Published in: Psychologica Belgica (2006), vol.46, iss.1-2, pp.5-36.
Status: Postprint (Author's version)

EVENT-RELATED BRAIN POTENTIALS IN PSYCHOPATHOLOGY: CLINICAL AND COGNITIVE PERSPECTIVES

Michel HANSENNE

University of Liège, Faculty of Psychology and Educational Sciences, Department of Cognitive Sciences 5, Bld du Rectorat (B32), 4000 Liège

Abstract: Since the discovery of the P300 component, a large number of studies have been conducted with the aim to find abnormalities of this psychophysiological marker among the main psychiatric disorders. The first studies were very promising, but successive findings were rather controversial resulting in two main positions (the pros and the cons) as regard to the usefulness of P300 in clinical psychopathology. However, P300 studies provide interesting findings concerning information processing in psychopathology. Moreover, other Event-Related Potentials (ERPs), such as the Mismatch Negativity (MMN) and the Error-Related Negativity (ERN) are particularly interesting for the study of cognitive processes in psychopathology. In this review, the author will give an overview of the main findings of P300, MMN and ERN values in psychopathology from a clinical and a cognitive point of view. After a brief description of the rationale of ERPs, the findings in schizophrenia, depression, alcoholism, posttraumatic stress disorder, panic disorder, and obsessive-compulsive disorder will be sequentially reviewed. The diagnostic usefulness of P300 in psychopathology is limited, but could be increased if variables known to influence P300 amplitude or latency are controlled. Doubtless, grouping two or more different ERP components would greatly improve the usefulness of the clinical applications of brain potentials. On the other hand, a growing number of studies have provided evidence of the relevance of ERPs to investigate cognitive processes in clinical psychopathology.

Introduction

Event-Related Potentials (ERPs) are useful tools to assess information processing in normal subjects as well as in clinical settings. ERPs are based, like the electroencephalogram (EEG), on the direct recording of brain electrical activity with the help of electrodes. More specifically, an ERP is a change in an EEG recording from the scalp that is related to the presentation of an external or internal stimulus. It is considered as a response from the brain, which is time-locked to the stimulus or event, that is, the potential either coincides with or follows the stimulus after a brief delay. ERPs provide online information about neurophysiological processes related to a range of cognitive tasks. Because ERPs occur as a consequence of an event, they are called "event-related" rather than simply "evoked potential". Classically, there are two kinds of evoked potentials: exogenous and endogenous ones. Exogenous potentials reflect the first neural processing of the physical characteristics of a stimulus, and the magnitude of the response is not dependent on the cognitive processing of the stimulus. They can be recorded without any consciousness from the subject and they represent the sensory responses evoked by the stimuli (e.g., visual or auditory stimuli). Conversely, endogenous potentials are elicited in complex experimental situations and usually require active participation of the subject. They involve higher cognitive processes such as attention and memory. Endogenous potentials are also called ERPs.

ERPs exhibit an excellent time resolution, that is, they reflect the processing of the information delivered by the stimulus or required by the task, millisecond by millisecond. Hence, the different stages of information processing may be distinguished. ERPs are classically composed of several deflections, or components, some positive and some negative. The positive components are called "P", and the negative ones "N", following by their latency (e.g., P300 for a positive component with a latency of 300 milliseconds). The latency of a component is usually considered as the time required by the brain to evaluate different features of the stimulus (i.e., the speed of information processing), with the rationale that longer latencies reflect more complex processing in normal subjects or delayed processing such as in aging or in degenerative diseases. On the other hand, the amplitude, or magnitude of the component is usually viewed as the energetical aspects of information processing (i.e., amount of the resources allocated to the task).

ERPs: a big family

There are different kinds of endogenous components. The most studied are the P300 and the Mismatch Negativity (MMN), and more recently, the Error-Related Negativity (ERN), or Error Negativity (EN) (ERN/EN). P300 is a positive wave that occurs 300 milliseconds after the presentation of the stimulation (Desmedt, Debrecker, & Manil, 1965; Sutton, Braren, Zubin, & John, 1965). It appears when a subject detects an informative task-related stimulus. P300 reflects memory updating (Donchin & Coles, 1988), or context closure

(Desmedt, 1980; Verleger, 1988). P300 is related to an external control that favours attentional mechanisms to the environment (Kok, 1990), and might represent the transfer of relevant information to consciousness (Picton, 1992). P300 amplitude is related to stimulus probability, stimulus significance, task difficulty, motivation, and vigilance (Johnson, 1986, 1993; Sommer & Matt, 1990). P300 latency reflects the time of stimulus evaluation (Kutas, McCarthy, & Donchin, 1977). P300 latency is mainly influenced by the task complexity and it is only weakly influenced by response selection processes (McCarthy & Donchin, 1981; Smulders, Kok, Kenemans, & Bashore 1995). The paradigm usually used to record P300 is the oddball paradigm in which two different stimuli are delivered with different probabilities (e.g., a frequent sound of 1000 Hz at 80%, and a rare sound of 2000 Hz at 20%) and the subject is required to discriminate the infrequent target stimulus from the frequent standard stimulus by noting the occurrence of the target, typically by pressing a button or mentally counting. The P300 elicited by target stimulus in this task is a large positive response that is of maximum amplitude over the parietal electrode sites with a peak latency of about 300-350 milliseconds for auditory and 350-450 milliseconds for visual stimuli in normal young adults.

Classically, the P300 response is divided into two sub-components: P3a and P3b (Squires, Squires, & Hillyard, 1975). The P3a component is mainly distributed in frontal regions, and its usual latency ranges from 220 to 280 milliseconds. It is elicited by infrequent, unpredictable shifts of either intensity or frequency in a train of tone pips when the subject is ignoring (reading a book) the tones. P3a amplitude exhibits rapid habituation, which depends on the novelty of the stimuli. P3a reflects automatic cognitive processing, and the orientation response. The P3a component is also typically recorded in a "three stimuli paradigm" in which infrequent nontarget stimuli are inserted into the sequence of target and standard stimuli. Indeed, when novel stimuli are presented as infrequent nontarget stimuli in the series of more typical target and standard stimuli, a P300 component that is large over the frontal areas is produced (Courchesne, Hillyard, & Galambos, 1975; Yamaguchi & Knight, 1991). This novelty P300 is sometimes called the P3a. In contrast, the P3b component (considered as P300) presents a centro-pari-etal topography and a longer latency usually comprised between 280 to 600 milliseconds. The unpredictable and novelty characteristics of the stimulus are not sufficient to elicit the P3b component, the subjects here must produce an active discrimination by pressing a button.

The MMN is considered as a neurophysiological index of early sensory processing and automatic attention allocation, and it is related to the orienting reflex (Näätänen, 1990, 1995). The MMN is a fronto-central component elicited by a physically deviant auditory stimulus occurring among frequent stimuli with a latency of about 130 milliseconds from stimulus onset and lasting to about 250/300 milliseconds (Näätänen, 1995, 2001; Näätänen, Gaillard, & Mantysalo, 1978; Picton, Alain, Otten, Ritter, & Achim, 2000).

The deviant sounds may differ from the standard sound in pitch, duration, intensity, and spatial location. The latency of the MMN is inversely related, and its amplitude positively related, to the magnitude of the difference between the standard and the deviant stimuli (Näätänen & Gaillard, 1983). The MMN is presumably generated by a mismatch process between the sensory input from a deviant stimulus and a short-term memory (sensory-memory) trace representing the physical features of the standard stimuli. This process appears to be automatic since the MMN is elicited even by changes in unattended auditory stimuli. Recent findings have also suggested that the transient auditory sensory-memory representation underlying the MMN is facilitated by a long-term memory representation of the corresponding stimulus. This means that some characteristics of the sensory-memory traces involved in the elicitation of this component are stored in a more durable representation and that these memory traces can be reactivated (Winkler, Cowan, Csépé, Czigler, & Näätänen, 1996; Winkler & Cowan, 2005). Moreover, as opposed to P300, the MMN seems not to be affected by the predictability of the deviant stimuli (Näätänen, 1995, 2001). The MMN is usually recorded with an oddball paradigm in which the two stimuli differ slightly (e.g., a frequent sound of 1000 Hz at 80%, and a rare sound of 1050 Hz at 20%) and where the subject is distracted from the task by a second task like counting, or reading. The MMN is also called N2a because both components share common features. The difference between them is that the former is a difference-waveform component obtained by subtracting the ERP waveform in the infrequent, deviant condition from the corresponding waveform in the frequent, standard condition. Moreover, in attentive condition, the MMN is surimposed to the N2b, and cannot be therefore analysed. As regards the physiological aspects of the MMN and its association with cortical networks, several studies have suggested that two main generators exist; first, the supratemporal plane of the auditory cortex (Alho et al., 1998; Giard, Perrin, Pernier, & Bouchet, 1990), reflecting the preconscious detection of a change in the signal, and second, the frontal areas (Deouell, Bentin, & Giard, 1998; Giard et al., 1990; Rinne, Ahlo, Ilmoniemi, Virtanen, & Näätänen, 2000) reflecting the orienting of attention towards the detected change. It has been suggested that the first component (supratemporal plane) may activate the second component (frontal) leading to a switch of attention to conscious detection.

ERN/Ne is a component associated with action monitoring and error detection (Falkenstein, Hohnsbein, Hoormann, & Blanke, 1990; Falkenstein, Hoormann, Christ, & Hohnsbein, 2000; Gehring, Coles, Meyer, & Donchin, 1990; Gehring, Goss, Coles, Meyer, & Donchin, 1993). It is a sharp negative deflection that generally occurs from 50 to 150 milliseconds following response execution and it is associated with activity involving the anterior cingulate cortex (ACC). It is typically observed following an error (key press error commission). The typical protocol consists of an incongruent spatial choice reaction time (e.g., left side stimulus with right hand response, and right side stimulus with left hand response).

ERPs in psychopathology: two perspectives

Since the discovery of the P300 component by Sutton and colleagues in the USA (Sutton et al., 1965) and by Desmedt and colleagues in Belgium (Desmedt et al., 1965), a large number of studies have been carried out with the aim to find abnormalities of this psychophysiological marker among the main psychiatric disorders. Following the disappointment that the EEG was not very valuable in psychiatry, some expectations have been formulated towards this component. This is the main perspective of ERPs in psychopathology, in which one distinguishes three sorts of markers: state, trait and vulnerability markers. A state marker characterises a biological parameter (here an ERP component) that is altered during the disease but that stabilises after clinical remission, a trait marker characterises a biological parameter that is changed during the disease and after the remission, and a vulnerability marker characterises a biological parameter that is modified before the emergence of the disease. For instance, the reduction of P300 amplitude is a state marker of depression, a trait marker of schizophrenia and a vulnerability marker of alcoholism, respectively.

Besides this main perspective, ERPs are also used to study the cognitive functions and processes in psychopathological conditions. There is no doubt that ERPs are useful tools to assess cognitive functions in psychopathology. This is demonstrated by a growing literature showing that specific psychiatric disorders exhibit abnormalities of ERPs' components recorded in particular conditions (Polich, 2000).

