia and addiction in humans. Thus these findings between theta EROs and *KCNJ6* have important implications for neural excitability and alcohol addiction.

Together, these results indicate that the neurophysiological endophenotypes implicate some of the transmitter genes important for modulating and maintaining neural excitability; variations in this excitability may underlie the predisposition or susceptibility for AUDs and related disorders.

CONCLUSION

In conclusion, the vulnerability to alcohol effects and AUDs may be associated with a modulation of excitability of some neural circuits more than others. These changes affect networks associated with cognitive domains of attention and self-monitoring that are part of the rubric of the frontal executive function which is impacted with both acute and chronic alcohol use. Both ERP and ERO studies discussed here provide evidence for impaired attention, response inhibition, and monitoring functions. Source localization of these components highlights impaired loci in frontal lobes, suggesting the utility of a multimodal approach. Future studies that integrate neuroelectrophysiology and neuroimaging are essential to understanding these complex structure–function interactions.

Studies conducted so far suggest that there are several common substrates (e.g., theta oscillations, beta oscillations, P3 amplitude) that are influenced by alcohol in both acute and chronic use and this in turn may reflect the underlying vulnerability of the brain to alcohol. The potential to isolate genetic underpinnings of impaired neuroelectrophysiological features associated with alcohol use is another exciting direction that may provide viable targets for intervention. Although no functional variant affecting the neuroelectrophysiological characteristics has yet been identified at the molecular level, a large body of pharmacological evidence attests to the relevance of these receptors for aspects of cognitive function. This approach has the unprecedented potential to unravel the complex interplay of various neural subsystems relevant to the generation of brain oscillations elicited under different cognitive conditions and in disease states.

Alcohol dependence results from a complex interaction of changing genetic and environmental liabilities across development. Genetic studies have successfully used these endophenotypes to reveal significantly associated SNPs from the same genes that are also associated with alcohol dependence and related disorders. Thus, genes underlying the variations in endophenotypes are also associated with the disease. Therefore, understanding genetic control of brain electrical activity can provide clues about cerebral function and also shed light on mechanisms involved in psychiatric disorders, such as AUDs, where impairment in brain electrical activity is apparent. Prospective studies of young individuals with “risk genotypes” can lead to an improved understanding of how neural and cognitive

changes contribute to susceptibility across development, which in turn can lead to the design of well-targeted prevention initiatives.

References

Abi-Dargham A, Krystal JH, Anjilvel S, et al. Alterations of benzodiazepine receptors in type II alcoholic subjects measured with SPECT and [123I]iomazenil. Am J Psychiatry. 1998; 155:1550–1555. [PubMed: 9812116]

Agrawal A, Edenberg HJ, Foroud T, et al. Association of GABRA2 with drug dependence in the collaborative study of the genetics of alcoholism sample. Behav Genet. 2006; 36:640–650. [PubMed: 16622805]

Ahveninen J, Escera C, Polo MD, et al. Acute and chronic effects of alcohol on preattentive auditory processing as reflected by mismatch negativity. Audiol Neurootol. 2000; 5:303–311. [PubMed: 11025330]

Andrew C, Fein G. Event-related oscillations versus event-related potentials in a P300 task as biomarkers for alcoholism. Alcohol Clin Exp Res. 2010a; 34:669–680. [PubMed: 20102573]

Andrew C, Fein G. Induced theta oscillations as biomarkers for alcoholism. Clin Neurophysiol. 2010b; 121:350–358. [PubMed: 20074999]

Anokhin A, Steinlein O, Fischer C, et al. A genetic study of the human low-voltage electroencephalogram. Hum Genet. 1992; 90:99–112. [PubMed: 1427795]

Ardekani BA, Choi SJ, Hossein-Zadeh GA, et al. Functional magnetic resonance imaging of brain activity in the visual oddball task. Brain Res Cogn Brain Res. 2002; 14:347–356. [PubMed: 12421658]

Bartholow BD, Pearson M, Sher KJ, et al. Effects of alcohol consumption and alcohol susceptibility on cognition: a psychophysiological examination. Biol Psychol. 2003; 64:167–190. [PubMed: 14602361]

Bartholow BD, Pearson MA, Dickter CL, et al. Strategic control and medial frontal negativity: beyond errors and response conflict. Psychophysiology. 2005; 42:33–42. [PubMed: 15720579]

Basar, E. Neurophysiology and cognitive processes. Berlin: Springer; 1999. Brain function and oscillations. Vol.II, Integrative brain function.

Basar-Eroglu C, Basar E, Demiralp T, et al. P300-response: possible psychophysiological correlates in delta and theta frequency channels. A review. Int J Psychophysiol. 1992; 13:161–179. [PubMed: 1399755]

Bauer LO. Predicting relapse to alcohol and drug abuse via quantitative electroencephalography. Neuropsychopharmacology. 2001; 25:332–340. [PubMed: 11522462]

Bauer LO, Hesselbrock VM. EEG, autonomic and subjective correlates of the risk for alcoholism. J Stud Alcohol. 1993; 54:577–589. [PubMed: 8412148]

Begleiter, H.; Platz, A. The effects of alcohol on the central nervous system in humans. In: KISSIN, B.; BEGLEITER, H., editors. The Biology of Alcoholism, Vol. 2, Physiology and Behavior. New York: Plenum; 1972.

Begleiter H, Porjesz B. What is inherited in the predisposition toward alcoholism? A proposed model. Alcohol Clin Exp Res. 1999; 23:1125–1135. [PubMed: 10443977]

Begleiter H, Porjesz B, Bihari B, et al. Event-related brain potentials in boys at risk for alcoholism. Science. 1984; 225:1493–1496. [PubMed: 6474187]

Benegal V, Jain S, Subbukrishna DK, et al. P300 amplitudes vary inversely with continuum of risk in first degree male relatives of alcoholics. Psychiatr Genet. 1995; 5:149–156. [PubMed: 8750356]

Bentin S. Electrophysiological studies of visual word perception, lexical organization, and semantic processing: a tutorial review. Lang Speech. 1989; 32:205–220. [PubMed: 2701178]

Berman SM, Whipple SC, Fitch RJ, et al. P3 in young boys as a predictor of adolescent substance use. Alcohol. 1993; 10:69–76. [PubMed: 8447968]

Birbaumer N, Elbert T, Canavan AG, et al. Slow potentials of the cerebral cortex and behavior. Physiol Rev. 1990; 70:1–41. [PubMed: 2404287]

Boha R, Molnar M, Gaal ZA, et al. The acute effect of low-dose alcohol on working memory during mental arithmetic: I. Behavioral measures and EEG theta band spectral characteristics. Int J Psychophysiol. 2009; 73:133–137. [PubMed: 19414050]

Bohman M, Cloninger R, Sigvardsson S, et al. The genetics of alcoholisms and related disorders. J Psychiatr Res. 1987; 21:447–452. [PubMed: 3326937]

Buzsaki G. The hippocampo-neocortical dialogue. Cereb Cortex. 1996; 6:81–92. [PubMed: 8670641]

Buzsaki G, Draguhn A. Neuronal oscillations in cortical networks. Science. 2004; 304:1926–1929. [PubMed: 15218136]

Cadaveira F, Grau C, Roso M, et al. Multimodality exploration of event-related potentials in chronic alcoholics. Alcohol Clin Exp Res. 1991; 15:607–611. [PubMed: 1928634]

Cadoret RJ, Cain CA, Grove WM. Development of alcoholism in adoptees raised apart from alcoholic biologic relatives. Arch Gen Psychiatry. 1980; 37:561–563. [PubMed: 7377912]

Campbell KB, Lowick BM. Ethanol and event-related potentials: the influence of distractor stimuli. Alcohol. 1987; 4:257–263. [PubMed: 3620094]

Ceballos NA, Nixon SJ, Phillips JA, et al. Semantic processing in alcoholics with and without antisocial symptomatology. J Stud Alcohol. 2003; 64:286–291. [PubMed: 12713204]

Ceballos NA, Houston RJ, Smith ND, et al. N400 as an index of semantic expectancies: differential effects of alcohol and cocaine dependence. Prog Neuropsychopharmacol Biol Psychiatry. 2005; 29:936–943. [PubMed: 15967560]

Celesia GG, Brigell M. Event-related potentials. Curr Opin Neurol Neurosurg. 1992; 5:733–739. [PubMed: 1392146]

Chen AC, Porjesz B, Rangaswamy M, et al. Reduced frontal lobe activity in subjects with high impulsivity and alcoholism. Alcohol Clin Exp Res. 2007; 31:156–165. [PubMed: 17207114]

Chen ACH, Tang Y, Rangaswamy M, et al. Association of single nucleotide polymorphisms in a glutamate receptor gene (GRM8) with theta power of event-related oscillations and alcohol dependence. Am J Med Genet Part B: Neuropsychiatric Genet. 2008a; 150B:359–368.

Chen CC, Hsieh JC, Wu YZ, et al. Mutual-information-based approach for neural connectivity during self-paced finger lifting task. Hum Brain Map. 2008b; 29:265–280.

Chorlian DB, Tang Y, Rangaswamy M, et al. Heritability of EEG coherence in a large sib-pair population. Biol Psychol. 2007; 75:260–266. [PubMed: 17498861]

Chorlian DB, Rangaswamy M, Porjesz B. EEG coherence: topography and frequency structure. Exp Brain Res. 2009; 198:59–83. [PubMed: 19626316]

Cohen HL, Porjesz B, Begleiter H. EEG characteristics in males at risk for alcoholism. Alcohol Clin Exp Res. 1991; 15:858–861. [PubMed: 1755520]

Cohen HL, Porjesz B, Begleiter H. The effects of ethanol on EEG activity in males at risk for alcoholism. Electroencephalogr Clin Neurophysiol. 1993a; 86:368–376. [PubMed: 7686471]

Cohen HL, Porjesz B, Begleiter H. Ethanol-induced alterations in electroencephalographic activity in adult males. Neuropsychopharmacology. 1993b; 8:365–370. [PubMed: 8512622]

Cohen HL, Wang W, Porjesz B, et al. Auditory P300 in young alcoholics: regional response characteristics. Alcohol Clin Exp Res. 1995; 19:469–475. [PubMed: 7625584]

Cohen HL, Projesz B, Begleiter H. Temporal recovery of auditory evoked potentials in individuals at risk for alcoholism. Alcohol. 1996; 13:333–339. [PubMed: 8836320]

Cohen HL, Porjesz B, Begleiter H, et al. Neuroelectric correlates of response production and inhibition in individuals at risk to develop alcoholism. Biol Psychiatry. 1997a; 42:57–67. [PubMed: 9193742]

Cohen HL, Porjesz B, Begleiter H, et al. Neurophysiological correlates of response production and inhibition in alcoholics. Alcohol Clin Exp Res. 1997b; 21:1398–1406. [PubMed: 9394110]

Cohen HL, Porjesz B, Stimus AT, et al. Effects of ethanol on temporal recovery of auditory-evoked potentials in individuals at risk for alcoholism. Alcohol Clin Exp Res. 1998; 22:945–953. [PubMed: 9660327]

Colrain IM, Taylor J, Mclean S, et al. Dose dependent effects of alcohol on visual evoked potentials. Psychopharmacology (Berl). 1993; 112:383–388. [PubMed: 7871046]

Colrain IM, Sullivan EV, Ford JM, et al. Frontally mediated inhibitory processing and white matter microstructure: age and alcoholism effects. Psychopharmacology (Berl). 2011; 213:669–679. [PubMed: 21161189]

Comings DE, Wu S, Rostamkhani M, et al. Association of the muscarinic cholinergic 2 receptor (CHRM2) gene with major depression in women. Am J Med Genet. 2002; 114:527–529. [PubMed: 12116189]

Conte A, Attilia ML, Gilio F, et al. Acute and chronic effects of ethanol on cortical excitability. Clin Neurophysiol. 2008; 119:667–674. [PubMed: 18083628]

Corbetta M, Kincade JM, Ollinger JM, et al. Voluntary orienting is dissociated from target detection in human posterior parietal cortex. Nat Neurosci. 2000; 3:292–297. [PubMed: 10700263]

Costa L, Bauer L. Quantitative electroencephalographic differences associated with alcohol, cocaine, heroin and dual-substance dependence. Drug Alcohol Depend. 1997; 46:87–93. [PubMed: 9246556]

