Brain Response to Unexpected Novel Noises in Children with Low and High Trait Anxiety

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Abstract

■ The behavioral inhibition system [Gray, J. A. *The neuropsychology of anxiety: An enquiry into the functions of the septohippocampal system*. Oxford: Oxford University Press, 1982] proposes that anxiety is associated with the processing of novel stimuli. We aimed to explore this relationship by recording auditory event-related potentials associated with unexpected novel noises in typically developing children. Children aged 10–14 years with low (n = 12) and high (n = 11) self-report trait anxiety were assessed using a novelty oddball task. The N1 associated with novel stimuli, specifically the ''N1c'' component maximal at temporal lobe sites, was of significantly longer latency (p = .014) and greater amplitude (p = .004) in the high compared with the low anxious group. This group difference was supported by linear correlations between N1c amplitude and trait anxiety scores. There was no effect of anxiety on the later novelty P3. These data suggest a subtle moderating role of trait anxiety on brain response to novelty, and further research with clinically anxious children is indicated. ■

INTRODUCTION

Behavioral inhibition in childhood is defined as a trait-like behavioral style associated with an avoidance of unfamiliar people or objects and with a diagnosis of anxiety disorder in later life (e.g., Schwartz, Snidman, & Kagan, 1999; Kagan & Snidman, 1991; review by Fox, Henderson, Marshall, Nichols, & Ghera, 2005). Early childhood research has focused on identifying the behavioral parameters associated with individual variation in behavioral inhibition and children's response to unfamiliar situations or people (e.g., Kagan & Snidman, 1991). More recently, research has aimed to explore the neuropsychology of behavioral inhibition and anxiety. Gray (1982) and Gray and McNaughton (2000), for example, proposed that anxiety is associated with overactivation of the behavioral inhibition system (BIS), a system that responds to threat situations, including those involving some element of novelty. This model predicts that conflict generated by novelty and unfamiliarity leads to increased vigilance and attention and greater behavioral inhibition.

The pioneering studies of Fox et al. (2005) have explored the relationship between electrophysiological (electroencephalographic [EEG]) activity and individual differences in approach and withdrawal behaviors in infancy and childhood. These studies have made an important contribution to our understanding of the development and the biological underpinning of anxiety disorders. Specifically, patterns of frontal lobe EEG asymmetry recorded from infants have been found to predict the later manifestation of a behaviorally inhibited style (Calkins, Fox, & Marshall, 1996). Complementary information may be provided by examining event-related potential (ERP) components associated with novel events, but such data are lacking. The aim of the present study was to explore the relationship between trait anxiety and brain response to unexpected novel sounds in children aged 10–14 years by using an auditory novelty oddball ERP paradigm.

Modulation of the auditory ERP response has been demonstrated as early as 100 msec (''N1'') after stimulus presentation in adults (Hillyard, Hink, Schwent, & Picton, 1973) and children (Määta, Pääkkönen, Saavalainen, & Partanen, 2005). This component was originally described as reflecting a redirection of attentional focus (Näätänen, 1988) and, more recently, as a preattentive gating mechanism in the posterior auditory cortex that determines the extent to which novel sounds capture awareness (Jääskelälnen et al., 2004). Unexpected novel stimuli, such as vocalizations or mechanical noise, also elicit a subsequent P3 response that is independent of task relevance (Friedman, Cycowicz, & Gaeta, 2000; Courchesne, Kilman, Galambos, & Lincoln, 1984) and is maximal over the frontal cortex, suggesting a frontal lobe generator (e.g., Dien, Spencer, & Donchin, 2003). The novelty P3 is frequently described in terms of an orienting response, defined by rapid processing of new or unexpected information (Friedman et al., 2000).

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There is currently only limited evidence to suggest that anxiety may influence the auditory ERP response, and to our knowledge, no studies have administered the novelty auditory oddball task to explore anxiety in children. N1 amplitude is nevertheless increased in adults with panic disorder (Iwanami, Isono, Okajima, & Kamijima, 1997; Knott, Lapierre, Fraser, & Johnson, 1991), although studies of adults with generalized anxiety disorder and social phobia have also reported decreased N1 amplitude (Sachs et al., 2004; Drake, Pakalnis, Phillips, Padamadan, & Hietter, 1991). A modulating effect of anxiety on the no-go-related N1 component has been described in children (Baving, Rellum, Laucht, & Schmidt, 2004; see also Lewis & Stieben, 2004). In the study by Baving et al. (2004), anxious children had larger N1 amplitude compared to controls. Moreover, N1 amplitude may be reduced by administration of diazepam (e.g., Abduljawad, Langley, Bradshaw, & Szabadi, 2001) and is hypothesized to reflect serotonergic activity (Senokowski, Linden, Zubragel, Bar, & Gallinat, 2003), suggesting that this component may be of particular interest in anxious populations.