In this review, we will give an overview of the main findings of ERPs' values in psychopathology from a clinical and a cognitive point of view. We will sequentially review the findings in schizophrenia, depression, alcoholism, posttraumatic stress disorder, panic disorder and obsessive-compulsive disorder. Some psychopathological disorders will not be reviewed here due to limited space. Several studies have reported interesting findings concerning P300 modulation in other disorders, such as autism, substance abuse (e.g., heroin addicts, and cannabis use), and personality disorders (e.g., schizoid, antisocial and borderline personality disorders).

Briefly, autistic subjects are characterised by reduced P300 amplitude, which indicates alteration of attention (Lotspeich & Ciaranello, 1993; Kemner, van der Gaag, Verbaten, & van Engeland, 1999). Papageorgiou et al. (2004) reported that abstinent heroin addicts exhibit reduced P300 amplitude at centro-frontal regions as compared to current heroin users and controls in a short memory task, and Kouri, Lukas, and Mendelson (1996) found a reduction of P300 amplitude in heroin addicts following detoxification and that buprenorphine treatment significantly reversed this P300 amplitude decrement. Regular cannabis users are characterised by an enhancement of P300 latency (Solowij, Michie, & Fox, 1991; 1995), and chronic cocaine users exhibit reduced P3a amplitude and prolonged latency in a three stimuli paradigm (Biggins, McKay, Clark, & Fein, 1997), suggesting frontal deficits. Concerning personality disorders, Kutcher, Blackwood, Gaskell, Muir, and St Clair (1989) reported that P300 was not different among schizotypical, borderline or controls subjects, but that the two clinical groups showed prolonged P300 latency. Other studies confirmed that schizotypical subjects did not have an alteration of P300 amplitude (Kalus et al., 1991; Trestman, Horvath, Kalus, & Peterson, 1996). However, Salisbury, Voglmaier, Seidman, and McCarley (1996) indicated that schizotypical subjects exhibit similar topographical alterations of P300 to those found in schizophrenia. Some studies have also demonstrated that borderline subjects are characterised by reduced P300 amplitude and prolonged latency (Blackwood, St Clair, & Kutcher, 1986; Kutcher, Blackwood, St Clair, Gaskell, & Muir, 1987). Lastly, reduced P300 amplitude over frontal regions is observed among antisocial subjects (Bauer, Hesselbrock, O'Connor, & Roberts, 1994; Costa et al., 2000), and Iacono, Malone, and McGue (2003) provided evidence supporting that P300 amplitude reduction could be considered as an index of genetic vulnerability for the spectrum of behaviours and traits characterised by behavioural disinhibition.

Schizophrenia

Most studies using P300 in clinical psychopathology have been performed in schizophrenia. The first study showed that schizophrenic patients exhibited lower P300 amplitude compared to controls, and that habituation of P300 amplitude was not observed in the clinical group (Roth & Cannon, 1972). Since no biological markers of

the disease had been identified at the time, this result was considered as a big progress for the diagnosis of schizophrenia. From this initial finding, several studies have confirmed that schizophrenia is characterised by lower P300 amplitude (Hill & Weisbrod, 1999; Pfefferbaum, Wenegrat, Ford, Roth, & Kopell, 1984; Souza et al., 1995; Verleger, Bode, Arolt, Wascher, Kömpf, 1994). The reduction of P300 found in schizophrenia is not due to lack of motivation (Brecher & Begleiter, 1983; Verleger et al., 1994), or latency variation (Ford, White, Lim, & Pfefferbaum, 1994), but probably because the task requires a cognitive effort that is impaired (Verleger et al., 1994). However, several findings show that patient characteristics and ERPs' methodologies affect P300, and that a better understanding of these factors is a necessary step towards developing the clinical usefulness of the findings.

As regards the sensorial modality, the strongest P300 effect is observed with the auditory oddball paradigm (Ford, 1999; Pfefferbaum, Ford, White, & Roth, 1989), and some studies have not reported differences between schizophrenic patients and controls with a visual discrimination protocol (Ducan 1988; Heinz & Emser, 1987). The interpretation given by these authors is that schizophrenia is mainly characterised by auditory information processing abnormalities rather than visual ones. In contrast, some studies demonstrated that schizophrenic patients had lower P300 amplitude in a visual paradigm (Pass, Klorman, Salzman, Klein, & Kaskey, 1980).

Although the main P300 abnormalities found in schizophrenia are related to amplitude, alterations of the latency and the topography have also been reported in different studies. Concerning latency, a number of studies report that schizophrenic patients and controls do not differ (Stefánsson & Jónsdóttir, 1996; Stranburg, Marsch, & Brown, 1987), whereas other studies observe prolonged P300 latency in the clinical group (Ducan, Morihisa, Fawcet, & Kirch, 1987; Roth & Cannon, 1972). An explanation of these contradictory findings is that the difficulty of the task was not equivalent between the studies, with some of them requiring more attentional resources than others.

Concerning P300 topography, various studies show that schizophrenic patients, compared to controls, are characterised by an alteration of the distribution over the scalp (Faux, Shenton, McCarley, Nestor, Marcy, & Ludwig, 1990; Hill & Weisbrod 1999). In schizophrenic patients, P300 is particularly lowered in the left temporal regions, and this finding is not influenced by the medication of the patients (Faux et al., 1993), but is reversed among left-handed patients (Holinger, Faux, & Shenton, Sokol, Seidman, Green, & McCarley, 1992), suggesting a hand dominance effect. In contrast, other studies do not report hemispherical abnormalities (Ford, Mathalon, White, & Pfefferbaum, 2000; Pfefferbaum et al., 1989). However, a metaanalysis on P300 asymmetry in schizophrenia is in agreement with left reduction amplitude (Jeon & Polich, 2001).

Anatomical abnormalities, and more particularly reduction in the volume of gray matter in the left anterior hippocampus-amygdala, the left parahip-pocampal gyrus, and the left superior temporal gyrus, have been observed in schizophrenia (Shenton et al., 1992). In addition, evidences suggest that some structural brain abnormalities in schizophrenia are neurodevelopmen-tal in origin (Weinberger, 1996, 1997). Some authors propose that these anatomical abnormalities could induce the modifications of P300 found in schizophrenia (Blackwood et al., 1991; McCarley et al., 2002). McCarley et al. (1989) found that left Sylvian fissure enlargement, which reflects temporal lobe tissue loss, was highly correlated with a left temporal scalp region feature of the auditory P300 measure (T3 electrode) that differentiated schizophrenics and controls, and that both left Sylvian fissure enlargement and the P300 measure were highly correlated with positive symptoms. The same authors also report that gray matter volume reduction in the left posterior superior temporal gyrus was highly and specifically associated with both P300 amplitude reduction and left topographic asymmetry (McCarley et al., 1993). In contrast, ventricule sizes were not correlated with P300 reduction, although alterations of these structures have been observed in schizophrenia (Juckel, Reischies, Müller-Schubert, Vogel, Gaebel, & Hegerl, 1994).

Epidemiological and genetic studies suggest evidence of predispositions to schizophrenia (Baron, 1986). Consequently, several studies have been conducted on children of schizophrenic patients to find a vulnerability marker of the disease (Bharath, Gangadhar, & Janakiramaiah, 2000; Winterer, Egan, Radler, Coppola, & Weinberger, 2001). Saitoh, Niwa, Hiramatsu, Kayemaya, Rymar, and Itoh (1984) found, during a syllable discrimination task in siblings of schizophrenic probands, that mean amplitudes of the P300 component elicited by target stimuli in the attended channel for siblings were nearly equivalent to those of unmedicated schizophrenics, and that these values in siblings were significantly smaller compared to those of controls. Based on these results, it was concluded that abnormalities of the late positive component in siblings could reflect a genetic predisposition to schizophrenia. Similar findings have been observed in other studies (Blackwood et al., 1991, Ebmeier et al., 1990). Conversely, some studies have not confirmed these results (Friedman, Cornblatt, Vaughan, & Erlenmeyer-Kimling, 1986), and Schreiber, Strolz-Born, Rothmeier, Kornhuber, Kornhuber, and

Born (1991) did not find any differences between children at risk for schizophrenia and controls for P300 amplitude, but reported prolonged P300 latency in children of schizophrenic patients. However, due to the variability of P300 during ontogenesis, it is impossible to conclude from these findings. On the other hand, Bharath et al. (2000) concluded that the P300 findings from families with schizophrenia are too varied to give conclusive statements, because of excessive variability of ERP methodology and sample selections. For these reasons, P300 is not a definitive indicator of risk of schizophrenia.

An interesting question arising from some P300 studies in schizophrenia concerns the "trait" versus "state" status of this biological marker. Rao, Ananthnarayanan, Gangadhar, and Janakiramaiah (1995) found that P300 amplitude was significantly smaller among schizophrenic patients in remission as compared to controls. Moreover, no differences for either P300 amplitude or latency were observed between schizophrenic patients in an acute phase compared to patients in a remitted phase (Blackwood, Whalley, & Christie, 1987; St Clair, Blackwood, & Muir, 1989). Taken together, these findings suggest that P300 is probably a "trait" marker of schizophrenia.

In a recent meta-analysis, Jeon and Polich (2003) tried to identify the factors that contribute to the P300 differences found in schizophrenia compared to controls, in an attempt to characterise the clinically relevant information underlying P300 deficits. The results showed that paranoid symptoms and age of onset were associated with stronger effect sizes, whereas the severity of symptoms, disease duration, and medication status were not. Moreover, a high-pass filter of 0.5 Hz or lower produced smaller P300 amplitude and latency effect sizes than those employing improper higher settings. Indeed, some studies with control subjects have demonstrated that the value of the high-pass filter can considerably alter the P300 amplitude and latency (i.e., reduction of P300 amplitude and delayed P300 latency with filter higher than 0.5 Hz). Lastly, gender proportion, educational level, and stimulus and task variables also seem to affect P300 amplitude and latency effect sizes.

Several data show that the amplitude of the MMN is lower in schizophrenia (Alain, Bernstein, Cortese, Yu, & Zipursky 2002; Javitt, Grochowski, Shelley, & Ritter, 1998; Shelley, Silipo, & Javitt, 1999). Javitt et al. (1998) suggested that the reduction of MMN amplitude reflects sensory memory deficits and could be responsible for later processing. The reason is that since the first steps of information processing (automatic attention, MMN) are altered, the next steps could not work normally. Therefore, it is possible that P300 reduction found in schizophrenia is caused by earlier sensory deficit. However, van der Stelt, Frye, Lieberman, and Belger (2004) showed that high-level attention-dependent cognitive deficits central to schizophrenia did not originate from potential preceding impairments at lower levels of sensory, perceptual, or cognitive processing.

Several studies have demonstrated that patients with schizophrenia are impaired in recognising emotions (Brune, 2005). Some studies have also reported that schizophrenia showed more profound impairment of negative emotion processing than of positive emotion processing (Bell, Bryson, & Lysaker, 1997). This question has been investigated within an ERP paradigm (An et al., 2003). The results showed that P300 amplitudes associated with negative emotional photographs, in normal controls, were significantly larger than those of positive stimuli. Unlike the controls, in patients with schizophrenia, P300 amplitudes generated by negative emotional targets were significantly smaller than those of positive stimuli. These results support previous neurobehavioural studies, in which patients with schizophrenia showed greater impairment in the recognition of negative emotions.

