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The emergence of childhood bipolar disorder: a prospective study from 4 months to 7 years of age

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Abstract

The present study reviews the development from 4 to 84 months of age of a boy diagnosed with bipolar mood disorder (BPD) and attention deficit hyperactivity disorder (ADHD) at 7 years of age. Extensive data were collected in four central domains: psychophysiology (EEG and ECG), child temperament, mother–child interactions, and peer interactions. The target child's development was traced across time and compared with a cohort of 81 normally developing children. The target child displayed an unusual psychophysiological pattern from early infancy. His highly active central nervous system was coupled with an under-aroused autonomic nervous system. By preschool, his social interactions were marked by inappropriate affect and behavioral disinhibition, along with impulsivity and aggression. Possible links between the child's psychophysiological pattern and his behavior are discussed.

Keywords: Longitudinal research; Bipolar mood disorder; ADHD; Psychophysiology; Temperament; Childhood

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1. Introduction

1.1. Background

While the formal diagnosis of a clinical disorder may be thought of as a discrete event isolated in time, the symptoms or behaviors that lead to diagnosis clearly are not. Psychiatric conditions in childhood do not appear *de novo*. Rather, they evolve from preexisting traits and tendencies and are influenced by a variety of factors (Biederman, Rosenbaum, Chaloff, & Kagan, 1995). In particular, specific behavioral and psychophysiological traits that cluster together, and are stable over time, may serve as early markers for an underlying predisposition for later psychopathology. Furthermore, the systematic study of such behavioral and psychophysiological characteristics could assist in revealing risk as well as protective factors that may prove relevant to effective interventions.

The present study traces from early infancy the behavioral, physiological, and emotional development of a child diagnosed with bipolar mood disorder (BPD) at age 7. Much of the research concerning childhood BPD has focused on uncovering the potential links between childhood and adult presentations of the disorder. For example, Geller et al. (1998) suggested that the chronic and ultrarapid mood cycling typically found in children might signify a developmental stage that then evolves into a pattern of more discrete (adult-like) depressive and manic episodes. While retrospective reviews of the developmental characteristics of individuals with adolescent-onset BPD have been informative, they have not been able to fully address questions concerning the developmental course of childhood-onset BPD. In this study, the child in question, Jason,[1] was recruited as part of a normative sample of 81 infants participating in a longitudinal study of the physiological and temperamental correlates of social and emotional development (Fox, Henderson, Rubin, Calkins, & Schmidt, 2001). Following initial recruitment, extensive psychophysiological and behavioral data were collected at 4, 9, 14, 24, 48, and 84 months of age. As such, data collected from multiple sources at multiple points in time were available for review.

Exploiting the wealth of data generated by the longitudinal study, this present report attempts to identify stable characteristics that are candidates for incorporation into future studies of BPD. Due to the unique nature of the data set, we were able to trace Jason's development across time and functional domains, both as an individual and against the backdrop of the larger cohort of normally developing children. Integrating information from diverse sources (e.g., behavior, physiology, parental reports) has proven to be extremely fruitful in the study of normative development, particularly in the field of child temperament (e.g., Kagan, Snidman, & Arcus, 1995; Rothbart, Posner, & Hershey, 1995; Rubin & Burgess, 2001). A similar approach to the study of psychopathology revealed significant associations between behavioral inhibition in early childhood and later anxiety disorders (Biederman et al., 1990). Indeed, one could make the case that the study of complex phenomena, such as temperamental shyness, is dependent on research strategies that move

[1] The child's real name has been changed in order to protect his anonymity.

across empirical and temporal domains. This is imperative if we wish to adequately reflect the nuanced and multileveled theories that often guide empirical research. It is our hope that this approach could prove beneficial to the study of developmental psychopathology in general and childhood onset BPD in particular. With this in mind, the present investigation focused on three core dimensions of child development that are of immediate interest to the study of the developmental course of childhood onset BPD: Psychophysiology (the electroencephalogram [EEG] as an index of central nervous system activation and the electrocardiogram [ECG] as an index of peripheral autonomic system activation), temperamental reactivity, and social behavior.

1.2. Diagnosis and clinical presentation

Clinical diagnosis was based on a structured research diagnostic interview (Schedule for Affective Disorders and Schizophrenia for School-Age Children—Present and Lifetime Version [K-SADS-PL]; Kaufman, Birmaher, Brent, & Rao, 1997) administered separately to parent and child by a child psychiatrist and a psychiatric nurse who had been trained in the use of the instrument. The K-SADS-PL indicated that Jason met DSM-IV criteria for past and current diagnoses of: Bipolar I Disorder with psychotic features, attention deficit hyperactivity disorder (ADHD) (combined type), oppositional defiant disorder (ODD), enuresis, and encopresis. Jason also met criteria for past (and not current) diagnosis of obsessive compulsive disorder.

Three standardized diagnostic scales were also administered: The parent report version of the Child Behavior Checklist/4–18 (CBCL; Achenbach, 1991a), the teacher report form of the Child Behavior Checklist (TRF; Achenbach, 1991b), and the BASC Parent Rating Scales (Kamphaus, Reynolds, & Hatcher, 1999). The CBCL indicated that Jason scored in the clinical range on the following scales: Anxious/depressed, thought problems, and aggressive behavior. He also scored in the borderline range on the attention scale. On the TRF, Jason scored in the clinical range for self-destructive, obsessive–compulsive, and aggressive behaviors. Finally, the overall behavioral symptom index of the BASC was in the clinically significant range at the 99th percentile. The subscales showing clinical significance were hyperactivity, aggression, conduct-problems, and depression. The attention subscale was in the at-risk range (90th percentile).

