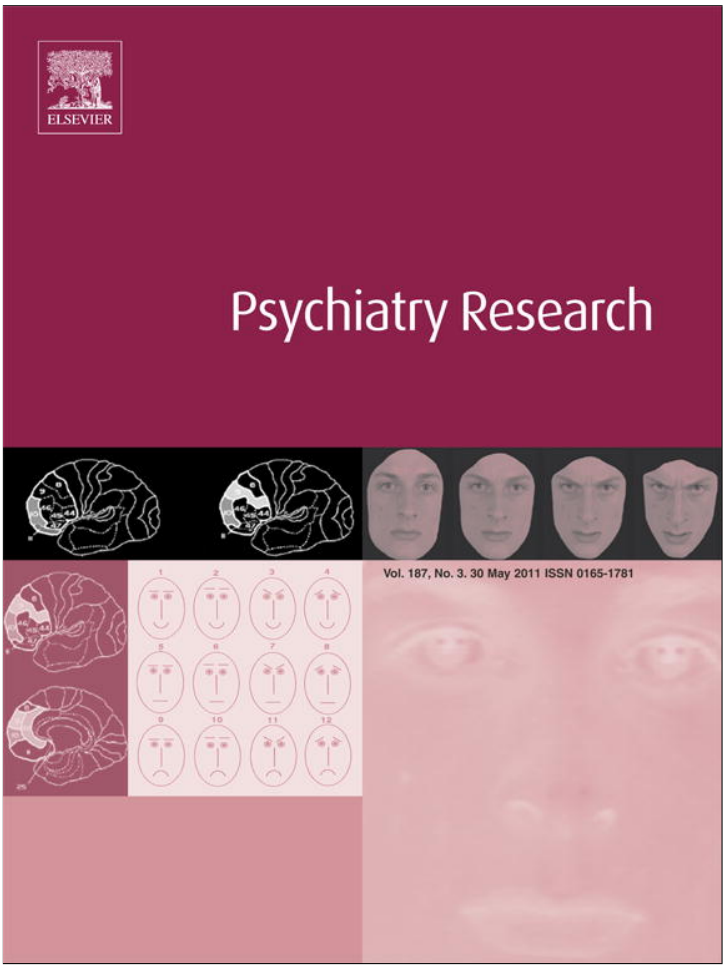

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Event-related potentials in impulsively aggressive juveniles: A retrospective chart-review study ☆

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ABSTRACT

The assessment, treatment and management of aggressive youth represent a major clinical challenge facing pediatric mental health professionals today. Although a number of studies have examined physiological differences among aggressive patients vs. controls, the current literature lacks a comprehensive examination of the electroencephalographic activity of impulsively aggressive juveniles. The current study was designed to fill this void in the literature via a retrospective chart review of 80 male and female juveniles undergoing inpatient treatment for pathologically impulsive aggression. Clinical reports for mid- and late-latency event-related potentials (ERPs) were examined to determine their correlations with aggression characteristics, as well as any differential predictive utility of hemispheric differences and auditory vs. visual potentials. Results indicated that decrements of mid-latency potentials and ERPs evoked by auditory stimuli (vs. late-latency components and visual ERPs) were more highly predictive of aggressive behavior. No significant hemispheric differences were noted. Taken together, these results have theoretical significance for the etiology of impulsive aggression, and perhaps also clinical relevance for the treatment of this condition.

1. Introduction

The assessment, treatment and management of aggressive youth represent a major clinical challenge facing pediatric mental health professionals today. Although no nationally representative survey of pediatric mental health treatment centers exists, smaller, single-site studies suggest that aggressive behavior is prevalent, occurring in lifetime rates of 50–90% among psychiatrically referred juveniles, ages 5 to 19 (Fritsch et al., 1992; Connor et al., 1997). In general, research concerning maladaptive human aggression often makes a distinction between premeditated (cold-blooded, predatory or proactive) aggression and impulsive (hot-tempered, affective or reactive) aggression (Connor, 2002). Impulsive aggression is more *emotional*, and is considered to be more biological in origin (McEllistrem, 2002; Slever, 2002); whereas, premeditated aggression is considered an instrumental, purposeful, controlled aggressive behavior that is more likely to be learned or influenced by psychosocial factors (Stanford et al., 2003).

Within the literature pertaining to impulsive aggression, two etiological factors have been identified (Coccaro, 2003). The first factor, emotion control, appears to involve the sub-cortical, temporal-limbic regions of the brain, abnormalities of which may manifest behaviorally as explosive temper, or extreme emotional outbursts (Best et al., 2002; Coccaro et al., 2007). The second factor, impulse control, is thought to involve the prefrontal regions of the brain, abnormalities of which may manifest behaviorally as symptoms of impulsivity and the failure to inhibit reactions when it would be appropriate to do so (Best et al., 2002). Thus, emotion-control problems are thought to be linked to impairments within the limbic system; whereas, impulse-control problems may be linked to impairments in the prefrontal cortex. Neural imaging studies of murderers, psychopaths and habitual criminals have suggested more normal frontal lobe function in premeditated criminal behavior but more frontal dysfunction in impulsive crimes of passion (Raine et al., 1998; McEllistrem, 2004). In his comprehensive review of the literature on psychopathy, Kiehl (2006) implicates frontal lobe dysfunction among individuals engaging in acts of primarily impulsive or reactive aggression. On the other hand, premeditated aggressors tend to exhibit frontal lobe functioning that is more similar to that of 'normal' controls, as assessed by both neuropsychological and neurophysiological testing.