Lastly, a number of researchers have proposed that a failure of internal monitoring of errors contributes to the generation of schizophrenic symptoms. For example, Frith and Done (1989) proposed that failure to monitor self-generated activity contributes to delusions of alien control. Others, such as McGrath (1991), have suggested that failure of the internal monitoring of speech output might contribute to formal thought disorder. Within this line of hypothesis, the recording of ERN/NE in schizophrenia is of interest. Alain, McNeely, He, Christensen, and West (2002) showed that ERN/NE was not present in a S troop paradigm, providing evidence that deficits in error monitoring in schizophrenia arise from a disruption of error-detection processes, possibly attributable to anterior cingulate dysfunction. Other studies have revealed that ERN/NE is reduced in schizophrenia (Bates, Liddle, Kiehl, & Ngan, 2004; Mathalon, Fedor, Faustman, Gray, Askari, & Ford, 2002). Interestingly, Bates et al. (2004) reported that ERN/NE amplitude was significantly reduced in schizophrenic patients when acutely ill, and increased significantly following treatment. Moreover, ERN/NE amplitude remained significantly larger in the healthy group than in the patients with schizophrenia after the treatment. This study suggests that error negativity amplitude is modulated by clinical state in schizophrenia and provides further support for findings that decreased ERN/NE amplitude is a potentially useful trait marker for schizophrenia.

In summary, schizophrenia is characterised by reduced P300 amplitude, which can be considered as a trait marker, but not a genetic one. This alteration of the P300 component could be related to the anatomical

abnormalities found in schizophrenia. P300 is particularly lowered in the left temporal regions. MMN amplitude is also reduced in schizophrenia, suggesting sensory-memory deficits. Lastly, ERN/NE seems to be modulated by the clinical state.

Depression

Since the first study conducted by Levit, Sutton, and Zubin (1973), a number of studies have found reduced P300 amplitude in depression (Blackwood et al., 1987; Diner, Holcomb, & Dyknian, 1985), although others have failed to replicate this finding (Bruder, Towey, Steward, Friedman, Tenke, & Quitkin, 1991; Have, Kolbeinson, & Pétursson, 1991). Some authors suggest that depressed patients exhibit mainly attentional deficits, which influence earlier ERP components (i.e., N100 and N200) (the auditory N100 component presents a central distribution, it is related to selective attention, and the neural substrate is localised over the temporal cortex involving the primary auditory cortex; the N200 component can be thought of as a cortical concomitant of the orienting response with a fronto-central distribution, and whose cortical generators include temporal and frontal cortexes) and that do not interfere with the P300 component (Smith, Banquet, El Massioui, & Widlocher, 1991). Several studies have also reported that P300 latency is not altered in depression (Gangadhar, Ancy, Janakiramaiah, & Umapathy, 1993; Partiot, Pierson, Le Houezec, Dodin, Renault, & Jouvent, 1993), but that reaction time is (Bolz & Giedke, 1981; Diner et al., 1985; El Massioui & Lesèvre, 1988; Thier, Axmann, & Gierdke, 1986). Thus, information processing alterations found in depression could be localised on preparation, selection and motor processes (prolonged reaction time) rather than on later stages of information processing (normal P300 latency).

However, one possible explanation as to why the majority of the studies have not found evidence of any modification of P300 latency in depression could be due to the protocol used, and the clinical sub-types of depressed patients included in these studies. Particularly, when patients were divided into two subgroups, one having a typical major depression (melancholia or simple mood reactive depression) and one having an atypical depression, Bruder et al. (1991), using auditory temporal and spatial discrimination tasks, found that typical depressives had abnormally long P300 latency for the spatial task but not for the temporal one. They also showed an abnormal lateral asymmetry, with longer P300 latency for stimuli in the right hemifield than in the left. In contrast, atypical depressives did not differ from controls.

While the diagnostic criteria proposed by the DSM-IV (American Psychiatric Association, 1994) are very useful for the diagnosis of depression, the heterogeneity of the samples of depressed patients included in the different P300 studies may have obscured effects that could be specific to only a subgroup of depressed patients and thus could be responsible for the controversial results. In this direction, studies have reported that some clinical variables associated with depression have an impact on either P300 latency or amplitude, such as impulsivity, the severity of depression, anhedonia, psychotic symptoms, and suicidal behaviours (Bruder et al., 1991, Gangadhar et al., 1993, Hansenne, Pitchot, Gonzalez Moreno, Urcelay Zaldua, & Ansseau, 1996, Partiot et al., 1993, Pierson, Ragot, van Hooff, Partiot, Renault, & Jouvent, 1996).

Pierson et al. (1991) and Partiot et al. (1993) showed that P300 amplitude was reduced among the retarded and blunted affect depressed patients compared to the anxious-agitated and impulsive depressed patients. Some studies have also shown that P300 amplitude is significantly reduced in depressed patients who had attempted suicide compared with patients who had not (Hansenne et al., 1996). Moreover, a significant correlation was found between P300 amplitude and the suicidal risk scale (Hansenne et al., 1996). It was postulated that the reduction of cortical activity reported in depressed patients with a past history of suicidal attempts reflected the concept of hopelessness and helplessness described in depression and particularly in relation to suicide.

The reduction of P300 amplitude found in several studies is probably related to the clinical state, and thus could be considered as a "state" marker of the disease. Indeed, Blackwood et al. (1987) have shown that P300 amplitude increased after four weeks of antidepressant treatment. Gangadhar et al. (1993) also reported that P300 amplitude significantly increased in depressed patients following recovery from electroconvulsive therapy.

Many studies suggest an impairment of executive control functions in depression (Merriam, Thase, Haas, Keshavan, & Sweeney, 1999). Kaiser, Unger, Kiefer, Markela, Mundt, and Weisbrod (2003) investigated whether depressive patients showed a specific impairment of executive control in a response inhibition task (Go/Nogo task). It was postulated that depressive patients would perform similarly to controls in the Go task, and in contrast, they would perform worse in the Nogo task, which requires response inhibition. Behavioural results showed that depressed patients exhibited lower performance for the Nogo task. Psychophysiological results revealed no differences between depressed and controls within the Go task. In contrast, within the Nogo

task, increasing frontal positivity was found among controls, and parietal activities that resemble the Go task were found in depressed subjects. This deficit is thought to reflect dysfunctional activation of the network subserving executive control during an early stage of cortical processing.

Perceived failure is reported to have detrimental effects on subsequent performance in patients with major depressive disorder (Elliott et al., 1997). Therefore, Ruchsow, Herrnberger, Wiesend, Gron, Spitzer, and Kiefer (2004) investigated the ERN/NE in patients with major depressive disorder in an Eriksen flanker task with continuous performance feedback that signaled monetary reward. Compared to controls, patients with major depressive disorder showed a less negative ERN/NE following error trials. This result might reflect impaired response monitoring processes in major depressive disorder due to hypo-activity in a central reward pathway and/or a deficit in strategic reasoning.

In summary, depression is associated with P300 modifications. P300 amplitude is usually reduced when the patient is ill (state marker), but some clinical features modulate this reduction. P300 latency is only prolonged in some paradigms requiring more attention than the oddball one. ERN/NE amplitude is reduced in depression, suggesting impaired response monitoring processes.

Alcoholism

P300 abnormalities have been reported in alcoholism in several studies. Basically, P300 amplitude is reduced and P300 latency is prolonged (Cohen, Wang, Porjesz, & Begleiter, 1995; Porjesz, Begleiter, Bihari, & Kissin, 1989; Whipple, Berman, & Noble, 1991). The explanation usually given is that alcoholic patients exhibit arousal, attentional, and memory disturbances. However, other studies have failed to report significant differences between alcoholics and controls (Biggins, McKay, Poole, & Fein, 1995; Hill, Locke, & Steinhauer, 1999; Keenan, Freeman, & Harrell, 1997; Steinhauer, Hill, & Zubin, 1987).

Several studies have reported that in adult alcoholics P300 amplitude reduction, but not prolonged P300 latency, could be related to a family history of alcoholism rather than to personal alcohol abuse or consumption history (Begleiter, Porjesz, Bihari, & Kissin, 1984; Porjesz & Begleiter, 1990). Indeed, since the decreased P300 amplitude does not recover with prolonged abstinence, it is unlikely to be related to drinking history but more likely to be genetically influenced (Carlson, Iacono, & McGue, 2002). This is supported by findings showing that P300 amplitudes were reduced in subjects at high-risk for alcoholism compared to subjects at low-risk (Hill & Steinhauer, 1993; Iacono, Carlson, & Malone, 2000; Reese & Polich, 2003). Particularly, the sons of alcoholic fathers have reduced P300 amplitude as elicited by a variety of tasks when compared to the sons of non-alcoholics (Hill, Yuan, & Locke, 1999). Greater effects have been found with difficult tasks involving visual rather than auditory stimuli, and for subjects whose fathers had undergone treatment for alcoholism. In addition to the paternal risk effect, the sons of alcoholic mothers also show reduced P300 amplitude (Hill, Steinhauer, & Locke, 1995). The parental risk effect is seen in high-risk children who have not yet been exposed to the potentially neurotoxic effects of alcohol (Begleiter et al., 1984). However, a comprehensive meta-analysis of at-risk P300 studies indicated that P300 amplitude differences were most evident in young prepubescent male subjects when a difficult visual discrimination task was used. The results in older offspring were more variable, particularly those involving easy auditory tasks (Polich, Pollock, & Bloom, 1994). Since Hill, Locke, et al. (1999) did not report significant differences for P300 amplitude between adult alcoholics and controls, they suggested that P300 amplitude reduction seen in children at high-risk for developing alcoholism seems to represent a neurodevelopmental delay that normalises by adulthood.

While most studies have focused on men, recent studies indicate that women are equally vulnerable to developing alcoholism. Prabhu, Porjesz, Chorlian, Wang, Stimus, and Begleiter (2001) indicated that alcoholic women had significantly smaller P300 amplitudes in the frontal and central regions compared with controls. In another study, alcoholic women had significantly lower P300 amplitude compared to controls, and the reduction of P300 was not associated with depression comorbidity (Suresh et al., 2003). In contrast, Hill, Locke, et al. (1999) reported that female alcoholics showed reduced P300 amplitude only when a comorbid lifetime diagnosis of depression was present.

Using an emotional paradigm, cue-reactivity (P300 peak amplitude elicited by alcohol-related words minus peak amplitude elicited by neutral stimuli) was found in alcohol-dependent patients, but not in controls (Herrmann, Weijers, Wiesbeck, Aranda, Boning, & Fallgatter, 2000). Moreover, increased P300 and decreased N100 amplitudes to alcohol-related pictures as compared to neutral pictures were found in heavy drinkers, but not in light drinkers (Herrmann, Weijers, Wiesbeck, Boning, & Fallgatter, 2001). The increased P300 amplitude could reflect a shift of attention toward alcohol-related stimuli (i.e., more emotional evaluation of these stimuli). In

contrast, with a visual oddball paradigm using alcohol-related words as target stimuli, Hansenne, Olin, Pinto, Pitchot and Ansseau (2003) did not report an impact of alcohol-related words on P300 amplitude, suggesting that alcoholic patients did not allocate more attention to alcohol-related words than controls. However, this study showed that alcoholic men exhibited shorter P300 latency compared to controls, and that alcoholic women had longer P300 latency compared to controls. This suggests that alcoholic men tend to process the information associated with alcohol cues more quickly, implying a facilitation mechanism of an alcoholic semantic network.

