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Developmental frontal lobe imaging in moral judgment: Arthur Benton's enduring influence 60 years later

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Early prefrontal cortex damage has been associated with developmental deficits in social adaptation, moral behavior, and empathy that alter the maturation of social cognition and social emotions. The seminal case of Ackerly and Benton (1948) continues to provide the most striking clinical example of prefrontal-related neurodevelopmental impairments, with more recent case reports confirming and elaborating these influential observations. This study investigated the prefrontal hypothesis of moral decision making in healthy, typically developing children and adolescents (10–17 years of age) using functional magnetic resonance imaging (fMRI). Participants judged the actions in age-appropriate moral vignettes as right or wrong, and results were contrasted to a nonsocial/nonmoral baseline condition requiring similar right versus wrong judgments. Results confirmed a predominant cluster of activity in the most rostral-medial (frontal polar) prefrontal region across moral judgment conditions, along with left lateroposterior orbitofrontal/ventrolateral prefrontal, left temporoparietal junction, midline thalamus and globus pallidus, and bilateral inferior occipital clusters. Trials entailing ambiguous moral situations activated considerably more prefrontal and parietal regions than did routine moral situations, suggesting the need for more neurocognitive resources. While age regression analysis identified a few regions of greater or lesser activity with age, the frontal polar activations did not change with age. Findings confirm a significant role for anterior-medial prefrontal cortex in the typical development and maturation of moral decision making, consistent with clinical lesion case descriptions.

Keywords: Functional magnetic resonance imaging; Moral judgment; Frontal lobe; Brain development.

FOREWORD

While helping to prepare this manuscript, I (PJE) came across Donald Hebb's influential book *The*

Organization of Behavior: A Neuropsychological Theory, published in 1949. The book was a historical and seminal work aimed at delineating "a general theory of behavior that attempts to bridge

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the gap between neurophysiology and psychology, as well as that between laboratory psychology and the problems of the clinic. The book is written, consequently, with the hope that it will be intelligible to the clinician and the physiologist as well as to psychologists" (p. vii) I was especially pleased by the reminder that this was Arthur Benton's personal copy of Hebb's work, graciously handed to me in 1980 when I was a postdoctoral fellow in the Department of Neurology at the University of Iowa Hospitals and Clinics in Iowa City. In this context (and with deserving respect to the late Professor Hebb) I found the most revealing parts of the book to be the portions that Professor Benton had underlined and commented on in the margins. There were many brief queries (e.g., "But it would be half anatomy and half behavior", "What does this mean?") and unmistakable indications that Professor Benton saw a natural compatibility rather than chasm between brain and behavior. Paging through the book also reminded me that at the time Hebb was putting pen to paper, Arthur Benton was engaged in writing and presenting an equally historical neuropsychological contribution, his case study of J.P. with Dr Spafford Ackerly. Their presentation took place in December 1947 at the meeting of the Association for Research in Nervous and Mental Disease and published in 1948 as "Report of Case of Bilateral Frontal Lobe Defect" (Ackerly & Benton, 1948) Now, 60 years or nearly 22,000 days later, I find that I am still learning from the Ackerly and Benton case study. Professor Benton kindly elaborated on this seminal case in a 1991 special issue of Developmental Neuropsychology devoted to "Perspectives on the Developmental Consequences of Early Frontal Lobe Damage" (Benton, 1991), instantly lending credibility to this fledgling clinical-scientific topic. His guiding words provided insightful and reflective analyses of the emerging field of early frontal and executive function development, a topic that now draws psychologists, educators, physicians, and neuroscientists to international conferences. To have provided observations that are still discussed after that length of time is remarkable and would give one pause to wonder whether they may have contributed something of lasting value, but that is an honor for Arthur Benton and one indication of the kind of intellectual influence he continues to wield. With the speed, breadth, and diverse methodologies of contemporary clinical scientific investigation, it is intriguing to speculate what seminal neuropsychological studies we encounter today will continue to be read 60 years from now, in 2068. (Paul Eslinger)

INTRODUCTION

The Ackerly and Benton (1948) case of J.P. continues to provide unique observations and raise fundamental questions regarding the neural substrate of human cognitive, emotional, and social maturation. J.P. began formal evaluations at about 13 years of age in the Louisville Mental Hygiene Clinic because of persistent and increasing behavioral self-regulatory deficits. No interventions proved of lasting value. Later neurological, neuropsychological, and psychiatric examinations supported a developmental pattern of self-regulatory and interpersonal difficulties dating to at least 3 years of age related to congenital atrophy of the left prefrontal region and absence of right prefrontal cortex. These took the forms of habitual wandering, even at 3 years of age without apparent anxiety and often for long distances (a habit that continued into adulthood and sometimes entailed thousands of miles), overpoliteness, and "a smooth, ingratiating manner toward adults." These Chesterfieldian manners were noteworthy as J.P. could charm adults, even health professionals, but none of these relationships proved reciprocal or could be maintained in a healthy fashion as his "shallow surface feature" would become evident. Although early cognitive impairments were not evident, differences in social emotions and social cognition do appear to have been evident. For example, J.P. seemed not to experience or express much gratitude, humility, social anxieties, embarrassment, or regret, though he could become very intolerant and indignant over others' shortcomings. Social relationships were shallow with very constrained modes of interpersonal sharing such as empathy, reciprocity, theory of mind, and even agreement about game rules whenever he was at a disadvantage. Hence J.P.'s moral behavior and socialmoral judgment became progressively problematic throughout childhood and adolescence, leading Ackerly and Benton (1948) to characterize these neurodevelopmental difficulties as a "primary social defect."