Courchesne E, Hillyard SA, Galambos R. Stimulus novelty, task relevance and the visual evoked potential in man. Electroencephalogr Clin Neurophysiol. 1975; 39:131–143. [PubMed: 50210]

Courtney KE, Polich J. Binge drinking in young adults: Data, definitions, and determinants. Psychol Bull. 2009; 135:142–156. [PubMed: 19210057]

Courtney KE, Polich J. Binge drinking effects on EEG in young adult humans. Int J Environ Res Public Health. 2010; 7:2325–2336. [PubMed: 20623027]

Coutin-Churchman P, Moreno R. Intracranial current density (LORETA) differences in QEEG frequency bands between depressed and non-depressed alcoholic patients. Clin Neurophysiol. 2008; 119:948–958. [PubMed: 18289936]

Covault J, Gelernter J, Hesselbrock V, et al. Allelic and haplotypic association of GABRA2 with alcohol dependence. Am J Med Genet B Neuropsychiatr Genet. 2004; 129:104–109. [PubMed: 15274050]

Crego A, Holguin SR, Parada M, et al. Binge drinking affects attentional and visual working memory processing in young university students. Alcohol Clin Exp Res. 2009; 33:1870–1879. [PubMed: 19673739]

Crego A, Rodriguez-Holguin S, Parada M, et al. Reduced anterior prefrontal cortex activation in young binge drinkers during a visual working memory task. Drug Alcohol Depend. 2010; 109:45–56. [PubMed: 20079980]

Crego A, Cadaveira F, Parada M, et al. Increased amplitude of P3 event-related potential in young binge drinkers. Alcohol. 2012; 46:415–425. [PubMed: 22459872]

Crews FT, Braun CJ, Hoplight B, et al. Binge ethanol consumption causes differential brain damage in young adolescent rats compared with adult rats. Alcohol Clin Exp Res. 2000; 24:1712–1723. [PubMed: 11104119]

Crews FT, Mdzinarishvili A, Kim D, et al. Neurogenesis in adolescent brain is potently inhibited by ethanol. Neuroscience. 2006; 137:437–445. [PubMed: 16289890]

Cristini P, Fournier C, Timsit-Berthier M, et al. ERPs (N200, P300 and CNV) in alcoholics: relapse risk assessment. Neurophysiol Clin. 2003; 33:103–119. [PubMed: 12909389]

Cuzen NL, Andrew C, Thomas KG, et al. Absence of p300 reduction in South African treatment-naive adolescents with alcohol dependence. Alcohol Clin Exp Res. 2013; 37:40–48. [PubMed: 22676302]

De Bruin EA, Bijl S, Stam CJ, et al. Abnormal EEG synchronisation in heavily drinking students. Clin Neurophysiol. 2004; 115:2048–2055. [PubMed: 15294207]

De Bruin EA, Stam CJ, Bijl S, et al. Moderate-to-heavy alcohol intake is associated with differences in synchronization of brain activity during rest and mental rehearsal. Int J Psychophysiol. 2006; 60:304–314. [PubMed: 16150505]

Desmedt, JE. P300 in serial tasks: An essential post–decision closure mechanism. In: Kornhuber, HH.; Deecke, L., editors. Motivation, Motor and Sensory Processes of the Brain. Amsterdam: Elsevier; 1980.

Dick DM, Bierut L, Hinrichs A, et al. The role of GABRA2 in risk for conduct disorder and alcohol and drug dependence across developmental stages. Behav Genet. 2006; 36:577–590. [PubMed: 16557364]

Dick DM, Agrawal A, Wang JC, et al. Alcohol dependence with comorbid drug dependence: genetic and phenotypic associations suggest a more severe form of the disorder with stronger genetic contribution to risk. Addiction. 2007; 102:1131–1139. [PubMed: 17567401]

Dierks T, Frolich L, Ihl R, et al. Event-related potentials and psychopharmacology. Cholinergic modulation of P300. Pharmacopsychiatry. 1994; 27:72–74. [PubMed: 7913237]

Easdon C, Izenberg A, Armilio ML, et al. Alcohol consumption impairs stimulus- and error-related processing during a Go/No-Go Task. Brain Res Cogn Brain Res. 2005; 25:873–883. [PubMed: 16256319]

Edenberg HJ, Dick DM, Xuei X, et al. Variations in GABRA2, encoding the alpha 2 subunit of the GABA(A) receptor, are associated with alcohol dependence and with brain oscillations. Am J Hum Genet. 2004; 74:705–714. [PubMed: 15024690]

Ehlers CL, Phillips E. EEG low-voltage alpha and alpha power in African American young adults: relation to family history of alcoholism. Alcohol Clin Exp Res. 2003; 27:765–772. [PubMed: 12766620]

Ehlers CL, Schuckit MA. EEG response to ethanol in sons of alcoholics. Psychopharmacol Bull. 1988; 24:434–437. [PubMed: 3153504]

Ehlers CL, Schuckit MA. EEG fast frequency activity in the sons of alcoholics. Biol Psychiatry. 1990; 27:631–641. [PubMed: 2322623]

Ehlers CL, Schuckit MA. Evaluation of EEG alpha activity in sons of alcoholics. Neuropsychopharmacology. 1991; 4:199–205. [PubMed: 2064719]

Ehlers CL, Wall TL, Schuckit MA. EEG spectral characteristics following ethanol administration in young men. Electroencephalogr Clin Neurophysiol. 1989; 73:179–187. [PubMed: 2475322]

Ehlers CL, Phillips E, Parry BL. Electrophysiological findings during the menstrual cycle in women with and without late luteal phase dysphoric disorder: relationship to risk for alcoholism? Biol Psychiatry. 1996; 39:720–732. [PubMed: 8731460]

Ehlers CL, Garcia-Andrade C, Wall TL, et al. Determinants of P3 amplitude and response to alcohol in Native American Mission Indians. Neuropsychopharmacology. 1998a; 18:282–292. [PubMed: 9509496]

Ehlers CL, Havstad J, Prichard D, et al. Low doses of ethanol reduce evidence for nonlinear structure in brain activity. J Neurosci. 1998b; 18:7474–7486. [PubMed: 9736666]

Ehlers CL, Wall TL, Garcia-Andrade C, et al. Auditory P3 findings in mission Indian youth. J Stud Alcohol. 2001; 62:562–570. [PubMed: 11702795]

Ehlers CL, Phillips E, Sweeny A, et al. Event-related potential responses to alcohol-related stimuli in African-American young adults: relation to family history of alcoholism and drug usage. Alcohol Alcohol. 2003; 38:332–338. [PubMed: 12814900]

Ehlers CL, Phillips E, Wall TL, et al. EEG alpha and level of response to alcohol in Hispanic- and non-Hispanic-American young adults with a family history of alcoholism. J Stud Alcohol. 2004; 65:301–308. [PubMed: 15222586]

Ehlers CL, Phillips E, Finnerman G, et al. P3 components and adolescent binge drinking in Southwest California Indians. Neurotoxicol Teratol. 2007; 29:153–163. [PubMed: 17196788]

Ehlers CL, Wills DN, Havstad J. Ethanol reduces the phase locking of neural activity in human and rodent brain. Brain Res. 2012; 1450:67–79. [PubMed: 22410292]

Eimer M. Effects of attention and stimulus probability on ERPs in a Go/Nogo task. Biol Psychol. 1993; 35:123–138. [PubMed: 8507742]

Elmasian R, Neville H, Woods D, et al. Event-related brain potentials are different in individuals at high and low risk for developing alcoholism. Proc Natl Acad Sci U S A. 1982; 79:7900–7903. [PubMed: 6961459]

Enoch MA, Rohrbaugh JW, Davis EZ, et al. Relationship of genetically transmitted alpha EEG traits to anxiety disorders and alcoholism. Am J Med Genet. 1995; 60:400–408. [PubMed: 8546153]

Enoch MA, White KV, Harris CR, et al. Association of low-voltage alpha EEG with a subtype of alcohol use disorders. Alcohol Clin Exp Res. 1999; 23:1312–1319. [PubMed: 10470973]

Enoch MA, Xu K, Ferro E, et al. Genetic origins of anxiety in women: a role for a functional catechol-*O*-methyltransferase polymorphism. Psychiatr Genet. 2003; 13:33–41. [PubMed: 12605099]

Euser AS, Van Meel CS, Snelleman M, et al. Acute effects of alcohol on feedback processing and outcome evaluation during risky decision-making: an ERP study. Psychopharmacology (Berl). 2011; 217:111–125. [PubMed: 21475971]

Falkenstein M, Hoormann J, Hohnsbein J. ERP components in Go/Nogo tasks and their relation to inhibition. Acta Psychol (Amst). 1999; 101:267–291. [PubMed: 10344188]

Fallgatter AJ, Wiesbeck GA, Weijers HG, et al. Event-related correlates of response suppression as indicators of novelty seeking in alcoholics. Alcohol Alcohol. 1998; 33:475–481. [PubMed: 9811199]

Fein G, Chang M. Visual P300s in long-term abstinent chronic alcoholics. Alcohol Clin Exp Res. 2006; 30:2000–2007. [PubMed: 17117965]

Fein G, Chang M. Smaller feedback ERN amplitudes during the BART are associated with a greater family history density of alcohol problems in treatment-naive alcoholics. Drug Alcohol Depend. 2008; 92:141–148. [PubMed: 17869027]

Fein G, Whitlow B, Finn P. Mismatch negativity: no difference between controls and abstinent alcoholics. Alcohol Clin Exp Res. 2004; 28:137–142. [PubMed: 14745312]

Fell J, Fernandez G, Laver P, et al. Is synchronized neuronal gamma activity relevant for selective attention? Brain Res Brain Res Rev. 2003; 42:265–272. [PubMed: 12791444]

Fellous JM, Sejnowski TJ. Cholinergic induction of oscillations in the hippocampal slice in the slow (0.5–2 Hz), theta (5–12 Hz), and gamma (35–70 Hz) bands. Hippocampus. 2000; 10:187–197. [PubMed: 10791841]

Filipovic SR, Jahanshahi M, Rothwell JC. Cortical potentials related to decision-making: comparison of two types of go/no-go decision. Neuroreport. 1999; 10:3583–3587. [PubMed: 10619648]

Fillmore MT, Vogel-Sprott M. An alcohol model of impaired inhibitory control and its treatment in humans. Exp Clin Psychopharmacol. 1999; 7:49–55. [PubMed: 10036609]

Fillmore MT, Vogel-Sprott M. Response inhibition under alcohol: effects of cognitive and motivational conflict. J Stud Alcohol. 2000; 61:239–246. [PubMed: 10757134]

Finn PR, Justus A. Reduced EEG alpha power in the male and female offspring of alcoholics. Alcohol Clin Exp Res. 1999; 23:256–262. [PubMed: 10069554]

Folstein JR, Van Petten C. Influence of cognitive control and mismatch on the N2 component of the ERP: a review. Psychophysiology. 2008; 45:152–170. [PubMed: 17850238]

Fries P. A mechanism for cognitive dynamics: neuronal communication through neuronal coherence. Trends Cogn Sci. 2005; 9:474–480. [PubMed: 16150631]

Frodl-Bauch T, Bottlender R, Hegerl U. Neurochemical substrates and neuroanatomical generators of the event-related P300. Neuropsychobiology. 1999; 40:86–94. [PubMed: 10474063]

Fuentemilla L, Marco-Pallares J, Gual A, et al. Impaired theta phase-resetting underlying auditory N1 suppression in chronic alcoholism. Neuroreport. 2009; 20:337–342. [PubMed: 19188856]

Gabrielli WF Jr, Mednick SA, Volavka J, et al. Electroencephalograms in children of alcoholic fathers. Psychophysiology. 1982; 19:404–407. [PubMed: 7122778]

Gehring WJ, Willoughby AR. The medial frontal cortex and the rapid processing of monetary gains and losses. Science. 2002; 295:2279–2282. [PubMed: 11910116]

Gevins A, Chan CS, Sam-Vargas L. Towards measuring brain function on groups of people in the real world. PLoS One. 2012; 7:e44676. [PubMed: 22957099]

Giesbrecht B, Woldorff MG, Song AW, et al. Neural mechanisms of top-down control during spatial and feature attention. Neuroimage. 2003; 19:496–512. [PubMed: 12880783]