Although the understanding of the etiology of impulsive aggression among juveniles is in its infancy, measurement of the neurophysiological characteristics of this population has generated considerable interest to date. In particular, physiological explanations for heightened impulsive aggression in children range from impaired emotional processing (Cappadocia et al., 2009; Lewis et al., 2008) to deficits in performance monitoring (Corbetta and Shulman, 2002; Crowe and

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Blair, 2008) to the most recent theories regarding an overactive hypothalamic-pituitary-adrenal axis response (van Goozen and Fairchild, 2008; Lopez-Duran et al., 2009) and various genetic factors (Craig and Halton, 2009). Certainly, a combination of these factors might lead to the development of aggressive behaviors in childhood, as well as the potential for persistence of these behaviors into adulthood. In fact, studies have shown that these types of issues tend to exist not only in impulsively aggressive children, but also in impulsively aggressive adults (Hawes et al., 2009).

In clinical practice, the electroencephalogram, (EEG) is frequently used to evaluate juvenile patients with impulsive aggression. Historically, increased inter-ictal irritability and impulsive aggression have been noted among individuals with temporal-limbic epilepsy (Spiers et al., 1985). Also consistent with a neurobiological focus, a large number of studies have shown a relationship between EEG abnormalities and impulsive aggression (Stein et al., 1995). Enhanced cortical slow wave activity, particularly in the delta frequency range, (e.g., less than 4 Hz) is one relatively consistent finding that has been successfully replicated (Volavka, 1990; Houston and Stanford, 2005; Patrick, 2008). In addition, slow wave EEG activity in adolescence has been shown to predict the emergence of antisocial behavior later in life (Raine et al., 1990; Patrick, 2008). The aforementioned authors have interpreted these findings as evidence of cortical immaturity resulting in impaired inhibitory control, and cortical underarousal that predisposes towards compensatory stimulation seeking (See Patrick, 2008 for review).

More recently, the examination of event related potentials (ERPs) in aggressive, juvenile populations has become more prevalent (Pogarell, et al., 2007). Like the EEG, the ERP can measure abnormal brain activity associated with impulsive aggression; however, the ERP differs from traditional EEG measures, in that it is thought to reflect the brain's time-locked, electrical response to a specific stimulus. According to Connor (2002), the first 100 ms of ERP signal may correspond with very basic brainstem activity; whereas, the next 200 to 300 ms of ERP signal may correspond to limbic processing, and the next stage of 300–500 ms following stimulus presentation may correspond to cortical perceptual and cognitive processing. Using the negative components as an example, the N100 (e.g., negative peak 100 ms following stimulus presentation) reflects processing of simple sensory parameters of the stimulus (intensity, duration, complexity), while the N200 may reflect response inhibition (the opposite of impulsivity), and the N400 reflects higher level linguistic and semantic processing.

Decrements of the amplitude and latency of these characteristic waveforms have been noted among populations with impulsive aggression (vs. controls), most frequently in the P300 ERP, which occurs approximately 300–900 ms following the presentation of a rare, target stimulus (Branchey et al., 1988; Barratt et al., 1997; Gerstle et al., 1998; Mathias and Stanford, 1999; Patrick, 2008). Similarly, such findings have also been noted among individuals with antisocial personality disorder, specifically with regard to abnormal maturation of the pre-frontal cortical generators of the P300 waveform (Bauer et al., 1994; Bauer and Hesselbrock, 1999, 2001, 2003; Patrick, 2008). Patrick (2008) suggests that this dispositional vulnerability to impulse control problems, reflected in the specific ERP decrements described above, may be the key to understanding impulsive aggression. Such findings are supported by our own recent studies of impulsively aggressive juvenile populations, in which long latency ERPs (e.g., 500 ms following stimulus presentation) were found to be more sensitive than traditional EEG measures to the neuroelectric characteristics of impulsive aggression (Fisher et al., 2008).

The literature regarding examination of earlier components of the ERP (e.g., P100, N100, and P200) among impulsive aggressors vs. controls is sparse. One study, by Houston and Stanford (2001) examined psychophysiological differences in arousability among adults displaying impulsive aggressive outbursts. Photic stimulation was used to evoke P100, N100 and P200 waveforms, components occurring 100 and 200 ms following stimulus presentation, respectively, and reflecting the integrity of participants' sensory gating mechanisms. Results indicated reduced P100 amplitude, increased N100 amplitude, and a shorter latency of the P100, N100, and P200 complex. The authors suggested that these findings reflected inefficient sensory gating mechanisms, enhanced orientation of attention to stimuli, and a quicker orienting and processing of stimuli among impulsively aggressive individuals, and that these characteristics may reflect an attempt to compensate for low arousal levels. This interpretation supports previous assertions associated with EEG studies, that impaired inhibitory control and cortical underarousal, as reflected in the EEG, may predispose individuals towards compensatory stimulation seeking (See Patrick, 2008 for review).

