THE Earliest Behavioral Expression OF Focal Damage TO HUMAN PREFRONTAL CORTEX

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ABSTRACT

Damage to the prefrontal cortex in childhood can produce long-term impairments of emotion, behavior regulation, and executive functions, but little is known regarding the earliest expression of these impairments. We describe here detailed behavioral studies of a boy at 14 months of age (‘PF1’) who sustained focal damage in the right inferior dorsolateral prefrontal cortex due to resection of a vascular malformation on day 3 of life. The surgery was followed by a good medical recovery, and he reached developmental milestones at a normal rate. His neurological examination was normal, as were his mother’s ratings of communication abilities, daily living skills, socialization, and motor skills. Multiple standardized laboratory paradigms were used to evaluate his behavior in structured and relatively unstructured situations designed to elicit positive and negative emotions and to place demands on attention. Relative to a comparison group of 50 age-matched boys with no neurological history, PF1 demonstrated significant impairments in the regulation of emotion and engagement of attention, particularly in unstructured conditions. These findings indicate that damage to prefrontal cortex in infancy begins to impact on emotional and cognitive development already during the first months of life.

Key words: prefrontal cortex, emotion, attention, executive function

INTRODUCTION

Injury to the mammalian prefrontal region early in life results in impairments in aspects of social behavior, emotion, arousal, attention, and higher-order integrative functions. Dysfunction within ventral and medial sectors is most strongly associated with social and emotional deficits, while dorsolateral damage appears to impact more on attentional and integrative functions. (e.g., Ackerly and Benton, 1948; Anderson et al., 1999; Bowden et al., 1971; Eslinger et al., 1992; Harlow et al., 1964; Kolb et al., 2004; Max et al., 2005; Price et al., 1990). In humans, early damage in the ventromedial prefrontal region places individuals at risk for failure to develop normal social or occupational competencies in adolescence or adulthood, due to chronic emotional disruption and impairments of decision-making, planning, and behavior regulation (Anderson et al., 2004), while early damage to dorsolateral regions may have greater impact on the development of aspects of executive functions (e.g., Eslinger and Biddle, 2000). The often debilitating neuropsychological impairments that persist for decades following childhood prefrontal injuries stand in marked contrast to the relatively good functional recovery and development that occur following childhood damage to certain other brain regions, such as the relatively normal development of language following early damage to the left perisylvian region.

Early-onset lesions with clear boundaries between damaged and normal tissue and no involvement of non-prefrontal regions are not common, but study of such cases can aid in understanding more common conditions in which prefrontal cortex may be damaged together with more widespread damage (e.g., traumatic brain injury – TBI). Levin et al. (2004) found that school-aged children who had sustained TBI and had evidence of damage to the frontal lobes on magnetic resonance imaging (MRI) were twice as likely to be disabled as children who had sustained TBI but had no evidence of frontal lobe damage. Location of injury in TBI likely interacts with several other factors in determining outcome, including injury severity, pre-injury adaptive abilities, and post-injury environment (Anderson et al., 2004).

Although much has been learned about the long-term consequences of childhood prefrontal injury, the earliest behavioral expression of such injury remains poorly characterized. In a recent review of the published cases of childhood-onset prefrontal lesions (Eslinger et al., 2004), the youngest research participant at the time of evaluation was 6 years of age (Marlowe, 1992), by which time behavioral impairments already were prominent. Currently, information regarding the expression of dysfunction in human prefrontal cortex during the first 5 years of life is based primarily on the retrospective reports of parents or other care providers.

Because of the lack of evidence from early childhood, it is not known when the behavioral...
impairments resulting from prefrontal injury first become apparent. It has been proposed that, in nonhuman primates at least, a certain degree of maturation is required for the impairments resulting from prefrontal lesions to be expressed. For example, Franzen and Myers (1973) found that the behavior of infant and 1 year old monkeys with bilateral prefrontal lesions did not differ from normal age-matched monkeys, but that behavioral deficits in the lesioned monkeys became increasing evident in 2 and 3 year old juveniles and adults.