Gilmore CS, Fein G. Theta event-related synchronization is a biomarker for a morbid effect of alcoholism on the brain that may partially resolve with extended abstinence. Brain Behav. 2012; 2:796–805. [PubMed: 23170242]

Glenn SW, Sinha R, Parsons OA. Electrophysiological indices predict resumption of drinking in sober alcoholics. Alcohol. 1993; 10:89–95. [PubMed: 8442897]

Glenn S, Parsons OA, Sinha R. Assessment of recovery of electrophysiological and neuropsychological functions in chronic alcoholics. Biol Psychiatry. 1994; 36:443–452. [PubMed: 7811840]

Goodwin DW, Schulsinger F, Hermansen L, et al. Alcohol problems in adoptees raised apart from alcoholic biological parents. Arch Gen Psychiatry. 1973; 28:238–243. [PubMed: 4684290]

Gorenstein EE, Newman JP. Disinhibitory psychopathology: a new perspective and a model for research. Psychol Rev. 1980; 87:301–315. [PubMed: 7384345]

Grau C, Polo MD, Yago E, et al. Auditory sensory memory as indicated by mismatch negativity in chronic alcoholism. Clin Neurophysiol. 2001; 112:728–731. [PubMed: 11336886]

Haas LF. Hans Berger (1873–1941), Richard Caton (1842–1926), and electroencephalography. J Neurol Neurosurg Psychiatry. 2003; 74:9. [PubMed: 12486257]

Hada M, Porjesz B, Begleiter H, et al. Auditory P3a assessment of male alcoholics. Biol Psychiatry. 2000; 48:276–286. [PubMed: 10960158]

Hada M, Porjesz B, Chorlian DB, et al. Auditory P3a deficits in male subjects at high risk for alcoholism. Biol Psychiatry. 2001; 49:726–738. [PubMed: 11313040]

Hajcak G, Moser JS, Holroyd CB, et al. The feedback-related negativity reflects the binary evaluation of good versus bad outcomes. Biol Psychol. 2006; 71:148–154. [PubMed: 16005561]

Halgren E, Squires NK, Wilson CL, et al. Endogenous potentials generated in the human hippocampal formation and amygdala by infrequent events. Science. 1980; 210:803–805. [PubMed: 7434000]

Hammond EJ, Meador KJ, Aung-Din R, et al. Cholinergic modulation of human P3 event-related potentials. Neurology. 1987; 37:346–350. [PubMed: 3808322]

Harper C. The neuropathology of alcohol-related brain damage. Alcohol Alcohol. 2009; 44:136–140. [PubMed: 19147798]

Heath AC, Bucholz KK, Madden PA, et al. Genetic and environmental contributions to alcohol dependence risk in a national twin sample: consistency of findings in women and men. Psychol Med. 1997; 27:1381–1396. [PubMed: 9403910]

Hermens DF, Lagopoulos J, Tobias-Webb J, et al. Pathways to alcohol-induced brain impairment in young people: A review. Cortex. 2013; 49:3–17. [PubMed: 22789780]

Hicks BM, Krueger RF, Iacono WG, et al. Family transmission and heritability of externalizing disorders: a twin-family study. Arch Gen Psychiatry. 2004; 61:922–928. [PubMed: 15351771]

Hill SY, Steinhauer SR. Event-related potentials in women at risk for alcoholism. Alcohol. 1993; 10:349–354. [PubMed: 8216879]

Hill SY, Muka D, Steinhauer S, et al. P300 amplitude decrements in children from families of alcoholic female probands. Biol Psychiatry. 1995a; 38:622–632. [PubMed: 8573664]

Hill SY, Steinhauer S, Lowers L, et al. Eight-year longitudinal follow-up of P300 and clinical outcome in children from high-risk for alcoholism families. Biol Psychiatry. 1995b; 37:823–827. [PubMed: 7647169]

Hillyard SA, Hink RF, Schwent VL, et al. Electrical signs of selective attention in the human brain. Science. 1973; 182:177–180. [PubMed: 4730062]

Holmes AJ, Pizzagalli DA. Spatiotemporal dynamics of error processing dysfunctions in major depressive disorder. Arch Gen Psychiatry. 2008; 65:179–188. [PubMed: 18250256]

Houston RJ, Bauer LO, Hesselbrock VM. Depression and familial risk for substance dependence: a P300 study of young women. Psychiatry Res. 2003; 124:49–62. [PubMed: 14511795]

Hummel F, Gerloff C. Larger interregional synchrony is associated with greater behavioral success in a complex sensory integration task in humans. Cereb Cortex. 2005; 15:670–678. [PubMed: 15342429]

Iacono WG, Carlson SR, Malone SM, et al. P3 event-related potential amplitude and the risk for disinhibitory disorders in adolescent boys. Arch Gen Psychiatry. 2002; 59:750–757. [PubMed: 12150652]

Iacono WG, Malone SM, Mcgue M. Substance use disorders, externalizing psychopathology, and P300 event-related potential amplitude. Intl J Psychophysiol. 2003; 48:147–178.

Itoh T, Sumiyoshi T, Higuchi Y, et al. LORETA analysis of three-dimensional distribution of delta band activity in schizophrenia: relation to negative symptoms. Neurosci Res. 2011; 70:442–448. [PubMed: 21641943]

Jaaskelainen IP, Pekkonen E, Alho K, et al. Dose-related effect of alcohol on mismatch negativity and reaction time performance. Alcohol. 1995; 12:491–495. [PubMed: 8590608]

Jaaskelainen IP, Naatanen R, Sillanaukee P. Effect of acute ethanol on auditory and visual event-related potentials: a review and reinterpretation. Biol Psychiatry. 1996; 40:284–291. [PubMed: 8871775]

Jaaskelainen IP, Schroger E, Naatanen R. Electrophysiological indices of acute effects of ethanol on involuntary attention shifting. Psychopharmacology (Berl). 1999; 141:16–21. [PubMed: 9952060]

Jaaskelainen IP, Hirvonen J, Saher M, et al. Dose-dependent suppression by ethanol of transient auditory 40-Hz response. Psychopharmacology (Berl). 2000; 148:132–135. [PubMed: 10663427]

Jodo E, Kayama Y. Relation of a negative ERP component to response inhibition in a Go/No-go task. Electroencephalogr Clin Neurophysiol. 1992; 82:477–482. [PubMed: 1375556]

Jones KA, Porjesz B, Almasy L, et al. Linkage and linkage disequilibrium of evoked EEG oscillations with CHRM2 receptor gene polymorphisms: implications for human brain dynamics and cognition. Int J Psychophysiol. 2004; 53:75–90. [PubMed: 15210286]

Jones KA, Porjesz B, Almasy L, et al. A cholinergic receptor gene (CHRM2) affects event-related oscillations. Behav Genet. 2006a; 36:627–639. [PubMed: 16823639]

Jones KA, Porjesz B, Chorlian D, et al. *S*-transform time-frequency analysis of P300 reveals deficits in individuals diagnosed with alcoholism. Clin Neurophysiol. 2006b; 117:2128–2143. [PubMed: 16926113]

Kahkonen S, Kesaniemi M, Nikouline VV, et al. Ethanol modulates cortical activity: direct evidence with combined TMS and EEG. Neuroimage. 2001; 14:322–328. [PubMed: 11467906]

Kamarajan C, Porjesz B, Jones KA, et al. The role of brain oscillations as functional correlates of cognitive systems: a study of frontal inhibitory control in alcoholism. Intl J Psychophysiol. 2004; 51:155–180.

Kamarajan C, Porjesz B, Jones KA, et al. Alcoholism is a disinhibitory disorder: neurophysiological evidence from a Go/No-Go task. Biol Psychol. 2005a; 69:353–373. [PubMed: 15925035]

Kamarajan C, Porjesz B, Jones KA, et al. Spatial-anatomical mapping of NoGo-P3 in the offspring of alcoholics: evidence of cognitive and neural disinhibition as a risk for alcoholism. Clin Neurophysiol. 2005b; 116:1049–1061. [PubMed: 15826845]

Kamarajan C, Porjesz B, Jones K, et al. Event-related oscillations in offspring of alcoholics: neurocognitive disinhibition as a risk for alcoholism. Biol Psychiatry. 2006; 59:625–634. [PubMed: 16213472]

Kamarajan C, Porjesz B, Rangaswamy M, et al. Brain signatures of monetary loss and gain: outcome-related potentials in a single outcome gambling task. Behav Brain Res. 2009; 197:62–76. [PubMed: 18775749]

Kamarajan C, Rangaswamy M, Tang Y, et al. Dysfunctional reward processing in male alcoholics: an ERP study during a gambling task. J Psychiatric Res. 2010; 44:576–590.

Kamarajan C, Rangaswamy M, Manz N, et al. Topography, power, and current source density of theta oscillations during reward processing as markers for alcohol dependence. Hum Brain Mapp. 2012; 33:1019–1039. [PubMed: 21520344]

Kang SJ, Rangaswamy M, Manz N, et al. Family-based genome-wide association study of frontal theta oscillations identifies potassium channel gene KCNJ6. Genes Brain Behav. 2012; 11:712–719. [PubMed: 22554406]

Kaplan RF, Glueck BC, Hesselbrock MN, et al. Power and coherence analysis of the EEG in hospitalized alcoholics and nonalcoholic controls. J Stud Alcohol. 1985; 46:122–127. [PubMed: 3990297]

Kaplan RF, Hesselbrock VM, O'connor S, et al. Behavioral and EEG responses to alcohol in nonalcoholic men with a family history of alcoholism. Prog Neuropsychopharmacol Biol Psychiatry. 1988; 12:873–885. [PubMed: 3241870]

Karakas S, Erzengin OU, Basar E. The genesis of human event-related responses explained through the theory of oscillatory neural assemblies. Neurosci Lett. 2000a; 285:45–48. [PubMed: 10788704]

Karakas S, Erzengin OU, Basar E. A new strategy involving multiple cognitive paradigms demonstrates that ERP components are determined by the superposition of oscillatory responses. Clin Neurophysiol. 2000b; 111:1719–1732. [PubMed: 11018485]

Kathmann N, Wagner M, Rendtorff N, et al. Delayed peak latency of the mismatch negativity in schizophrenics and alcoholics. Biol Psychiatry. 1995; 37:754–757. [PubMed: 7640331]

Kendler KS, Prescott CA, Myers J, et al. The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. Arch Gen Psychiatry. 2003; 60:929–937. [PubMed: 12963675]

Kenemans JL, Hebly W, Van Den Heuvel EH, et al. Moderate alcohol disrupts a mechanism for detection of rare events in human visual cortex. J Psychopharmacol. 2010; 24:839–845. [PubMed: 19028837]

Kiehl KA, Liddle PF. An event-related functional magnetic resonance imaging study of an auditory oddball task in schizophrenia. Schizophr Res. 2001; 48:159–171. [PubMed: 11295369]

Klimesch W, Doppelmayr M, Wimmer H, et al. Theta band power changes in normal and dyslexic children. Clin Neurophysiol. 2001; 112:1174–1185. [PubMed: 11516729]

Klimesch W, Sauseng P, Hanslmayr S, et al. Event-related phase reorganization may explain evoked neural dynamics. Neurosci Biobehav Rev. 2007; 31:1003–1016. [PubMed: 17532471]

Knight RT, Scabini D. Anatomic bases of event-related potentials and their relationship to novelty detection in humans. J Clin Neurophysiol. 1998; 15:3–13. [PubMed: 9502509]

Koskinen SM, Ahveninen J, Kujala T, et al. A longitudinal twin study of effects of adolescent alcohol abuse on the neurophysiology of attention and orienting. Alcohol Clin Exp Res. 2011; 35:1339–1350. [PubMed: 21463336]

Kovacevic S, Azma S, Irimia A, et al. Theta oscillations are sensitive to both early and late conflict processing stages: effects of alcohol intoxication. PLoS One. 2012; 7:e43957. [PubMed: 22952823]

Krause CM, Aromaki A, Sillanmaki L, et al. Alcohol-induced alterations in ERD/ERS during an auditory memory task. Alcohol. 2002; 26:145–153. [PubMed: 12057775]

Krieger S, Timmer J, Lis S, et al. Some considerations on estimating event-related brain signals. J Neural Transm. 1995; 99:103–129.