A thorough examination of the neuroelectric characteristics of impulsively aggressive juveniles is lacking in the current literature, and a number of issues remain to be addressed. For instance, it is not known definitively whether or not the neuroelectric deficits associated with impulsive aggression in this population are most accurately reflected via early or late components of the ERP. Further, it is unclear whether or not hemispheric differences in electrical activity may be characteristic in this population, or whether auditory or visual ERPs may be most revealing. The current study was the first of its kind to address these issues via retrospective chart review in a population of 80 male and female juveniles undergoing inpatient treatment for pathological levels of impulsive aggression. Based on previous work, the authors hypothesized that, compared to late ERP components, early ERP components would be more highly correlated with impulsive aggression. Given the sparse literature on this topic, differential correlations of auditory vs. visual components and left hemisphere vs. right hemisphere activity with impulsive aggression, were examined as empirical questions.

2. Methods

2.1. Participants

Data were extracted from the medical records of 80 juvenile patients admitted to a residential treatment center in Central Texas for the treatment of pathological impulsive aggression. For admission, the patient were required to have had at least three discrete episodes of failure to resist aggressive impulses, resulting in assaultive acts causing serious physical harm to others (i.e., with bruising, bleeding, or broken bones). Additionally, the degree of aggression expressed during the episodes was grossly out of proportion to any precipitating psychosocial provocation. All patients demonstrated prior psychometric evidence of an intellect (e.g., IQ) of 70 or above. Excluded from admission were individuals who had severe language disorders or who did not speak English, were deaf, blind, or had severe mobility problems, suffered with severe medical illness (e.g., AIDS), were pregnant, had a history of arson, or had other conditions that could be a safety concern or would prevent them from participating in individual, group, and family psychotherapy.

For this population, psychiatric diagnoses were determined upon admission to the treatment center. A complete listing of the participants' psychiatric diagnoses and their frequency is listed in Table 1. It is important to note that patients with conduct disorder, antisocial personality disorder, borderline personality disorder, pervasive developmental disorder, or any psychotic disorder not associated with a mood disorder were excluded by the treatment facility based on their admissions policies. The admitting psychiatrist screened out patients whose history of aggression did not appear to be impulsive in nature. The neuropsychiatry unit described in this study was designed to include only youth who were irritable or “hot-tempered” and had been known to impulsively over-react to trivial provocation. Patients with a history of premeditated, planned aggression meant to serve some instrumental purposes were therefore excluded from the neuropsychiatry unit. In addition, the admitting psychiatrist also screened out individuals whose aggression appeared to be related to substance abuse or medication side effects. Lastly, participants whose aggressive behavior may have been due to a general medical or neurological condition were excluded, unless the condition was prenatal or perinatal in origin and was considered chronic rather than progressive. The admitting psychiatrist determined whether or not a given patients' aggression was due to a general or neurological condition.

For the purposes of this study, the data extracted from medical records were cleared of all identifying information and patient privacy was protected using a coded number to represent the participant. Any datum that could be reasonably used to identify the patients was removed. All procedures were approved by the Texas State University Institutional Review Board, as well as the residential treatment facility where data were collected.

2.2. Demographic characteristics

Participants ranged in age from 6 to 17 years, with a mean age of 13 years. The participants were predominantly male (56 males and 24 females) and were predominately right hand dominant (74 right handed, 6 left handed). With few exceptions, the

Table 1
Rank order of diagnoses.

Rank*	%	N**	Diagnoses
1.	82.4%	61	Personality Change due to Complex Partial Seizure Disorder of limbic origin
2.	75.7%	56	Attention Deficit Hyperactivity Disorder
3.	45.9%	34	Major Depression
4.	40.5%	30	Oppositional Defiant Disorder
5.	22.9%	17	Bipolar Disorder
6.	21.6%	16	Cognitive Disorder NOS
7.	10.8%	8	Personality Change due to Encephalopathy
8.	9.5%	7	Conduct Disorder
9.	9.5%	7	Post-Traumatic Stress Disorder
10.	8.1%	6	Mixed Receptive and Expressive Language Disorder
11.	6.8%	5	Poly-substance Abuse
12.	5.4%	4	Dysthymia
13.	5.4%	4	Substance Abuse
14.	5.4%	4	Learning Disorder (reading/writing)
15.	5.4%	4	Asperger's Disorder
16.	5.4%	4	Mathematics Disorder

Diagnoses at 5% or less included: Intermittent Explosive Disorder (3), Anxiety Disorder NOS (3), Pervasive Developmental Disorder (3), Paraphilia NOS (2), Sexual Disorder NOS (2), Obsessive–Compulsive Disorder (2), Impulse Control Disorder (1), Disorder of written expression (1), Schizoaffective Disorder (1), Reading Disorder (1), Reactive Attachment Disorder (1), Psychotic Disorder (1), and Receptive Language Disorder (1).
* Ranked by percent of sample with diagnosis.
** $n = 74$, with 6 missing values.

participants were Caucasian, and self-reported their state of residence as either Texas or California. Fifty percent of participants had completed 7th grade or higher.