Currently, Jason is being treated at an inpatient facility for children with severe emotional disabilities. Manic and depressive episodes are observed nearly every day. When elated, Jason experiences mood-congruent delusions (e.g., believing that he has been given special powers by superheroes or the devil). Aggressive and assaultive behaviors are most prominent when Jason exhibits grandiosity and feels entitled to special treatment. For example, Jason will overturn furniture when behavior rules are not relaxed to accommodate his special status. Depressed phases are often accompanied by suicidal remarks and ideation. Jason's sleep-activity cycles are disturbed, typically shifting with his moods. In the early morning, he is tired, irritable, and difficult to awaken. During mid-morning, he is often elated, verbose, and unable to sit still. By late morning, he becomes irritable or depressed, refuses to move or follow directions, and many times falls into a comatose-like sleep. If not allowed to sleep, he becomes verbally and physically aggressive. Throughout the day, this cycle repeats every few hours. Late in the evening and into the early morning hours, Jason experiences bouts of insomnia and hyperenergy. Nightmares and restlessness are common during sleep. In addition to the grandiose delusions noted above, Jason also experiences persecutory delusions and auditory and visual hallucinations. Jason has assaulted peers on several occasions under the belief that attacks were imminent. He has heard voices and seen or felt the presence of monsters. These episodes are quite intense, leading him to run away when he has perceived the monsters to be nearby. Jason never experienced psychosis in the absence of prominent mood symptoms. His medication regimen includes dextroamphetamine, valproate sodium, risperidone, and carbamazepine. Medications, as well as other medical conditions, were ruled out as the cause of his mood disorder and psychotic features.

Finally, a review of Jason's clinical records indicates a significant family history of mental illness. His father, now deceased, was diagnosed with BPD, but never followed an approved course of treatment. On the maternal side of the family, Jason's grandmother and his 14-year-old half-sister are also diagnosed with BPD. Jason's mother, maternal grandmother, and five of his mother's siblings have agoraphobia and major depression. His mother also suffers from panic disorder and other phobias.

While this is a complex case, especially considering the co-diagnoses of ADHD and ODD, the symptom presentation along with the bilineal family history of BPD support the primary diagnosis of Bipolar I Disorder with psychotic features. Although Jason's comorbidity limits this report's ability to discuss BPD in isolation, the data presented here may help guide future studies attempting to shed light on the controversy concerning the diagnostic boundaries among these psychiatric disorders (e.g., Biederman, Russell, Soriano, Wozniak, & Faraone, 1998; Carlson, 1998; Geller et al., 1998; Kovaks & Pollock, 1995; Sachs, Baldassano, Truman, & Guille, 2000).

2. Method

2.1. Psychophysiology

2.1.1. EEG

Resting EEG during a quiet and attentive state was collected at 9, 14, 24, 48, and 84 months of age. Data were collected from F3, F4, Fz, C3, C4, P3, P4, Pz, O1, and O2, as well as the reference site (Cz), using lycra stretch caps (Electro-Cap, Eaton, OH) with tin EEG electrodes placed according to the International 10–20 system (Jasper, 1958). The central sites (C3 and C4) were not used during the visit at 84 months. The EEG channels at all ages were re-referenced via software to an average reference configuration. EEG data was not collected from Jason as 14 months due to technical difficulties.

Prior to the recording of EEG from each participant at each age, a 50-μV 10-Hz signal was input into each of the channels and this amplified signal was recorded for calibration purposes. Following gentle abrasion, a small amount of electrolytic conducting gel was inserted in each site. Impedances were measured at each site and were kept below 5 kΩ.

EEG was collected with band pass filters of either 1–100 Hz using individual Grass AC bioamplifiers (ages 9–48 months) or 0.1–100 Hz with SA Instruments (San Diego, CA) isolated bioelectric amplifiers (84 months). At every visit from 9 to 48 months, one channel of EOG was recorded from the right eye using two Beckman mini-electrodes, one placed at the outer canthus and the second placed at the supra orbit position. At 84 months, vertical eye movements were recorded from electrodes placed above and below the right eye, while horizontal eye movements were monitored with electrodes placed at the external canthi of each eye. The digitized EEG data were displayed graphically for artifact scoring. Portions of the EEG record marked by eye blinks, horizontal eye movement, or motor movement artifact were removed from all channels of the EEG record prior to subsequent analysis. EEG data collected during the visits were submitted to a Discrete Fourier Transform analysis (DFT) that utilized a 1-s Hanning window with 50% overlap between adjacent windows. This analysis quantified the spectral power in picowatt ohms (or microvolts squared) for each electrode site in single Hz frequency bins from 1 to 12 Hz. Power across three frequency bands (1–3, 4–6, and 6–9 Hz) was computed for each site by summing the spectral power of the single hertz bins in these three frequencies. These three bands were used at 9, 24, and 48 months. At 84 months, the frequency bands used were 1–3, 4–6, and 7–11 Hz. The change in the higher frequency band was prompted by previous research indicating that in older children, the 7–11-Hz band better captures alpha functioning (Marshall, Bar-Haim, & Fox, 2002). At every age, average power was calculated for the frontal (F3, Fz, F4), central (C3, Cz, C4), parietal (P3, Pz, P4), and occipital (O1, O2) regions as well as in the right hemisphere, left hemisphere, and total power across all collection sites.

It is important to note that there is an inverse relationship between power and electrocortical activation (Davidson, 1988; Lindsley & Wicke, 1974). That is, high power reflects low activation at a particular electrode site, while low power reflects high activation.

In addition to the quantitative analysis, Jason's EEG records were visually inspected for abnormalities such as spiking and excessive display of alpha spindles.