Krueger RF, Hicks BM, Patrick CJ, et al. Etiologic connections among substance dependence, antisocial behavior, and personality: modeling the externalizing spectrum. J Abnorm Psychol. 2002; 111:411–424. [PubMed: 12150417]

Kutas M, Federmeier KD. Electrophysiology reveals semantic memory use in language comprehension. Trends Cogn Sci. 2000; 4:463–470. [PubMed: 11115760]

Kutas M, Federmeier KD. Thirty years and counting: finding meaning in the N400 component of the event-related brain potential (ERP). Annu Rev Psychol. 2011; 62:621–647. [PubMed: 20809790]

Kutas M, Hillyard SA. Reading senseless sentences: brain potentials reflect semantic incongruity. Science. 1980; 207:203–205. [PubMed: 7350657]

Laukka SJ, Jarvilehto T, Alexandrov Yu I, et al. Frontal midline theta related to learning in a simulated driving task. Biol Psychol. 1995; 40:313–320. [PubMed: 7669839]

Lingford-Hughes AR, Acton PD, Gacinovic S, et al. Reduced levels of GABA-benzodiazepine receptor in alcohol dependency in the absence of grey matter atrophy. Br J Psychiatry. 1998; 173:116–122. [PubMed: 9850223]

Llinas RR, Ribary U, Jeanmonod D, et al. Thalamocortical dysrhythmia: A neurological and neuropsychiatric syndrome characterized by magnetoencephalography. Proc Natl Acad Sci U S A. 1999; 96:15222–15227. [PubMed: 10611366]

Logan GD, Cowan WB. On the ability to inhibit thought and action: A theory of an act of control. Psychol Rev. 1984; 91:295–327.

Lopez-Caneda E, Cadaveira F, Crego A, et al. Hyperactivation of right inferior frontal cortex in young binge drinkers during response inhibition: a follow-up study. Addiction. 2012; 107:1796–1808. [PubMed: 22487028]

Luck, SJ. An introduction to the event-related potential technique. Cambridge, MA: MIT Press; 2005.

Lukas SE, Mendelson JH. Electroencephalographic activity and plasma ACTH during ethanol-induced euphoria. Biol Psychiatry. 1988; 23:141–148. [PubMed: 2825820]

Lukas SE, Mendelson JH, Woods BT, et al. Topographic distribution of EEG alpha activity during ethanol-induced intoxication in women. J Stud Alcohol. 1989; 50:176–185. [PubMed: 2927132]

Lukas SE, Mendelson JH, Kouri E, et al. Ethanol-induced alterations in EEG alpha activity and apparent source of the auditory P300 evoked response potential. Alcohol. 1990; 7:471–477. [PubMed: 2222851]

Luo X, Kranzler HR, Zuo L, et al. CHRM2 gene predisposes to alcohol dependence, drug dependence and affective disorders: results from an extended case-control structured association study. Hum Mol Genet. 2005; 14:2421–2434. [PubMed: 16000316]

Luscher C, Slesinger PA. Emerging roles for G protein-gated inwardly rectifying potassium (GIRK) channels in health and disease. Nat Rev Neurosci. 2010; 11:301–315. [PubMed: 20389305]

Marco-Pallares J, Ruffini G, Polo MD, et al. Mismatch negativity impairment associated with alcohol consumption in chronic alcoholics: a scalp current density study. Int J Psychophysiol. 2007; 65:51–57. [PubMed: 17449124]

Marinkovic K, Halgren E, Klopp J, et al. Alcohol effects on movement-related potentials: a measure of impulsivity? J Stud Alcohol. 2000; 61:24–31. [PubMed: 10627093]

Marinkovic K, Halgren E, Maltzman I. Arousal-related P3a to novel auditory stimuli is abolished by a moderately low alcohol dose. Alcohol Alcohol. 2001; 36:529–539. [PubMed: 11704618]

Marinkovic K, Halgren E, Maltzman I. Effects of alcohol on verbal processing: an event-related potential study. Alcohol Clin Exp Res. 2004; 28:415–423. [PubMed: 15084899]

Marinkovic K, Rosen BQ, Cox B, et al. Event-related theta power during lexical-semantic retrieval and decision conflict is modulated by alcohol intoxication: anatomically constrained MEG. Front Psychol. 2012; 3:121. [PubMed: 22536192]

Masaki H, Takeuchi S, Gehring WJ, et al. Affective-motivational influences on feedback-related ERPs in a gambling task. Brain Res. 2006; 1105:110–121. [PubMed: 16483556]

Maurage P, Pesenti M, Philippot P, et al. Latent deleterious effects of binge drinking over a short period of time revealed only by electrophysiological measures. J Psychiatry Neurosci. 2009; 34:111–118. [PubMed: 19270761]

Maurage P, Joassin F, Speth A, et al. Cerebral effects of binge drinking: respective influences of global alcohol intake and consumption pattern. Clin Neurophysiol. 2012; 123:892–901. [PubMed: 22055841]

McCarthy G, Nobre AC. Modulation of semantic processing by spatial selective attention. Electroencephalogr Clin Neurophysiol. 1993; 88:210–219. [PubMed: 7684969]

Menon V, Ford JM, Lim KO, et al. Combined event-related fMRI and EEG evidence for temporal-parietal cortex activation during target detection. Neuroreport. 1997; 8:3029–3037. [PubMed: 9331910]

Michael A, Mirza KA, Mukundan CR, et al. Interhemispheric electroencephalographic coherence as a biological marker in alcoholism. Acta Psychiatr Scand. 1993; 87:213–217. [PubMed: 8465670]

Mitrofanis J, Guillery RW. New views of the thalamic reticular nucleus in the adult and the developing brain. Trends Neurosci. 1993; 16:240–245. [PubMed: 7688166]

Molnar M, Boha R, Czigler B, et al. The acute effect of low-dose alcohol on working memory during mental arithmetic: II. Changes of nonlinear and linear EEG-complexity in the theta band, heart rate and electrodermal activity. Int J Psychophysiol. 2009; 73:138–142. [PubMed: 19414053]

Moselhy HF, Georgiou G, Kahn A. Frontal lobe changes in alcoholism: a review of the literature. Alcohol Alcohol. 2001; 36:357–368. [PubMed: 11524299]

Muralidharan K, Venkatasubramanian G, Pal PK, et al. Abnormalities in cortical and transcallosal inhibitory mechanisms in subjects at high risk for alcohol dependence: a TMS study. Addict Biol. 2008; 13:373–379. [PubMed: 18422835]

Näätänen R. The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. Behav Brain Sci. 1990; 13:201–233.

Näätänen R, Gaillard AW, Mäntysalo S. Early selective-attention effect on evoked potential reinterpreted. Acta Psychol (Amst). 1978; 42:313–329. [PubMed: 685709]

Newlin DB, Thomson JB. Alcohol challenge with sons of alcoholics: a critical review and analysis. Psychol Bull. 1990; 108:383–402. [PubMed: 2270234]

Niedermayer, E.; Lopes Da Silva, FH., editors. Electroencephalography: Basic Principles, Clinical Applications and Related Fields. New York: Williams & Wilkins; 1999.

Nieuwenhuis S, Holroyd CB, Mol N, et al. Reinforcement-related brain potentials from medial frontal cortex: origins and functional significance. Neurosci Biobehav Rev. 2004; 28:441–448. [PubMed: 15289008]

Nixon SJ, Tivis R, Ceballos N, et al. Neurophysiological efficiency in male and female alcoholics. Prog Neuropsychopharmacol Biol Psychiatry. 2002; 26:919–927. [PubMed: 12369267]

Nunez, PL. Neocortical dynamics and Human EEG rhythms. New York: Oxford University Press; 1995.

Oddy BW, Barry RJ. The relationship of N2 and P3 to inhibitory processing of social drinkers in a Go/NoGo task. Int J Psychophysiol. 2009; 72:323–330. [PubMed: 19250950]

O'Donnell BF, Swearer JM, Smith LT, et al. A topographic study of ERPs elicited by visual feature discrimination. Brain Topogr. 1997; 10:133–143. [PubMed: 9455604]

Olbrich HM, Maes H, Gann H, et al. Auditory and visual event-related potentials in alcoholics: abnormalities of components and brain electrical field. Eur Arch Psychiatry Clin Neurosci. 2000; 250:215–220. [PubMed: 11097163]

Overbeek TJM, Nieuwenhuis S, Ridderinkhof KR. Dissociable Components of Error Processing. J Psychophysiol. 2005; 19:319–329.

Padilla ML, Colrain IM, Sullivan EV, et al. Electrophysiological evidence of enhanced performance monitoring in recently abstinent alcoholic men. Psychopharmacology (Berl). 2011; 213:81–91. [PubMed: 20941595]

Padmanabhapillai A, Porjesz B, Ranganathan M, et al. Suppression of early evoked gamma band response in male alcoholics during a visual oddball task. Int J Psychophysiol. 2006a; 60:15–26. [PubMed: 16019097]

Padmanabhapillai A, Tang Y, Ranganathan M, et al. Evoked gamma band response in male adolescent subjects at high risk for alcoholism during a visual oddball task. Int J Psychophysiol. 2006b; 62:262–271. [PubMed: 16887227]

Pandey AK, Kamarajan C, Tang Y, et al. Neurocognitive deficits in male alcoholics: An ERP/sLORETA analysis of the N2 component in an equal probability Go/NoGo task. Biol Psychol. 2012; 89:170–182. [PubMed: 22024409]

Pascual-Marqui RD. Standardized low-resolution brain electromagnetic tomography (sLORETA): technical details. Methods Find Exp Clin Pharmacol. 2002; 24 (Suppl D):5–12. [PubMed: 12575463]

Patterson BW, Williams HL, Mclean GA, et al. Alcoholism and family history of alcoholism: effects on visual and auditory event-related potentials. Alcohol. 1987; 4:265–274. [PubMed: 3620095]

Pekkonen E, Ahveninen J, Jaaskelainen IP, et al. Selective acceleration of auditory processing in chronic alcoholics during abstinence. Alcohol Clin Exp Res. 1998; 22:605–609. [PubMed: 9622438]

Perry E, Walker M, Grace J, et al. Acetylcholine in mind: a neurotransmitter correlate of consciousness? Trends Neurosci. 1999; 22:273–280. [PubMed: 10354606]

Petit G, Kornreich C, Maurage P, et al. Early attentional modulation by alcohol-related cues in young binge drinkers: an event-related potentials study. Clin Neurophysiol. 2012; 123:925–936. [PubMed: 22119177]

Pfefferbaum A, Ford JM. ERPs to stimuli requiring response production and inhibition: effects of age, probability and visual noise. Electroencephalogr Clin Neurophysiol. 1988; 71:55–63. [PubMed: 2446846]

Pfefferbaum A, Ford JM, Weller BJ, et al. ERPs to response production and inhibition. Electroencephalogr Clin Neurophysiol. 1985; 60:423–434. [PubMed: 2580694]

Pfefferbaum A, Ford JM, White PM, et al. Event-related potentials in alcoholic men: P3 amplitude reflects family history but not alcohol consumption. Alcohol Clin Exp Res. 1991; 15:839–850. [PubMed: 1755518]

Polich J, Bloom FE. P300 from normals and adult children of alcoholics. Alcohol. 1987; 4:301–305. [PubMed: 3620099]

Polich J, Herbst KL. P300 as a clinical assay: rationale, evaluation, and findings. Int J Psychophysiol. 2000; 38:3–19. [PubMed: 11027791]

Polich J, Pollock VE, Bloom FE. Meta-analysis of P300 amplitude from males at risk for alcoholism. Psychol Bull. 1994; 115:55–73. [PubMed: 8310100]

Pollock VE. Meta-analysis of subjective sensitivity to alcohol in sons of alcoholics. Am J Psychiatry. 1992; 149:1534–1538. [PubMed: 1415821]

Pollock VE, Volavka J, Goodwin DW, et al. The EEG after alcohol administration in men at risk for alcoholism. Arch Gen Psychiatry. 1983; 40:857–861. [PubMed: 6870482]

Pollock VE, Schneider LS, Zemansky MF, et al. Topographic quantitative EEG amplitude in recovered alcoholics. Psychiatry Res. 1992; 45:25–32. [PubMed: 1410076]

Pollock VE, Earleywine M, Gabrielli WF. Personality and EEG beta in older adults with alcoholic relatives. Alcohol Clin Exp Res. 1995; 19:37–43. [PubMed: 7771661]

Polo MD, Escera C, Gual A, et al. Mismatch negativity and auditory sensory memory in chronic alcoholics. Alcohol Clin Exp Res. 1999; 23:1744–1750. [PubMed: 10591590]

Porjesz, B.; Begleiter, H. Brain dysfunction and alcohol. In: KISSIN, B.; BEGLEITER, H., editors. The pathogenesis of alcoholism: biological factors. New York: Plenum Press; 1983.