2.3. Electrophysiological procedure

Participants were seated in a comfortable chair in an electrically shielded room located in a quiet section of the residential treatment facility. The EEG was conducted by a trained EEG technician employed by the residential treatment facility, under the supervision of a licensed, board certified, neurologist with specialty training as an electroencephalographer. The technician explained the procedure to the participant. The patient's head was measured and marked according to the International 10/20 System of Electrode Placement and 6 mm, Grass Gold EEG electrodes applied using standard technique (e.g., collodion, Grass paste/tape or electrode cap). The instrument was calibrated for a 50 μV signal (60 cycle filters off), 5 μV/mm sensitivity, high linear frequency filter of 70 Hz, and low frequency filter at 1.0 Hz, and the electrodes were checked for proper impedance (more than 0.5 k-Ohm and less than or equal to 5 k-Ohms). All ERP procedures were conducted in accordance with recommendations of Cognitrace, the manufacturers of the EEG machine used by the facility (see Duffy et al., 1979). It is important to note that some aspects of Cognitrace methodology are proprietary in nature and cannot be included in the current manuscript. The authors realize that this reduces the ability of other researchers to replicate the findings of the current study; such issues are a caveat of retrospective chart review studies.

Auditory and visual ERPs were routinely conducted on juveniles admitted for pathologically impulsive aggression. The ERPs were long latency (500 ms) electrical responses time-locked to auditory (bilateral 86 dB SPL, 1000 Hz tone, rise and fall time 10 ms) or visual (Grass strobe light flash, 18 in from closed eyes) stimuli, averaged from the background EEG over 100 trials for each type of stimulus. All stimuli were presented in random format with at least 1000 ms intervals. Auditory and visual ERPs were collected in separate blocks. The test results were interpreted by a board certified pediatric neurologist with specialty training as an electroencephalographer. The neurologist was blind to the participants' diagnoses (e.g., only participants' age and gender were given). The auditory and the visual ERPs consisted of averaged records taken from periods of artifact-free EEG. Data were baseline corrected and eye movement artifacts were corrected using proprietary software from Cognitrace (e.g., manufacturers of the EEG machine; see Duffy et al., 1979). For each of the 19 electrodes (F_{p1}, F_{p2}, F_7, F_3, F_Z, F_4, F_8, T_3, C_3, C_Z, C_4, T_4, T_5, P_3, P_Z, P_4, T_6, O_1, and O_2), the raw records available to the neurologist consisted of a graph of the averaged ERPs, time locked from the moment of stimulation, with data points taken every 20 ms for a total of 500 ms. For each auditory and visual ERP, the neurologist had access to individual ERP graphs as well as to averaged graphs, which were computerized and compared to age- and gender-matched, proprietary norms provided by Cognitrace (e.g., manufacturers of the EEG machine) (Duffy et al., 1979). The following procedure was used: each point on the ERP graph was converted to a Z score, and these scores were used to create a normative ERP to compare to the participant's ERP. Norms provided from Cognitrace were based on 100 normal participants in each of the following age groups: 5 to 7 years, 8 years, 9 to 13 years, and 14 to 19 years. The use of these norms allowed the neurologist to employ an operational definition of amplitude abnormality by comparing the number of S.D.s by which a participant's ERP amplitude differed from the norm amplitude at specific points on the ERP waveform. ERP peaks were defined by visual inspection of the waveform for inflection points. ERP components were grouped by the neurologist into early components (P100, P200, N100 and N200) and late components (P300 only), and this information was recorded in the patients' charts. Due to the dichotomous nature of the neurologist's coding scheme, data from individual ERPs were not available for analysis in the chart-review study. Only data related to the "early" and "late" *groupings* were available to the authors.

The operational definition of abnormal referred to a condition in which participants' ERP wave amplitudes differed from the norm amplitude by at least 2.5 S.D. In this way, the amplitude or latency of the waveforms (auditory and visual) was considered normal or abnormal at each peak. However, if the amplitude of any of peak did not reach 5 μV in negative or positive amplitude, the ERP was considered absent and abnormal. Also, in terms of latency at each peak, the ERP was considered abnormal if the latency was early or late by 50 ms or more.

Using the standards described above, for both auditory and visual paradigms, ERPs were categorized as either "abnormal" or "normal" by the facility's pediatric neurologist. The activity of all available electrodes was taken into consideration during this categorization. Information regarding how many abnormalities were due to amplitude and/or latency differences in particular was not available, nor was the actual amplitude and latency values. The criterion of 5 μV for abnormal ERPs was determined by the aforementioned pediatric neurologist. Due to the dichotomous nature of the neurologist's coding for the normality (or abnormality) of the ERPs, the percentage of patients who were deemed "abnormal" due to the 5 μV criteria is not known.