In our experience, the retrospective reports of parents of children with early-onset prefrontal lesions often are consistent with the notion that there may be increasingly severe deficits with increasing age throughout childhood and adolescence. These reports also often suggest that relatively subtle precursors appeared during infancy of the more aberrant behaviors that develop later. This developmental profile is illustrated by J.P., the case of Ackerly and Benton (1948), who had a congenital bilateral prefrontal lesion and was first evaluated at age 13. J.P. was reported to have acquired normal early developmental milestones and was not recalled as being particularly disruptive in early childhood. However, he had a tendency to wander long distances without fear at age 2 or 3, foreshadowing the severe impairments in social behavior and judgment that became evident in later childhood and persisted into adulthood.

Identification of the earliest deficits resulting from prefrontal damage will be important for achieving a better understanding of subsequent impairments in the development of mature social and occupational competencies. Also, evaluation of early social and emotional behaviors and cognitive abilities may eventually, with further study, come to have predictive validity that could be of considerable benefit to parents, educators, and care providers. It is reasonable to think that if effective interventions are to be developed for these neurobehavioral disorders, the greatest probability of success will be associated with early intervention, which in turn depends on early identification.

The purpose of this study was to begin to investigate the early signs of circumscribed damage to human prefrontal cortex when that damage is incurred in infancy. We expected that such injury could impact on emotion, attentional and integrative functions, and behavior regulation from the earliest age, with the specific profile of these deficits depending on location of the lesion in the prefrontal cortex. In this study, a 14-month-old boy with a focal right prefrontal lesion was examined with regard to neurologic and developmental status, and his behavioral responses were compared to those of an age-matched group of boys on a battery of standardized laboratory challenges of emotion and attention.

**Methods**

**Participants**

The participants in this study were 51 boys between the ages of 13 and 15 months. One boy (‘PF1’; age 14 months) had a focal lesion in the right prefrontal region, and the other 50 boys (group NC) were neurologically normal.

**PF1 History**

PF1 was the product of a normal and uncomplicated pregnancy and delivery. Ultrasounds during pregnancy did not reveal any abnormality. He was the third child born into a stable family, and his siblings were healthy and normal. His parents were college graduates. There was no family history of neurologic or psychiatric disease. At birth, the child appeared to be healthy except for prominent swelling under the skin in the right forehead area. Computed tomography (CT) and magnetic resonance (MR) imaging of the head revealed an enhancing mass extending through the skull and occupying much of the right frontal region. A craniotomy was done at the age of 3 days, and a right frontal mass was removed. The pathology indicated a cavernous angioima with no malignant transformation. Total resection of the tumor was accomplished, and there has been no evidence of regrowth. During the resection, the surgeons entered into the frontal horn of the right lateral ventricle to inspect the cavity, but there was no evidence of abnormality there. PF1 recovered well from the surgery, and his subsequent medical history has been unremarkable.

Comparing the first 14 months of PF1’s development to that of his 3 siblings, his parents felt he was on target. He started crawling at 8 months and walking at 12 months. By 1 year of age, he was speaking single words. He seemed to have normal exploratory behavior toward objects in his environment, and he seemed normally attentive and responsive to people. His mother felt he had a tendency to chew on or attempt to eat items that exceeded that seen in their other children.

**PF1 Neurologic Examination**

The neurological examination was normal. Cranial nerves II-XII were normal. The face was symmetric and extraocular movements were full. Muscle bulk, tone, and movement were normal in all four extremities. Reflexes were normal, and gait was normal.

**PF1 Neuroimaging**

MRI revealed a circumscribed lesion in the right inferior dorsolateral prefrontal cortex, at the juncture of the orbital and inferior dorsolateral
sectors (Figure 1). In the anterior-posterior axis, the lesion extends from the lateral polar region back to the anterior horn of the lateral ventricle. Although there is extension deep from the lateral surface, the lesion remains almost entirely within the cortex. There is limited white matter in this region at this age. There is no damage to the mesial prefrontal cortex.

Group NC

The comparison sample included 50 age-matched, normally developing boys who had entered a longitudinal study of social-emotional development at 7 months. They were seen at 15 months for a follow-up assessment (mean = 15.10, SD = .46; 46 boys were either 14 or 15 months). The families responded to letters sent to parents of newborns identified through birth records and to broadly disseminated advertisements in Iowa. Most boys were first (46%) or second (26%) born. The families were all intact at the entry. Most were well educated: 25% of mothers and 28% of fathers had no more than high school education; 12% of mothers and 18% of fathers had an associate degree, 35% of mothers and 36% of fathers completed college, and 29% of mothers and 18% of fathers had post-college education.
Procedure