Although J.P.'s case remains unique because of its probable congenital nature, several similar cases have been described as a result of frontal brain injuries acquired early in life. These were reviewed in a joint effort with Professor Benton and were published in 2004 (Eslinger, Flaherty-Craig, & Benton, 2004). Although not every case of early frontal damage leads to such disabling outcomes, those with the poorest outcomes seem to have damage that involved the frontal polar and/or orbito-medial cortical regions (Eslinger, Biddle, & Grattan, 1997; Eslinger et al., 2004). Such cases

continue to be encountered in occasional striking clinical presentations, as we have seen recently in 2 new cases (see Figure 1 for examples), but also in more mixed and subtle forms in acquired and neurodevelopmental disorders involving frontal pathophysiology (Powell & Voeller, 2004).

The case description of J.P. and more recent confirmatory cases that carefully extend and elaborate on Ackerly and Benton's (1948) observations underscore the severe social adaptation deficits associated with early frontal damage (Anderson, Barrash, Bechara, & Tranel, 2006; Eslinger et al., 1997; Eslinger et al., 2004; Eslinger, Grattan, Damasio, & Damasio, 1992; Grattan & Eslinger, 1991, 1992; Marlowe, 1992; Mateer & Williams, 1991; Price, Daffner, Stowe, & Lesulam, 1990). These individuals are unable to thrive and independently function within home, school, and community settings and often encounter significant legal, financial, and interpersonal conflicts. An important aspect of their social adaptation deficits involves poor social and moral judgment that we suspect emerges in part from the impaired acquisition and elaboration of social concepts, moral knowledge, and adaptive moral decision making. Such impairments have been evident not only on standardized measures of social-moral development, but also in their daily behaviors that depict impulsive actions, inability to learn from experience (particularly from negative consequences), impaired emotion and interpersonal relationships, and a shallow form of social-moral cognition and social emotion (e.g., gratitude, embarrassment) that revolve primarily around meeting their own immediate needs in socially primitive ways. However, confirmatory evidence for a prefrontal neural substrate for development of moral judgment is scarce. It is largely within this context that the current functional magnetic resonance imaging (fMRI) study of moral judgment in children and adolescents was undertaken.

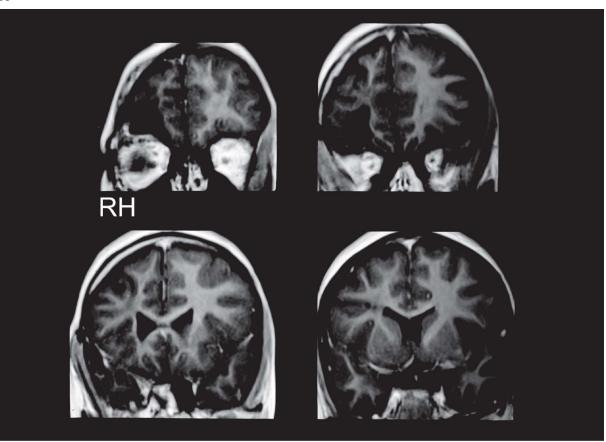
Moral judgment depends upon the acquisition of rules and concepts that help guide personal decisions and actions according to interests that extend beyond the self to others and to society as a whole. Moral behavior and its underpinnings have been of interest to humans for thousands of years as social interactions have evolved, become more complex, and provided the bases for shared cultures, values, and economics. Social—moral considerations provide much of the foundation for formal legal systems, laws, and governmental institutions, but also are apparent in many ordinary social interactions. The implications of these processes are substantial as antisocial behavior is at the root of numerous social problems, abuses, and criminality (Stams et al., 2006).

Understanding moral processes spans many disciplines including philosophy, psychology, sociology, and, more recently, neuroscience. Moral psychology research has largely emphasized the cognitive capacities to analyze dilemmas and delineate the rational bases for judgments based on utilitarian and other principles (Kohlberg, 1964, 1984). From the developmental perspective, which is the emphasis in this paper, Piaget (1968) identified cognitive developmental stages that also frame the acquisition of social-moral rules and knowledge, particularly in middle childhood. We and others have argued that the prefrontal cortex and interconnected systems provide some of the neural bases for acquisition and maturation of cooperation, reciprocity, empathy, self-other considerations in agreeing on rules, fair play, and consequences of actions (Eslinger et al., 2004; Eslinger et al., 1992). Prefrontal systems have also been implicated in perception of intentionality, theory of mind, emotion, and self-other representations that provide further mechanisms crucial for understanding others and linking to moral knowledge and development (Baron-Cohen et al., 1993; Decety & Sommerville, 2003; Flavell, Miller, & Miller, 1993).