Porjesz B, Begleiter H. The use of event-related potentials in the study of alcoholism: implications for the study of drugs of abuse. NIDA Res Monogr. 1985; 62:77–99. [PubMed: 3935933]

Porjesz, B.; Begleiter, H. Individuals at risk for alcoholism: Neurophysiologic processes. In: CLONINGER, CR.; BEGLEITER, H., editors. Genetics and biology of alcoholism. New York: Cold Spring Harbor Laboratory Press; 1990.

Porjesz, B.; Begleiter, H. Neurophysiological factors associated with alcoholism. In: NIXON, SJ.; HUNT, WA., editors. Alcohol-induced brain damage. Rockville, MD: NIH Publication; 1993.

Porjesz, B.; Begleiter, H. Effects of alcohol on electrophysiological activity of the brain. In: BEGLEITER, H.; KISSIN, B., editors. Alcohol and Alcoholism: The Pharmacology of Alcohol and Alcohol Dependence. New York: Oxford University Press; 1996.

Porjesz B, Rangaswamy M. Neurophysiological endophenotypes, CNS disinhibition, and risk for alcohol dependence and related disorders. ScientificWorldJournal. 2007; 7:131–141. [PubMed: 17982586]

Porjesz B, Begleiter H, Bihari B, et al. Event-related brain potentials to high incentive stimuli in abstinent alcoholics. Alcohol. 1987a; 4:283–287. [PubMed: 3620097]

Porjesz B, Begleiter H, Bihari B, et al. The N2 component of the event-related brain potential in abstinent alcoholics. Electroencephalogr Clin Neurophysiol. 1987b; 66:121–131. [PubMed: 2431876]

Porjesz B, Begleiter H, Reich T, et al. Amplitude of visual P3 event-related potential as a phenotypic marker for a predisposition to alcoholism: preliminary results from the COGA Project. Collaborative Study on the Genetics of Alcoholism. Alcohol Clin Exp Res. 1998; 22:1317–1323. [PubMed: 9756048]

Porjesz B, Begleiter H, Wang K, et al. Linkage and linkage disequilibrium mapping of ERP and EEG phenotypes. Biol Psychol. 2002a; 61:229–248. [PubMed: 12385677]

Porjesz B, Almasy L, Edenberg HJ, et al. Linkage disequilibrium between the beta frequency of the human EEG and a GABAA receptor gene locus. Proc Natl Acad Sci U S A. 2002b; 99:3729–3733. [PubMed: 11891318]

Porjesz B, Rangaswamy M, Kamarajan C, et al. The utility of neurophysiological markers in the study of alcoholism. Clin Neurophysiol. 2005; 116:993–1018. [PubMed: 15826840]

Potter DD, Pickles CD, Roberts RC, et al. Scopolamine impairs memory performance and reduces frontal but not parietal visual P3 amplitude. Biol Psychol. 2000; 52:37–52. [PubMed: 10686371]

Prabhu VR, Porjesz B, Chorlian DB, et al. Visual p3 in female alcoholics. Alcohol Clin Exp Res. 2001; 25:531–539. [PubMed: 11329493]

Prescott CA. The genetic epidemiology of alcoholism – Sex differences and future directions. Alcohol in Health and Disease. 2001:125–149.

Prescott CA, Aggen SH, Kendler KS. Sex differences in the sources of genetic liability to alcohol abuse and dependence in a population-based sample of U.S. twins. Alcohol Clin Exp Res. 1999; 23:1136–1144. [PubMed: 10443978]

Propping P, Kruger J, Mark N. Genetic disposition to alcoholism. An EEG study in alcoholics and their relatives. Hum Genet. 1981; 59:51–59. [PubMed: 10819022]

Rangaswamy M, Porjesz B. From event-related potential to oscillations: genetic diathesis in brain (dys)function and alcohol dependence. Alcohol Res Health. 2008a; 31:238–242. [PubMed: 23584866]

Rangaswamy M, Porjesz B. Uncovering genes for cognitive (dys)function and predisposition for alcoholism spectrum disorders: a review of human brain oscillations as effective endophenotypes. Brain Res. 2008b; 1235:153–171. [PubMed: 18634760]

Rangaswamy M, Porjesz B, Chorlian DB, et al. Beta power in the EEG of alcoholics. Biol Psychiatry. 2002; 52:831–842. [PubMed: 12372655]

Rangaswamy M, Porjesz B, Chorlian DB, et al. Theta power in the EEG of alcoholics. Alcohol Clin Exp Res. 2003; 27:607–615. [PubMed: 12711923]

Rangaswamy M, Porjesz B, Ardekani BA, et al. A functional MRI study of visual oddball: evidence for frontoparietal dysfunction in subjects at risk for alcoholism. Neuroimage. 2004a; 21:329–339. [PubMed: 14741671]

Rangaswamy M, Porjesz B, Chorlian DB, et al. Resting EEG in offspring of male alcoholics: beta frequencies. Int J Psychophysiol. 2004b; 51:239–251. [PubMed: 14962576]

Rangaswamy M, Jones KA, Porjesz B, et al. Delta and theta oscillations as risk markers in adolescent offspring of alcoholics. Int J Psychophysiol. 2007; 63:3–15. [PubMed: 17129626]

Realmuto G, Begleiter H, Odencrantz J, et al. Event-related potential evidence of dysfunction in automatic processing in abstinent alcoholics. Biol Psychiatry. 1993; 33:594–601. [PubMed: 8329490]

Ridderinkhof KR, De Vlugt Y, Bramlage A, et al. Alcohol consumption impairs detection of performance errors in mediofrontal cortex. Science. 2002; 298:2209–2211. [PubMed: 12424384]

Rodriguez Holguin S, Corral M, Cadaveira F. Mismatch negativity in young children of alcoholics from high-density families. Alcohol Clin Exp Res. 1998; 22:1363–1368. [PubMed: 9756054]

Rodriguez Holguin S, Porjesz B, Chorlian DB, et al. Visual P3a in male subjects at high risk for alcoholism. Biol Psychiatry. 1999; 46:281–291. [PubMed: 10418704]

Rohrbaugh JW, Stapleton JM, Parasuraman R, et al. Dose-related effects of ethanol on visual sustained attention and event-related potentials. Alcohol. 1987; 4:293–300. [PubMed: 3620098]

Roopesh BN, Rangaswamy M, Kamarajan C, et al. Priming deficiency in male subjects at risk for alcoholism: the N4 during a lexical decision task. Alcohol Clin Exp Res. 2009; 33:2027–2036. [PubMed: 19764939]

Roopesh BN, Rangaswamy M, Kamarajan C, et al. Reduced resource optimization in male alcoholics: N400 in a lexical decision paradigm. Alcohol Clin Exp Res. 2010; 34:1905–1914. [PubMed: 20659074]

Sable JJ, Low KA, Maclin EL, et al. Latent inhibition mediates N1 attenuation to repeating sounds. Psychophysiology. 2004; 41:636–642. [PubMed: 15189486]

Saletu-Zyhlarz GM, Arnold O, Anderer P, et al. Differences in brain function between relapsing and abstaining alcohol-dependent patients, evaluated by EEG mapping. Alcohol Alcohol. 2004; 39:233–240. [PubMed: 15082461]

Sauseng P, Klimesch W. What does phase information of oscillatory brain activity tell us about cognitive processes? Neurosci Biobehav Rev. 2008; 32:1001–1013. [PubMed: 18499256]

Schellekens AF, De Bruijn ER, Van Lankveld CA, et al. Alcohol dependence and anxiety increase error-related brain activity. Addiction. 2010; 105:1928–1934. [PubMed: 20840190]

Schoepp DD. Unveiling the functions of presynaptic metabotropic glutamate receptors in the central nervous system. J Pharmacol Exp Ther. 2001; 299:12–20. [PubMed: 11561058]

Schuckit MA. Low level of response to alcohol as a predictor of future alcoholism. Am J Psychiatry. 1994; 151:184–189. [PubMed: 8296886]

Schuckit MA, Gold EO, Croot K, et al. P300 latency after ethanol ingestion in sons of alcoholics and in controls. Biol Psychiatry. 1988; 24:310–315. [PubMed: 3401524]

Squires NK, Squires KC, Hillyard SA. Two varieties of long-latency positive waves evoked by unpredictable auditory stimuli in man. Electroencephalogr Clin Neurophysiol. 1975; 38:387–401. [PubMed: 46819]

Stassen HH, Lykken DT, Propping P, et al. Genetic determination of the human EEG. Survey of recent results on twins reared together and apart. Hum Genet. 1988; 80:165–176. [PubMed: 3169741]

Steele CM, Josephs RA. Drinking your troubles away. II: An attention-allocation model of alcohol's effect on psychological stress. J Abnorm Psychol. 1988; 97:196–205. [PubMed: 3385073]

Steele CM, Josephs RA. Alcohol myopia. Its prized and dangerous effects. Am Psychol. 1990; 45:921–933. [PubMed: 2221564]

Steinhauer SR, Hill SY, Zubin J. Event-related potentials in alcoholics and their first-degree relatives. Alcohol. 1987; 4:307–314. [PubMed: 3620100]

Stenberg G, Sano M, Rosen I, et al. EEG topography of acute ethanol effects in resting and activated normals. J Stud Alcohol. 1994; 55:645–656. [PubMed: 7861791]

Steriade M. Cholinergic control of thalamic function. Arch Int Physiol Biochim. 1990; 98:A11–A46. [PubMed: 1696459]

Stockwell RG, Mansinha L, Lowe Rp. Localization of the complex spectrum: The S-transform. IEEE Trans on Sig Proc. 1996; 44:998–1001.

Suresh S, Porjesz B, Chorlian DB, et al. Auditory P3 in female alcoholics. Alcohol Clin Exp Res. 2003; 27:1064–1074. [PubMed: 12878912]

Teo RK, Ferguson DA. The acute effects of ethanol on auditory event-related potentials. Psychopharmacology (Berl). 1986; 90:179–184. [PubMed: 2878457]

Tiesinga PH, Fellous JM, Jose JV, et al. Computational model of carbachol-induced delta, theta, and gamma oscillations in the hippocampus. Hippocampus. 2001; 11:251–274. [PubMed: 11769308]

Toyomaki A, Murohashi H. Discrepancy between feedback negativity and subjective evaluation in gambling. Neuroreport. 2005; 16:1865–1868. [PubMed: 16237344]

Trim RS, Schuckit MA, Smith TL. The relationships of the level of response to alcohol and additional characteristics to alcohol use disorders across adulthood: a discrete-time survival analysis. Alcohol Clin Exp Res. 2009; 33:1562–1570. [PubMed: 19485971]

Uhlhaas PJ, Singer W. Neural synchrony in brain disorders: relevance for cognitive dysfunctions and pathophysiology. Neuron. 2006; 52:155–168. [PubMed: 17015233]

Uhlhaas PJ, Roux F, Rodriguez E, et al. Neural synchrony and the development of cortical networks. Trends Cogn Sci. 2010; 14:72–80. [PubMed: 20080054]

Van Baal GC, De Geus EJ, Boomsma DI. Genetic influences on EEG coherence in 5-year-old twins. Behav Genet. 1998; 28:9–19. [PubMed: 9573642]

Van Beijsterveldt CE, Boomsma DI. Genetics of the human electroencephalogram (EEG) and event-related brain potentials (ERPs): a review. Hum Genet. 1994; 94:319–330. [PubMed: 7927323]

Van Beijsterveldt CE, Molenaar PC, De Geus EJ, et al. Heritability of human brain functioning as assessed by electroencephalography. Am J Hum Genet. 1996; 58:562–573. [PubMed: 8644716]

Van Beijsterveldt CE, Molenaar PC, De Geus EJ, et al. Genetic and environmental influences on EEG coherence. Behav Genet. 1998; 28:443–453. [PubMed: 9926613]

Van Der Stelt O, Gunning WB, Snel J, et al. No electrocortical evidence of automatic mismatch dysfunction in children of alcoholics. Alcohol Clin Exp Res. 1997; 21:569–575. [PubMed: 9194906]

Van Veen V, Carter CS. The anterior cingulate as a conflict monitor: fMRI and ERP studies. Physiol Behav. 2002; 77:477–482. [PubMed: 12526986]

Van Vugt MK, Sederberg PB, Kahana MJ. Comparison of spectral analysis methods for characterizing brain oscillations. J Neurosci Methods. 2007; 162:49–63. [PubMed: 17292478]

Varela F, Lachaux JP, Rodriguez E, et al. The brainweb: phase synchronization and large-scale integration. Nat Rev Neurosci. 2001; 2:229–239. [PubMed: 11283746]

Verleger R. Event-related potentials and cognition: A critique of the context updating hypothesis and an alternative interpretation of P3. Behavioral and Brain Sciences. 1988; 11:343–427.