*Vineland Adaptive Behavior Scales (VABS)*
(Sparrow et al., 1984)

The VABS (Survey Form) is a semi-structured interview administered to parents regarding their child's behavioral sufficiency in four domains: Communication, Daily Living Skills, Socialization, and Motor Skills. The parents' responses are compared to a national standardization sample, which included 200 children between the ages of 12 and 23 months for the purposes of this study. Standardized scores with the mean = 100 and a SD = 15 are derived in each of the four domains. For the age group involved in this study, the content of items in each domain is as follows. The Communication domain includes questions regarding attention to and comprehension of spoken language, as well as verbal and gestural expression. The Daily Living Skills domain refers primarily to eating behaviors at this age, and to a lesser extent, early dressing and toileting behaviors. The Socialization domain includes questions regarding interest in other people, emotional responses to others, and imitation behavior. The Motor Skills domain focuses primarily on walking and manually manipulating items.

**Behavioral Observations in Standardized Laboratory Paradigms**

PF1 and his mother participated in a 1-hour long laboratory session. The laboratory includes a naturally furnished "living room" and a sparsely furnished play room. A female staff member (E) conducted the session. All procedures and the coding systems were identical to those employed with the comparison group of boys. The procedures included several mother-child naturalistic interaction contexts (snack, play, etc.), standard emotion-eliciting episodes (joy, fear, and anger), and a paradigm assessing the child’s internalization of maternal prohibition or restraint, and attention tasks. The session was videotaped through a one-way mirror.

In the study of the normative sample, all data were coded from videotapes by independent teams of coders, and approximately 20% of cases were used for reliability. Those reliability data are reported below. Coders also periodically realigned to prevent drift. PF1’s videotapes were coded by some of those experienced coders.

Because the coding systems yield extensive data on various dimensions, data reduction procedures tend to be extensive as well. We describe those data reduction procedures for the NC sample below. PF1’s scores were processed following identical procedures. Whenever composite measures were used to characterize children’s behavior in a given paradigm, component scales were standardized and averaged. In these instances, PF1’s raw component scale scores were standardized relative to the mean and SD of the comparison sample.

**Emotion Measures**

The emotion measures encompassed “free-flowing” expression of emotion in naturalistic interactive contexts with the mother (cumulatively 22 minutes) and standardized emotion-eliciting episodes. The latter were carefully scripted procedures drawn from the Laboratory Temperament Assessment Battery (Lab-Tab; Goldsmith and Rothbart, 1999) and our own earlier work (Kochanska et al., 1998). The Lab-Tab battery employs traditional emotion stimuli, known to elicit joy, anger, and fear in most young children.

Coding judgments of emotions in “free-flowing” naturalistic contexts are made in 30-second segments and are global or molar in nature. In contrast, the judgments in standardized emotion paradigms from Lab-Tab are made in shorter segments, e.g., 5 sec segments. Further, these judgments consider small changes in emotion expression in multiple modalities (facial, vocal, bodily) and multiple parameters of the emotional response (latency, intensity, and duration).

**Mother-Child Interactive Contexts**

**Procedure**

In these contexts, we assessed “free-flowing” expression of emotions. It was coded for each 30 sec segment of the naturalistic interactions (total of 44 segments).

**Coding and Reliability**

All discrete positive affects and all discrete negative emotions were coded. More than one discrete emotion could be coded in a 30 sec segment, but each only once. If no clear discrete emotion was present, the prevalent mood was coded as “neutral positive” or “neutral negative”. The discrete emotions were marked if the affect was particularly intense or pervasive (lasting more than half a segment). Reliability, kappas, ranged from .74 to .87.

**Data Aggregation**

We tallied all instances when the child’s emotion was coded as moderately or strongly positive, all instances when the child’s emotion was coded as moderately or strongly negative, and all instances when the child was in neutral mood (positive or negative). We then divided each tally by the total number of segments. All analyses were conducted on those three scores separately.
Standardized Emotion Paradigms

Joy

Procedure. Joy was assessed in a Puppet episode, a playful dialogue enacted by E, who held two colorful hand puppets. The episode ended with the puppets gently tickling the child. E operated and spoke for the puppets, but she remained “in the background” and did not involve the child.