A small number of functional brain imaging studies in healthy adults have identified neural activation patterns associated with cognition and emotion involved in moral judgments (Greene, Nystron, Engell, Darley, & Cohen, 2004; Moll, Eslinger, & Oliveira-Souza, 2001; Moll et al., 2002; Moll, Zahn, Oliveira-Zouza, Kruger, & Grafman, 2005; Moll et al., 2007; Zahn et al., 2007) but no studies have investigated similar substrates in children. Studies in healthy adults have identified that when participants undertake specific right-wrong judgments of social-moral situations, there is prominent activation of prefrontal cortices, particularly around the frontal poles. When asked to process moral dilemmas or act as witnesses to moral violations, a broader range of activations involved the superior temporal sulcus, temporalparietal junction, mesial and orbital prefrontal cortices, and limbic and paralimbic systems, suggesting a network of prominent frontal-temporal and subcortical regions underlying both cognitive and emotional aspects of social-moral processing.

The objective of the present study was to investigate the neural substrates associated with making moral judgments in a healthy, typically developing sample of children and adolescents. We designed and implemented two moral judgment tasks that provided short vignettes of characters and actions that were age appropriate to children and adolescents. The first were straightforward vignettes and actions that were highly rule based and judged as

A



В

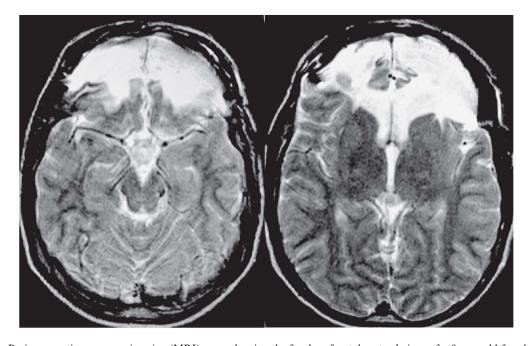


Figure 1. Brain magnetic resonance imaging (MRI) scans showing the focal prefrontal cortex lesions of a 9-year-old female (A) and 16-year-old male (B) who both suffered traumatic damage from falls early in life. Note the asymmetric right prefrontal lesion and surrounding tissue volume loss in A and the extensive bilateral lesion in B. Both patients showed significant developmental self-regulatory and executive deficits.

right or wrong in out-of-magnet testing with very high agreement. The second set of vignettes comprised more ambiguous social circumstances and actions (e.g., telling "white lies" to spare another's feelings, stealing food to feed a poor, starving family) that garnered much more varied right versus wrong responses. We hypothesized that these judgments would activate prefrontal regions predominantly and possibly recruit activity also in the anterior lateral temporal, temporal-parietal junction, and subcortical limbic areas.

METHOD

Study participants

The sample was composed of 9 volunteers (1 lefthanded) between the ages of 10-17 years (4 male, 5 female) who had no history of medical, neurological, or psychiatric illness, learning disability, or current medication usage. Participants were first administered standardized tests of general intellect, academic achievement, and executive functions and completed inventories of emotional intelligence and social behavior in order to characterize several aspects of cognitive, emotional, and social development relevant to the experimental protocol. All measures indicated development and achievement within the normal range (varying average to above average), with one exception on the Home and Community Social Behavior Scale, where a participant was scored "at risk" for social incompetence and antisocial behavior.

fMRI study procedures

Preparation and positioning

The fMRI studies were conducted on a 3.0-T MRI scanner. Stimuli were presented to participants through VisuaStim Digital Glasses (Resonance Technology Inc., Northridge, CA), and responses were recorded through a handheld device. All participants were first introduced to the tasks and response device in out-of-magnet training that included introduction and instruction slides as well as sample trials of baseline and experimental stimuli on a laptop computer. Questions about the tasks and procedures were clarified with participants until they fully understood the tasks for the fMRI session. Training was geared at alleviating any anxiety during the actual fMRI study and thoroughly familiarizing participants with the modes of stimulus presentation, task requirements, and response options. Instruction slides were repeated in-magnet, and task readiness cues were presented through the two-way intercom.

Participants laid supine in a head restrainer that minimized motion and provided precise positioning and comfort. A boxcar fMRI paradigm was used, which consisted of interleaved time intervals of baseline and cognitive activation. During fMRI scanning, participants were instructed to respond to visual stimulation by pressing either the left or the right button with their respective thumb on a two-button handheld device.

Image acquisition

Functional MRI images were acquired on a whole-body 3-tesla imaging spectrometer (Med-Spec S300, Bruker BioSpin Corporation, Ettlingen, Germany) with a TEM head coil for radio frequency (RF) transmission and reception. A fast spin-echo sequence (time to repetition/echo time, TR/TE = 4,000 ms/58.5 ms; flip angle = 180° ; field of view, FOV = 23×23 cm²; 20 axial slices, 5 mm thick, with 1-mm distance between slices; acquisition matrix = 256×192 , number of average = 1) and 3D gradient-echo sequence (TR/TE = 25 ms/5 ms; flip angle = 15° ; FOV= $23 \times 23 \times 13.5 \text{ cm}^3$; acquisition matrix = $256 \times 192 \times 50$; number of average = 1) were used to scan the whole brain, to exclude participants with any potential neuroanatomic abnormalities. Functional images were acquired with an echo planar imaging sequence (TR/TE = 3,000 ms/35 ms; flip angle = 90° ; FOV = $23 \times 23 \text{ cm}^2$; 24.5-mm-thick axial slices with no gap between slices; acquisition matrix = 64×64 ; number of average = 1). Two study paradigms were administered in each participant session. For the moral judgment paradigm, 259 images were acquired during the alternating blocks of stimulation and baseline.