The deviant P3 component is influenced by anxiety in adults (Drake et al., 1991) and its topography is atypical in anxious children (Daruna, Rau, & Strecker, 1991). In the active auditory oddball study by Daruna et al. (1991), typically developing children were divided into low and high trait anxiety groups based on scores obtained from the Conners Behavior Rating Scale. The P3 elicited by deviant stimuli was greater over the right compared with the left hemisphere in high anxious children, whereas the opposite pattern was obtained in low anxious children. By contrast, the topography of an earlier component (N2) was not sensitive to anxiety. More recently, by using a passive paradigm, Bar-Haim, Marshall, Fox, Schorr, and Gordon-Salant (2003) investigated the mismatch negativity and P1–N1 complex elicited by low-probability (deviant) tones in socially withdrawn children. Compared to controls, socially withdrawn children had reduced amplitude of the mismatch negativity, but there was no modulation of the P1–N1 complex.[1] Because only two types of stimuli were presented in the studies by Daruna et al. and Bar-Haim et al., it is not possible to infer that the altered brain response was due to the ''novelty'' of the deviant stimuli rather than their lower probability.

A more direct test of Gray's (1982) hypothesis that anxious children respond atypically to novel events would be to administer a novelty auditory oddball paradigm. In this paradigm, two types of deviant stimuli of equal probability (novel noises and deviant, e.g., high-tone stimuli) are embedded in a train of standard (e.g., low-tone) stimuli. We predicted that only the amplitude and/or latency of ERP components (N1, novP3) associated with novel stimuli would be influenced by increased trait anxiety in typically developing children.

METHODS

Permission for this study was granted by the Ethics Committee of the School of Psychology, University of Southampton, UK. All children lived in the mixed urban–rural county of Hampshire and were Caucasian. They were recruited via university employees and local schools and attended for one session lasting approximately 1 hr.

Anxiety Measure

The State-Trait Anxiety Inventory for Children (STAIC; Spielberger, 1973) is a self-report measure designed to assess state (current) anxiety (STAIC A-State) and trait (enduring or chronic) anxiety (STAIC A-Trait) in children. The STAIC A-State consists of 20 statements (maximum score = 60) asking children to report how they feel at ''that particular moment in time.'' The STAIC A-Trait scale also consists of 20 statements (maximum score = 60) and asks participants to report how they ''generally feel.'' The trait scale is, therefore, suggested to indicate ''relatively stable individual differences in anxiety proneness, that is, differences between children in the tendency to experience anxiety states'' (Spielberger, 1973, p. 3). Evidence for the reliability and validity of the test has been shown (Seligman, Ollendick, Langley, & Baldacci, 2004; Muris, Merckelbach, Ollendick, King, & Bogie, 2002; Spielberger, 1973). The total STAIC A-Trait score has been found to be highly correlated with other self-report measures of childhood anxiety (e.g., Revised Children's Manifest Anxiety Scale; Muris et al., 2002). In addition, it has been found to discriminate between children with and without anxiety disorders, and has shown some sensitivity to treatment outcome (Seligman et al., 2004).

The mean STAIC A-State score was 30.04 (SD = 2.70) with a range of 24 to 34, and the mean STAIC A-Trait score was 34.70 (SD = 6.24) with a range of 23 to 50. The range of scores indicates that the majority of the sample fell within a typical range of anxiety (only one child's STAIC A-Trait score reached a clinically significant level). Children were split at the STAIC A-Trait median score (33) into ''high'' and ''low'' anxious groups. For the low anxious group, the mean STAIC A-Trait score was 29.8 (n = 12, SD = 2.7, range 23–33; 5 boys; age, M = 12 years 2 months, SD = 1 year 7 months). For the high anxiety group, the mean STAIC A-Trait score was 40.1 (n = 11, SD = 4.0, range, 36–50; 7 boys; age, M = 12 years 2 months, SD = 1 year 11 months). There was no difference in STAIC A-State scores between the two groups (M [low anxious] = 29.6, SD = 3.1, range 24–34; M [high anxious] = 30.5, SD = 2.0, range 27–34; p = .407) and there was no significant correlation between trait and state anxiety (R = .154, p = .241). Trait anxiety reflects a more stable emotional bias and

we describe the interaction of these scores with ERP component amplitude and latency.