Coding and reliability. The episode was divided into short epochs consistent with its script, for example, from the appearance of the puppets to the first tickle, from the first to second tickle, from the second to third tickle. For each epoch, the coders recorded the presence or absence of smiling, laughter, positive vocal acts, such as squealing, babbling, and positive motor acts, such as clapping, waving arms, reaching for the object. Peak intensity of smiling was coded from none, to mild, to moderate, to strong. Latency to smile, in seconds, was also coded. Reliability, kappas, ranged from .79 to .87. Alpha for the latency to the first smile was .99.

Data aggregation. Latency to the first joy reaction was reversed; peak intensity of smiling was weighted by its duration (measured in percent epochs a smile was noted); and percent epochs when the infant engaged in each of three classes of discrete acts, i.e., laughter, positive vocals, and positive motor acts, were summed. Each of these three component scales was standardized and averaged to form the joy composite measure.

Anger

Procedure. Anger was assessed in a Car Seat episode that involved a 1-min confinement in a commercially available car seat.

Coding and reliability. The episode was divided into 5 sec coding segments. The coding captured presence or absence of facial, vocal, and bodily expression of anger. Facial anger peak intensity was coded with a scale from 0 (none) to 3 (strong), bodily anger peak intensity was coded with a scale from 0 (none) to 4 (strong), distress vocalization peak intensity was coded with a scale from 0 (none) to 5 (strong cry) in 30 sec segments. The latencies to express emotion were also coded. The kappas ranged from .79 to .87. Alpha for the latency to the first anger expression was 1.00.

Data aggregation. Latency to first anger response was reversed. Duration of facial, vocal, and bodily anger expressions was computed (percent of segments when anger was present in each modality). Those scores were then weighted by the average peak intensity across two 30 sec segments. Those four component scales were standardized and averaged to form the anger composite measure.

Fear

Procedure. E drew attention to herself by saying the child’s name in a neutral tone, and then put on four consecutive masks (each for 10 sec): ghost, clown, gorilla, and a gas mask. She then leaned slightly toward the child, saying his name.

Coding and reliability. The approach to coding was analogous to that used for the Puppets episode. The episode was divided into four epochs, each corresponding to one mask. Each epoch was divided into two 5 sec coding segments. For each segment, the coders recorded presence or absence of facial fear, distress vocalization, and bodily fear. Facial and bodily fear peak intensities were coded with a scale from 0 (none) to 3 (strong), and distress vocalizations were coded with a scale from 0 (none) to 5 (strong cry). Latency to fear response was coded in seconds. Reliabilities, kappas, ranged from .65 to .96. Alpha for latency to the first fear expression was 1.00.

Data aggregation. Latency to first fear reaction was reversed. Peak intensity of fear responses in each modality was weighted by the average duration of fear responses in that modality. Each of those modality specific fear responses were standardized and averaged to form the fear composite measure.

Restraint

Procedure

In the laboratory “living room”, very attractive toys were displayed on a shelf easily accessible to children. Those toys were designated as off-limits, and at the outset of the session, the mother was asked to enforce the prohibition. Toward the end of the session, the child was left alone in the room and the mother was seated in the adjoining room, with her back to the child, visible through a crack in the door. Prior to departure, the mother reminded the child about the prohibition, and asked him to engage in a dull sorting task, set up directly in front of the shelf. After 1 minute, an unfamiliar female came in and played with some of the toys for one minute. Then, the child was alone again for 6 minutes.

Coding and Reliability

Children’s behavior was coded for each of 96 5-sec segments using mutually exclusive and exhaustive categories. Those behaviors included looking at the toys without touching, touching and playing (deviating), and being engaged in other activities (doing the sorting task, walking around, snacking, playing with permitted toys, etc.). Latencies to the first look at the toys and to the first touch were also recorded, in terms of the number of 5 sec segments. Reliability, kappa, for
child behavior was .90, and alphas for the latency to look and to touch were .99 and 1.00, respectively.

Data Aggregation

We tallied all instances of “touching/playing with prohibited toys”, and all instances of behaviors that avoided touching/playing with the prohibited toys, for example, doing the sorting task, playing with permitted toys. Those tallies were divided by the total number of segments when the child was in the living room (the segments when the child left the room to sit on mother’s lap were not included). In addition, we computed the number of segments that elapsed between looking at the toys without touching them and touching the prohibited toys. All three component scores were standardized and averaged to form a restraint composite (touching/playing with prohibited toys was reversed in this average).