Cognitive activation task—moral judgment

The boxcar design used for this task was composed of alternating experimental and baseline blocks. There were 15 experimental blocks, 15 baseline blocks, and 5 rest periods. Experimental blocks were divided into three conditions: moral right (6 blocks), moral wrong (6 blocks), and moral ambiguous (3 blocks). Each block lasted 27 seconds, consisting of three statements presented for 6 seconds with an additional 3 seconds per statement for the participant to respond using the two-button handheld device. Participants were asked to judge whether they believed the statement was "right" or "wrong" by pressing either the right or the left key, respectively. All experimental statements contained moral-social situations. The moral right and wrong conditions presented vignettes of moral actions that were judged in out-of-magnet testing to be highly rule-based decisions, having high agreement and a definite right or wrong response (see Table 1 for examples). In the moral ambiguous condition, the "correct" moral actions were less clear than they were for straightforward right versus wrong judgments (See Table 1 for example). These trials contained vignettes such as "white lies" and stealing food to feed a starving family. The baseline blocks each lasted 18 seconds and consisted of two statements each presented for 6 seconds with an additional 3 seconds for a right or wrong response. Baseline blocks were neutral statements that lacked a moral component but were either factually right or wrong (See Table 1 for examples). To avoid anticipatory effects in responding, the moral right, moral wrong, moral ambiguous, and baseline blocks were intermixed. Rest periods were evenly dispersed throughout the paradigm, and each lasted 18 seconds, allowing the blood-oxygen-level-dependent (BOLD) response to return to baseline after a series of stimulation blocks. Participants viewed reminder instruction windows before each task. Stimuli across all conditions were controlled for word length (11-15), names used (short common female and male names), sentence structure, exposure time, and screen presentation (i.e., font, size, location). The timing and switching of visual stimuli were automatically controlled by transistor-transistor logic (TTL) signals incorporated in the pulse-timing program. The total in-magnet time for this paradigm was 12 minutes 57 seconds.

Data analysis

The fMRI image data were processed with SPM2 software (Wellcome Department of Cognitive Neurology, London, UK) implemented in Matlab

TABLE 1
Examples of the moral stimuli used for this study

Moral category	Example of stimuli in fMRI session
Moral right	At recess, I saw a classmate playing alone so I went to play with him.
Moral wrong	Everyone else was picking on Toby, so I started picking on him, too.
Moral ambiguous	When my very overweight friend asked if she was fat I said "no."
Neutral right	On a clear and sunny day, the color of the sky is blue.
Neutral wrong	In the game of basketball, a soccer ball is kicked back and forth.

Note. The experimental and baseline tasks are listed on the left, with one example of a corresponding stimulus on the right.

(Mathworks, Inc.). The first four images of each fMRI data set were discarded to remove the initial transit signal fluctuations, and subsequent images were realigned within the session to remove any minor movements. The T₁-weighted high-resolution anatomical images were coregistered with fMRI images and spatially normalized according to the Montreal Neurological Institute brain template. The time-course images were normalized using the same normalization parameters and were then smoothed with a $5 \times 5 \times 12.5$ -mm³ (full width at half maximum) Gaussian smoothing kernel. A statistic parametric map (SPM) was generated for each participant under each condition by fitting the stimulation paradigm to the functional data, convolved with a hemodynamic response function. The pixels representing the active regions were overlaid on the 3-D T₁-weighted anatomic image in Talairach coordinates. In this process, brain activations generated by the moral judgment (experimental) task were contrasted with the nonmoral judgment (baseline) task, isolating cognitive processes of morality and the related judgments made in social moral contexts.

Group analysis was undertaken to generate an average activation map (one-sample t test), with a rigorous statistical threshold set at p < .005 and a minimal voxel threshold of 10. In addition, developmental analyses were undertaken by computing linear regressions between age and activations clusters in the experimental tasks.

RESULTS

Similar to the ratings of out-of-magnet controls, fMRI participants performed with an average agreement of 98% in judgment of both moral right-wrong and baseline nonmoral statements and were nearly evenly split in their judgment of the ambiguous condition actions (57%). The mean reaction/response times averaged across fMRI participants were 3,820.92 ms, 3,786.48 ms, and 5,007.33 ms for moral right, moral wrong, and moral ambiguous conditions, respectively. As expected, the ambiguous condition mean reaction/response time was significantly longer (p < .0001, two-tailed t test), suggesting that the situational uncertainty engaged additional decision-making time and processing.

Activation maps were generated for the moral judgment conditions (right, wrong, ambiguous combined) and then separately for the rule-based moral right—wrong condition and the moral ambiguous conditions, with respective figures and tables of activated regions following. Two-way contrasts were generated between the moral right—wrong and

moral ambiguous conditions, and age regressions were computed to identify any developmental shifts in activations.