Novelty Auditory Oddball

A series of pure sinusoidal tones and novel sounds was presented in one 10-min session: (i) standard tone (1 kHz, 200 msec long, 5 msec rise and fall time, 75 dB sound pressure level, 80% probability); (ii) deviant high tones (1.5 kHz, 10% probability); (iii) computer-generated novel sounds, for example, dog bark, car horn, whistle (10% probability). Stimulus onset asynchrony was 900 msec. Children were instructed to press a mouse button when they heard a deviant (''target'') tone, and were not informed about novel stimuli. Between 550 and 750 events were administered depending on the child's level of cooperation.

Electroencephalography

Continuous EEG data were recorded at a sampling rate of 500 Hz (band-pass 0.05–70 Hz) from electrodes individually positioned at lateral (left hemisphere: F3, T3, T5; right hemisphere: F4, T4, T6) and midline (Fz, Cz, Pz, Oz) sites, using a linked-mastoid reference and a ground lead located at FP1. Vertical (right eye) and lateral ocular electrodes enabled off-line blink reduction according to a standard algorithm (Semlitsch, Anderer, Schuster, & Presslich, 1986). Impedance was kept below 5 kΩ.

ERP Processing

EEG data were divided into epochs centered on stimulus presentation (−200 to 1000 msec), baseline corrected (−200 to 0 msec), artifact rejected (±75 μV), low-pass filtered at 20 Hz, and averaged according to stimulus type. The percentage of total trials rejected due to movement artifact was comparable between groups [low anxious: $M = 5.9\%$, $SD = 4.7$; high anxious: $M = 8.8\%$, $SD = 6.6$; $t(21) = -1.25$, $p = .225$). Similarly, the mean number of trials included in the grand averages for each stimulus type did not significantly differ between groups (standard tones: low anxious, $M = 520$, $SD = 80$; high anxious, $M = 481$, $SD = 71$; $t(21) = 1.22$, $p = .233$; high tones: low anxious, $M = 62$, $SD = 8$; high anxious, $M = 56$, $SD = 8$; $t(21) = 1.62$, $p = .119$; novel noises: low anxious, $M = 60$, $SD = 10$; high anxious, $M = 55$, $SD = 8$; $t(21) = 1.35$, $p = .191$]. The present study focused on two prominent components: the N1 (70–190 msec), and the (novelty) P3 (250–450 msec).

Statistical Analysis

Group differences were tested at locations where they appeared maximal by using a mixed-factorial model with the within-subjects factors stimulus (× 3) and side (× 2: T3, T4) and the between-subjects factor group (× 2) for the N1; for the P3 component, side was replaced by site (× 3: Fz, Cz, Pz). Due to evidence that N1 (''lateral N1'') amplitude declines with age in children aged 6–12 years (Gomes et al., 2001), we repeated those models with significant group differences with age as a covariate. *t* Tests and correlation analyses (across groups) were conducted to explore significant group effects.

RESULTS

Behavior

Behavioral response to the deviant (target) tones did not differ between groups (hit rate: low anxious, $M = 85.8\%$, $SD = 14.3$; high anxious, $M = 84.6\%$, $SD = 14.9$; response time: low anxious, $M = 205.0$ msec, $SD = 17.9$; high anxious, $M = 218.3$ msec, $SD = 25.1$). Children in both groups sometimes responded incorrectly to novel noises perhaps in association with a degree of startle (low anxious: $M = 13.5\%$, $SD = 14.4$; high anxious: $M = 10.1\%$, $SD = 15.9$).

ERP Components

The N1 consists of multiple components (Näätänen & Picton, 1987), including the ''T complex'' (Wolpaw & Penry, 1975). An early negativity at 70–80 msec (''N1b'') is followed by a larger negativity at approximately 150 msec (''N1c'' or ''Tb'') that is maximal over the auditory cortex (Woods, 1995). The N1c, which is particularly prominent in children (Tonnquist-Uhlen, Ponton, Eggermont, Kwong, & Don, 2003; Bruneau, Dourneau, Garreau, Pourcelot, & Lelord, 1997; see also Gomes et al., 2001), was evident in both groups in the present study (see Figure 1).