Several studies have demonstrated that alcoholics exhibit increased latency of short auditory evoked potentials, such as delayed peak V and an increase in the III-V and I-V intervals of the auditory brainstem potential and increased PIOO latency of visual evoked potential (Cadaveira, Grau, Roso, & Sanchez-Turet, 1991; Chan, Mc Leod, Tuck, Walsh, & Feary, 1986; Nicolas et al., 1997) (the PIOO component is largest over the occipital regions and it represents the activation of the area 17 in the visual cortex). These abnormalities were related to the lifetime consumption of ethanol (Nicolas et al., 1997), and improvement of P100 abnormalities have been found after a period of abstinence (Chan et al., 1986). Consequently, the hypothesis made for schizophrenia, namely that the P300 reduction may be caused by earlier sensory deficit, could also be suggested for alcoholism.

In summary, P300 amplitude is reduced and P300 latency is prolonged in alcoholism, which reflect arousal, attentional, and memory deficits. P300 amplitude reduction could be related to a family history of alcoholism. With emotional paradigm, increased P300 amplitude and reduced latency were observed to alcohol-related pictures or words, suggesting a shift of attention towards alcohol-related stimuli.

Posttraumatic stress disorder

Several ERPs' studies have been published in posttraumatic stress disorder (PTSD) (Orr & Roth, 2000; Pitman, Orr, Shalev, Metzger, & Bellman, 1999). The first study was conducted by McFarlane, Weber and Clark (1993), and the results showed reduced N100 and P300 amplitudes in PTSD patients compared to controls and prolonged P300 latency. Charles et al. (1995) also found lower P300 amplitude in PTSD subjects compared to subjects who were exposed to a traumatic event without developing the disorder. However, the two groups did not differ in terms of P300 latency. Some studies have replicated findings of reduced P300 amplitude in PTSD (Felmingham, Bryant, Kendall, & Gordon, 2002; Metzger, Orr, Lasko, & Pitman, 1997), but others have failed to reproduce this finding (Kimble, Kaloupek, Kaufman, & Deldin 2000; Neylan et al., 2003). Moreover, Felmingham et al. (2002) reported a significant negative correlation between the intensity of numbing symptoms in PTSD patients and P300 amplitude. Neylan et al. (2003) provided evidence for greater variability over time of P300 amplitude in PTSD subjects compared to subjects exposed to a trauma without developing the disorder, and they proposed that this increased variability of P300 amplitude in PTSD subjects could account for the inconsistent findings reported in some P300 studies on PTSD.

Attias, Bleich, Furman and Zinger (1996) recorded visual ERPs in response to three sets of visual stimuli, presented in the form of a modified oddball paradigm, which included domestic animal pictures (targets), emotionally neutral pictures of furnishings (non-targets), and combat-related pictures (non-target probes). Target stimuli elicited enhanced P300 amplitudes in controls and PTSD patients. The non-target combat-related pictures elicited enhanced P300 and N100 amplitudes in the PTSD patients only. N200 amplitudes were also accentuated in PTSD patients for both targets and combat-related pictures, and P300 latency and reaction time to target stimuli were prolonged in PTSD patients. These findings suggested that PTSD is characterised by an altered state of early and late cognitive selective attention processing, in addition to a vulnerability to traumatic reminiscences, as expressed by the higher P300 amplitude for the non-target combat-related stimuli.

Interestingly, Stanford, Vasterling, Mathias, Constans and Houston (2001) reported that the increased P300 amplitude was found only for trauma-stimuli that were relevant for Vietnam veterans with a PTSD diagnosis but not for trauma-stimuli irrelevant for the subjects. In this study, PTSD veterans and veterans without the disorder were presented with two visual oddball tasks (trauma-relevant words, trauma-irrelevant words) counterbalanced for order. Blomhoff, Reinvang and Malt (1998), using a paradigm in which non-words and words with negative or positive emotional valences were used as distractors in an oddball paradigm, reported that PTSD subjects had increased P300 amplitude to both words and non-words compared to controls. Moreover, P300 amplitudes to emotionally meaningful words were significantly related to psychometric assessment of PTSD dimensions, particularly avoidance and arousal.

PTSD is characterised by intrusive memories, avoidance behaviours and hyperarousal. This latter clinical feature enhances attentional processes. Moreover, disturbances in sensory processing have been hypothesised in individuals with PTSD. Within this framework, Morgan and Grillon (1999) recorded the MMN among women

with sexual assault-related PTSD. The results showed that the amplitude of the MMN was significantly greater among PTSD women compared to controls. This study provides evidence for abnormalities in preconscious auditory sensory memory in PTSD, whereas earlier studies have reported abnormalities in conscious processing (i.e., P300 amplitude reduction). These data suggest an increased sensitivity to stimulus changes in PTSD and implicate the auditory cortex in the pathophysiology of the disorder.

In summary, alterations of P300 amplitude and latency have been reported in PTSD. However, the main interesting result is the increased P300 amplitude for trauma-stimuli that are relevant for the subjects. MMN amplitude is also increased, reflecting a greater sensitivity to stimuli changes.

Panic disorder

A central feature of panic disorder is the loss in the capacity to integrate incoming information with a cognitive context. Panic attacks can be triggered in a variety of situations, but most common are those providing complex, unstructured stimulation such as supermarkets and crowds where patients are distracted by salient, but extraneous stimuli. In normal subjects, automatic processing involves an efficient orientation of attention to previously experienced significant stimuli, and a concomitant orientation of attention away from stimuli of low significance. Therefore, Clark, McFarlane, Lee Weber and Battersby (1996) investigated P300 in panic disorder patients and controls during an auditory three-stimuli paradigm. The results showed that P300 amplitude was higher for both infrequent target tones and infrequent tones across frontal and central regions. Based on the topography of the component, the authors suggested that they had identified a P3a sub-component, although they did not distinguish explicitly between P3a and P3b sub-components in their methodology. While accepting this hypothesis, this finding provides evidence of an enhancement of automatic attentional processing (i.e., preconscious stimulus overactivity) in patients suffering from panic disorder. Indeed, higher P3a amplitude suggests that panic disorder involves the processing of stimuli that should have been filtered out at an earlier stage, thereby engaging conscious attention unnecessarily (i.e., inability to filter out stimuli on the basis of their novelty).

In contrast, using a classical auditory oddball paradigm, Iwanami, Isono, Okajima and Kamijima (1997) did not demonstrate any differences between panic disorder patients and controls for P300 amplitude or latency. However, the results revealed that both N100 and N200 amplitudes for target tones and the N100 amplitude for non-target tones were significantly larger in the panic disorder patients than those in the controls, suggesting an alteration of early information processing in panic disorder. Conversely, Turan, Esel, Karaaslan, Basturk, Oguz and Yabanoglu (2002) reported a significant prolongation of P300 latency in a panic disorder group using an auditory oddball paradigm without any differences for earlier components. Moreover, Wang, Miyazato, Randall, Hokama, Hiramatsu and Ogura (2003) found a reduction of the N200 component in female subjects suffering from panic disorder during an active discrimination task, and no differences for the P300 component were described between patients and controls.

In an original study, Pauli et al. (1997) recorded P300 using a visual paradigm in which body-related words and non-somatic words were presented tachistoscopically to panic disorder patients and controls. The results showed that, in panic disorder patients, body related-words as compared with non-somatic words elicited significantly larger P300 amplitudes. These results are consistent with cognitive models of panic disorder, assuming that certain bodily sensations are perceived and processed automatically. In another study, the same group showed that panic patients are characterised by an early automatic and elaborated processing of panic-related stimuli (Pauli, Amrhein, Muhlberger, Dengler, & Wiedemann, 2005).

The contradictory findings observed in the different studies could arise from the possibility that P300 amplitude is unpredictable in panic disorder, with some patients exhibiting higher P300 amplitude whereas other patients showing normal or lower P300 amplitude. Indeed, Gordeev, Ryabokon, Fedotova, Tabeeva and Vein (2003) reported decreased as well as increased P300 amplitude in panic disorder patients. These authors assumed that the decreasing of P300 amplitude could reflect increased activity of the cerebral reticulothalamic structures, while the increasing of P300 amplitude could be associated with the activation of the septohippocampal limbic system. However, the heterogeneity of the subjects included and the differences in the methodology, particularly the inability to distinguish between P3a and P3b sub-components, could explain the discrepancies between the studies. Consequently, no conclusion can be given, and further studies should be conducted to enlarge the findings.

Published in: Psychologica Belgica (2006), vol.46, iss.1-2, pp.5-36.
Status: Postprint (Author's version)

Obsessive-compulsive disorder

Initially, Beech, Ciesielski and Gordon (1983) reported that N200 and P300 amplitudes were reduced in patients suffering from obsessive-compulsive disorder (OCD) compared to controls in a visual paradigm. Moreover, while the latencies of both N200 and P300 components increased with the task difficulty in controls, OCD patients exhibited the opposite pattern. These results suggested that OCD patients did not allocate so much energetical resources or attention towards the task. However, the speed of information processing was accelerated in the clinical group. Towey et al. (1990) aimed to replicate these findings using an auditory oddball paradigm. Their results also showed reductions of N200 and P300 latencies when the task increased in difficulty, but they reported higher N200 amplitudes in OCD patients compared to controls. The N200 component exhibited a left topographical dominance. In another study, the same authors confirmed and extended their previous results by showing a significant correlation between the amplitude of the N200 component and the severity of the OCD assessed by the Yale-Brown scale (Towey et al., 1993).

Miyata, Matsunaga, Kiriike, Iwasaki, Takei and Yamagami (1998) as well as de Groot, Torello, Boutros and Allen (1997) replicated these findings (decreased P300 and N200 latencies, and greater N200 amplitudes in OCD patients compared to controls), whereas Kivircik, Yener, Alptekin, and Aydin (2003) found reduced P300 latencies in OCD patients, but no differences for the N200 component. Kim, Kang, Youn, Kang, Kim and Kwon (2003) also reported reduced P300 in a group of OCD patients without any effects on P300 latency and N200 component, but found that the reduction of P300 amplitude is related to neuropsychological deficit of controlled attention and self-guided, flexible behaviour, which are mediated by the fronto-striatal system.

According to these findings, the reduction of either P300 or N200 latencies in OCD could reflect the possibility that those patients are more efficient as regard to the speed of information processing (i.e., faster information processing). Moreover, the enhancement of the N200 component could suggest that OCD patients are characterised by cortical hyperarousal and overfocused automatic attention, and that they present some difficulties in inhibiting such cognitive processing. Lastly, the left topographical dominance of the N200 component was congruent with brain neuroimaging studies (Baxter, Phelps, Mazziotta, Guze, Schwartz, & Selin, 1987). As regards the general finding of reduced P300 amplitude and prolonged latency in most of the other psychiatric patients, it is outstanding that OCD is one of the few psychiatric diseases characterised by larger P300 amplitude and shorter latency.