3. Results

3.1. Electrophysiology

In order to determine the "abnormal" or "normal" designation for each patient's ERP, the facility's pediatric neurologist examined the activity of all 20 electrodes. A designation of "abnormal" ERP refers to an either/or situation in which the patient exhibited either abnormal amplitude, or abnormal latency, or the combination of both abnormal amplitude and latency. As noted previously, amplitude and latency information was not available for analysis; thus, the following results apply only to the dichotomous categorization available in the neurologist's report for each patient. Separate diagnostics were conducted for left hemisphere vs. right hemisphere, early ERPs vs. late ERPs, and auditory ERPs vs. visual ERPs.

Analysis of electrophysiological data indicated a tendency for larger proportion of ERP abnormalities in the left hemisphere compared to the right but these differences were not statistically significant. Significant findings were observed in the auditory (AERP) versus visual (VERP) comparisons and in the early component (100–300 ms) versus late component (300–500 ms) comparisons, using McNemar's test for correlated proportions. For auditory versus visual comparisons, McNemar's test for the difference was significant ($p<0.01$, two tailed), showing a greater proportion of ERP abnormalities in the auditory ERPs. For the early versus the late component comparisons, McNemar's test for the difference was also significant ($p<01$, two tailed), showing a greater proportion of ERP abnormalities for the early component ERPs. Results are shown in Table 2.

4. Discussion

The current study was designed to fill a void in the literature regarding the neuroelectric characteristics of impulsively aggressive juveniles. The study hypothesis that shorter-latency ERP's (100–300 ms) would show more abnormalities than long-latency ERP's (300–500 ms) was confirmed by a small, but statistically significant

Table 2
Proportion of abnormal ERPs.

Comparison type		McNemar's test
AERP	VERP	
59.31%	40.69%	$p<0.01$, two tailed
100–300 ms	300–500 ms	
55.63%	44.37%	$p<0.01$, two tailed
Left hemisphere	Right hemisphere	
35.84%	21.99%	$p>0.05$, non-sig.

difference. Further, auditory ERPs were found to show more abnormalities than visual ERPs in this population. No statistically significant hemispheric differences were noted. Taken together, these results have theoretical significance for the etiology of impulsive aggression, and perhaps also clinical relevance for the treatment of this condition. For instance, abnormality of short-latency (100–300 ms) ERP's may reflect disordered limbic activity (Wong, 1991; Connor, 2002), and auditory ERP's may be more sensitive to temporal-limbic abnormalities than visual ERP's (Matthews and Fisher, 2004). These findings lend support to the Limbic Dysmodulation Hypothesis of the etiology of impulsive aggression. According to the Limbic Dysmodulation Theory (Matthews and Fisher, 2004), electrical abnormalities in the temporal-limbic region may be associated with the clinical symptom of impulsive aggression. This electrical disorder of the limbic system could lead to extreme emotions, with a lowering of the threshold for aggressive behavior. The theorized electrical disorder is referred to as "limbic kindling", as described by Kraus (2000), which means that impulsive aggression is not a form of epilepsy but, rather, an increased neuronal sensitization. This type of limbic kindling, or electrical sensitization in the limbic areas of the brain, refers to the development of an exaggerated response to a stimulus that was previously "sub-threshold". In clinical terms, a juvenile who develops limbic kindling may subsequently show impulsive or explosive aggression to minor provocations that previously would have been innocuous.

According to the Limbic Dysmodulation Theory, it is because of this limbic electrical disorder that such juveniles become hypersensitive to trivial provocations and show persistent impulsive aggression that may become pathological (e.g., too severe, too frequent, and out of proportion to the provocation). Frequently, pathologically impulsive aggression leads to eventual psychiatric hospitalization or placement in a psychiatric residential treatment facility. It is also interesting to note (Olvera, 2002; Fisher, et al., 2007) that psychiatrists often report that the medications most helpful in treating this type of impulsive aggression are anti-epileptic medications (which might be stabilizing electrical abnormalities in the limbic system). Thus, the findings of the current study lend physiological support to the clinical lore surrounding impulsive aggression. Further support for stabilization treatment may be found in a number of recent reports linking the use of phenytoin (an anti-epileptic drug) to improvement of impulsive aggressive outbursts (Stanford et al., 2001, 2005, 2009; Huband et al., 2010).

Further, it is important to note that similar theories have been proposed by other researchers. For instance, Kiehl's (2006) paralimbic system dysfunction model of psychopathology has particular significance for the current work. This model highlights both limbic and paralimbic brain regions including the orbital frontal cortex, insula, anterior and posterior cingulated, amygdala, parahippocampal gyrus, and anterior superior temporal gyrus. Patterns of dysfunction with these regions have been associated with various types of impulsivity and aggression. Reactive aggression and impulsivity have been noted among individuals with damage to the orbitofrontal cortex, a region which may serve to modulate the activity of the emotional areas of the temporal lobe (Stuss et al., 1983; Malloy et al., 1993; Kiehl, 2006). These individuals are unlikely to demonstrate the type of goal-directed or instrumental aggression frequently seen among psychopaths (Hare, 1993; Blair, 2001; Kiehl, 2006).