In the low anxious group, N1c latency was shortest for novel stimuli and longest for standard stimuli, whereas the opposite pattern was found in the high anxious group (see Table 1). There was a significant interaction between stimulus and group, $F(2,42) = 7.11$, $p = .002$, which remained significant when age was added as a covariate, $F(2,40) = 6.84$, $p = .003$, but no main effect of stimulus. Post hoc tests revealed a group main effect for both standard, $F(1,21) = 4.85$, $p = .039$, and novel, $F(1,21) = 7.15$, $p = .014$, stimuli. However, individual *t* tests did not support a significant group difference for standard latency at either left (T3: $p = .079$) or right (T4: $p = .114$) sites, or for T4 novel latency ($p = .177$). There was a significant difference for T3 novelty latency ($p = .033$), but a correlation with trait anxiety scores fell just short of statistical significance ($R = .338$, $p = .057$).

A main effect of stimulus, $F(2,42) = 16.6$, $p < .005$, reflected increased omnibus N1c amplitude for deviant

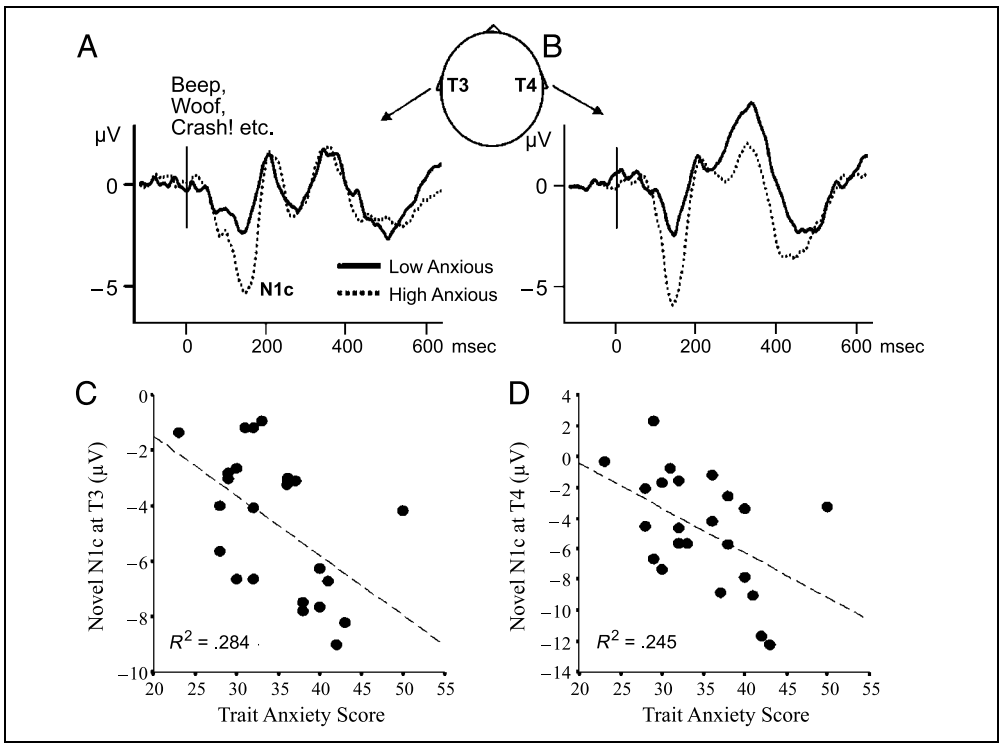

Figure 1. Increased N1c amplitude in high compared to low trait anxious children in relation to unexpected novel stimuli over the left (A) and right (B) temporal lobe. The group difference is supported by a significant linear correlation between trait anxiety scores and novelty N1c amplitude on the left (C) and right (B) side.

and novel stimuli compared to standard stimuli. Amplitude was highest for deviant stimuli in the low anxious group, and highest for novel stimuli in the high anxious group. A significant interaction between stimulus and group was obtained, $F(2,42) = 3.37$, $p = .044$, that remained significant when age was added as a covariate, $F(2,40) = 3.28$, $p = .048$. Post hoc testing revealed a main effect of group only for novel stimuli, $F(1,21) = 10.33$, $p = .004$ (see Figure 1). t Tests confirmed a significant group difference at both left (T3: $p = .006$) and right (T4: $p = .036$) sites, and there were significant linear correlations (one tailed) between N1c amplitude and trait anxiety scores (T3: $R = -.533$, $p = .004$; T4: $R = -.496$, $p = .008$; Nb; the N1c is negative: Figure 1), consistent with the finding that increased trait anxiety was associated with higher component amplitude.

In order to explore the specificity of trait-anxiety modulation of the novelty N1 to temporal lobe sites, we compared the amplitude of this component between groups at midline sites also (central N1). A mixed-factorial model was tested with one within-subject factor (site: Fz, Cz, Pz) and one between-subject factor (group: low and high anxious), but there were no significant effects (all $p > .05$). At midline locations, the novelty N1 was of similar amplitude in the low and high anxious groups (see Figure 2 for Cz).