Volavka J, Czobor P, Goodwin DW, et al. The electroencephalogram after alcohol administration in high-risk men and the development of alcohol use disorders 10 years later. Arch Gen Psychiatry. 1996; 53:258–263. [PubMed: 8611063]

Volkow ND, Wang GJ, Begleiter H, et al. Regional brain metabolic response to lorazepam in subjects at risk for alcoholism. Alcohol Clin Exp Res. 1995; 19:510–516. [PubMed: 7625590]

Von Stein A, Sarnthein J. Different frequencies for different scales of cortical integration: from local gamma to long range alpha/theta synchronization. Int J Psychophysiol. 2000; 38:301–313. [PubMed: 11102669]

Wang JC, Hinrichs AL, Stock H, et al. Evidence of common and specific genetic effects: association of the muscarinic acetylcholine receptor M2 (CHRM2) gene with alcohol dependence and major depressive syndrome. Hum Mol Genet. 2004; 13:1903–1911. [PubMed: 15229186]

Weschke S, Niedeggen M. Differential effects of moderate alcohol consumption on motion and contrast processing. Psychophysiology. 2012; 49:833–841. [PubMed: 22332779]

Whittington MA, Traub RD, Kopell N, et al. Inhibition-based rhythms: experimental and mathematical observations on network dynamics. Int J Psychophysiol. 2000; 38:315–336. [PubMed: 11102670]

Winterer G, Kloppel B, Heinz A, et al. Quantitative EEG (QEEG) predicts relapse in patients with chronic alcoholism and points to a frontally pronounced cerebral disturbance. Psychiatry Res. 1998; 78:101–113. [PubMed: 9579706]

Winterer G, Enoch MA, White KV, et al. EEG phenotype in alcoholism: increased coherence in the depressive subtype. Acta Psychiatr Scand. 2003a; 108:51–60. [PubMed: 12807377]

Winterer G, Mahlberg R, Smolka MN, et al. Association analysis of exonic variants of the GABA(B)-receptor gene and alpha electroencephalogram voltage in normal subjects and alcohol-dependent patients. Behav Genet. 2003b; 33:7–15. [PubMed: 12645817]

Winterer G, Smolka M, Samochowiec J, et al. Association of EEG coherence and an exonic GABA(B)R1 gene polymorphism. Am J Med Genet. 2003c; 117B:51–56. [PubMed: 12555235]

Yeung N, Sanfey AG. Independent coding of reward magnitude and valence in the human brain. J Neurosci. 2004; 24:6258–6264. [PubMed: 15254080]

Yordanova J, Kolev V. Brain theta response predicts P300 latency in children. Neuroreport. 1996; 8:277–280. [PubMed: 9051795]

Yordanova J, Banaschewski T, Kolev V, et al. Abnormal early stages of task stimulus processing in children with attention-deficit hyperactivity disorder – evidence from event-related gamma oscillations. Clin Neurophysiol. 2001; 112:1096–1108. [PubMed: 11377270]

Zahr NM, Pitel AL, Chanraud S, et al. Contributions of studies on alcohol use disorders to understanding cerebellar function. Neuropsychol Rev. 2010; 20:280–289. [PubMed: 20809198]

Zahr NM, Kaufman KL, Harper CG. Clinical and pathological features of alcohol-related brain damage. Nat Rev Neurol. 2011; 7:284–294. [PubMed: 21487421]

Zucker RA, Heitzeg MM, Nigg JT. Parsing the undercontrol/disinhibition pathway to substance use disorders: a multilevel developmental problem. Child Dev Perspect. 2011; 5:248–255. [PubMed: 22116786]

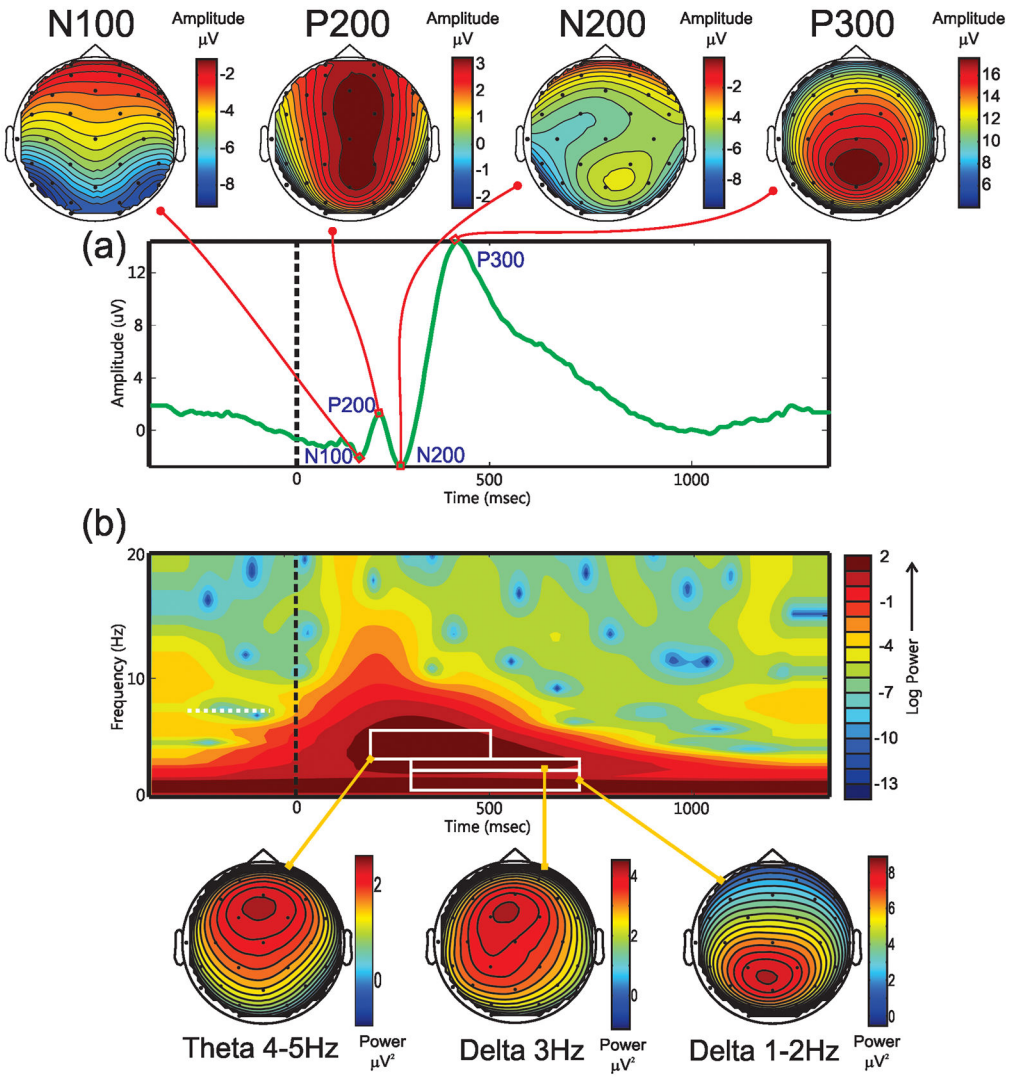

Fig. 23.1. Visual oddball event-related potential (ERP) and corresponding event-related oscillations using time frequency transformation. (Data from Jones et al., 2006.)

(**A**) Responses to rare targets in a visual oddball task at the vertex (Cz electrode): Typical grand mean waveform from 100 normal control subjects showing the major sequential ERP components and their topography, namely N100 (N1), P200 (P2), N200 (N2), and P300 (P3). These components are discussed in the text and described here:

The N1 (N100) component, a negative deflection occurring around 100 ms, is involved in an early attentional selection process; it is dampened to unattended stimuli and enhanced to attended ones (Hillyard et al., 1973; Nataanen et al., 1978). The vertex P200 component has been associated with visual feature discrimination (O'Donnell et al., 1997) and is sensitive to salient features of target stimuli (Luck and Hillyard, 1994a). The posterior N200 reflects the degree of attention required for processing stimuli and is sensitive to target probability (Folstein and Van Petten, 2008). The P3 (P300) is a large positive deflection seen 300–700 ms after a rare stimulus embedded in a series of unattended standard stimuli. It is proposed to reflect attentional allocation and context updating (Polich and Herbst, 2000) and cognitive closure (Desmedt, 1980; Verleger, 1988), while its time of occurrence (latency) reflects

mental processing speed; the earlier and larger the P3, the easier the processing. Evidence indicates that P3 has multiple sources, with contributions from frontal cortex (including anterior cingulate) and hippocampus (Halgren et al., 1980; Menon et al., 1997; Kiehl and Liddle, 2001; Ardekani et al., 2002).

(**B**) Time–frequency transformation using the S-transform (same data from top panel), illustrating the distribution of power over time during processing of the target. The white boxes indicate time–frequency regions of interest (TFROI) in specific band widths and their topography in the head plots at the bottom. It can be seen that during target detection theta (4–7 Hz) has a frontal distribution while delta (1–2 Hz) has a posterior distribution (Jones et al., 2006b).

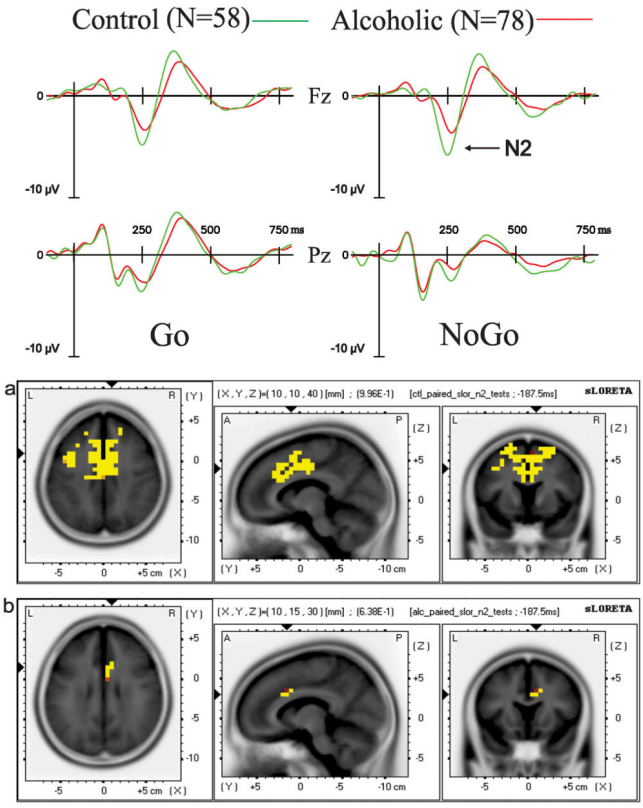

Fig. 23.2. Event-related potential waveforms and source localization of N2 component with low-resolution brain electromagnetic tomography (LORETA). (Data from Pandey et al., 2012.)

(Top panel) Waveforms from response inhibition task (Go/NoGo) comparing alcoholics and normal controls showing enhanced N2 wave and a frontal P3 during response inhibition (NoGo). Reduced N2 amplitudes are seen to both Go and NoGo condition, particularly for NoGo at frontal (Fz) lead.

(Bottom panel) sLORETA images for controls (**A**) and alcoholics (**B**) indicating areas in the brain which are significantly more activated for NoGo when compared to Go. Controls show a strong bilateral activation of anterior cingulate and also right medial frontal cortex. Alcoholics show a much smaller region of activation in anterior cingulate that does not involve bilateral areas.