It is important to note that, during the juvenile period of development, the frontal lobes are still undergoing the process of maturation (See Marsh et al., 2009; Raznahan et al., 2010). Thus, taken together, these theories may explain in part how juveniles experiencing neural hypersensitivity might have difficulty regulating aggressive behavior. The still-developing frontal regions of the brain may fail to exert adequate control over aggressive behaviors mediated through lower brain regions associated with emotion. For this reason, the period of adolescence may present a unique opportunity for intervention and treatment of impulsive aggression.

4.1. Limitations

There are limitations in this study inherent in any retrospective endeavor, such as lack of control variables, lack of availability of records, and the quality and completeness of available data. For instance, although information regarding the patients' medications would certainly have enhanced the manuscript, this information was not reliably available for the 'snapshot' period in which the electrophysiological procedures were performed. Certainly, this is one of the caveats of a retrospective chart-review study in which information was originally documented for clinical, rather than research, purposes. Future studies, utilizing a prospective research design could address this issue more thoroughly. Also, as there was no random assignment to the intake of the residential treatment facility from which participants were derived, any circumstances (e.g., managed care, low socio-economic status) which might have precluded patients from being admitted to the treatment facility could have also impacted the ecological validity of the results.

Additionally, the neurologist's dichotomous coding scheme for the "early" components of the ERP (P100, P200, N100 and N200) versus the single "late" component of the ERP (P300) prohibited the analysis of any individual waveforms. Because the cognitive correlates of the P1, N1, P2 and N2 may differ, individual analysis of these ERPs could provide additional information on the electrophysiological correlates of impulsive aggression. Similarly, as the amplitude and latency data for individual ERPs were not available for study, the neurologists' reports in the medical record were the only basis for gaging the normality (e.g., normal vs. abnormal) of the visual and auditory ERPs. Future studies, including a more in-depth analysis of the amplitudes and latencies of individual ERPs may provide additional insight into juveniles with impulsive aggression.

In addition, future studies examining the potential correlations between ERP findings and neuropsychological assessments of memory could help to clarify the nature of neural dysfunction in this population. To partially address this issue, post-hoc analyses were conducted on the current dataset using neuropsychological data from patients' intake assessment. Summary variables of absolute memory differences (e.g., verbal minus visual memory from the Wide Range Assessment of Memory and Learning, Version 2; Sheslow and Adams, 2003) and a summary variable of visual + auditory ERP data ("any ERP abnormality") were found to be significantly positively correlated. Although this correlation supports the notion of limbic dysfunction among impulsive aggressors, further study of this population, measuring a broader range of cognitive functions and using a complete psychometric battery is warranted.

Given the high degree of co-morbidity in the present patient sample (See Table 1) and the ERP abnormalities associated with some of these diagnoses (for instance, Attention Deficit Hyperactivity Disorder), it is possible that some of the ERP findings of the current study might not be specifically related to impulsive aggression per se. Future studies should more closely examine overlapping diagnoses and their contributions to both impulsive aggressive behaviors, and variations in neural function. Further, the range of ages included in this study was fairly broad. As mentioned previously, brain maturation differences could greatly affect ERPs over this particular age range. In addition, males and females may mature at different rates (Raznahan et al., 2010). However, in the current study, when post-hoc analyses were conducted on data coded for yes/no as to the presence of "any ERP abnormality", males and females didn't differ statistically with regard to their distribution in these categories. Although a longitudinal assessment was beyond the scope of the current study, future work should consider how aging might affect the potential neural substrates of impulsive aggression.

4.2. Conclusion

Impulsive aggression is a complex and multifaceted behavior with both biological and psychological influences. With regard to biological

etiology, theories have focused on neuroelectric abnormalities. The current study provides a comprehensive assessment of ERP characteristics of a large group of male and female inpatients undergoing treatment for pathological impulsive aggression. Results suggest that auditory ERPs in the range of 100 to 300 ms after stimulus presentation are most frequently associated with impulsive aggression. These findings lend support to the notion that impulsive aggression may be related to the phenomenon of 'limbic kindling' (Kraus, 2000) and may have implications for improved clinical treatment of this condition.

References

Barratt, E.S., Stanford, M.S., Kent, T.A., Felthous, A.R., 1997. Neuropsychological and cognitive psychophysiological substrates of impulsive aggression. Biological Psychiatry 41, 1045–1061.

Bauer, L.O., Hesselbrock, V.M., 1999. P300 decrements in teenagers with conduct problems: implications for substance abuse risk and brain development. Biological Psychiatry 46, 263–272.

Bauer, L.O., Hesselbrock, V.M., 2001. CSD/BEM localization of P300 sources in adolescents "at risk": evidence of frontal cortex dysfunction in conduct disorder. Biological Psychiatry 15, 600–608.

Bauer, L.O., Hesselbrock, V.M., 2003. Brain maturation and subtypes of conduct disorder: interactive effects on P300 amplitude and topography in male adolescents. Journal of the American Academy of Child and Adolescent Psychiatry 42, 106–115.