It could also be argued that the reduction of P300 latency found in OCD patients could mean that these patients develop a P3a sub-component overlapping with the P3b one. Indeed, hyperactivity in the frontal cortex, leading to acceleration of attentional and cognitive processes, is discussed as a pathogenetic factor in OCD, and P3a could index this dysfunction because this sub-component is mainly generated in frontal regions. Mavrogiorgou et al. (2002) investigated this possibility using a classic auditory oddball paradigm and dipole source analysis to identify the sub-components P3a and P3b. No difference for P3a amplitude between OCD patients and controls was found. However, OCD patients showed larger P3b amplitudes and a shorter P3b latencies.

According to Schwartz (1997), OCD is characterised by the generation of an inappropriate or hyperactive error-detection signal, manifesting phenome-nologically as a feeling that "something is wrong", and thus giving rise to the urge for adjustment. The associated brain circuit comprises the basal ganglia and the anterior cingulate, two brain structures implicated in the generation of ERN/NE. As an initial test of this hypothesis, Gehring, Himle and Nisenson (2000) investigated whether patients with OCD exhibit higher ERN/NE amplitude in a two-choice response task. They found that OCD patients did indeed show increased ERN/NE amplitude. This finding was confirmed by Johannes et al. (2001). In a subsequent study, Hajcak and Simons (2002) found that ERN/NE was significantly larger among college undergraduates with obsessive-compulsive characteristics. However, Nieuwenhuis, Nielen, Mol, Hajcak and Veltman (2005) found that OCD patients and healthy controls did not differ in the amplitude of the ERN/NE associated with errors and negative feedback in a probabilistic learning task. Methodological differences between the studies could explain the discrepancies. Indeed, in the study of Nieuwenhuis et al. (2005), participants received feedback at the end of each trial, and it is possible that OCD patients experienced this as reassuring, and consequently reduced the response-monitoring system. No feedbacks were delivered in the previous studies. Moreover, the severity of the OCD patients was higher in the study of Nieuwenhuis et al. (2005).

In summary, OCD is characterised by reduction of either P300 or N200 latencies suggesting that those patients are more efficient as regard to the speed of information processing. Moreover, the increased ERN/NE in OCD confirms a hyperactive error-detection process among this disorder.

Conclusions

After reviewing the main findings of ERPs' studies in major psy-chopathological disorders, what conclusions can be drawn? First, it should be noted that several controversial results have been reported. Concerning the P300 component, after the first promising studies, successive findings revealed that the problem was complex, and consequently, the enthusiasm that P300 would become a convincing biological marker of psychopatholog-ical disorders gradually disappeared. Nevertheless, before developing arguments to explain the potential sources of discrepancies, we can summarise the robust findings: P300 amplitude reduction in schizophrenia, with a left temporal reduction; P300 amplitude reduction and P300 latency prolongation in alcoholism; P300 amplitude enhancement in PTSD with stimuli recalling the traumatism; P300 amplitude enhancement in panic disorder; P300 amplitude enhancement and shortened P300 latency in OCD. One can reasonably argue that while attentional mechanisms, memory, and more generally cognitive functions are disturbed in psychopathological disorders, it is consequently logical to find a reduction of P300 amplitude and a prolongation of P300 latency in these clinical affections.

Different reasons could be stressed to explain the contradictory findings. As already mentioned, the diversity of ERP methodologies and the heterogeneity of the patient samples, as well as individual variables such as gender, age, the severity of the symptoms, and medication, are implicated to the incongruent findings. The inability to distinguish between P3a and P3b subcomponents contribute probably also to the weak diagnostic value of this biological marker. It should be noted that this distinction is not always possible using the classic oddball paradigm, and that the use of more complex paradigms, or just a three-stimuli paradigm, is more adequate. Particularly, Polich (2004) argued that the use of reliable P3a paradigms in conjunction with P3b tasks promises dramatically to augment the applicability and sensitivity of ERPs.

The diagnosis usefulness of P300 in psychopathology is thus limited, but this statement is not so unanticipated. Indeed, given the complexity and richness of psychopathological disorders, it would be illusive to reduce a psychiatric disorder to an electric phenomenon. However, different facts may temper this negative conclusion. First, as Polich has explained exhaustively in several articles (Polich, 1998, 2004; Polich & Herbst, 2000), P300 brain potential can provide information about cognition that is quantitatively comparable to other clinically used biomedical assays. When appropriate procedures are used, the P300 can provide a highly useful means to quantify human cognitive aptitudes.

Besides the diagnostic usefulness of P300, a growing number of studies have provided evidence of the relevance of P300 to investigate cognitive processes in clinical psychopathology. Lastly, the MMN and ERN/NE components are useful tools to assess psychopathological disorders. Almost certainly, grouping two or more different ERP components would greatly improve the clinical usefulness of brain potentials.

Acknowledgements

Many thanks to Frank Larøi for his useful comments on a previous version of the mansucript

References

Alain, C, Bernstein, L.J., Cortese, R, Yu, H., & Zipursky, R.B. (2002). Deficits in automatically detecting changes in conjunction of auditory features in patients with schizophrenia. *Psychophysiology, 39,* 599-606.

Alain, C, McNeely, H.E., He, Y., Christensen, B.K., & West, R. (2002). Neurophysiological evidence of error-monitoring deficits in patients with schizophrenia. *Cerebral Cortex, 12,* 840-846.

Alho, K., Winkler, I., Escera, C, Huotilainen, M., Virtanen, J., Jaaskelainen, I.R, Pekkonen, E., & Ilmoniemi, R.J. (1998). Processing of novel sounds and frequency changes in the human auditory cortex: magnetoencephalographic recordings. *Psychophysiology, 35,* 211-224.

American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders, Fourth edition (DSM-IV).* Washington: American Psychiatric Press.

An, S.K., Lee, S.J., Lee, C.H., Cho, H.S., Lee, P.G., Lee, C.I., Lee, E., Roh, K.S., & Namkoong, K. (2003). Reduced P3 amplitudes by negative facial emotional photographs in schizophrenia. *Schizophrenia Research, 64,* 125-135.

Attias, J., Bleich, A., Furman, V., & Zinger, Y. (1996). Event-related potentials in posttraumatic stress disorder of combat origin. *Biological Psychiatry, 40,* 373-381.

Baron, M. (1986). Genetics in schizophrenia, II: vulnerability traits and gene markers. *Biological Psychiatry, 21,* 1189-1211.

Bauer, L., Hesselbrock, V.M., O'Connor, S., & Roberts, L. (1994). P300 differences between non-alcoholic young men at average and above-average risk for alcoholism: effects of distraction and task modality. *Progress in Neuropsychopharmacology and Biological Psychiatry, 18,* 263-277.

Bates, A.T., Liddle, P.E, Kiehl, K.A., & Ngan E.T. (2004). State dependent changes in error monitoring in schizophrenia. *Journal of Psychiatric Research, 38,* 347-356.

Baxter, L.R., Phelps, M.E., Mazziotta, J.C., Guze, B.H., Schwartz, J.M., & Selin C.E. (1987). Local cerebral glucose metabolic rates in obsessive-compulsive disorder: a comparison with rates in unipolar depression and normal controls. *Archives of General Psychiatry, 44,* 211-218.

Beech, H.R., Ciesielski, K.T., & Gordon, P.K. (1983). Further observations of evoked potential in obsessional patients. *British Journal of Psychiatry, 142,* 605-609.

Begleiter, H., Porjesz, B., Bihari, B., & Kissin, B. (1984). Event-related brain potentials in boys at risk for alcoholism. *Science, 225,* 1493-1496.

Bell, M., Bryson, G, & Lysaker, P., (1997). Positive and negative affect recognition in schizophrenia: a comparison with substance abuse and normal control subjects. *Psychiatry Research, 73,* 73-82.

Bharath, S., Gangadhar, B.N., & Janakiramaiah, N. (2000). P300 in family studies of schizophrenia: review and critique. *International Journal of Psychophysiology, 38,* 43-54.

Biggins, C.A., McKay, S., Poole, N., & Fein, G. (1995). Delayed P3a in abstinent elderly male chronic alcoholics. *Alcoholism-Clinical and Experiment Research, 19,* 1032-1042.

Biggins, C.A., McKay, S., Clark, W., & Fein, G. (1997). Event-related potential evidence for frontal cortex effects of chronic cocaine dependence. *Biological Psychiatry, 42:* 472-485.

Blackwood, D.H.R., St Clair, D.M., & Kutcher, S.P. (1986). P300 eventrelated potential abnormalities in borderline personality disorder. *Biological Psychiatry, 21,* 560-564.

Blackwood, D.H.R., Whalley, L.J.O., & Christie, J.E. (1987). Changes in auditory P3 Event-Related Potential in schizophrenia and depression. *British Journal of Psychiatry, 150,* 154-160.

Blackwood, D.H.R, Young, A.H., McQueen, J.K., Martin, M.J., Roxborough, H.M., Muir, W.J., St Clair, D.M., & Kean, D.M. (1991). Magnetic resonance imaging in schizophrenia: altered brain morphology associated with P300 abnormalities and eye tracking dysfunction. *Biological Psychiatry, 30,* 753-759.

Blomhoff, S., Reinvang, I., & Malt, U.F. (1998). Event-related potentials to stimuli with emotional impact in posttraumatic stress patients. *Biological Psychiatry, 44,* 1045-1053.

Bolz, J., & Giedke, H. (1981). Controllability of an adverse stimulus in depressed patients and healthy controls: a study using slow brain potentials. *Biological Psychiatry, 16,* 441-452. Brecher, M., & Begleiter, H. (1983). Event-related brain potentials to high incentive stimuli in unmedicated schizophrenic patients. *Biological Psychiatry, 18,* 661-674.

Bruder, G.E., Towey, J.P, Stewart, J.W., Friedman, D., Tenke, C, & Quitkin, F.M. (1991). Event-related potentials in depression: influence of task, stimulus hemi-field and clinical features on P3 latency. *Biological Psychiatry,* 30, 233-246.

Brune, M. (2005). Emotion recognition, 'theory of mind,' and social behavior in schizophrenia. *Psychiatry Research, 133,* 135-147.

Cadaveira, E, Grau, C, Roso, M., & Sanchez-Turet, M. (1991). Multimodality exploration of event-related potentials in chronic alcoholics. *Alcoholism-Clinical and Experiment Research, 15,* 607-611.

Carlson, S.R., Iacono, W.G., & McGue, M. (2002). P300 amplitude in adolescent twins discordant and concordant for alcohol use disorders. *Biological Psychology, 61,* 203-227.

Chan, Y.W., McLeod, J.G., Tuck, R.R., Walsh, J.C., & Feary, P. A. (1986). Visual evoked responses in chronic alcoholics. *Journal of Neurology, Neurosurgery and Psychiatry, 49,* 945-950.

Charles, G, Hansenne, M., Pitchot, W., Ansseau, M., Machowsky, R., Schittecatte, M., & Wilmotte, J. (1995). P300 in posttraumatic stress disorder. *Neuropsychobiology, 32, 72-74.*

Clark, C.R., McFarlane, A.C., Lee Weber, D., & Battersby, M. (1996). Enlarged frontal P300 to stimulus change in panic disorder. *Biological Psychiatry, 39,* 845-856.