Attention Measures

Procedures

Attention was assessed during two age-appropriate problem-solving tasks (Willats, 1990). In both, children were presented with attractive toys. The toys were not accessible by reaching, but could be accessed upon a correct analysis of the task structure (for example, by pulling the end of the cloth on which a toy was placed). Each task required children to focus attention on the elements of its structure to achieve the solution. In the first task, three identical attractive toys were placed on three respective pieces of cloth. Because of the specific barrier set up between the child and the toy, or because of a cut in the cloth, only one piece of cloth, when pulled, would bring the toy toward the child. In the second task, the child could gain access to an attractive toy by pulling a string attached to the toy. Each task involved two trials, separated by a period when E demonstrated how to solve the problem.

Coding and Reliability

Each trial was coded in 5 sec segments. Coders noted the type of attentional engagement in each 5 sec segment using a mutually exclusive and exhaustive set of categories. Child’s gaze could be coded as “good attentional engagement”, indicating the child was actively focused on the task, scanning various task objects or acting on them often with “furrowed brows”. Alternatively, child’s gaze could be coded as “poor attentional engagement”, indicating the child was looking at task objects, but rather than being focused on solving the task, the child was mostly delighted with the toys, perhaps giggling, laughing and deriving joy from the props. Finally, the child could be coded as “off-task”, indicating his gaze was on non-task objects. The reliability, kappa, for the type of attentional engagement was .80.

Data Aggregation

The instances of “good attentional engagement”, “poor attentional engagement”, and “off-task” were each tallied and divided by the number of coded segments in each trial and each task. Because the results were very similar across the two tasks, each type of attention in Trial 1 and Trial 2 (after demonstrating the solution) was averaged across the two tasks. Thus, the scores expressed rates of different attentional engagement upon first presentation (Trial 1) and second presentation (Trial 2) of the problem.

Results

Behavioral Observations

PF1 was observed to be a happy and pleasant child. His behavior outside of the standardized laboratory paradigms was generally not distinguishable from that of other children his age. The only exception to this was an apparent lack of fear response to strangers and new settings; he happily interacted with multiple examiners and others whom he had never met before, and seemed to approach each novel situation with enthusiasm.

Vineland Adaptive Behavior Scales

The responses of PF1’s mother on the VABS placed him near the mean for the standardization sample (mean = 100; SD = 15) in all four domains. His scores were: Communication = 96; Daily Living Skills = 96; Socialization = 110; and Motor Skills = 104.

Behavioral Observations in Standardized Laboratory Paradigms

In comparing PF1 to his age and gender matched peers we used both descriptive and inferential methods. Given the relative novelty of the tasks used in this study, we provided a substantial amount of descriptive information on the nature of the measures collected from the normative sample. For example, in addition to sample mean and standard deviation, we provided the 95% confidence interval (CI) for the sample mean to allow the reader to gauge the degree of individual difference variability in these measures. Furthermore, because our matched comparison sample is considered small, we did not treat our sample statistics as though they were population parameters, free of measurement error and sampling fluctuation. Rather, we used modified t-statistics to
evaluate whether PF1’s scores constituted statistically significant departures from those of his peers and provided 95% CIs for PF1’s estimated percentile rank (PR) on all measures (Crawford and Howell, 1998; Crawford and Garthwaite, 2002). The modified t-statistics and the CIs associated with estimated percentile ranks were obtained using the program available from John Crawford’s web site, http://www.abdn.ac.uk/~psy086/dept/psychom.htm.

Table I presents the findings comparing PF1 to the normative sample of age and gender-matched toddlers. The first three columns present the mean, SD and 95% CI for the sample mean for the comparison sample. The last three columns present the statistics pertinent to the comparison of PF1’s data relative to the normative sample. The third column presents PF1’s scores, the fourth column shows the estimated PR of PF1’s score and the final column shows the modified t-statistic. Figure 2 presents the 95% CI for PF1’s estimated PR on emotion measures and Figure 3 presents the 95% CI for PF1’s estimated PR on restraint and attention measures.

The first three rows of Table I show that rates of moderate or intense positive and negative affect were generally low while the rates of neutral mood were generally high in free-flowing dyadic contexts. While PF1’s affective expressions conformed to that pattern in general, his rate of moderate or intense positive affect was three times that of his peers. Furthermore, that elevation represented a statistically significant departure from his peers. PF1’s estimated PR was at 99%. Figure 2 depicts the tight CI around that estimate.