Bauer, L.O., O'Connor, S., Hesselbrock, V.M., 1994. Frontal P300 decrements in antisocial personality disorder. Alcoholism, Clinical and Experimental Research 18, 1300–1305.

Best, M., Williams, J.M., Coccaro, E.F., 2002. Evidence for a dysfunctional prefrontal circuit in patients with an impulsive aggressive disorder. Proceedings of the National Academy of Sciences 99, 8448–8453.

Blair, R.J., 2001. Neurocognitive models of aggression, the antisocial personality disorders, and psychopathy. Journal of Neurology, Neurosurgery and Psychiatry 716, 727–731.

Branchey, M.H., Buydens-Branchey, L., Lieber, C.S., 1988. P300 in alcoholics with disordered regulation of aggression. Psychiatry Research 25, 49–58.

Cappadocia, M.C., Desrocher, M., Pepler, D., Schroeder, J.H., 2009. Contextualizing the neurobiology of conduct disorder in an emotion dysregulation framework. Clinical Psychology Review 29, 506–518.

Coccaro, E.F., 2003. Aggression: psychiatric assessment and treatment. Marcel Dekker, New York.

Coccaro, E.F., McCloskey, M.S., Fitzgerald, D.A., Phan, K.L., 2007. Amygdala and orbitofrontal reactivity to social threat in individuals with impulsive aggression. Biological Psychiatry 62, 168–178.

Connor, D.F., 2002. Aggression and antisocial behavior in children and adolescents. The Guilford Press, New York, NY.

Connor, D.F., Ozbayrak, K.R., Kisuak, K.A., Caponi, A.B., Melloni Jr., R.H., 1997. Combined pharmacotherapy in children and adolescents in a residential treatment center. Journal of the American Academy of Child and Adolescent Psychiatry 36, 248–254.

Corbetta, M., Shulman, G.L., 2002. Control of goal-directed and stimulus-driven attention in the brain. Nature Reviews. Neuroscience 3, 201–215.

Craig, I.W., Halton, K.E., 2009. Genetics of human aggressive behavior. Human Genetics 126, 101–113.

Crowe, S.L., Blair, R.J.R., 2008. The development of antisocial behavior: what can we learn from functional neuroimaging studies? Development and Psychopathology 20, 1145–1159.

Duffy, F., Burchfiel, J., Lombroso, C., 1979. Brain electrical activity mapping (BEAM). Annals of Neurology 5, 309–321.

Fisher, W., Kroll, G., Matthews, D., Fisher, L., 2007. Youth with impulsive aggression: anticonvulsant medication compliance and outcome. The Journal of Neuropsychiatry and Clinical Neurosciences 19, 213–235.

Fisher, W., Matthews, D., Fisher, W., Ceballos, N., 2008. Neurophysiological correlates of impulsive aggression. Poster at the International Society for Research on Aggression, Budapest, Hungary.

Fritsch, R.C., Heinssen, R.K., Delga, I., Goodrich, W., Yates, B.T., 1992. Predicting hospital adjustment by adolescent inpatients. Hospital & Community Psychiatry 43, 49–53.

Gerstle, J.E., Mathias, C.W., Stanford, M.S., 1998. Auditory P300 and self-reported impulsive aggression. Progress in Neuropsychopharmacology & Biological Psychiatry 22, 575–583.

Hare, R.D., 1993. Without conscience: the disturbing world of the psychopaths among us. Pocket Books, New York.

Hawes, D.J., Brennan, J., Dadds, M.R., 2009. Cortisol, callous-unemotional traits, and pathways to antisocial behavior. Current Opinion in Psychiatry 22, 357–362.

Houston, R.J., Stanford, M.S., 2001. Mid-latency evoked potentials in self-reported impulsive aggression. International Journal of Psychophysiology 40, 1–15.

Houston, R.J., Stanford, M.S., 2005. Electrophysiological substrates of impulsiveness: potential effects on aggressive behavior. Progress in Neuropsychopharmacology & Biological Psychiatry 29, 305–313.

Huband, N., Ferriter, M., Nathan, R., Jones, H., 2010. Antiepileptics for aggression and associated impulsivity. Cochrane Database Systems Review 2, CD003499.

Kiehl, K., 2006. A cognitive neuroscience perspective on psychopathy: evidence for paralimbic system dysfunction. Psychiatry Research 142, 107–128.

Kraus, J.E., 2000. Sensitization phenomenon in psychotic illness: lessons from the kindling model. The Journal of Neuropsychiatry and Clinical Neurosciences 12, 328–343.

Lewis, M.D., Granic, I., Lamm, C., Zelazo, P.D., Stieben, J., Todd, R.M., Moadab, I., Pepler, D., 2008. Changes in the neural bases of emotion regulation associated with clinical improvement in children with behavior problems. Developmental Psychopathology 20, 913–939.

Lopez-Duran, N.L., Olson, S.L., Hajal, N.J., Felt, B.T., Vazquez, D.M., 2009. Hypothalamic pituitary adrenal axis functioning in reactive and proactive aggression in children. Journal of Abnormal Child Psychology 37, 169–182.