Cohen, H.L., Wang, W., Porjesz, B., & Begleiter, H. (1995). Auditory P300 in young alcoholics: regional response characteristics. *Alcoholism-Clinical and Experiment Research, 19,* 469-475.

Courchesne, E. Hillyard, S.A., & Galambos, R. (1975). Stimulus novelty, task relevance and the visual evoked potential in man. *Electroencephalography and Clinical Neurophysiology, 39,* 131-143.

Costa, L., Bauer, L., Kuperman, S., Porjesz, B., O'Connor, S., Hesselbrock, V., Rohrbaught, J, & Begleiter, H. (2000). Frontal P300 decrements, alcohol dependence, and antisocial personality disorder. *Biological Psychiatry, 47,* 1064-1071.

de Groot, CM., Torello, M.W., Boutros, N.N., & Allen, R. (1997). Auditory event-related potentials and statistical probability mapping in obsessive-compulsive disorder. *Clinical Electroencephalography, 28,* 148-154.

Deouell, L.Y., Bentin, S., & Giard, M.-H. (1998). Mismatch negativity in dichotic listening: evidence for interhemispheric differences and multiple generators. *Psychophysiology, 35,* 355-365.

Desmedt, J.E. (1980). P300 in serial tasks: an essential post-decision closure mechanism. *Progress in Brain Research, 54,* 682-686.

Desmedt, J.E., Debrecker, J., & Manil, J. (1965). Mise en evidence d'un signe élec-trique cérébral associé à la détection par le sujet d'un stimulus sensoriel tactile. *Bulletin de l'Académie Royale de Médecine de Belgique, 5,* 887-936.

Diner, C.B., Holcomb, P.J., & Dykman, R.A. (1985). P300 in major depressive disorder. *Psychiatry Research, 15,* 175-184.

Donchin, E. & Coles, M.G.H. (1988). Context updating and the P300. *Behavioral and Brain Sciences, 21,* 149-154.

Duncan, C.C. (1988). Event-related brain potentials: a window in information processing in schizophrenia. *Schizophrenia Bulletin, 14,* 199-203.

Duncan, C.C, Morihisa, J.M., Fawcet, R.W., & Kirch, D.G. (1987). P300 in schizophrenia: State or trait marker? *Psychopharmacological Bulletin, 23,* 497-501.

Ebmeier, K.P, Potter, D.D., Cochrane, R.H.B., Mackenzie, A.R., MacAllister, H., Besson, J.A.O., & Salzen, E.A. (1990). P300 and smooth eye pursuit: concordance of abnormalities and relation to clinical features in DSM-III schizophrenia. *Acta Psychiatrica Scandinavia, 82,* 283-288.

Elliott, R., Baker, S., Rogers, R., O'Leary, D., Paykel, E., Frith, C, Dolan, R., & Sahakian, B. (1997). Prefrontal dysfunction in depressed patients performing a complex planning task: A study using positron emission tomography. *Psychological Medicine, 27,* 931-942.

El Massioui, F. & Lesévre, N. (1988). Attention impairment and psychomotor retardation in depressed patients: an event-related potential study. *Electroencephalography and Clinical Neurophysiology, 70,* 46-55.

Falkenstein, M., Hoormann, J., Christ, S., & Hohnsbein, J. (2000). ERP components on reaction errors and their functional significance: a tutorial. *Biological Psychology, 51,* 87-107.

Falkenstein, M., Hohnsbein, J., Hoormann, J., & Blanke L. (1990). Effects of errors in choice reaction tasks on the ERP under focused and divided attention. In C.H.M. Brunia, A.W.K. Gaillard, & Kok, A. (Eds.), *Psychophysiological Brain Research,* (pp. 192-195). Tilburg, Tilburg University Press.

Faux, S.F., McCarley, R.W., Nestor, P.G., Shenton, M.E., Pollak, S.D., Penhune, V., Mondrow, E., Marcy, B., Peterson, A., Horvath, T., & Davis, K.L. (1993). P300 topographic asymmetries are present in unmedicated schizophrenics. *Electroencephalography and Clinical Neurophysiology, 88,* 32-41.

Faux, S.F., Shenton, M.E., McCarley, R.W., Nestor, P.G., Marcy, B., & Ludwig, A. (1990). Preservation of P300 event-related potential topographic asymmetries in schizophrenia with use of either linked ear or nose reference sites. *Electroencephalography and Clinical Neurophysiology, 75,* 378-391.

Felmingham, K.L., Bryant, R.A., Kendall, C, & Gordon, E. (2002). Event-related potential dysfunction in posttraumatic stress disorder: the role of numbing. *Psychiatry Research, 109,* 171-179.

Ford, J.M. (1999). Schizophrenia: the broken P300 and beyond. *Psychophysiology,* 36, 667-682.

Ford, J.M., Mathalon, D.H., White, P.M., & Pfefferbaum, A. (2000). Left temporal deficit of P300 in patients with schizophrenia: effects of task. *International Journal of Psychophysiology, 38,* 71-79.

Ford, J.M., White, P., Lim, K.O., & Pfefferbaum, A. (1994). Schizophrenics have fewer and smaller P300s: a single-trial analysis. *Biological Psychiatry, 35,* 96-103.

Friedman, D., Cornblatt, B., Vaughan, H.G., & Erlenmeyer-Kimling, L. (1986). Event-related potentials in children at risk for schizophrenia during two versions of the continuous performance test. *Psychiatry Research, 18,* 161-177.

Frith, C.D., & Done, D.J. (1989). Experiences of alien control in schizophrenia reflect a disorder in the central monitoring of action. *Psychological Medicine, 19,* 359-363.

Gangadhar, B.N., Ancy, J., Janakiramaiah, N., & Umapathy, C. (1993). P300 amplitude in non-bipolar, melancholic depression. *Journal of Affective Disorders, 28,* 57-60.

Gehring, W.J., Coles, M.G.H., Meyer, D.E., & Donchin, E. (1990). The error-related negativity: an event-related brain potential accompanying errors. *Psychophysiology, 27,* S34.

Gehring, W.J., Goss, B., Coles, M.G.H., Meyer, D.E., & Donchin, E. (1993). A neural system for error detection and compensation. *Psychological Science, 4,* 385-390.

Gehring, W.J., Himle, J., & Nisenson, L.G. (2000). Action-monitoring dysfunction in obsessive-compulsive disorder. *Psychological Science, 11,* 1-6.

Giard, M-H., Perrin, E, Pernier, J., & Bouchet, P. (1990). Brain generators implicated in the processing of auditory stimulus deviance: a topographic event-related potential study. *Psychophysiology, 27,* 627-640.

Gordeev, S.A., Ryabokon, I.V., Fedotova, A.V., Tabeeva, G.R., & Vein, A.M. (2003). Evaluation of nonspecific brain systems in patients with panic disorders by the method of P300 cognitive evoked potentials. *Bulletin of Experimental Biology and Medicine, 136,* 522-524.

Hajcak, G, & Simons, R.F. (2002). Error-related brain activity in obsessive-compulsive undergraduates. *Psychiatry Research, 110,* 63-72.

Hansenne, M., Olin, C, Pinto, E., Pitchot, W., & Ansseau, M. (2003). Event-Related Potentials to emotional and neutral stimuli in alcoholism. *Neuropsychobiology, 48,* 77-81.

Hansenne, M., Pitchot, W., Gonzalez Moreno, A., Urcelay Zaldua, I., & Ansseau M. (1996). Suicidal behavior in depressive disorder: an event-related potential study. *Biological Psychiatry, 40,* 116-22.

Have, G, Kolbeinson, H., & Pétursson, H. (1991). Dementia and depression in old age: psychophysiological aspects. *Acta Psychiatrica Scandinavia, 83,* 329-333.

Heinz, G, & Emser, W. (1987). The P300 component of event-related potentials in schizophrenic patients. *Neurophysiologie Clinique, 17,* 193-201.

Herrmann, M.J., Weijers, H.G., Wiesbeck, G.A., Aranda, D., Boning, J., & Fallgatter, A.J. (2000). Event-related potentials and cue-reactivity in alcoholism. *Alcoholism-Clinical and Experimental Research, 24,* 1724-1729.

Herrmann, M.J., Weijers, H.G., Wiesbeck, G.A., Boning, J., & Fallgatter, A.J. (2001). Alcohol cue-reactivity in heavy and light social drinkers as revealed by event-related potentials. *Alcohol Alcoholism, 36,* 588-593.

Hill, H., & Weisbrod, M. (1999). The relationship between asymmetry and amplitude of the P300 field in schizophrenia. *Clinical Neurophysiology, 110,* 1611-1617.

Hill, S.Y., & Steinhauer, S.R. (1993). Assessment of prepubertal and post pubertal boys and girls at risk for developing alcoholism with P300 from a visual discrimination task. *Journal of Studies on Alcohol, 54,* 350-358.

Hill, S.Y., Locke, J., & Steinhauer, S.R. (1999). Absence of visual and auditory P300 reduction in nondepressed male and female alcoholics. *Biological Psychiatry, 46,* 982-989.

Hill, S.Y., Steinhauer, S.R., & Locke, J. (1995). Event-related potentials in alcoholic men, their high-risk male relatives, and low-risk male controls. *Alcoholism-Clinical and Experimental Research, 19,* 567-576.

Hill, S.Y., Yuan, H., & Locke, J. (1999). Path analysis of P300 amplitude of individuals from families at high and low-risk for developing alcoholism. *Biological Psychiatry, 45,* 346-359.

Holinger, D.P, Faux, S.F., Shenton, M.E., Sokol, N.S., Seiman, L.J., Green, A.I., & McCarley, R.W. (1992). Reversed temporal region asymmetries of P300 topography in left and right-handed schizophrenic subjects. *Electroencephalography and Clinical Neurophysiology, 84,* 532-537.

Iacono, W.G., Carlson, S.R., & Malone, S.M. (2000). Identifying a multivariate endophenotype for substance use disorders using psychophysiological measures. *International Journal of Psychophysiology, 38,* 81-96.

Iacono, W.G., Malone, S.M., & McGue, M. (2003). Substance use disorders, externalizing psychopathology, and P300 event-related potential amplitude. *International Journal of Psychophysiology, 48,* 147-178.

Iwanami, A., Isono, H., Okajima, Y, & Kamijima, K. (1997). Auditory event-related potentials in panic disorder. *European Archives Psychiatry Clinical Neuroscience, 247,* 107-111.

Javitt, D.C., Grochowski, S., Shelley, A.M., & Ritter, W. (1998). Impaired mismatch negativity (MMN) generation in schizophrenia as a function of stimulus deviance, probability, and interstimulus/interdeviant interval. *Electroencephalography and Clinical Neurophysiology, 108,* 143-153.

Jeon, Y.W., & Polich, J. (2001). P300 asymmetry in schizophrenia: a meta-analysis. *Psychiatry Research, 104,* 61-74.

Jeon, Y.M., & Polich, J. (2003). Meta-analysis of P300 and schizophrenia: patients, paradigms, and practical implications. *Psychophysiology,* 40, 684-701.

Johnson, R. (1986). A triarchic model of P300 amplitude. *Psychophysiology, 23,* 67-84.

Johnson, R. (1993). On the neural generators of the P300 component of the event-related potential. *Psychophysiology, 30,* 90-97.