Moral judgment activations

When averaging across the moral activation tasks (moral right, moral wrong, and ambiguous) and contrasting to the nonmoral judgment baseline in a one-sample t test (p < .005, v = 10), the following regions of activation were observed: bilateral superior medial prefrontal cortex extending just to the anterior cingulate, left superior frontal, left lateroposterior orbitofrontal extending to left ventrolateral prefrontal cortex, left temporoparietal junction, midline thalamus extending to the globus pallidus, left amygdala-hippocampus, and bilateral inferior occipital cortices (see Figure 2A). The medial frontal polar cluster predominated, followed by the orbitofrontal and occipital clusters. Cluster locations and sizes are summarized in Table 2.

Activations in the moral right-wrong condition

We further analyzed the overall moral judgment activations according to the two main tasks. During the more straightforward moral right—wrong condition in comparison to baseline (one sample t test, p < .005, v = 10), participants generated similar predominant activity in the superior medial prefrontal regions and the temporoparietal junction, this time with the temporoparietal activation being bilateral (see Figure 2B). In addition, significant recruitment also occurred in the left anterior temporal pole, the precuneus bilaterally, and the left superior frontal region. Activation size was again dominant in the superior medial region, but with similar-sized clusters also in the midline precuneus and left temporoparietal region (see Table 3).

Activations in the moral ambiguous condition

A one-sample t test (p < .005, v = 10) contrasting the moral ambiguous task to baseline identified significant activations in the left frontal polar, midline precuneus, left temporoparietal junction, and left cerebellar regions (see Table 4 and Figure 2B).

Contrasts of moral ambiguous and moral right—wrong conditions

Two-sample t tests were conducted (p < .005, v = 10) contrasting the moral ambiguous condition to the moral right—wrong condition and vice versa.

The moral ambiguous condition elicited specific activations in the frontal polar region bilaterally, the superior parietal region bilaterally, the right middle and superior frontal gyri, right precuneus, and fusiform/cerebellar region bilaterally. In contrast, the left temporal pole, left insula, left superior temporal, right occipital gyrus, and bilateral hippocampal regions were specifically activated in the moral right—wrong condition (see Figure 2C; Table 5).

Age regression analyses

After conducting age regression analyses for the moral judgment activations, we found some shifts in activation with age. Across moral judgment tasks combined, the right superior temporal sulcus and temporoparietal junction became less active with age (p < .005), whereas the bilateral anterior temporal region became more active with age (p < .005). In the moral ambiguous condition, the Rolandic operculum bilaterally was recruited more actively with age (p < .005), whereas the right temporoparietal junction was less active with age (p < .05). Lastly, in the moral right-wrong condition, there was significant reduction of activity in the right posterior middle temporal gyrus, middle frontal gyrus, and left superior temporal gyrus with age (p < .005). Importantly, there were no age-related changes identified in the superior-medial prefrontal region.

DISCUSSION

Results of fMRI study in healthy, typically developing children and adolescents provide confirmatory evidence that the prefrontal cortex is crucially involved in the development and maturation of moral judgment. The significant activation detected in the superior medial frontal polar region of prefrontal cortex was not only the largest cluster across the developmental sample, but also in an anatomical location that has been associated with poor developmental outcomes after early frontal damage and poor adaptation after adult-onset damage (Ackerly & Benton, 1948; Anderson, Bechara, Damasio, Tranel, & Damasio, 1999; Eslinger & Damasio, 1985; Eslinger et al., 2004; Eslinger et al., 1992; Harlowe, 1868). Therefore, both clinical and fMRI cognitive neuroscience data appear to converge in their support of a crucial role for superior-medial prefrontal regions in development and actualization of moral judgment throughout the lifespan and the conclusion that early damage to this region significantly alters the typical maturational trajectory of moral cognition and behavior. Moreover, this region interacts with other important cortical and