Malloy, P., Bihrle, A., Duffy, J., Cimino, C., 1993. The orbitomedial frontal syndrome. Archives of Clinical Neuropsychology 8, 185–201.

Marsh, R., Maia, T.V., Peterson, B.S., 2009. Functional disturbances within frontostriatal circuits across multiple childhood pathologies. The American Journal of Psychiatry 166, 664–674.

Mathias, C.W., Stanford, M.S., 1999. P300 under standard and surprise conditions in self-reported impulsive aggression. Progress in Neuro-Psychopharmacology & Biological Psychiatry 23, 1037–1051.

Matthews, D., Fisher, L., 2004. Anticonvulsant medication for impulsive aggression: an outcome study. Paper presented at the American Neuropsychiatric Association, Feb., Bal Harbour, Florida.

McEllistrem, J.E., 2002. Affective and predatory violence: a bimodal classification system of human aggression and violence. Aggression and Violent Behavior 10, 1–30.

McEllistrem, J.E., 2004. Affective and predatory violence: a bimodal classification system of human aggression and violence. Aggression and Violent Behavior 10, 1–30.

Olvera, R.L., 2002. Intermittent explosive disorder: epidemiology, diagnosis and management. CNS Drugs 16, 517–526.

Patrick, C.J., 2008. Psychophysiological correlates of aggression and violence: an integrative overview. Philosophical Transactions of the Royal Society B: Biological Sciences. 363, 2543–2555.

Pogarell, O., Mulert, C., Hegeri, U., 2007. Event-related potentials in psychiatry. Clinical EEG and Neuroscience 38, 25–34.

Raine, A., Venables, P.H., Williams, M., 1990. Relationships between N1, P300 and CNV recorded at age 15 and criminal behavior at age 24. Psychophysiology 27, 567–575.

Raine, A., Meloy, J.R., Bihrle, S., Stoddard, J., LaCasse, L., Buchsbaum, M.S., 1998. Reduced prefrontal and increased subcortical brain functioning assessed using positron emission tomography in predatory and affective murderers. Behavioral Sciences and the Law 16, 319–332.

Raznahan, A., Lee, Y., Stidd, R., Long, R., Greenstein, D., Clasen, L., Addington, A., Gogtay, N., Rapoport, J.L., Giedd, J.N., 2010. Longitudinally mapping the influence of sex and androgen signaling on the dynamics of human cortical maturation in adolescence. Proceedings of the National Academy of Sciences of the United States of America 107, 16988–16993.

Sheslow, D., Adams, W., 2003. Wide Range Assessment of Memory and Learning Second Edition administration and technical manual. Psychological Assessment Resources, Lutz, FL.

Slever, L.J., 2002. Neurobiology of impulsive-aggressive personality-disordered patients. Psychiatric Times 19, 74–79.

Spiers, P.A., Schomer, D.L., Blume, H.W., Mesulam, M., 1985. Temporolimbic epilepsy and behavior. In: Mesalum, M. (Ed.), Principles of Behavioral Neurology. F.A. Davis, Philadelphia, pp. 289–325.

Stanford, M.S., Houston, R.J., Mathias, C.W., Greve, K.W., Villemarette-Pittman, N.R., Adams, D., 2001. A double-blind placebo-controlled crossover study of phenytoin in individuals with impulsive aggression. Psychiatry Research 103, 193–203.

Stanford, M.S., Houston, R.J., Mathias, C.W., Villemarette-Pittman, N.R., Helfritz, I.E., Conklin, S.M., 2003. Characterizing aggressive behavior. Assessment 10, 183–190.

Stanford, M.S., Helfritz, L.E., Conklin, S.M., Villemarette-Pittman, N.R., Greve, K.W., Adams, D., Houston, R.J., 2005. A comparison of anticonvulsants in the treatment of impulsive aggression. Experimental and Clinical Psychopharmacology 13, 72–77.

Stanford, M.S., Anderson, N.E., Lake, S.L., Baldridge, R.M., 2009. Pharmacologic treatment of impulsive aggression with antiepileptic drugs. Current Treatment Options in Neurology 11, 383–390.

Stein, D.J., Towey, J., Hollander, E., 1995. The neuropsychiatry of impulsive aggression. In: Hollander, Stein (Eds.), Impulsivity and Aggression. Wiley, New York, pp. 99–100.

Stuss, D.T., Benson, D.F., Kaplan, E.F., 1983. The involvement of orbitofrontal cerebrum in cognitive tasks. Neuropsychologia 21, 235–248.

van Goozen, S.H., Fairchild, G., 2008. How can the study of biological processes help design new interventions for children with severe antisocial behavior? Developmental Psychopathology 20, 941–973.

Volavka, J., 1990. Aggression, electroencephalography, and evoked potentials: a critical review. Neuropsychiatry, Neuropsychology, and Behavioral Neurology 3, 249–259.

Wong, P.K.H., 1991. Introduction to brain topography. Plenum Press, N.Y.