Johannes, S., Wieringa, B.M., Nager, W., Rada, D., Dengler, R., Emrich, H.M., Münte, T.F., & Dietrich, D.E. (2001). Discrepant target detection and action monitoring in obsessive-compulsive disorder. *Psychiatry Research, 108,* 101-110.

Juckel, G., Reischies, F.M., Müller-Schubert, A., Vogel, A.C., Gaebel, W., & Hegerl, U. (1994). Ventricle size and P300 in schizophrenia. *European Archives of Psychiatry and Clinical Neuroscience, 243,* 352-354.

Kaiser, S., Unger, J., Kiefer, M., Markela, J., Mundt, G, & Weisbrod, M. (2003). Executive control deficit in depression: event-related potentials in a Go/Nogo task. *Psychiatry Research, 122,* 169-184.

Kalus, O., Horvath, T.B., Peterson, A., Cocarro, E.R, Mitropoulou, V., Davidson, M., Davis, K.L., & Siever, L.J. (1991). Event-related potentials in schizotypal personality disorder and schizophrenia. *Biological Psychiatry, 29,* 137.

Keenan, J.P., Freeman, PR, & Harrell R. (1997). The effects of family history, sobriety length, and drinking history in younger alcoholics on P300 auditory-evoked potentials. *Alcohol Alcoholism, 32,* 233-239.

Kemner, C, van der Gaag, R.J., Verbaten, M., & van Engeland, H. (1999). ERP differences among subtypes of pervasive developmental disorders. *Biological Psychiatry, 46,* 781-789.

Kim, M.S., Kang, S.S., Youn, T., Kang, D.H, Kim, J.J., & Kwon, J.S. (2003). Neuropsychological correlates of P300 abnormalities in patients with schizophrenia and obsessive-compulsive disorder. *Psychiatry Research, 123,* 109-123.

Kimble, M., Kaloupek, D., Kaufman, M., & Deldin, P. (2000). Stimulus novelty differentially affects attentional allocation in PTSD. *Biological Psychiatry, 47,* 880-890.

Kivircik, B.B., Yener, G.G., Alptekin, K., & Aydin, H. (2003). Event-related potentials and neuropsychological tests in obsessive-compulsive disorder. *Progress in Neuropsychopharmacology and Biological Psychiatry, 27,* 601-606.

Kok, A. (1990). Internal and external control: a two factors model of amplitude change of event-related potentials. *Acta Psychologica, 74,* 203-36.

Kouri, E.M., Lukas, S.E., & Mendelson, J.H. (1996). P300 assessment of opiate and cocaine users: effects of detoxification and buprenorphine treatment. *Biological Psychiatry, 40,* 617-628.

Kutas, M., McCarthy, G, & Donchin, E. (1977). Augmenting mental chronometry: the P300 as a measure of stimulus evaluation time. *Science, 197,* 792-795.

Kutcher, S.P, Blackwood, D.H.R., Gaskell, D.E, Muir, W.J., & St Clair, D. (1989). Auditory P300 does not differentiate borderline personality disorder from schizotypical personality disorder. *Biological Psychiatry, 26, 766-774.*

Kutcher, S.P, Blackwood, D.H.R., St Clair, D., Gaskell, D.E, & Muir, W.J. (1987). Auditory P300 in borderline personality disorder and schizophrenia. *Archives of General Psychiatry, 44,* 645-650.

Levit, R. A., Sutton, S., & Zubin, J. (1973). Evoked potential correlates of information processing in psychiatric patients. *Psychological Medicine, 3, 487-494.*

Lotspeich, L.J, & Ciaranello, R,.D. (1993). The neurobiology and genetics of infantile autism. *International Review of Neurobiology, 35,* 87-129.

Mathalon, D.H., Fedor, M., Faustman, W.O., Gray, M., Askari, N., & Ford, J.M. (2002). Response-monitoring dysfunction in schizophrenia: an event-related brain potential study. *Journal of Abnormal Psychology, 111,* 22-41.

Mavrogiorgou, P., Juckel, G, Frodl, T, Gallinat, J., Hauke, W., Zaudig, M., Dammann, G., Moller, H.J., & Hegerl, U. (2002). P300 subcomponents in obsessive-compulsive disorder. *Journal of Psychiatric Research, 36,* 399-406.

McCarley, R.W., Faux, S.F., Shenton, M., Le May, M., Cane, M., Ballinger, R., & Duffy, FG. (1989). CT abnormalities in schizophrenia: a preliminary study of their correlation with P300/N200 electrophysiological features and positive/negative symptoms. *Archives of General Psychiatry, 46,* 698-708.

McCarley, R.W., Salisbury, D.F., Hirayasu, Y., Yurgelun-Todd, D.A., Tohen, M., Zarate, C, Kikinis, R., Jolesz, F.A., & Shenton, M.E. (2002). Association between smaller left posterior superior temporal gyrus volume on magnetic resonance imaging and smaller left temporal

P300 amplitude in first-episode schizophrenia. *Archives of General Psychiatry, 59,* 321-331.

McCarley, R.W., Shenton, M.E., O'Donnell, B.F., Faux, S.F., Kikinis, R., Nestor, P.G., & Jolesz, F.A. (1993). Auditory P300 abnormalities and left posterior superior temporal gyrus volume reduction in schizophrenia. *Archives of General Psychiatry, 50,* 190-197.

McCarthy, G., & Donchin, E. (1981). A metric for thought: a comparison of P300 latency and reaction time. *Science, 211,* 77-80.

McFarlane, A.C., Weber, D.L., & Clark, C.R. (1993). Abnormal stimulus processing in posttraumatic stress disorder. *Biological Psychiatry, 34,* 311-320.

McGrath, J. (1991). Ordering thoughts on thought disorder. *British Journal of Psychiatry, 158,* 307-316.

Merriam, E.P, Thase, M.E., Haas, G.L., Keshavan, M.S., Sweeney, J.A. (1999). Prefrontal cortical dysfunction in depression determined by Wisconsin Card Sorting Test performance. *American Journal of Psychiatry, 156,* 780-782.

Metzger, L.J., Orr, S.P, Lasko, N.B., & Pitman, R.K. (1997). Auditory event-related potentials to tone stimuli in combat-related posttraumatic stress disorder. *Biological Psychiatry, 42,* 1006-1015.

Miyata, A., Matsunaga, H., Kiriike, N., Iwasaki, Y., Takei, Y., & Yamagami S. (1998). Event-related potentials in patients with obsessive-compulsive disorder. *Psychiatry and Clinical Neurosciences, 52,* 513-518.

Morgan, C.A., & Grillon, C. (1999). Abnormal mismatch negativity in women with sexual assault-related posttraumatic stress disorder. *Biological Psychiatry, 45,* 827-832.

Näätänen, R. (1990). The role of attention in auditory information processing as revealed by event-related potentials and other brain measures of cognitive function. *Behavioral and Brain Sciences, 13,* 201-288.

Näätänen, R. (1995). The mismatch negativity—a powerful tool for cognitive neuro-science. *Ear and Hearing, 16,* 6-18.

Näätänen, R. (2001). The perception of speech sounds by the human brain as reflected by the mismatch negativity (MMN) and its magnetic equivalent (MMNm). *Psychophysiology, 38,* 1-21.

Näätänen, R., & Gaillard, A. W. K. (1983). The orienting reflex and the N2 detection of the event-related potentials (ERP). In A. W. K. Gaillard & W. Ritter (Eds.), *Tutorials in event related potential research: endogenous components* (pp. 119-141). Amsterdam: North Holland.

Näätänen, R., Gaillard, A. W. K., & Mantysalo, S. (1978). Early selective-attention effect on evoked potential reinterpreted. *Acta Psychologia, 42,* 313-329.

Neylan, T.C., Jasiukaitis, P.A., Lenoci, M., Scott, J.C., Metzler, T.J., Weiss, D.S., Schoenfeld, KB., & Marmar, C.R. (2003). Temporal instability of auditory and visual event-related potentials in posttraumatic stress disorder. *Biological Psychiatry, 53,* 216-225.

Nicolas, J.M., Estruch, R., Salamero, M., Orteu, N., Fernandez-Sola, J., Sacanella, E., & Urbano-Marquez, A. (1997). Brain impairment in well-nourished chronic alcoholics is related to ethanol intake. *Annals of Neurology, 41,* 590-598.

Nieuwenhuis, S., Nielen, M.M., Mol, N., Hajcak, G., & Veltman, D.J. (2005). Performance monitoring in obsessive-compulsive disorder. *Psychiatry Research, 134,* 111-122.

Orr, S.P., & Roth, W.T. (2000). Psychophysiological assessment: Clinical applications for PTSD. *Journal of Affective Disorders, 61,* 225-240.

Papageorgiou, C.C., Liappas, I.A., Ventouras, E.M., Nikolaou, C.C., Kitsonas, E.N., Uzunoglu, N.K., & Rabavilas, A.D. (2004). Long-term abstinence syndrome in heroin addicts: indices of P300 alterations associated with a short memory task. *Progress in Neuropsychopharmacology and Biological Psychiatry, 28,* 1109-1115.

Partiot, A., Pierson, A., Le Houezec, J., Dodin, V., Renault, B., & Jouvent, R. (1993). Loss of automatic processes and blunted-affect in depression: a P3 study. *European Psychiatry, 8,* 309-318.

Pass, H.L., Klorman, R., Salzman, L.F., Klein, R.H., & Kaskey, G.B. (1980). The late positive component of the evoked response in acute schizophrenics during a test of sustained attention. *Biological Psychiatry, 15,* 9-20.

Pauli, P., Amrhein, C, Muhlberger, A., Dengler, W., & Wiedemann, G. (2005). Electrocortical evidence for an early abnormal processing of panic-related words in panic disorder patients. *International Journal of Psychophysiology, 57,* 33-41.

Pauli, P., Dengler, W., Wiedemann, G., Montoya, P., Flor, PL, Birbaumer, N, & Buchkremer, G. (1997). Behavioral and neurophysiological evidence for altered processing of anxiety-related words in panic disorder. *Journal of Abnormal Psychology, 106,* 213-220.

Pfefferbaum, A., Ford, J.M., White, P.M., & Roth, W.T. (1989). P3 in schizophrenia is affected by stimulus modality, response requirements, medication status, and negative symptoms. *Archives of General Psychiatry, 46,* 1035-1044.

Pfefferbaum, A., Wenegrat, B.G., Ford, J.M., Roth, W.T, & Kopell, B.S. (1984). Clinical application of P3 component of event-related potentials II. Dementia, depression and schizophrenia. *Electroencephalography and Clinical Neurophysiology, 59,* 104-124.

Picton, T.W. (1992). The P300 wave of the human event-related potential. *Journal of Clinical Neurophysiology, 9,* 456-479.

Picton, T. W., Alain, C, Otten, L., Ritter, W., & Achim, A. (2000). Mismatch negativity: different water in the same river. *Audiology and Neuro-Otology, 5,* 111-139.

Pierson, A., Partiot, A., Ammar, S., Dodin, V., Loas, G, Jouvent, R., & Renault, B. (1991). ERP differences between anxious-impulsive and blunted-affect depressive inpatients. In M. Ansseau, R. von Frenckell, & G. Frank (Eds.), *Biological markers of depression: State of the art* (pp. 121-129). Amsterdam: Elsevier.