In contrast, PF1’s rate of moderate or intense negative affect was quite similar to his peers with an estimated PR around 40%. Figure 2 shows the wide CI around that PR estimate and suggests he was quite typical of his peers. His rate of neutral mood was lower than his peers but that estimate was not statistically significant.

The next three rows of Table I show levels of

![Fig. 2 – 95% confidence intervals (CIs) for PF1’s estimated percentile rank (PR) on emotion measures.](image1)

![Fig. 3 – 95% confidence intervals (CIs) for PF1’s estimated percentile rank (PR) on restraint and attention measures.](image2)
joy, anger, and fear reactions in standardized paradigms. The scores from these paradigms represent children’s emotional reactions from a variety of modalities and, thus the scales are centered at zero. As can be seen from standard deviations and the 95% CI’s for the sample means, there was considerable variability in children’s reactions in these paradigms.

Consistent with his affective profile in free-flowing naturalistic interactions, PF1’s joy responses to the Puppets were generally elevated. For example, the estimated PR of PF1’s score was at 85%. Figure 2 lower limit indicates that his joy was estimated to be higher than 75% of his peers but that score did not represent a statistically significant departure from his peers.

PF1’s anger responses in the Car Seat paradigm were also stronger than those of his peers. For example, PF1’s estimated PR on anger responses was at 97%, representing a marginally significant departure from his peers and the lower limit for the estimated PR was above the 90th percentile. On the other hand, PF1’s fear responses in the seated Masks paradigm were very typical of children’s reactions in this age group. In fact, his score was in the 95% CI for the normative sample mean. Figure 2 shows the wide CI for his fear response ranking.

The next row of Table I shows the overall composite score for children’s restraint while alone with the prohibited toys. That score reflects several robust characteristics of children’s behavior in this paradigm, including the extent of lack of restraint, extent of behavior deployed to avoid playing with prohibited toys, and the time it takes to lose restraint. The composite score is centered at zero. Standard deviations and the 95% CI for the sample mean in Table I indicate that there was considerable variability in the overall scores obtained from the normative sample. PF1’s score was generally low in this paradigm, consistent with the lack of restraint. His estimated PR was at 21% but that score did not represent a statistically significant departure from his peers. Figure 3 shows the wide 95% CI for his estimated rank to be generally low relative to his peers.

The last three rows of Table I show children’s attentional engagement data during Trial 1 and Trial 2 of the problem-solving tasks. As can be seen from Table I, on Trial 1, the NC group had generally high rates of good attentional engagement (with neutral affect) and low rates of no attention and poor attentional engagement (with positive affect). The 95% CI for the sample means for those three scores were relatively tight despite low sample sizes indicating limited individual difference variability.

PF1’s scores did not conform to that pattern, however. His rate of poor attentional engagement was twice the rate of his good attentional engagement. In fact, the PR for his score on good attentional engagement was estimated at 0% while the PR for his score on poor attentional engagement was estimated at 100%. Not surprisingly, those rates represent statistically significant departures from his peers. Figure 3 shows the 95% CIs consistent with those extremes. In fact, the lower and upper limit estimates show minimal or no variation. Although PF1 did not show any off-task behavior, the tasks were generally engaging for all children and he was similar to his peers in this respect. In contrast to this performance on Trial 1, PF1’s performance was unremarkable and comparable to that of his peers on Trial 2 (following modeling of the task solution).

**Discussion**

These results suggest that circumscribed dysfunction in human prefrontal cortex early in life can result in subtle impairments of emotional regulation and attentional engagement as early as 14 months of age. These conclusions are regarded as preliminary, as they are based on a single case. We are not yet able to comment on the effects that early focal lesions to other brain regions might have on these measures. Childhood injury to non-frontal regions can result in impairments of executive functions such as planning and problem-solving (Jacobs and Anderson, 2002), and it is clear that development of the complex behaviors under consideration here depend on the integrated function of multiple distributed brain regions.