EEG recordings and quantification followed standard guidelines (Pivik et al., 1993). Further details concerning EEG collection and quantification in infants and young children can be found in Fox et al. (1995) and Marshall et al. (2002).

2.1.2. ECG

ECG data were collected during a resting baseline condition at 4, 9, 14, 24, 48, and 84 months following the procedure outlined in Bar-Haim, Marshall, and Fox (2000). Three disposable self-adhesive electrodes (Kendall Hydro-Snap) were placed on the upper and opposite lower portions of the child's torso, and the ground electrode was placed on the back of their neck. For ages 4 through 48 months, the ECG signals were amplified by a Grass bioamplifier (Model 7DAG), and the signal was digitized using Snapshot-Snapstream acquisition software (HEM Data, Southfield, MI). The ECG data from 84 months of age were collected with a custom bioamplifier from SA Instruments, and the signal was digitized with the Snap-Master Data Acquisition System (HEM Data). For all children, processing of the ECG signal was carried out using the IBI Analysis System from James Long (Caroga Lake, NY).

R-waves[2] were detected offline using a four-pass self-scaling peak detection algorithm. This gave a file containing the onset times of each detected R-wave in the physiological record. For artifact editing, the sampled ECG signal was viewed graphically alongside tick marks representing the times of software-detected R-waves. In the rare case of an obscured R-wave that was not detected by the software, a tick mark was inserted into the graphical ECG record. If the undetected R-wave was visible in the ECG, it was marked manually. If the R-wave was not visible, the tick mark was placed based on the specific editing rules of Byrne and Porges (1993).

Two measures of cardiac activity were calculated and used in subsequent analyses: Mean heart period (HP, the time between two R-waves)[3] and vagal tone (an index of parasympathetic autonomic nervous system activity which reflects respiratory-associated oscillations in HP, also referred to as "respiratory sinus arrhythmia"). For the quantification of vagal tone at 4, 9, 14, 24, and 48 months of age, the HP series was detrended using a third-order 21-point moving polynomial filter (Porges, 1985, U.S. Patent No.: 4,510,944; Porges & Bohrer, 1990). The detrended HP series was then filtered with a frequency band of 0.24–1.04 Hz. Vagal tone was calculated as the natural logarithm of the spectral power (in milliseconds squared) in this frequency band.

At 84 months of age, vagal tone was taken as the natural logarithm of the residual variability remaining in the HP series after the application of a moving polynomial serving as a high-pass filter with a frequency equivalent to 0.19 Hz (for details on age appropriate filtering bands in the quantification of vagal tone, see Bar-Haim et al., 2000). The specific cardiovascular measures of HP and vagal tone are well established as valid indices of the neurobehavioral organization underlying processes of emotion expression and regulation (for review, see Porges, Doussard-Roosevelt, & Maiti, 1994).

2.2. Temperament

2.2.1. Observed behavior

Behavioral reactivity to novel sensory stimulation at 4 months of age was used as the central determinant in selecting the children for the original longitudinal study. Testing was conducted in each infant's home where he or she was presented with visual, auditory, and olfactory stimulation (for details, see Kagan & Snidman, 1991).

The videotapes from each encounter where coded for major motoric activity, positive affect, and negative affect. Children selected for the study fell into one of three categories: (1) high motor activity and high negative affect, (2) high motor activity and high positive affect, or (3) low motor activity and low overall affect. For a complete description of this procedure, see Calkins, Fox, and Marshall (1996).

[2] An R-wave is the sharp up-tick in the ECG signal seen in visual outputs. The peak contraction of the heart's ventricles occurs near the peak of the R-wave. Therefore, the time between two consecutive R-waves is considered an accurate measure of the frequency with which the heart beats.

[3] Note that HP is inversely related to heart rate (i.e., the longer the HP the slower the heart rate).

At 14 and 24 months, individual differences in children's temperamental disposition when reacting to novelty were assessed. During each visit, the children were observed in a playroom for a set of brief episodes that included free play, an encounter with a stranger and a clown, and the presentation of novel objects. A single summary index score of behavioral inhibition was computed based on the child's physical and verbal behavior (for details, see Calkins & Fox, 1992; Calkins et al., 1996).

2.2.2. Maternal reports

At 14 and 24 months of age, mothers completed the Toddler Behavior Assessment Questionnaire (TBAQ; Goldsmith, 1987). The TBAQ is a 111-item rating form that produces five reported behavior scales: activity, pleasure, social fear, interest, and anger. Reliability and validity data may be found in Goldsmith (1996).

At 48 and 84 months, mothers completed the Colorado Child Temperament Inventory (CCTI; Buss & Plomin, 1984; Rowe & Plomin, 1977). This 30-item measure yields six scales pertaining to different dimensions of child temperament. These include emotionality, activity, attention, soothability, shyness, and sociability. Two additional scores of "impulsivity" (i.e., emotionality plus activity) and "emotion disregulation" (i.e., emotionality minus soothability) were computed (see Coplan, Rubin, Fox, & Calkins, 1994; Rubin, Coplan, Fox, & Calkins, 1995, respectively). Data on the reliability and validity of the CCTI can be found in Rowe and Plomin (1977).

2.3. Mother–child interaction

Mother–child interaction data were collected at 14 and 24 months of age. At the 14-month visit, mother–child dyads were videotaped in the standard Ainsworth and Witting (1969) Strange Situation procedure. The Strange Situation is a procedure consisting of eight episodes designed to exert a gradual increase in infant stress through the introduction of a stranger, and two sets of separations from the mother. The tapes were coded for major attachment classifications (secure, insecure–avoidant, insecure–ambivalent) and their corresponding subgroups. Raters were trained in the Strange Situation classification system (Ainsworth, Blehar, Waters, & Wall, 1978) and had achieved reliability with an experienced coder.