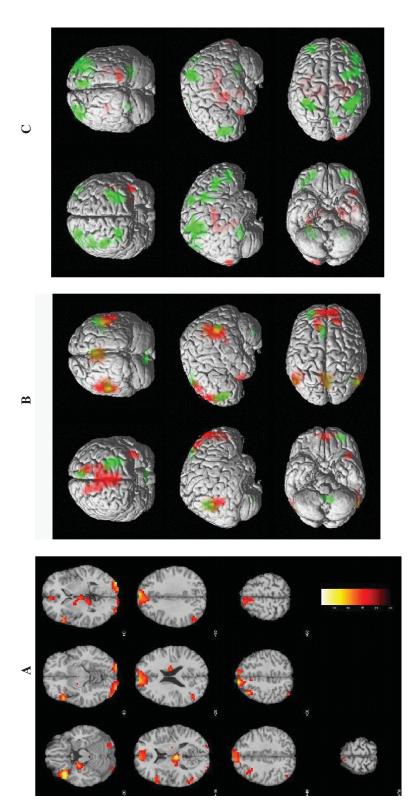


Figure 2. (A) Activation map associated with moral judgment in a healthy developmental sample (statistical threshold: p < .005, v = 10) overlaid on multislice axial images. Areas of activation tion maps generated during the moral right-wrong (red) and moral ambiguous (green) conditions overlaid on a 3D-rendered image (p < .01, $\nu = 10$). Areas of yellow represent common, overlapping regions of activation in both tasks. Regions of individual activation in the frontal polar region were slightly different for the two tasks, while temporo-parietal and precuneus areas of activity were included a large prominent cluster in the superior mesial prefrontal polar region extending just to the anterior cingulate and significant clusters in the left lateroposterior orbitofrontal and left ventrolateral prefrontal region, the left temporoparietal junction, midline thalamus extending to the globus pallidus, left amygdala-hippocampus, and bilateral inferior occipital cortices. (B) Average activa-(C) Contrast maps of moral right—wrong versus moral ambiguous (red) and moral ambiguous versus moral right—wrong (green) conditions overlaid on a 3D-rendered image (p < .005, v = 10). Most notably, the moral ambiguous condition elicited bilateral activation in the frontal polar and superior parietal cortices and right prefrontal regions, with an overall right hemispheric dominance. In contrast, bilateral hippocampal and left temporal-insula regions were recruited in the rule-based moral right-wrong condition. This comparative analysis revealed that the moral ambiguous condition recruited areas associated with mentalizing functions whereas the routine right-wrong condition recruited more semantic and memory related regions such as the left superior temporal gyrus and the hippocampus.

TABLE 2Moral judgment tasks: Average activation clusters

		MNI ^a coordinates			Activation size	
Area		X	Y	Z	(pixels)	t value
Frontal	Superior medial frontal (96%)	-12	44	45	332	7.32
	L superior frontal	-36	20	45	41	6.80
	L orbitofrontal cortex	-36	24	-15	113	9.83
Temporal-parietal	L temporal-parietal junction	-56	-56	5	60	8.20
Occipital	L inferior middle occipital	-24	-84	-40	100	7.46
•	R inferior middle occipital	32	-100	0	107	7.66
Thalamus	Midline thalamus/globus pallidus	0	-20	5	77	9.71
Limbic/paralimbic	Anterior cingulate-midline (4%)	-12	44	45	14	7.32
	L amygdala & hippocampus	-24	-12	-25	30	7.06

Note. Average activated regions during moral judgments by the developmental participants (one-sample t test, p < .005). Anatomical labels, corresponding coordinates, voxel size of activation, and t value for each cluster are displayed.

 TABLE 3

 Moral right-wrong judgment task: Average activation clusters

		MNI ^a coordinates			4 .: .: .	
Area		X	Y	Z	Activation size (pixels)	t value
Frontal	Superior medial frontal	0	60	10	124	6.61
	L superior medial frontal	-12	36	55	23	4.38
Parietal	Midline precuneus (90%) & posterior cingulate (10%)	0	-60	35	128	5.22
Temporal-parietal	L temporal-parietal junction	-56	-60	10	116	4.63
	R temporal-parietal junction	60	-64	15	40	4.60
Temporal	L anterior temporal lobe	-40	20	-25	10	3.62

Note. Average activated regions during the moral right-wrong judgment condition by the developmental participants (one-sample t test, p < .005). Anatomical labels, corresponding coordinates, voxel size of activation, and t value of clusters are summarized. ^aMNI: Montreal Neurological Institute.

 TABLE 4

 Moral ambiguous judgment task: Average activation clusters

		MNI ^a coordinates			4	
Area		X	Y	Z	Activation size (pixels)	t value
Frontal	L frontal polar	-28	52	0	30	6.55
Parietal	Midline precuneus/posterior cingulate	4	-60	35	27	3.98
Temporal-parietal	L temporal-parietal junction	-56	-64	15	11	4.13
Cerebellum	L cerebellum	-8	-56	-50	10	4.01

Note. Average activated regions during the moral ambiguous judgment condition by the developmental participants (one-sample t test, p < .005). Anatomical labels, corresponding coordinates, voxel size of activation, and t value of clusters are summarized. ^aMNI: Montreal Neurological Institute.

subcortical areas (e.g., orbitofrontal cortex, superior temporal gyrus and sulcus, temporoparietal junction, amygdala, midline thalamus) both developmentally and throughout the lifespan, as part of a network of structures that underlie current conceptions about the neurobiology of moral behavior, social cognition, social emotion, and adaptation to changing social demands and circumstances

(Davidson, Jackson, & Kalin, 2000; LeDoux, 2000; Moll, Oliveira-Souza, & Eslinger, 2003; Moll et al., 2005; Young, Cushman, Hauser, & Saxe, 2007).

Moral development entails the progressive acquisition and elaboration of social perception, social knowledge and concepts, event and action sequences, consequences, contingencies, and motivational and emotional systems. Embedded within

^aMNI: Montreal Neurological Institute.