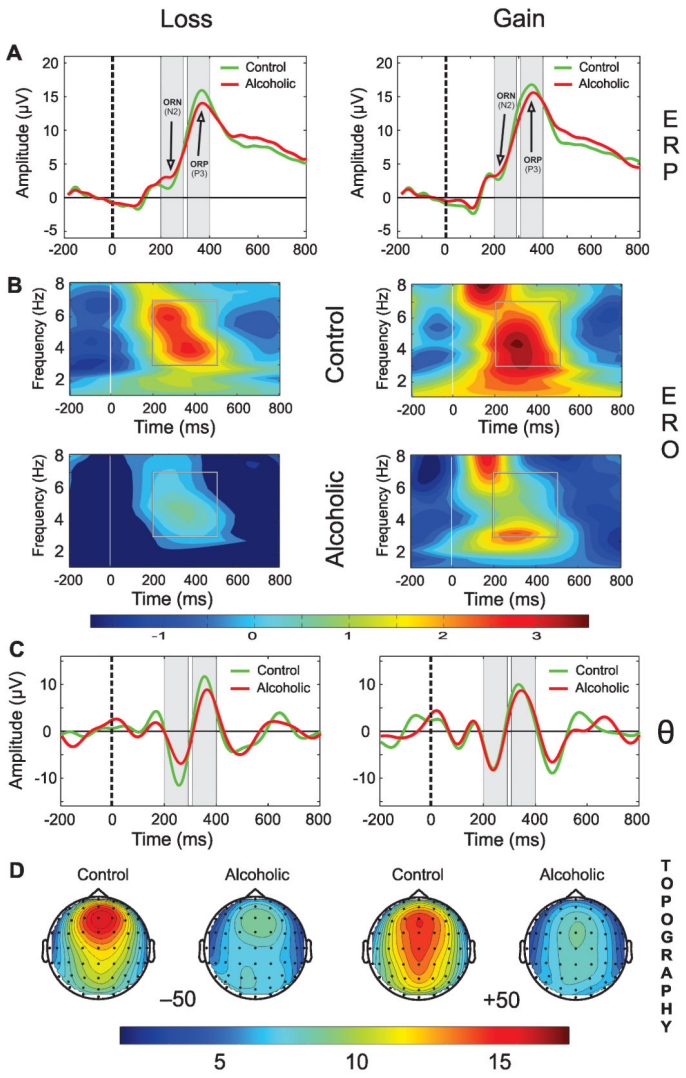

Fig. 23.3. Event-related potential, event-related oscillations, and theta topography in a gambling paradigm. (Data from Kamarajan et al., 2012.)

(**A**) Waveforms to loss and gain feedback stimuli in a gambling task showing erroneous responses (ERN)/outcome-related negativity (ORN) component and the outcome-related positivity (ORP) (P3) component in male controls (n = 38)and male alcoholics (n = 38).

(**B**) Time–frequency transformation of electroencephalogram epochs describing the total power in controls and alcoholics for loss and gain trials. Box indicates the region of interest – theta (3–7 Hz) band, 200–500 ms.

(**C**) Theta band response corresponding to the event-related potential traces in the above panel. Note differences between normal controls and alcoholics in the gray-shaded area.

(**D**) Theta power topography: note the sharply anterior peak for loss and a more diffuse slightly posterior spread for gain. Alcoholics have lower theta power, and the reduction is of greater magnitude for loss.

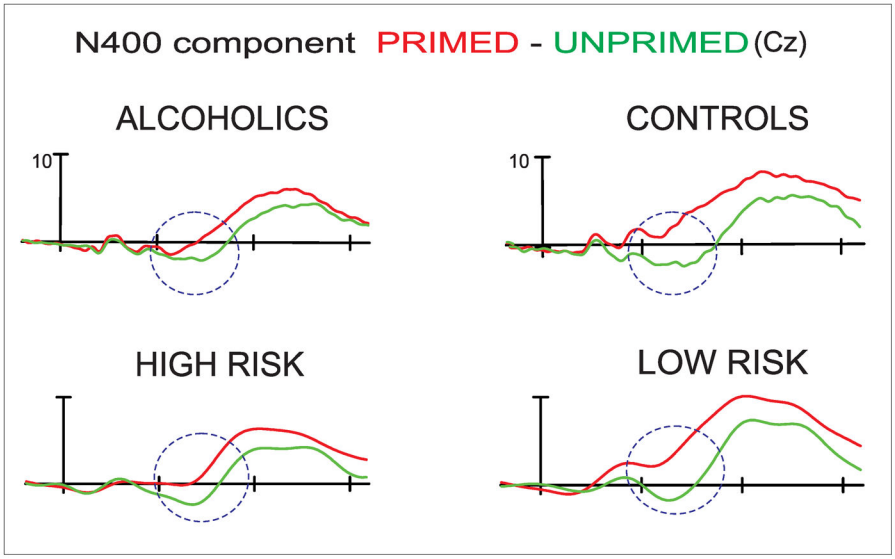

Fig. 23.4. Event-related potential waveforms from the semantic priming task. (Data from Roopesh et al., 2009, 2010.)

Waveforms from a semantic decision task for primed and unprimed words. The dotted circle marks the N400 component that is prominent in the case of unprimed words and highly attenuated for primed words, as seen in controls (n = 57) and low-risk (n = 28) individuals; alcoholics (n = 87) and high-risk (n = 23) individuals have less attenuation of this component.

N400 is a negative response seen between 200 and 600 ms in response to semantic incongruency (Kutas and Federmeier, 2011). The semantic priming task has been one of the most extensively used event-related potential paradigms to study the effect of priming on N400 (Bentin, 1989).

Table 23.1

Electroencephalogram (EEG) in Alcohol challenge studies

Study	Sample characteristics	Alcohol dose	EEG variable	Summary of findings
Pollock et al., 1983	31 FHP males, 17 FHN control males; 19–21 years	0.5 g/kg consumed over 15 minutes	EEG from C3, C4, T3, T4, P3, P4, O1, O2 slow alpha (7.42–9.46 Hz), fast alpha (9.75–12.1 Hz), theta (3.51–7.03 Hz), mean alpha frequency	Decrease in fast alpha and mean alpha frequency; increase in slow alpha and theta bands in both groups (postingestion), greater increase seen in high-risk patients. High-risk patients had greater decrease of fast alpha and mean alpha frequency than low-risk patients at 120 minutes. Largest effects seen on posterior electrodes
Ehlers and Schuckit, 1990	24 FHP males and 24 FHN males; 21–25 years	0.75 mL/kg dose Mean BAC at 90 minutes – 0.0726 g/dL	EEG from four bipolar derivations: F3–C3, F4–C4, P3–O1, P4–O2 Power: beta (12–20 Hz) at P3–O1, P4–O2	Increased beta power at 90 minutes only in FHP. Moderate drinkers had higher beta power at baseline and 90 minutes postingestion
Lukas et al., 1989	6 right-handed females; FHN (5), FHP (1); 21–27 years	0.7 g/kg consumed over 18 minutes Plasma ethanol 70–80 mg/dL	EEG power: delta (0.5–3.5) Theta (4.0–7.5) Slow alpha (7.5–9.5) Fast alpha (9.5–12.5) Beta1 (12–15.5) Beta2 (16.0–19.5) Beta3 (20.0–23.5)	Increased slow alpha (7.5–9.5) and fast alpha (9.5– 12.5) all over the scalp in FHN. FHP subject showed reduced alpha
Lukas et al., 1990	4 males; 25–39 years; light social drinkers; FHN (2), FHP (2)	0.7 g/kg consumed over 19 minutes	Power in alpha spectral band; auditory P300 amplitude and dipole	Increased alpha power all over the scalp in FHN. FHP showed no change. P3 amplitude lower in FHN at 30 minutes, no change in FHP. Dipole shows a shift to a more posterior distribution
Lukas and Mendelson, 1988	12 males; 21–35 years; light social drinkers	0.7 g/kg consumed over 15 minutes; plasma ethanol ~80 mg/dL	EEG power in four bands: 0.25–4 Hz; 4–8 Hz; 8–13 Hz, and 13–30 Hz	Increase in alpha power (8–13 Hz) 0–30 minutes; followed by a decrease in alpha power 35–60 minutes
Kaplan et al., 1988	25 high-risk + FHP males and 24 low-risk males; 21–28 years	Low dose; 2 12oz beer; ~18 g of alcohol	EEG alpha (9–12 Hz) power; subjective ratings of desire to drink and intoxication	Increase in alpha power after alcohol in both groups; the positive relationship of alpha activity with desire to drink was found only in FHP and not in FHN
Ehlers and Schuckit, 1988	30 males; 15 FHP and 15 FHN controls	0.75 mL/kg	EEG from two bipolar derivations: F4–C4, P4–O2 Power: theta (4–7.5 Hz), slow alpha (7.5–9 Hz), fast alpha (9–12 Hz), beta (12–20 Hz); EEG stability measure – coefficient of variation of mean power	Increase in alpha power at 90 minutes postethanol, especially in low alpha and a decrease in EEG stability for alpha band. This destabilizing effect was less intense in FHP
Ehlers et al., 1989	24 males; 21–25 years; FHN	0.75 mL/kg; BAC at 90 minutes = 0.0726 g/dL; at 150 minutes = 0.0562 g/dL	EEG from four bipolar derivations: F3–C3, F4–C4, P3–O1, P4–O2 Power: theta (4–7 Hz), slow alpha (7.5–9 Hz), fast alpha (9–12 Hz), beta (12–20 Hz)	Increased power in theta (all loci) and slow alpha (right frontal locus) at 90 and 150 minutes postingestion. Peak frequency in fast alpha (all loci) theta and beta bands (frontocentral loci) also decreased after alcohol ingestion. Drinking quantity/frequency associated with beta band in EEG; subjective response to ethanol associated with fast alpha

Study	Sample characteristics	Alcohol dose	EEG variable	Summary of findings
Stenberg et al., 1994	37 males – 22 (ethanol group) and 15 (placebo group); 21–29 years	Dose 1 0.5g/kg; dose 2 1.0 g/kg; mean BAC 31 mg/dL and 78 mg/dL	EEG power: delta (0.5–3.5) theta (4.0–7.5), alpha (8–12), beta (12.5–30)Hz	Robust dose-dependent increase in theta (parietal) and beta (frontal and parietal) in alcohol group; increase in alpha seen in both groups; left hemisphere effects of alcohol; low beta at baseline was associated with larger alpha increase to alcohol
Ehlers et al., 2004	FHP subjects; 79 Hispanic – 20 males and 59 females; 206 non-Hispanic – 78 males and 128 females; mean (SD) age 22 (2.9)	0.75 mL/kg (females), 0.90 mL/kg (males) consumed over 7 minutes	Bipolar leads: P3–O1, P4–O2; slow alpha (7.5–9 Hz), fast alpha (9–12 Hz)	Increased slow alpha power after ethanol ingestion. Decrease in fast alpha power following alcohol in Hispanic subjects; increases in fast alpha power following alcohol in non-Hispanic subjects
Ehlers et al., 1998b		0.75 mL/kg consumed over 7 minutes	EEG from bipolar P4–O2; coherence time; relative alpha power; relative theta power; non-linear analysis measures – slope asymmetry, Kaplan's delta epsilon intercept and slope; 1% radius and redundancy	Increase in coherence time; decrease in alpha relative power and increase in theta relative power. Significant changes in non-linear measures suggesting a reduction in non-linearity in EEG
Ehlers and Schuckit, 1991	24 FHP males, 24 FHN males		Fast alpha (9–12 Hz)	Decreased fast alpha (9–12 Hz) energy at 90 minutes in FHN. FHP had higher fast alpha energy than FHN at baseline
Cohen et al., 1993b	21 males; 19–39 years (mean 22); light social drinkers; FHN	0.5 mL/kg (low dose); 0.8 mL/kg (high dose) consumed in 10 minutes	Slow alpha 7.5–10 Hz; fast alpha 10.5–13.0 Hz Slow beta 13.5–19.5 Hz Fast beta 20–26 Hz	Increase in slow alpha for both low- and high-dose ethanol at frontal regions F3, F4, C3, and C4 35–70 minutes postdrink
Cohen et al., 1993a	21 high-risk (FHP) males, light drinkers, 19–39 years (mean 22 years) vs 21 low-risk (FHN) males, 19–29 years (mean 22 years)	0.5 mL/kg (low dose) 0.8 mL/kg (high dose) consumed in 10 minutes	Slow alpha 7.5–10 Hz; fast alpha 10.5–13.0 Hz Slow beta 13.5–19.5 Hz Fast beta 20–26 Hz	Increase in slow alpha for both low- and high-dose ethanol at frontal regions F3, F4, and right parietal P4 for high-risk and low-risk patients during ascending limb. High-risk patients showed higher increase. The descending limb revealed steeper decrease in slow alpha in high-risk patients and no decrease in low-risk patients

BAC, blood alcohol curve; FHP, family history-positive; FHN, family history-negative.