At 24 months of age, mother–child relations were assessed during a free-play session at the laboratory. The following behaviors were coded and then converted to z-scores: Frequency of positive or neutral vocalizations, number of smiles, frequency of bids for interaction, and total time spent in mutual play. In addition, a summary composite reflecting the overall quality of mother–child interaction was computed as the average of the four subcomponents.

2.4. Play with unfamiliar peers

At both 48 and 84 months of age, children participated in a group play session with three unfamiliar, same sex, same age peers. Each quartet consisted of one socially inhibited child, one noninhibited child, and two average children. At the 48-month visit, children were assigned to quartets based on the assessment of behavioral inhibition conducted at 24 months of age. At the 84-month visit, children were assigned to quartets based on their social play and reticence scores in the 48-month quartets (for details, see Fox et al., 1995, 2001). At both ages, Jason was assigned to the quartets as the noninhibited child.

The four children were led into a playroom where several age-appropriate toys were accessible. The visit was split into several episodes, a complete description of which may be found in Fox et al. (1995). For purposes of this study, data from two 15-minute free play sessions were used. Behaviors were coded with Rubin's (1989) Play Observation Scale (POS). Ten-second intervals were scored for social participation and the cognitive quality of play. Three independent observers, with reliability greater than .8, coded the POS. Three behavioral indices were computed: Solitary-passive behavior (summing the proportion of coding intervals spent in solitary-exploratory and/or solitary-constructive play), social reticence (the sum of onlooking and unoccupied behavior), and social play (the sum of peer conversation and group play; see Coplan et al., 1994).

2.5. Analyses

To systematically evaluate Jason's development as compared to the normative development of the studied cohort, *z*-scores were computed for each measure. We considered it noteworthy when Jason's scores were more than one standard deviation from the cohort's mean or when a significant directional pattern emerged over time. In an attempt to identify developmental precursors that might be related to Jason's overall condition, and to supplement the quantitative data with qualitative observations, behavioral data archived on videotapes were also reviewed in light of Jason's current psychiatric condition. Finally, data from children exhibiting a physiological pattern similar to Jason's was reviewed for any parallels in behavior.

To control for the possibility of gender differences, *z*-scores were calculated twice, first against the entire cohort and then against the male participants only. No gender differences were found for any measure. Therefore, only findings pertaining to the entire sample are reported.

3. Results

3.1. Psychophysiology

3.1.1. EEG

Raw power *z*-scores across age, scalp regions, and frequency bands are presented in Table 1. When compared to the cohort, Jason showed a consistent pattern of less power, in all frequency ranges, at all ages except for 1–3 Hz at 9 months of age. Most notable was the finding that Jason scored lower than the sample in raw EEG power in the 4–6-Hz band at all ages, most often over one standard deviation below the mean. In addition, at 48 and 84 months of age, Jason also scored below one standard deviation from the cohort's mean in the 1–3-Hz band. Across frequency bands and ages, the findings were not specific to a single scalp region. Rather, it appears to be a global trademark of Jason's electrocortical activity. Fig. 1 shows the cohort's distribution of total EEG power across ages and frequencies.

Table 1
Z-scores of Jason's EEG power across age and EEG frequency

Scalp region	9 months ($n = 72$)			24 months ($n = 66$)			48 months ($n = 65$)			84 months ($n = 60$)		
	1–3 Hz	4–6 Hz	6–9 Hz	1–3 Hz	4–6 Hz	6–9 Hz	1–3 Hz	4–6 Hz	6–9 Hz	1–3 Hz	4–6 Hz	7–11 Hz
Frontal	0.61	− 0.95	− 0.51	− 0.31	− 0.13	− 0.70	− 1.46	− 1.23	− 0.62	− 0.97	− 1.67	− 0.39
Central	0.06	− 0.78	− 0.58	− 0.99	− 1.11	− 0.31	− 1.18	− 0.84	− 0.45	–	–	–
Parietal	0.59	− 1.22	− 0.43	− 0.38	− 1.04	− 0.25	− 0.80	− 0.96	− 0.17	− 0.46	− 0.83	0.22
Occipital	0.36	− 1.01	− 0.40	− 0.55	− 0.89	− 0.49	− 1.15	− 0.84	− 0.41	− 1.36	− 1.57	− 0.71
Right hemisphere	0.85	− 1.00	− 0.46	− 0.44	− 1.11	− 0.49	− 1.29	− 1.07	− 0.45	− 1.09	− 1.45	− 0.39
Left hemisphere	0.20	− 1.20	− 0.65	− 0.67	− 1.05	− 0.35	− 1.22	− 1.01	− 0.42	− 0.90	− 1.53	− 0.25
Total	0.58	− 1.15	− 0.57	− 0.65	− 1.09	− 0.43	− 1.28	− 1.05	− 0.44	− 1.09	− 1.54	− 0.33

Despite the fact that Jason was awake and attentive during data collection, a visual inspection of the streaming EEG signal revealed occasional alpha spindles in frontal leads at 6–9 Hz. These unusual alpha spindles were first evident at 24 moths of age and became more pronounced at 48 months of age. By the age of 84 months, alpha rhythms (7–11 Hz) were prevalent throughout the entire EEG record. This, however, may have been due to Jason's medication regimen, which was fully implemented two months prior to the testing session at 84 months.