TABLE 5						
Moral right-wrong and moral ambiguous contrasts: Average activation clusters						

	Area	MNI ^a coordinates				
Condition		X	Y	Z	Activation size (voxels)	t value
Moral right-wrong	R hippocampal region	36	-32	-10	131	6.65
vs. moral ambigu-	L insula-superior temporal	-48	-8	5	44	4.44
ous contrast	L hippocampal region	-24	-12	-20	16	4.11
	L temporal pole	-40	20	-25	11	4.00
	R occipital pole	20	-104	-5	10	4.00
Moral ambiguous vs.	L frontal polar	-28	52	0	52	6.41
moral right-wrong	R superior parietal	36	-40	55	144	6.00
contrast	R cerebellum (58%) R fusiform (41%)	28	-56	-25	47	5.00
	R frontal polar	28	52	0	66	4.71
	L superior parietal	-36	-40	60	55	4.37
	L fusiform (67%) L cerebellum (30%)	-28	-48	-15	27	4.26
	R superior frontal	32	8	65	20	4.09
	R precuneus	12	-72	60	22	3.89
	R middle frontal	44	12	40	42	3.75

Note. Activated regions identified from contrast analysis of moral right—wrong versus moral ambiguous conditions and moral ambiguous versus moral right—wrong conditions in the developmental sample (two-sample t test, p < .005). Anatomical labels, corresponding coordinates, voxel size of activation, and t value of clusters are summarized.

these constructs are processes of social sensitivity and empathy, perspective taking, theory of mind, intentionality, and social emotions (e.g., gratitude, humility, guilt, embarrassment) that extend beyond the self to include others and society as a whole. It is these complex, integrated processes, mediated through more extensive frontal-temporal, parieto-occipital, and even subcortical limbic system structures, that underlie the full range of social cognition, emotion, and behavior that permit not only social adaptation but also social virtues such as altruism and self-sacrifice. Moll et al. (2005) have described these processes as occurring within event-feature-emotion complexes. In contrast to Piaget and Kohlberg's cognitive developmental approach, recent investigators have also emphasized the importance of affective or "hot" executive function processing in developmental learning, social decision making, and social interactions (Hoffman, 2000; Hongwanishkul, Happaney, Lee, & Zelazo, 2005). Hoffman (2000) emphasized the role of empathy in moral maturity. Recent adult functional brain imaging studies of empathy and self-other judgments, including meta-analysis, have identified consistent recruitment of specific clusters in the rostral medial portions of prefrontal cortex and the medial precuneus region, overlapping with the activations observed in this study (Kelley et al., 2002; Seger, Stone, & Keenan, 2004; Seitz, Nickel, & Azari, 2006). These correlations and activations, within the context of current

developmental theories, suggest that moral maturity coincides with cognitive, emotional, and executive function development along with increasingly complex socialization, transitioning from a superficial, self-centered mentality (that has been described in many cases of early prefrontal cortex damage) to development of a broader other- and social-centered perspective (Gibbs, 2003). As children are progressively incorporated into more complex and varied social contexts, their event sequence knowledge and mental models of social actions and circumstances increase, broadening their scope of social conceptual and conditional knowledge (Moll et al., 2005; Zahn et al., 2007). Hence, it is reasonable to speculate that the activations generated by the moral judgment tasks in this study are related to several aspects of developmental social cognition and social emotion.

The moral right and moral wrong conditions can be considered largely rule-based decisions about routine social actions, drawn from a knowledge base of generally clear and consistent concepts regarding right and wrong moral behavior. The activation detected in the anterior lateral temporal lobe in this task is consistent with the recent suggestion of Zahn et al. (2007) that the anterior temporal lobe may be an important substrate for social conceptual knowledge, as identified in adults. Furthermore, a stable social semantic knowledge store may be particularly important while making socialmoral judgments that entail considerations of

^aMNI: Montreal Neurological Institute.

contexts, agency, social sensitivity, intentionality, and consequences (Moll et al., 2003; Moll et al., 2002). The latter have been associated with prefrontal orbital and mesial limbic regions, which are strongly interconnected not only between themselves but also with the anterior temporal lobe and subcortical limbic nuclei (Carmichael & Price, 1996; Saleem, Kondo, & Price, 2008). We suspect that the acquisition of adaptive social knowledge and self-regulated actions depends upon important interactions among these regions throughout maturation.

The moral ambiguous condition in this study required additional considerations beyond the routine rules of moral right and wrong. Here we suspect that interpersonal processing involving empathy, theory of mind, and intentionality increased the load of processing and the decisionmaking time, as suggested by the longer reaction/ response times of the participants and the low agreement on the moral actions. Specific contrast of the moral ambiguous condition with the moral right-wrong condition uncovered extensive activations in the frontal polar regions bilaterally, the superior parietal lobe bilaterally, the right middle and superior frontal gyrus and precuneus, and the fusiform/cerebellar regions bilaterally. By comparison, activations specific to the moral right-wrong condition involved the hippocampal region bilaterally and left temporal pole, insula, and superior temporal areas. These findings suggest that when social judgments extend beyond highly rule-based events and entail novel or ambiguous situations, much greater neural resources are required and particularly extensive portions of the prefrontal and parietal regions. When the current fMRI results are taken together with the available early frontal lesion literature, the results are consistent with our proposal that early damage to frontal polar and orbital-medial regions fundamentally alters the typical developmental interplay of multiple frontal systems important to social maturation (e.g., fronto-temporal, frontal-parietal, fronto-subcortical limbic system regions). Thus, we contend that it is not a single core deficit, but rather an entirely altered psychology that seems to occur after early prefrontal damage. Not only are intrinsic mechanisms of self and emotion affected, but also the ensuing structure of social knowledge concepts, executive functions, and how actions are regulated. These multiple deficits have lifelong consequences that can be dramatic and very disabling, most compellingly in the unstructured, novel, and ambiguous social contexts of real life (Ackerly & Benton, 1948; Eslinger et al., 2004). Support for this clinical conclusion also comes, in part, from the developmental

analyses in this study. Age regressions identified that select cortical areas became more active or less active with age, but none of these involved the superior-medial frontal polar region. Hence, across a variety of studies, this region appears to be recruited in children, adolescents, and adults when encountering moral decisions. For example, Moll et al. (2006) identified that the frontal polar region was engaged when healthy adult participants weighed costly decisions and when altruistic decision making prevailed over self-interests.