A P3 component, evident at approximately 300 msec at all midline sites, was not significantly influenced by anxiety (waveforms at Cz, where the novelty P3 appeared maximal are presented in Figure 2). There was a main effect of stimulus, $F(2,42) = 27.1$, $p < .001$, reflecting the expected higher amplitude of the P3 associated with novel compared to standard and deviant stimuli across sites.

DISCUSSION

This study provides evidence for a moderating role of trait anxiety on brain function in typically developing children. Earlier reports in children reported reduced mismatch negativity amplitude in socially withdrawn children (Bar-Haim et al., 2003) and P3 topographic differences in high compared to low anxious children (Daruna et al., 1991). The present study extends this literature to highlight anxiety modulation of the ERP waveform associated with novel stimuli, controlling for stimulus probability. Furthermore, these data may be interpreted as supportive of the BIS model of anxiety (Gray, 1982).

Increased N1c latency and amplitude suggests an influence of anxiety at initial stages of sensory processing, within 200 msec of stimulus presentation. These data are compatible with the BIS model, which suggests that in anxious individuals, novel stimuli generate conflict leading to increased arousal. However, the subsequent P3 response, reflecting an evaluative stage of novelty processing (Friedman et al., 2000), was comparable between groups, indicating that the effect of trait anxiety on novelty processing is subtle in typically developing children. Whereas a previous study used a passive oddball paradigm (e.g., Bar-Haim et al., 2003), the use of an active oddball task enabled us to infer the extent to which children's attention was diverted from a

Table 1. Mean Amplitude and Latency (*SD*) for the N1c Component at Temporal Lobe Sites

	Low Anxious (n = 12)	*High Anxious (n = 11)*
T3		
Standard		
Amplitude (μV)	−1.8 (1.3)	−3.2 (2.1)
Latency (msec)	153.2 (14.9)	133.1 (34.3)
Deviant		
Amplitude (μV)	−4.6 (1.9)	−4.8 (3.2)
Latency (msec)	147.5 (18.9)	147.3 (21.2)
Novel		
Amplitude (μV)	−3.3 (2.1)	−6.1 (2.2)
Latency (msec)	128.3 (23.1)	147.1 (14.9)
T4		
Standard		
Amplitude (μV)	−2.2 (1.3)	−2.4 (2.4)
Latency (msec)	158.0 (19.9)	140.7 (29.8)
Deviant		
Amplitude (μV)	−4.7 (2.9)	−5.8 (5.9)
Latency (msec)	151.0 (21.5)	145.1 (21.3)
Novel		
Amplitude (μV)	−3.2 (2.9)	−6.4 (3.8)
Latency (msec)	134.3 (23.5)	146.2 (16.1)

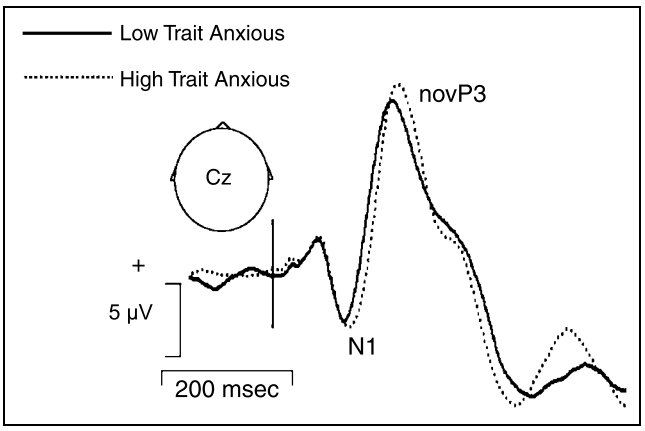

Figure 2. Novel waveforms at Cz in low and high trait anxious children. A prominent N1 and P3 component associated with novel stimuli is evident and comparable between groups.

selective attention task. We conclude that high trait anxious children have a heightened vigilance for unexpected novel stimuli, but that this is not associated with prolonged modulation of attentional processing or with increased (re)allocation of attentional resources. Compatible with this interpretation, an earlier study that administered a go/no-go paradigm also found increased N1 amplitude in anxious children, but no effect on the P3 (Baving et al., 2004). Modulation of the N1 but not the P3 has also been demonstrated in adults with panic disorder (Iwanami et al., 1997). Both authors concluded that there was an early attentional enhancement that did not appear to influence subsequent allocation of processing resources. However, it would be of interest to investigate the extent to which the novelty P3 component is sensitive to clinically significant anxiety in children.