3.1.2. ECG

The distribution and *z*-scores across age for HP and vagal tone are presented in Fig. 2 and Table 2, respectively. During each of the first five visits (4, 9, 14, 24, and 48 months), Jason showed a pattern of greater HP (slower heart rate) as compared to the cohort. While only exceeding one standard deviation from the mean at 4 and 14 months of age (1.80 and 1.43, respectively), the elevation in HP at 9 and 48 months was also pronounced (0.92 and 0.96, respectively). Jason showed elevated vagal tone at 4, 9, and 14 months of age as compared to the cohort (*z*-scores of 1.28, 1.94, and 1.46, respectively). At 84 months of age, Jason's cardiac pattern reverses. At this point, Jason was over one standard deviation below the mean in HP and showed decreased vagal tone. This shift in Jason's pattern of cardiac activity is most probably associated with Jason's medication, which included dextroamphetamine, an amphetamine known to produce tachycardia.

3.2. Temperament

At 4 months of age, Jason displayed low motor activity, low positive affect, and low negative affect to sensory stimulation. Compared to a screened population of 235 infants, Jason fell in the bottom 30% in each of these behavioral dimensions. Further inspection of the videotapes revealed that Jason displayed little overt affect.

At both 14 and 24 months of age, Jason showed little sign of behavioral inhibition during laboratory testing. At 14 months of age, Jason was − 1.03 standard deviations below the

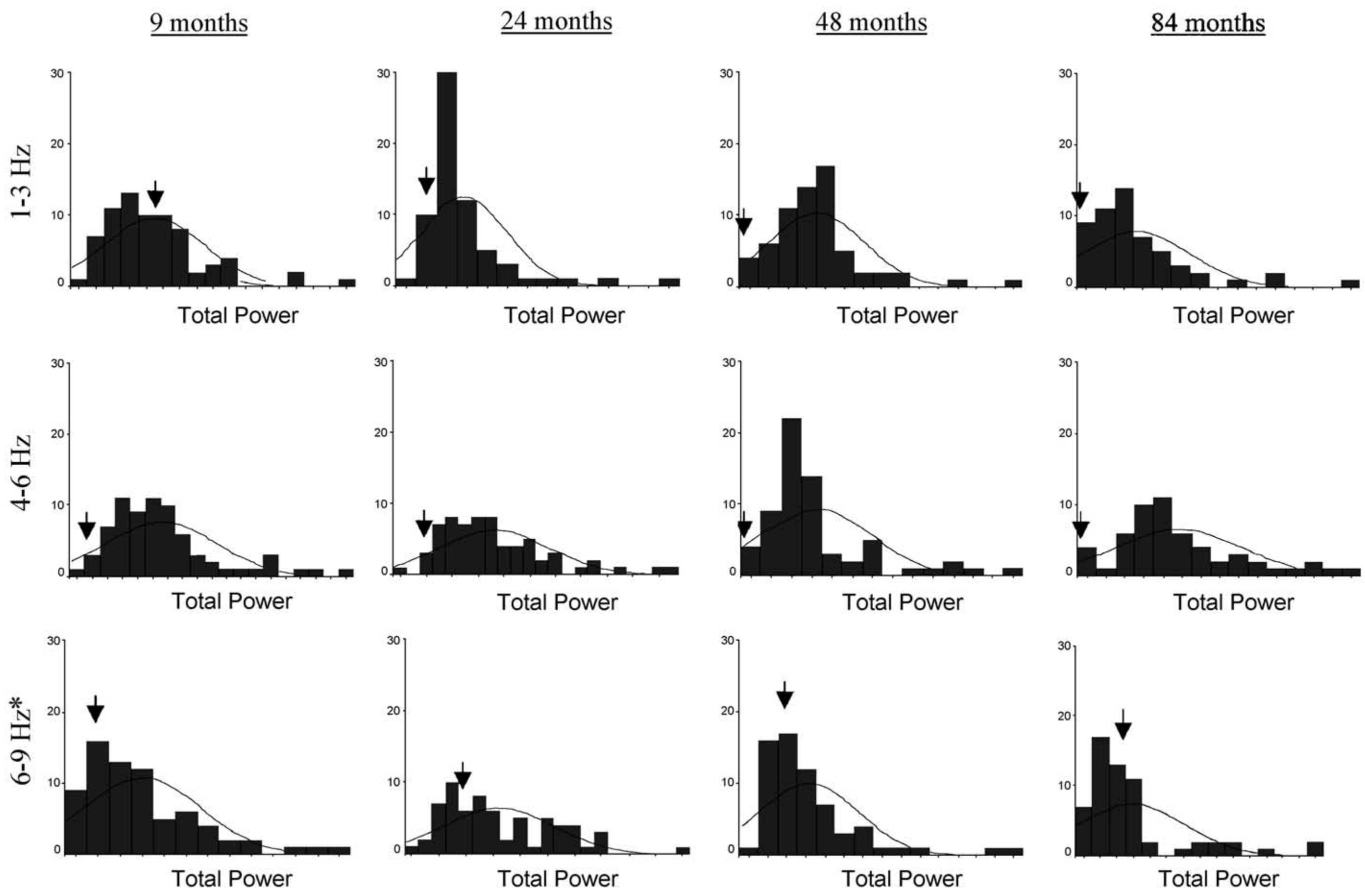

Fig. 1. Distribution of average total power across ages and frequencies. The arrow indicates Jason's position within each distribution. At 9, 24, and 48 months, the following frequency bands are used: 1–3, 4–6, and 6–9 Hz. At 84 months, the 7–11-Hz band replaces the 6–9-Hz band.