Table 23.2

Alcohol challenge studies using event-related potentials (ERP)

Study	Sample characteristics	Alcohol dose	Task and ERP components	Summary of findings
Elmasian et al., 1982	15 FHP males and 15 FHN males; 21–26 years. 1–84 drinks per month; three dose groups	Placebo, 0.56 g/kg and 0.94 g/kg consumed in 24 minutes. BAC peak 66 mg/100 mL and 97.6 mg/100 mL	Auditory oddball task; P3 peak latency and peak amplitude; non-target P2 peak	Reduction in P3 amplitude in FHN (most marked in high dose) and FHP (strong decrease at all three doses); alcohol increased latencies in both groups but FHP had more slowing
Teo and Ferguson, 1986	9 males and 4 females; 20–44 years	Placebo, 0.3 g/kg and 0.54 g/kg of total body weight	Auditory oddball task; Cz electrode; N100, P200, N200, and P300	High dose produced an increase in latency for N1, P2, N2 components for both stimuli. Target P3 amplitude reduced and latency increased (dose-dependent)
Rohrbaugh et al., 1987	Male social drinkers	Separate sessions of four doses ranging from 0 (placebo) to 1.05 g/kg lean body weight, with periodic maintenance dose of 0.12 g/kg	Visual sustained attention task requiring response to target digits in a stream of blurred non-target digits, presented one at a time. ERP – N1, P2, N2, and P3	Dose-related decrease of detection performance. Early ERP components (N1 and P2) not affected by alcohol. Ethanol caused dose-related delays in N2 and P3 latencies and reaction time increases. The amplitude of N2 also decreased over time on task, and P3 amplitude decreased both as a function of dose and time on task
Campbell and Lowick, 1987	10 subjects	Placebo; 1.0 mL/kg dosage of 94% ethanol	Auditory oddball task; ERP components – N1b, P2, and P3 to distractor and target waveforms	N1b and P2 amplitudes were significantly reduced. P3 to distractor stimuli was significantly reduced. No target P3 change
Schuckit et al., 1988	21 FHP males and 21 FHN males; 21–25 years	Placebo, 0.75 mL/kg, 1.1 mL/kg consumed in 10 minutes	Auditory oddball task; P3 peak latency	Increase in P3 latency postethanol in both groups for ascending BAC. For the high dose the FHP showed a faster recovery in P3 latency compared to FHN
Colrain et al., 1993	10 males; 18–25 years; social drinkers	Placebo; 0.28; 0.36; 0.54 and 0.72 g/kg consumed over 20 minutes	Reversing checkerboard in standard oddball paradigm. Peak and latency P1, P2, N2, P3. 11 Electrode sites (10–20 system)	Increase in reaction time, N2 and P3 latency with increasing dose. No effect on P1 and P2. Reduced RMS power of the P3 complex and N2–P3 amplitude difference at central and parietal sites at higher alcohol doses
Jaaskelainen et al., 1995	5 females; 5 males (n = 10); 20–30 years. Social drinkers	Placebo; 0.5 g/kg consumed in 40 minutes (BAC prior to test = 0.063%)	Two auditory oddball streams (target/non-target) presented to right and left ear. Subjects told to attend to one ear and ignore the other. ERP – N1(Cz), P2(Cz), MMN(Fz), N2b(Cz), P3b(Pz)	Attended and unattended N1 amplitudes were reduced after alcohol ingestion. Unattended P2 amplitudes also reduced after alcohol. MMN amplitude decreased significantly after alcohol, with no change on N2b and P3b amplitudes. Latency increased for MMN and N2b
Jaaskelainen et al., 1996	4 females, 5 males (n = 9); 23–29 years. Social drinkers	Placebo; 0.55 g/kg (BAC prior to test = 0.58); 0.85 g/kg (BAC prior to test = 1.04); consumed in 25 minutes	Auditory oddball with short and long interstimulus interval (ISI) while subjects read a book. Electrodes: F3, Fz, F4, C3, Cz, C4, Pz. ERP – MMN from Fz (rare-standard tone); N1 and P2 from Cz (standard tones)	N1, P2, and MMN amplitudes reduced for long ISI task. High alcohol dose reduced N1 amplitudes in both long and short ISI tasks. MMN decrease was primarily frontal
Porjesz and Begleiter, 1996	24 HR males and 24 LR males; 19–24 years	0.5 mL/kg (low dose) 0.8 mL/kg (high dose) consumed in 10 minutes	Visual oddball, with easy and difficult line discrimination. P3 amplitude, latency	Decrease in P3 amplitude in both; percent decrease from baseline to ascending limb was greater in HR. P3 latency was longer at peak BAC and descending limb for both; HR recovered faster to baseline level

Study	Sample characteristics	Alcohol dose	Task and ERP components	Summary of findings
Jaaskelainen et al., 1999	7 males and 4 females (n = 11) social drinkers; 24–30 years	Placebo; 0.3 g/kg; 0.6 g/kg; consumed in 25 minutes	Auditory forced choice task with two tones and rare deviations in tone frequency	Low dose: For standard tones N1, N2 amplitude decreased; N2 and P3 latency increased. P2 amplitude increased. For deviant tones P3a amplitude decreased. Higher dose did not produce any additive effects
Cohen et al., 1998	27 LR males, 23 HR males; 18–30 years; HR = light drinkers (n = 14), heavy drinkers (n = 9)	Placebo, 0.5 g/kg, 0.8 g/kg consumed in 10 minutes	AEP to binaural auditory clicks; measures: N100, P200	Within group – LR showed decreased N100 between placebo and high dose; HR showed decreased N100 and P200. Between group – HR N100 and P200 amplitude decrease is higher than LR during ascending BAC; HR – N100 and P200 amplitudes recover to baseline levels faster that LR in descending BAC
Ehlers et al., 1998a	28 FHP and 14 FHN males; 18–25 years; Native American heritage	Placebo, 0.75 mL/kg consumed over 7 minutes; BAC peak ~0.078 g/dL	Auditory oddball plus noise; ERP data from Fz, Cz, Pz; P3a (225–300 ms) and P3b (300–400 ms) amplitude	Alcohol significantly reduced P3a amplitude when compared to placebo
Marinkovic et al., 2000	12 males; 21–26 years; light social drinkers	Placebo, 0.4 g/kg consumed in 10–15 minutes	Word recognition task; 13 electrodes, 10–20 system. Lateralized readiness potential (LRP) (C3 subtracted from C4). Mu (12.5–17.5 Hz) band	Go (old words) condition shows no alcohol-related LRP changes, NoGo (novel words) condition shows enhanced LRP to alcohol. Mu band power reduced in NoGo trials
Marinkovic et al., 2001	12 males; 21–28 years; light social drinkers and non-smokers	Placebo, 0.4 g/kg consumed in 10–15 minutes	Three stimulus auditory oddball task; 13 electrodes, 10–20 system. ERP (average amplitude) – N1, N2, P3a, P3b, and slow wave	Increased frontal N2 and decreased frontal P3a average amplitude to ethanol. Decreased P3b to alcohol centroparietally
Ridderinkhof et al., 2002	14 right-handed males; social drinkers; age 20–40 years	Placebo, low-dose (0.45 g/kg), and high-dose (0.85 g/kg); BAC 0.4%, 0.97%	Subjects pretrained on Eriksen Flanker Task, then tested again after placebo and alcohol. ERP – N2 for congruent and incongruent correct responses; ERN for error responses	No effect of alcohol on N2; ERN was reduced significantly by both alcohol doses
Bartholow et al., 2003	42 adults (21 males and 21 females); age 21–30 years	Placebo; moderate dose (females 0.36 g/kg, males, 0.40 g/kg); high dose (females 0.72 g/kg, males 0.80 g/kg)	Version of Eriksen Flanker Task; EEG: 20 scalp electrodes (10–20 system). PCA was conducted on ERP data and two poststimulus epochs 200–350, 400– 500 were evaluated. Reaction time and accuracy	Dose-related decrease in P3 amplitude. Moderate dose increased P3 latency; high susceptibility to alcohol moderated an increase in ERN amplitude to both alcohol doses
Marinkovic et al., 2004	12 males; 21–26 years; light social drinkers	Placebo, 0.4 g/kg consumed in 10–15 minutes	Verbal/word recognition task; 13 electrodes, 10–20 system. ERP components – P/N180, N310, N450, P580	N180 at T5, T6 – reduced after alcohol ingestion. N450 and P580 latency was increased by alcohol
Easdon et al., 2005	Three groups with 4 males and 4 females: control (mean age = 27.75), low dose (mean age = 24.13) and high dose (mean age = 26.75)	Placebo, 0.56 g/kg (low dose) or 0.80 g/kg (moderate dose)	Sustained attention to response task (Go-NoGo) 64-channel EEG; stimulus-locked (P1,N170, N2, P3) and response-locked ERPs (correct: Nc, Pc; error: Ne, Pe)	Increase in error rate postethanol. Both doses of alcohol reduced N170 and P3 amplitudes during Go, No-Go, and error trials. Both doses of alcohol reduced the Ne amplitude whereas the Pe amplitude decreased only after moderate doses of alcohol
Euser et al., 2011	64 males; 30 males (placebo); 31 males (alcohol). Age 18–25 years	Placebo; 0.65 g/kg consumed over 8 minutes	Balloon analogue risk task (BART); Fz, FCz, and Cz; FRN (max. negativity 200–300 ms after feedback); P300	No alcohol effect on Feedback related negativity (FRN), reduced amplitude of P300 to loss feedback. Alcohol affects later stages of outcome evaluation
Kenemans et al., 2010	8 females and 8 males; 18–25 years; social drinkers	Placebo, moderate alcohol (BAC level between 0.04% and 0.07%)	Auditory MMN task; visual task - 2.4 versus 0.6 c/d gratings in pseudorandom sequence (deviant (10%), standard	MMN – alcohol decreased amplitudes significantly. RRN – moderate-dose alcohol significantly reduced RRN.

Study	Sample characteristics	Alcohol dose	Task and ERP components	Summary of findings
			(90%)); ERP component – rareness related negativity (RRN: difference between deviant and standard ERP between 120 and 1	SEM80 (RRN: difference between deviant and standard ERP between 120 and 1
			(90%)); ERP component – rareness related negativity (RRN: difference between deviant and standard ERP between 120 and 1	effects (RRN: difference between deviant and standard ERP between 120 and 1
			(90%)); ERP component – rareness related negativity (RRN: difference between deviant and standard ERP between 120 and 1	Data synchrony (RRN: difference between deviant and standard ERP between 120 and 1
			(90%)); ERP component – rareness related negativity (RRN: difference between deviant and standard ERP between 120 and 1	
			(90%)); ERP component – rareness related negativity (RRN: difference between deviant and standard ERP between 120 and 1	
Weschke and Niedeggen, 2012	29 subjects in two groups: alcohol and placebo. Alcohol (n =15; 8 males, 7 females); Placebo (n = 14; 7 males, 7 females)	Placebo; alcohol: females 0.30 g/kg, males 0.35 g/kg consumed within 30 minutes. BAC level 0.047%	Contrast perception task (subjects identified high contrast stimulus); Motion perception task (subjects identify stimulus with dots moving up). EEG – O1, O2, P3, P4. ERP components – contrast evoked negativity (110–170 ms); motion evoked negativity (160–240 ms); late positive complex (P300)	Alcohol reduced contrast-evoked negativity and P300; Motion-evoked negativity was reduced contralaterally by alcohol

BAC, blood alcohol curve; FHP, family history-positive; FHN, family history-negative; HR, high risk; LR, low risk; MMN, mismatch negativity; AEP, auditory evoked potential; PCA, principal component analysis.