Our data may reflect a degree of hypersensitivity to novelty in anxious children, perhaps associated with stimulus ambiguity. This is compatible with cognitive theories of anxiety (e.g., Eysenck, 1992) that argue that anxious individuals are sensitive to threatening, aversive, and/or ambiguous stimuli (see Hadwin, Garner, & Perez-Olivas, 2006, for a review). Indeed, in the early studies of behavioral inhibition it was reported that, although the children avoided unfamiliar objects and situations, they remained vigilant of their surroundings (Kagan, Reznick, & Gibbons, 1989; Kagan, Reznick, Snidman, Gibbons, & Johnson, 1988). The degree to which N1 modulation reflects a stable sensory-processing bias distinct from that associated with more transient emotional states, however, must be confirmed in future studies. Similarly, the extent to which anxiety-related ERP modulation is associated with altered cognitive function or behavior (see Vasa & Pine, 2004, for a review) is unknown; although in the present study low and high trait anxious groups had comparable levels of performance, the oddball task is simplistic and not an adequate reflection of cognitive function or everyday behavior.

Converging evidence indicates that the neural generators of the auditory N1 components are located in the auditory cortex of the temporal lobes (Jääskelälnen et al., 2004; Herrman & Knight, 2001; Wolpaw & Penry, 1975). In support, adult lesion studies have revealed diminished single-tone N1 amplitude in patients with temporal lobe lesions, specifically the superior temporal gyrus (Knight, Scabini, Woods, & Clayworth, 1988; Knight, Hillyard, Woods, & Neville, 1980). Magnetic resonance imaging studies of children with clinical anxiety have shown increased volume of the superior temporal gyrus (De Bellis et al., 2002) and amygdala (De Bellis et al., 2000; but see also Milham et al., 2005), compatible with earlier hypotheses suggesting an overactive amygdala in the development and maintenance of behavioral inhibition (e.g., Davidson, 2000). In line with these studies, the N1 group differences in the present study were maximal at EEG sites proximal to the temporal lobes. This effect was comparable over the left and right temporal cortex, consistent with the earlier report by

Daruna et al. (1991) who found laterality effects only for the later P300 component. The anxiety-related N1 modulation observed in our study may be consistent with atypical temporal lobe anatomy, although a direct relationship between structural (e.g., De Bellis et al., 2002) and functional (present study) abnormality and its relevance to the BIS model and anxiety disorder was not established.

In summary, this study found significantly increased N1 component latency and amplitude in children with increased self-report trait anxiety. It is important to acknowledge, however, that N1 modulation is not specific to anxiety. Similar findings have been reported, for example, in children with fragile X syndrome (Castren, Paakkonen, Tarkka, Rynanen, & Partanen, 2003) and autism (Ferri et al., 2003), as well as in adults with schizophrenia (Wood, Potts, Hall, Ulanday, & Netsiri, 2005). Nevertheless, it would be of interest to examine this ERP component in children with clinically diagnosed anxiety disorders.

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Note

1. It is noteworthy that in adults and in children N1 topography indicates the existence of central and lateral subcomponents (Gomes et al., 2001), the latter being maximal over those temporal lobe sites (e.g., T3, T4) not included in the EEG montage used by Bar-Haim et al.

REFERENCES

Abduljawad, K. A. J., Langley, R. W., Bradshaw, C. M., & Szabadi, E. (2001). Effects of clonidine and diazepam on prepulse inhibition of the acoustic startle response and the N1/P2 auditory evoked potential in man. *Journal of Psychopharmacology, 15,* 237–242.

Bar-Haim, Y., Marshall, P. J., Fox, N. A., Schorr, E., & Gordon-Salant, S. (2003). Mismatch negativity in socially withdrawn children. *Biological Psychiatry, 54,* 17–21.

Baving, L., Rellum, T., Laucht, M., & Schmidt, M. H. (2004). Attentional enhancement to NoGo stimuli in anxious children. *Journal of Neural Transmission, 111,* 985–999.

Bruneau, N., Dourneau, M. C., Garreau, B., Pourcelot, L., & Lelord, G. (1997). Temporal prominence of auditory evoked potentials (N1 wave) in 4–8-year-old children. *Psychophysiology, 34,* 32–38.

Calkins, S. D., Fox, N. A., & Marshall, T. R. (1996). Behavioural and physiological antecedents of inhibited and uninhibited behaviour. *Child Development, 67,* 523–540.