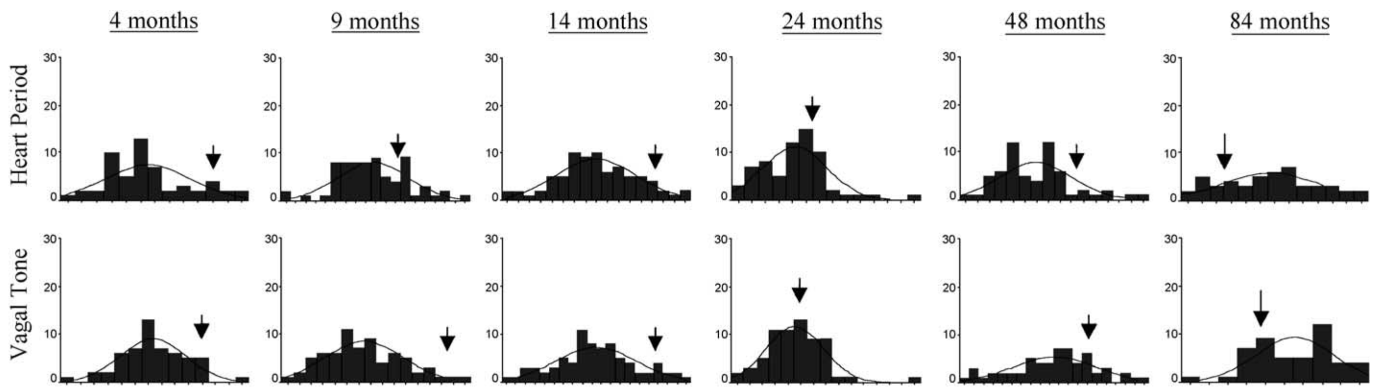

Fig. 2. Distribution of the cardiac data (HP and vagal tone) across ages. The arrow indicates Jason's position within each distribution.

Table 2
Z-scores of Jason's HP and vagal tone across age

	4 months ($n=55$)	9 months ($n=71$)	14 months ($n=79$)	24 months ($n=66$)	48 months ($n=60$)	84 months ($n=48$)
Heart period	1.80	0.92	1.43	0.16	0.96	− 1.23
Vagal tone	1.28	1.94	1.46	− 0.54	0.65	− 0.84

group's mean. By 24 months, he was − 1.61 standard deviations below the mean. This is not to imply that Jason displayed sociable behavior, as low inhibited children typically do. His involvement with objects, with his mother, and with a stranger was disorganized, fragmented, and marked by high levels of frustration. He was fidgety, constantly running in the room, and banging against the walls. This behavioral pattern was mirrored by maternal report on the TBAQ "anger" and "activity" scales, which were 1.04 and 0.93 standard deviations above the group's mean, respectively. The "interest in external events" scale was 1.20 standard deviations above the mean. At 24 months, when the same laboratory procedures were repeated, Jason's behavior seemed much better regulated. While signs of frustration and anger were still evident, these were not as extreme or deviant as before. Maternal reports validated these observations. The "anger" and "activity" scales of the TBAQ were no longer extreme. Interestingly, the "pleasure" scale was now 1.26 standard deviations above the group's mean.

At 48 months of age, maternal ratings on child temperament using the CCTI indicated that Jason was 1.10 standard deviations above the group's mean on both the emotionality scale and the impulsivity index. Jason was also 0.89 standard deviations above the mean on the emotion disregulation index. At 84 months, Jason's temperamental characteristics as reported by his mother were more extreme. This was seen in high scores on the emotionality scale (1.69) and the impulsivity (1.13) and emotion disregulation (1.70) indices. Jason was also − 1.19 and − 1.41 standard deviations below the mean on the soothability and sociability scales, respectively.

3.3. Mother–child interaction

In the Strange Situation at 14 months of age, Jason displayed an atypical behavior profile that was difficult to classify using the standard Ainsworth et al. (1978) classification system. The difficulty was in deciding between a secure (B2) classification and an avoidant (A2) classification. Further consultation with an experienced attachment researcher (A. Sagi) tipped the balance toward a secure classification. Jason did not seem distressed during episodes involving separation and reunion with his mother. He also showed little or no emotional response to epochs in which he was left in the room without his mother, either with a stranger or entirely alone. Upon the mother's return, there was minimal effort by Jason to achieve physical contact or proximity with her. However, his mother was quick to initiate contact during reunion. Jason seemed to accept the contact passively and gave the impression of liking it. Overall, there were no signs of active avoidance or resistance.

During free-play interaction with his mother at 24 months of age, Jason directed less positive vocalizations and smiles towards her, made fewer bids for interaction, and spent less time in mutual play as compared to the cohort's average. Jason's average z-score for the four measures was -0.76 standard deviations below the mean.

Overall, Jason's interactions with his mother seemed attuned and sensitive. However, in reviewing the archival videotapes, it became apparent that Jason's mother was primarily responsible for maintaining positive engagement, while Jason typically played a more passive role.

3.4. Play with unfamiliar peers

At 48 months, Jason displayed a high frequency of solitary-passive behavior and was 1.35 standard deviations above the group's mean for this measure. There were no signs of excessive anxious/reticent behavior and he was close to the group's mean on social play. At 84 months of age, Jason's solitary-passive behavior became even more pronounced, now 4 standard deviations above the group's mean. In addition, Jason's social play behavior had decreased to the level of -1.72 standard deviations below the mean. Once again, there were no excessive signs of reticent behavior. Further inspection of the tapes revealed that at both ages Jason's sparse attempts to join his peers in play were marked by aggression and obtrusive behavior. When entering social interactions he tried to dominate play and control the actions of the other children. These behaviors were met with peer rejection to the point of physical retaliation. In the rare occasions when the other children tried to join Jason in his solitary games, he seemed to interpret their bids as attempts to take toys away from him and reacted aggressively.