Pierson, A., Ragot, R., van Hooff, J., Partiot, A., Renault, B., & Jouvent R. (1996). Heterogeneity of information-processing alterations according to dimensions of depression: An event-related potentials study. *Biological Psychiatry, 40,* 98-115.

Pitman, R.K., Orr, S.P., Shalev, A.Y., Metzger, L.J., & Bellman, T.A. (1999). Psychophysiological alterations in post-traumatic stress disorder. *Seminars in Clinical Neuropsychiatry, 4,* 234-241.

Polich, J. (1998). P300 clinical utility and control of variability. *Journal of Clinical Neurophysiology, 15,* 14-33.

Polich, J. (2000). Introduction. *International Journal of Psychophysiology, 38,* 1-2.

Polich, J. (2004). Clinical application of the P300 event-related brain potential. *Physical Medicine and Rehabilitation Clinics of North America, 15,* 133-161.

Polich, J., & Herbst, K.L. (2000). P300 as a clinical assay: rationale, evaluation, and findings. *International Journal of Psychophysiology, 38,* 3-19.

Polich, J., Pollock, V.E., & Bloom, RE. (1994). Meta-analysis of P300 amplitude from males at risk for alcoholism. *Psychological Bulletin, 115,* 55-73.

Porjesz, B., & Begleiter, H. (1990). Event-related potentials in individuals at risk for alcoholism. *Alcohol,* 7, 465-469.

Porjesz, B., Begleiter, H., Bihari, B., & Kissin, B. (1989). Event-related brain potentials to high incentive stimuli in abstinent alcoholics. *Alcohol, 4,* 283-287.

Prabhu, V.R., Porjesz, B., Chorlian, D.B., Wang, K., Stimus, A., & Begleiter, H. (2001). Visual P3 in female alcoholics. *Alcoholism-Clinical and Experimental Research, 25,* 531-539.

Rao, K.M., Ananthnarayanan, C.V., Gangadhar, B.N., & Janakiramaiah, N.S. (1995). Smaller auditory P300 amplitude in schizophrenics in remission. *Neuropsychobiology, 32, 171-174.*

Reese, C, & Polich, J. (2003). Alcoholism risk and the P300 event-related brain potential: modality, task, and gender effects. *Brain and Cognition, 53,* 46-57.

Rinne, T., Alho, K., Ilmoniemi, R. J., Virtanen, J., & Näätänen, R. (2000). Separate time behaviors of the temporal and frontal mismatch negativity sources. *Neuroimage, 12,* 14-19.

Roth, W.T., & Cannon, E.H. (1972). Some features of the auditory evoked response in schizophrenics. *Archives of General Psychiatry, 27,* 466-471.

Ruchsow, M., Herrnberger, B., Wiesend, C, Gron, G., Spitzer, M., & Kiefer, M. (2004). The effect of erroneous responses on response monitoring in patients with major depressive disorder: a study with event-related potentials. *Psychophysiology, 41,* 833-840.

St Clair, D., Blackwood, D., & Muir, W. (1989). P300 abnormality in schizophrenic subtypes. *Journal of Psychiatric Research, 23,* 49-55.

Saitoh, O., Niwa, S.I., Hiramatsu, K., Kayemaya, T., Rymar, K., & Itoh, K. (1984). Abnormalities in late positive components of event-related potentials may reflect a genetic predisposition to schizophrenia. *Biological Psychiatry, 19,* 293-303.

Salisbury, D.F., Voglmaier, M.M., Seidman, L.J., McCarley, R.W. (1996). Topographic abnormalities of P3 in schizotypal personality disorder. *Biological Psychiatry, 40,* 165-172.

Schreiber, H., Strolz-Born, G., Rothmeier, J., Kornhuber, A., Kornhuber, H.H., & Born, J. (1991). Endogenous event-related brain potentials and psychometric performance in children at risk for schizophrenia. *Biological Psychiatry, 30,* 177-189.

Schwartz, J.M. (1997). Obsessive-compulsive disorder. *Science and Medicine,* 2, 14-23.

Shelley, A.M., Silipo, G., & Javitt, D.C. (1999). Diminished responsiveness of ERPs in schizophrenic subjects to changes in auditory stimulation parameters: implications for theories of cortical dysfunction. *Schizophrenia Research, 37,* 65-79.

Shenton, M.E., Kikinis, R., Jolesz, F.A., Pollack, S.D., LeMay, M., Wible, CO., Hokama, H., Martin, J., Metcalf, D., & Coleman M. (1992). Abnormalities of the left temporal lobe and thought disorder in schizophrenia. A quantitative magnetic resonance imaging study. *New England Journal of Medicine, 327,* 604-612.

Smith, M., Banquet, J-P., El Massioui, E, & Widlocher D. (1991). Measuring cognitive deficits in depressives through ERPs. In M. Ansseau, R. von Frenckell, & G. Frank (Eds.), *Biological markers of depression: State of the art* (pp. 131-144). Amsterdam: Elsevier.

Smulders, F.T.Y., Kok, A., Kenemans, J.L., & Bashore, T.R. (1995). The temporal selectivity of additive factor effects on the reaction process revealed in ERP component latencies. *Acta Psychologia, 90,* 97-109.

Sommer, W., & Matt, J. (1990). Awareness of P300-related cognitive processes: a signal detection approach. *Psychophysiology, 27,* 575-585.

Solowij, N., Michie, P.T., & Fox, A.M. (1991). Effects of long-term cannabis use on selective attention: an event-related potential study. *Pharmacolology and Biochemical Behavior, 40,* 683-688.

Solowij, N., Michie, P.T., & Fox, A.M. (1995). Differential impairments of selective attention due to frequency and duration of cannabisuse. *Biological Psychiatry, 37,* 731-737.

Souza, V.B., Muir, W.J., Walker, M.T., Glabus, M.F., Roxborough, H.M., Sharp, C.W., Dunan, J.R., & Blackwood, D.H. (1995). Auditory P300 event-related potentials and neuropsychological performance in schizophrenia and bipolar affective disorder. *Biological Psychiatry, 37,* 300-310.

Squires, N.K., Squires, K.C., & Hillyard, S.A. (1975). Two varieties of long latency positive waves evoked by unpredictable auditory stimuli in man. *Electroencephalography and Clinical Neurophysiology, 38,* 387-401.

Stanford, M.S., Vasterling, J.J., Mathias, C.W., Constans, J.I., & Houston, R.J. (2001). Impact of threat relevance on P3 event-related potentials in combat-related post-traumatic stress disorder. *Psychiatry Research, 102,* 125-137.

Steinhauer, S.R., Hill, S.Y., & Zubin, J. (1987). Event-related potentials in alcoholics and their first-degree relatives. *Alcohol, 4,* 307-314.

Stefánsson, S.B., & Jónsdóttir, T.J. (1996). Auditory event-related potentials, auditory digit span, and clinical symptoms in chronic schizophrenic men on neuroleptic medication. *Biological Psychiatry, 40,* 19-27.

Stranburg, R.J., Marsch, J.T., & Brown, W.S. (1987). P3, PCA and schizophrenia: amplitude or latency? In R. Johnson, J.W. Rohrbaugh, & R. Parasuraman (Eds.), *Current trends in event-related potential research: Electroencephalography and Clinical Neurophysiology suppl. 38* (pp. 756-761). Amsterdam: Elsevier.

Suresh, S., Porjesz, B., Chorlian, D.B., Choi, K., Jones, K.A., Wang, K., Stimus, A., & Begleiter, H. (2003). Auditory P3 in female alcoholics. *Alcoholism-Clinical and Experimental Research, 27,* 1064-1074.

Sutton, S., Braren, M., Zubin, J., & John, E.R. (1965). Evoked potential correlates of stimulus uncertainty. *Science,* 150, 1187-1188.

Thier, P., Axmann, D., & Gierdke, H. (1986). Slow brain potentials and psychomotor retardation in depression. *Electroencephalography and Clinical Neurophysiology, 63,* 570-581.

Towey, J.P., Bruder, G.E., Hollander, E., Friedman, D., Erhan, H., Liebowski, M., & Sutton, S. (1990). Endogenous event-related potentials in obsessive-compulsive disorder. *Biological Psychiatry, 28,* 92-98.

Towey, J.P, Bruder, G.E., Tenke, C.E., Leite, P., DeCaria, C, Friedman, D., & Hollander, E. (1993). Event-related potential and clinical correlates of neu-rodysfunction in obsessive-compulsive disorder. *Psychiatry Research, 49,* 167-181.

Trestman, R.L., Horvath, T., Kalus, O., & Peterson, A.E. (1996). Event-related potentials in schizotypal personality disorder. *Journal of Neuropsychiatry and Clinical Neurosciences, 8,* 33-40.

Turan, T., Esel, E., Karaaslan, E, Basturk, M., Oguz, A., & Yabanoglu, I. (2002). Auditory event-related potentials in panic and generalized anxiety disorders. *Progress in Neuropsychopharmacology and Biological Psychiatry, 26,* 123-126.

van der Stelt, O., Frye, J., Lieberman, J.A., & Belger, A. (2004). Impaired P3 generation reflects high-level and progressive neurocognitive dysfunction in schizophrenia. *Archives of General Psychiatry, 61,* 237-48.

Verleger, R. (1988). Event-related potentials and cognition: a critique of the context updating hypothesis and an alternative interpretation of P3. *Behavioral and Brain Sciences, 11,* 343-356.

Verleger, R., Bode, M., Arolt, V., Wascher, E., & Kömpf, D. (1994). Differences in P3 amplitudes between schizophrenics and healthy controls vary between the different events presented in a guessing task. *Neuropsychobiology, 30,* 114-123.

Wang, J., Miyazato, H., Randall, M., Hokama, H., Hiramatsu, K., & Ogura C. (2003). The N200 abnormalities of auditory event-related potentials in patients with panic disorder. *Progress in Neuropsychopharmacology and Biological Psychiatry, 27,* 1013-1021.

Weinberger, D.R. (1996). On the plausibility of "the neurodevelopmental hypothesis" of schizophrenia. *Neuropsychopharmacology, 14,* 1S-11S.

Weinberger, D.R. (1997). The biological basis of schizophrenia: new directions. *Journal of Clinical Psychiatry, 58, suppl. 10,* 22-27.

Whipple, S.C., Berman, S.M., & Noble, E.P (1991). Event-related potentials in alcoholic fathers and their sons. *Alcohol, 8,* 321-327.

Winkler, I., Cowan, N., Csépé, V., Czigler, I. & Näätänen, R. (1996). Interaction between transient and long-term auditory memory as reflected by Mismatch negativity. *Journal of cognitive neuroscience, 8,* 403-415.

Winkler, I. & Cowan, N. (2005). From sensory to long-term memory: Evidence from auditory memory reactivation studies. *Experimental Psychology, 52,* 3-20.

Winterer, G., Egan, M.F., Radler, T, Coppola, R., & Weinberger, DR. (2001). Event-related potentials and genetic risk for schizophrenia. *Biological Psychiatry, 50.* 407-417. Yamaguchi, S., & Knight, R.T. (1991). P300 generation by novel somatosensory stimuli. *Electroencephalography and Clinical Neurophysiology, 78,* 50-55.