Castren, M., Paakkonen, A., Tarkka, I. M., Rynanen, M., & Partanen, J. (2003). Augmentation of auditory N1 in children with fragile X syndrome. *Brain Topography, 15,* 165–171.

Courchesne, E., Kilman, B., Galambos, R., & Lincoln, A. (1984). Autism: Processing of novel auditory information assessed by event-related brain potentials. *Electroencephalography and Clinical Neurophysiology, 59,* 238–248.

Daruna, J. H., Rau, A. E., & Strecker, C. D. (1991). P3 amplitude in young children: Relation to anxiety. *Biological Psychiatry, 29,* 837–840.

Davidson, R. J. (2002). Anxiety and affective style: Role of prefrontal cortex and amygdala. *Biological Psychiatry, 51,* 68–80.

De Bellis, M. D., Casey, B. J., Dahl, R. E., Birmaher, B., Williamson, D. E., Thomas, K. M., et al. (2000). A pilot study of amygdala volumes in pediatric generalised anxiety disorder. *Biological Psychiatry, 48,* 51–57.

De Bellis, M. D., Keshavan, M. S., Shifflett, H., Iyengar, S., Dahl, R. E., Axelson, D. A., et al. (2002). Superior temporal gyrus volumes in pediatric generalized anxiety disorder. *Biological Psychiatry, 51,* 553–562.

Dien, J., Spencer, K. M., & Donchin, E. (2003). Localization of the event-related potential novelty response as defined by principal components analysis. *Cognitive Brain Research, 17,* 637–650.

Drake, M. E., Jr., Pakalnis, A., Phillips, B., Padamadan, H., & Hietter, S. A. (1991). Auditory evoked potentials in anxiety disorder. *Clinical Electroencephalography, 22,* 97–101.

Eysenck, M. W. (1992). *Anxiety: The cognitive perspective.* Hove, UK: Erlbaum.

Ferri, R., Elia, M., Agarwal, N., Lanuzza, B., Musumeci, S. A., & Pennisi, G. (2003). The mismatch negativity and the P3a components of the auditory event-related potentials in autistic and low-functioning subjects. *Clinical Neurophysiology, 114,* 1671–1680.

Fox, N. A., Henderson, H. A., Marshall, P. J., Nicholds, K. E., & Ghera, M. M. (2005). Behavioral inhibition: Linking biology and behavior within a developmental framework. *Annual Review of Psychology, 56,* 235–262.

Friedman, D., Cycowicz, Y., & Gaeta, H. (2000). The novelty P3: An event-related brain potential (ERP) sign of the brain's evaluation of novelty. *Neuroscience Biobehavioral Reviews, 25,* 355–373.

Gomes, H., Dunn, M., Ritter, W., Kurtzberg, D., Brattson, A., Druezer, J. A., et al. (2001). Spatiotemporal maturation of the central and lateral N1 components to tones. *Brain Research: Developmental Brain Research, 129,* 147–155.

Gray, J. A. (1982). *The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system.* Oxford: Oxford University Press.

Gray, J. A., & McNaughton, N. (2000). *The neuropsychology of anxiety: An enquiry into the functions of the septo-hippocampal system* (2nd ed.). Oxford: Oxford University Press.

Hadwin, J. A., Garner, M., & Perez-Olivas, G. (2006). The development of information processing biases in childhood anxiety: A review and exploration of its origins in parenting. *Clinical Psychology Review, 26,* 876–894.

Hillyard, S. A., Hink, R. F., Schwent, V. L., & Picton, T. W. (1973). Electrical signals of selective attention in the human brain. *Science, 182,* 177–180.

Herrman, C. S., & Knight, R. T. (2001). Mechanisms of human attention: Event-related potentials and oscillations. *Neuroscience Biobehavioral Reviews, 25,* 465–476.

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

Jääskelälnen, I. P., Ahvenlnen, J., Bonmassar, G., Dale, R. M., Ilmonlemi, R. J., Levänen, S., et al. (2004). Human posterior auditory cortex gates novel sounds to consciousness. *Proceedings of the National Academy of Sciences, U.S.A., 101,* 6809–6814.

Kagan, J., Reznick, J. S., & Gibbons, J. (1989). Inhibited and uninhibited types of children. *Child Development, 60,* 838–845.

Kagan, J., Reznick, J. S., Snidman, N., Gibbons, J., & Johnson, M. O. (1988). Childhood derivatives of inhibition to the unfamiliar. *Child Development, 59,* 1580–1589.

Kagan, J., & Snidman, N. (1991). Temperamental factors in human development. *American Psychologist, 46,* 856–862.