3.5. EEG/ECG patterns—extreme group assessment

Jason displayed a distinct physiological pattern of high central nervous system activation, coupled with a vegetative autonomic system. In order to further assess potential correlates of this physiological pattern, cohort children displaying a similar physiological pattern were selected for further analyses. Z-scores for EEG total power at 4–6 Hz and vagal tone were calculated for each age. These scores were then averaged to create aggregate measures of autonomic and central activation. Children in the top quartile on vagal tone and bottom quartile on EEG power were selected. This included Jason and four other children, indicating that this psychophysiological pattern is quite unusual. A scatterplot of EEG total power by vagal tone aggregates is displayed in Fig. 3.

An inspection of the temperamental characteristics of the children in the designated subgroup revealed that at 4 months of age, three of the children exhibited high motor reactivity and high positive affect to sensory stimulation, and one child displayed high motor reactivity coupled with high negative emotionality. Jason was the only child who displayed low motor reactivity and low affect. All five children showed low levels of behavioral inhibition at both 14 and 24 months of age. However, only Jason and one additional child were more than one standard deviation below the mean. At 48 months, all five children in the subgroup displayed low levels of social engagement with their peers during free play. For Jason and one other child, this was seen in very high

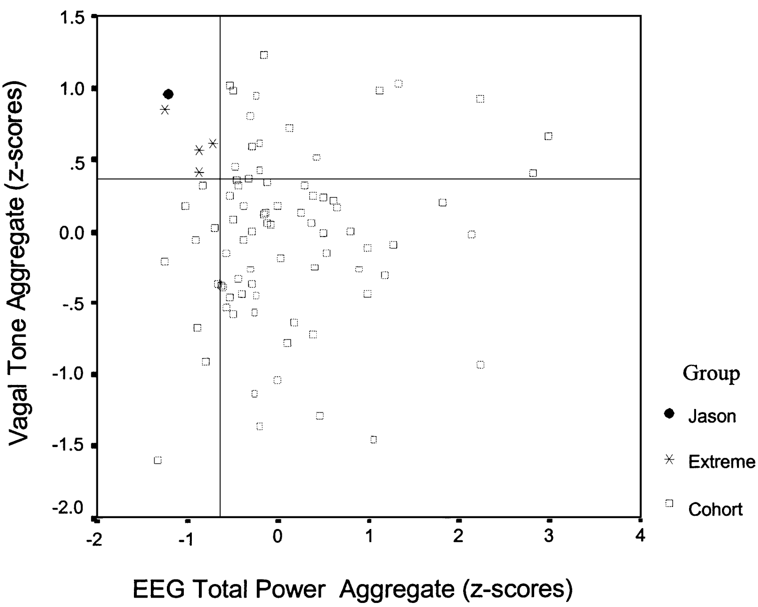

Fig. 3. Plotted distribution of the vagal tone aggregate by the EEG 4–6 Hz total power aggregate. Noted on the plot are the positions of Jason and the four children who also show dissociations between central and autonomic nervous system functioning.

frequencies of solitary-passive behavior. At 84 months of age, however, only Jason continued to display high frequencies of solitary behavior and low social play. By this age, the other children in the subgroup had moved closer to the cohort's mean in terms of their social behavior.

4. Discussion

This study has examined a broad range of physiological, psychological, and behavioral measures in an attempt to portray the developmental progression of a single child diagnosed with early-onset BPD (as well as ADHD and ODD). These data indicate that Jason's developmental difficulties cluster into three major domains that, when taken together, may be potential early precursors to his eventual diagnoses. These domains are: Psychophysiology (reduced autonomic nervous system activity coupled with abnormally increased activation in the central nervous system), emotion (inappropriate and disregulated affect), and self-regulation (behavioral disinhibition marked by impulsivity and aggression).

While aberrations in Jason's behavior only became apparent over time, deviations in psychophysiological patterns were observed early in infancy. Jason showed a pattern of increased electrocortical activity throughout the course of the study. This was most evident in the EEG signal at the low frequency ranges of 1–3 and 4–6 Hz across all recording sites. Previous work has found greater power in the lower frequency bands (0.5–2.5 and 2.5–7.5 Hz) for young children with ADHD (Clarke, Barry, McCarthy, & Selikowitz, 1998). This pattern was then reversed in the higher bands (7.5–13.5 and 13.5–20.5 Hz). These data are of interest in that they may help in teasing apart the difficult issue of co-morbidity between BPD and ADHD. In Jason's case, the data would seem to indicate that his pattern of electrocortical activity is not in line with that of a child with "pure" ADHD.

Jason displayed a pattern of high HP, coupled with high vagal tone. This pattern of cardiac activity is thought to reflect a "conservation" state that is typically associated with low reactivity to external stimulation (Porges, 1997). Vigilant or wary children, on the other hand, often display low HP and HP variability (e.g., Kagan, Reznick, & Snidman, 1987). High and unstable vagal tone positively correlates with temperamental difficultness (Porges, Doussard-Roosevelt, Portales, & Suess, 1994) and regulatory disorders (DeGangi, DiPietro, Greenspan, & Porges, 1991) in infancy and early childhood. Excessively high variability in cardiac activity might indicate irregularities in children's ability to mobilize responses to external stimulation and engage in productive social interactions. During interactions with others, metabolic output may need to be rapidly regulated in order to foster the behavioral and psychological processes required to engage and disengage with the environment (Porges, 1997). When these processes are imbalanced, behavioral and emotional regulation could be compromised.

Taken together, the EEG and ECG data suggest an incongruent psychophysiological profile. There is an apparent dissociation between Jason's highly activated central nervous system and his under-aroused autonomic nervous system. The psychophysiological dissociation described above was highly stable across time. However, Jason's behavior became increasingly unstable with age. It may be that the increasing bidirectional influence of the central and peripheral nervous systems led to impairment in Jason's ability to adjust to contextual demands. Without the support of more flexible nervous system activity that actively monitors and processes feedback from internal states and the environment, behavior is likely to become increasingly disregulated.