The key finding of the present study was that subject PF1, a 14-month-old boy with primarily normal behavior following a focal lesion in the right inferior dorsolateral prefrontal cortex, displayed difficulties in regulating the expression of disparate emotions (joy, approach, anger) when presented with standardized laboratory challenges. Further, these emotional difficulties appeared to impact on attentional regulation. PF1 showed markedly high positive affectivity and low restraint relative to his peers. This was particularly evident in his intense and positive affective expressions during free-flowing interactions, his unrestrained approach of desirable but prohibited stimuli, and to a lesser extent in his mildly atypical levels of anger and resistance when physically restrained. Faced with problem-solving tasks, when most of his peers displayed affectively neutral expressions and focused on finding the solutions, PF1 initially responded with strong and under-regulated positive emotion that interfered with attentional engagement on the task at hand.

At this age, there are substantial ongoing developmental neural changes in prefrontal cortex and concomitant developments in cognitive and social abilities. Among the major changes in brain structure is a volumetric increase in prefrontal gray matter from birth until sometime in later childhood (likely 4-12 years of age). Synaptic density in the PFC decreases substantially (by approximately
40%) during this time, likely due to selective pruning. Meanwhile, prefrontal white matter is increasing and will continue to do so for several years (e.g., Matsuzawa et al., 2001; Fuster, 2002). Age-related changes in the extent and rate of these and other neural developmental processes likely impact on the degree of plasticity in relevant systems that would allow compensation for early prefrontal injury. Extrapolating from research on critical periods of brain development in rodents, it is possible that for humans, the least favorable time for cortical injury is at the end of the gestational period, during the first months of life (Kolb et al., 2000). However, it is not at all yet evident how these developmental anatomical changes map onto cognitive development. It is generally agreed that, for humans, postnatal brain changes are strongly influenced by experience over the relatively delayed period of development (e.g., Johnson, 2001). If prefrontal cortex injury during infancy fundamentally alters the iterative child-environment interactions that normally would lead to social and emotional competency, there clearly would be potential for long-term repercussions (Damasio, 2000). The development of self-regulatory capacities, and that those capacities impact on their social-emotional development. Deficits in self-regulatory capacities have been linked to aggression and conduct problems in children and adults, as well as social withdrawal and other forms of psychopathology (Calkins and Fox, 2002; Keenan, 2000). Self-regulation skills, including executive function and emotion regulation, have been found to be an important protective factor for youths living in high-risk conditions (Buckner et al., 2003). Many related characteristics have been studied, including but not limited to, impulsivity (Maccoby, 1980; Milich and Kramer, 1984), self-control and self-regulation (Kopp, 1982, 1987; Kopp and Neufeld, 2003; Mischel, 1983; Shoda et al., 1990), ego-control and ego-resilience (Block and Block, 1980), and behavioral inhibition (Barkley, 1997). Recently, emotional regulation has emerged as a related critical topic, discussed in several special sections and separate volumes (for example, a special issue of Child Development, 2004; SRCD monograph, 1994). An exhaustive review is well beyond the scope of this article (see Kochanska et al., 2000 for a partial review).

The findings of our study support the value of complementing traditional clinical assessments with standardized procedures that capture subtle aspects of self-regulation and that allow for comparisons with normally developing age- and gender-matched children. Such paradigms can produce developmentally sensitive information that has not been available through other methods. In the present study, we were able to detect a subtle, yet coherent pattern of specific emotion regulation problems that were expressed across different emotions, tasks, and contexts. It appeared that PF1 experienced difficulty down-regulating and modulating the initial expression of affect according to situational and task demands. This was true for both positive and negative emotions. The scientific literature on emotion regulation has focused primarily on regulating negative affect, with deficits in this realm often linked to psychopathology (Keenan, 2000). There has been relatively little focus on difficulties pertaining to the regulation of positive emotions, as if implicitly assuming that joy and approach are associated with good adjustment. It appears likely, however, that optimal regulation requires a co-modulation of both negative and positive emotions, depending on circumstances and context. Under-regulated approach tendencies may lead to maladaptive choices or possibly antisocial behavior.
At this time, not enough is known to make predictions regarding the long-term consequences of PF1’s brain injury. As we continue to monitor his development, we hope to track his emotional regulation relative to his peers in relatively complex emotional reactions such as guilt and empathic distress, in addition to those pertinent to positive affectivity, anger, and fear systems. Furthermore, as he gets older, it will be possible to gauge the gains or lack thereof in other aspects of emerging self-regulation, such as restraint or inhibition that involve both effortful and voluntary systems, and to place these findings in the context of those from children with focal damage to other brain regions. It is hoped that the information gained will facilitate the design of rational interventions for children with impairments of emotional regulation and related functions.

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