Knight, R., Hillyard, S., Woods, D., & Neville, H. (1980). The effects of frontal and temporal–parietal lesions on the auditory evoked potential in man. *Electroencephalography and Clinical Neurophysiology, 50,* 112–124.

Knight, R. T., Scabini, D., Woods, D. L., & Clayworth, C. (1988). The effects of lesions of superior temporal gyrus and inferior parietal lobe on temporal cortex and vertex components of the human AEP. *Electroencephalography and Clinical Neurophysiology, 70,* 499–509.

Knott, V., Lapierre, Y. D., Fraser, G., & Johnson, N. (1991). Auditory evoked potentials in panic disorder. *Journal of Psychiatric Neuroscience, 16,* 215–220.

Lewis, M. D., & Stieben, J. (2004). Emotion regulation in the brain: Conceptual issues and direction for developmental research. *Child Development, 75,* 371–376.

Määtta, S., Pääkkönen, A., Saavalainen, P., & Partanen, J. (2005). Selective attention event-related potential effects from auditory novel stimuli in children and adults. *Clinical Neurophysiology, 116,* 129–141.

Milham, M. P., Nugent, A. C., Drevets, W. C., Dickstein, D. P., Leibenluft, E., Ernst, M., et al. (2005). Selective reduction in amygdala volume in pediatric anxiety disorders: A voxel-based morphometry investigation. *Biological Psychiatry, 57,* 961–966.

Muris, P., Merckelbach, H., Ollendick, T., King, N., & Bogie, N. (2002). Three traditional and three new childhood anxiety questionnaires: Their reliability and validity in a normal adolescent sample. *Behavioral Research Therapy, 40,* 753–772.

Näätänen, R. (1988). Implications of ERP data for psychological theories of attention. *Biological Psychology, 26,* 117–163.

Näätänen, R., & Picton, T. (1987). The N1 wave of the human electric and magnetic response to sound: A review and an analysis of the component structure. *Psychophysiology, 24,* 375–425.

Sachs, G., Anderer, P., Margreiter, N., Semlitsch, H., Saletu, B., & Katschnig, H. (2004). P300 event-related potentials and cognitive function in social phobia. *Psychiatry Research: Neuroimaging, 131,* 249–261.

Schwartz, C. E., Snidman, N., & Kagan, J. (1999). Adolescent social anxiety as an outcome of inhibited temperament in childhood. *Journal of the American Academy of Child and Adolescent Psychiatry, 38,* 1008–1015.

Seligman, L. D., Ollendick, T. H., Langley, A. K., & Baldacci, H. B. (2004). The utility of measures of child and adolescent anxiety: A meta-analytic review of the Revised Children's Manifest Anxiety Scale, the State-Trait Anxiety Inventory for Children, and the Child Behavior Checklist. *Journal of Clinical Child & Adolescent Psychology, 33,* 557–565.

Semlitsch, H. V., Anderer, P., Schuster, P., & Presslich, O. (1986). A solution for reliable and valid reduction of ocular artifacts, applied to the P300 ERP. *Psychophysiology, 23,* 695–703.

Senokowski, D., Linden, M., Zubragel, D., Bar, T., & Gallinat, J. (2003). Evidence for disturbed cortical signal processing and altered serotonergic neurotransmission in generalized anxiety disorder. *Biological Psychiatry, 53,* 304–314.

Spielberger, C. (1973). *Manual for the State-Trait Anxiety Inventory for Children.* Palo Alto, CA: Consulting Psychologists Press.

Tonnquist-Uhlen, I., Ponton, C. W., Eggermont, J. J., Kwong, B., & Don, M. (2003). Maturation of human central auditory system activity: The T-complex. *Clinical Neurophysiology, 114,* 685–701.

Vasa, R. A., & Pine, D. (2004). Neurobiology. In T. L. Morris & J. S. March (Eds.), *Anxiety disorders in children and adolescents.* London: Guilford Press.

Wolpaw, J. R., & Penry, J. K. (1975). A temporal component of the auditory evoked response. *Electroencephalography and Clinical Neurophysiology, 38,* 609–620.

Woods, D. L. (1995). The component structure of the N1 wave of the human auditory evoked potential. *Electroencephalography and Clinical Neurophysiology, Suppl. 44,* 102–109.

Wood, S. M., Potts, G. F., Hall, J. F., Ulanday, J. B., & Netsiri, C. (2005). Event-related potentials to auditory and visual selective attention in schizophrenia. *International Journal of Psychophysiology, 60,* 67–75.