In accord with his physiological irregularities, Jason's social behavior was difficult to characterize using traditional temperament and attachment measures. Typically, securely attached infants show distress during separation episodes in the Strange Situation and display contact seeking and contact maintaining behaviors at reunion. Such behaviors were absent from Jason's repertoire. Furthermore, disinhibited children make frequent attempts for social engagement, often involving the active expression of positive affect (Fox et al., 2001). As a toddler, Jason's affective displays were disjointed and he made only sparse attempts at social engagement. Jason's behavior in the presence of peers was marked by a solitary passivity, punctuated by aggressive and inappropriate attempts to join the ongoing activity. It may be that, over time, Jason's social skills became increasingly ineffective and disorganized. Lack of proper emotion regulation, increased isolation, and disregulated nervous system activity may have impeded Jason's development in the arena of interpersonal interaction. Such circumstances may have provided him with fewer opportunities to learn and practice the complexities of social engagement.

Taken together, the physiological and behavioral data reveal a relatively coherent developmental pattern. Abnormalities in Jason's developmental trajectory seem to revolve around difficulties in the regulation of biological rhythms, affect, and behavior. This pervasive regulatory problem was manifested in signs of vegetative autonomic system and under-reactive responsiveness to sensory stimulation as early as 4 month of age. This may have been exacerbated by Jason's family background, which placed him at greater risk for psychological difficulties. With increasing age, these temperamental dispositions and disregulated states became increasingly noticeable in interpersonal and task-oriented contexts.

Interestingly, Jason's psychiatric status mirrors the empirical observations of diagnostic co-morbidity between ADHD, BPD, and ODD. Boundaries between these childhood disorders are the focus of a great deal of debate (e.g., Biederman et al., 1998; Carlson, 1998; Geller et al., 1998; Kovaks & Pollock, 1995; Sachs et al., 2000). However, each of these diagnostic categories involves a core regulatory dysfunction (i.e., attentiveness and/or impulse control in ADHD, affective regulation in BPD, and behavioral inconformity in ODD). This may suggest that these disorders share a common etiologic core. Indeed, Biederman (Biederman, Newcorn, & Sprich, 1991) makes the case for a common vulnerability between ADHD and major mood disorders.

Furthermore, Jason's physiological predispositions seem to affect his ability to achieve important developmental milestones. Deficiencies in emotional and motor responsiveness might have compromised early mother–child bonding, which in turn might have lead to impaired two-way communication between Jason and his mother. Typically, even the most competent parents are not prepared to deal with under responsive and highly disregulated children. Parents carry an important role in helping infants and young children to achieve physiological, behavioral, and emotional regulation. For some children and parents, this task may prove exceptionally challenging. When the interactive regulatory processes occurring between parents and children are compromised, difficulties in impulse control, low behavioral inhibition, disregulated affective expression, and ultimately low competence and passivity in social interactions with peers are reasonably expected. Supporting this speculation concerning Jason's developmental ontogeny is the finding that all four children displaying a similar psychophysiological pattern showed relatively high levels of disinhibition at the younger ages and a tendency to be less social at 48 months of age. However, Jason was consistently the most extreme on these behaviors and only he continued to show this behavioral pattern at 84 months of age. It may be that Jason's genetic predisposition and/or the presence of psychopathology in his immediate parental environment made him more vulnerable to extreme behavioral and physiological disregulation.

5. Conclusion and practical implications

We believe that, despite the limitations associated with the study of a single case, the extensive developmental data available allowed for a unique description of several core domains in Jason's development, which seem to be related to the course of his psychiatric status. This multifaceted developmental description of a child eventually diagnosed with BPD and ADHD may serve to identify possible markers for further exploration and monitoring for professionals working with infants and young children displaying similar behaviors as those described for Jason. Additionally, the prospective nature of the dataset offers practitioners a unique glimpse at information that is typically not available to them when working with children and adolescents. However, since the data of the present report portray the development of a single child, it should be interpreted with caution. Several steps are needed before the findings could bear direct practical implications for diagnosis and treatment. First, it is necessary to establish that the presently identified physiology-behavior cluster is indeed characteristic of other children diagnosed with BPD and/or ADHD. Longitudinal studies involving larger samples will allow us to see if the potential core risk factors identified in the present data are also found in other infants and young children that are eventually diagnosed with the disorders in question. In that respect, future studies into the etiology of BPD and ADHD may wish to focus on the associations between temperamental affective regulation and the psychophysiological patterns of the central and the autonomic nervous systems.

Unfortunately, the uncertainty concerning the diagnostic boundaries between BPD and ADHD, and perhaps even ODD, could not be resolved in the present case. However, the cluster of stable characteristics described in this article may help guide future studies of ADHD and BPD. It may be the case that the unique psychophysiological pattern observed in Jason is in fact exclusively associated with BPD or ADHD, in which case the boundaries between these disorders may become better defined at the physiological level of analysis. As such, the second step must be to determine whether the identified psychophysiological risk factors can be efficiently used for case identification. Since the methods used here are noninvasive and sensitive to a young child's limited behavioral repertoire, they may allow researchers and clinicians to detect at-risk children earlier than currently possible with traditional psychodiagnostic measures. Finally, with the additional information at hand, it may become possible to develop early intervention programs that would target the specific disregulations (behavioral as well as physiological) associated with BPD and ADHD.

Lastly, this study indicates that the longitudinal and systematic research methodology employed in the field of developmental psychology may contribute to the understanding of psychiatric and psychological conditions. In particular, the study of the childhood onset of psychiatric disorders such as BPD and ADHD may benefit from prospective studies beginning early in infancy and collecting both physiological and behavioral data.

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