The findings support Ackerly and Benton's (1948) astute observations regarding the significance of the prefrontal cortex in social development and maturation. The combination of human lesion and functional brain imaging analysis in healthy samples provides a particularly strong set of converging data to support the importance of the prefrontal cortex and related regions in the neurobiology of social moral development and maturation. However, our understanding of underlying neural mechanisms, the role of social experiences, and the potential for rehabilitation after early brain pathophysiology still remains very limited and requires further studies. Despite these limitations, we suspect that Professor Benton would applaud current efforts to extend his and Dr Ackerly's seminal observations and advance the diagnosis and care of frontal brain injuries.

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REFERENCES

Ackerly, S. S., & Benton, A. L. (1948). Report of case of bilateral frontal lobe defect. Research Publications of the Association for Research in Nervous and Mental Disease Disorders, 27, 479–504.

Anderson, S. W., Barrash, J., Bechara, A., & Tranel, D. (2006). Impairments of emotion and real-world complex behavior following childhood- or adult-onset damage to ventromedial prefrontal cortex. *Journal of the International Neuropsychological Society*, 12, 224–235.

Anderson, S. W., Bechara, A., Damasio, H., Tranel, D., & Damasio, A. R. (1999). Impairment of social and moral behavior related to early damage in human prefrontal cortex. *Nature Neuroscience*, 2, 1032–1037.

Baron-Cohen, S. N., & Howlin, P. (1993). The theory of mind deficit in autism: Some questions for teaching and diagnosis. In S. N. Baron-Cohen, H. Tager-Flusberg, & D. J. Cohen (Eds.), *Understanding other minds: Perspectives from autism*. New York: Oxford University Press.

Benton, A. L. (1991). Prefrontal injury and behavior in children. Developmental Neuropsychology, 7, 275–281.

Carmichael, S. T., & Price, J. T. (1996). Connectional networks within the orbital and medial prefrontal cortex of macaque monkeys. *Journal of Comparative Neurology*, 371, 179–207.

- Davidson, R., Jackson, D., & Kalin, N. (2000). Emotion, plasticity, context, and regulation: Perspectives from affective neuroscience. *Psychological Bulletin*, 126, 890–909.
- Decety, J., & Sommerville, J. H. (2003). Shared representations between self and other: A social cognitive neuroscience view. *Trends in Cognitive Neuroscience*, 7(12), 527–533.
- Eslinger, P. J., Biddle, K. R., & Grattan, L. M. (1997). Cognitive and social development in children with prefrontal cortex lesions. In N. A. Krasnegor, G. R. Lyon, & P. S. Goldman-Rakic (Eds.), Development of the prefrontal cortex: Evolution, neurobiology, and behavior (pp. 295–335). Baltimore: Paul H. Brookes.
- Eslinger, P., & Damasio, A. (1985). Severe disturbance of higher cognition after bilateral frontal lobe ablation: Patient EVR. *Neurology*, *35*, 1731–1741.
- Eslinger, P. J., Flaherty-Craig, C. V., & Benton, A. L. (2004). Developmental outcome after early prefrontal cortex damage. *Brain & Cognition*, 55, 84–103.
- Eslinger, P., Grattan, L., Damasio, H., & Damasio, A. (1992). Developmental consequences of childhood frontal lobe damage. *Neurology*, 49, 764–769.
- Flavell, J. H., Miller, P. H., & Miller, S. A. (1993). Cognitive development (3rd ed.). Englewood Cliffs, NJ: Prentice Hall.
- Gibbs, J. (2003). Moral development and reality: Beyond the theories of Kohlberg and Hoffman. Thousand Oaks, CA: Sage Publications.
- Grattan, L. M., & Eslinger, P. J. (1991). Frontal lobe damage in children and adults: A comparative review. *Developmental Neuropsychology*, 7, 283–326.
- Grattan, L. M., & Eslinger, P. J. (1992). Long-term psychological consequences of childhood frontal lobe lesion in patient DT. *Brain and Cognition*, 20, 185–195.
- Greene, J. D., Nystron, L. E., Engell, A. D., Darley, J. M., & Cohen, J. D. (2004). The neural bases of cognitive conflict and control in moral judgment. *Neuron*, 44, 389–400.
- Harlow, J. M. (1868). Recovery from the passage of an iron bar through the head. *Publications of the Massachusetts Medical Society*, 2, 327–347.
- Hebb, D. (1949). The organization of behavior: A neuropsychological theory. New York: John Wiley & Sons.
- Hoffman, M. L. (2000). *Empathy and moral development: Implications for caring and justice*. New York: Cambridge University Press.
- Hongwanishkul, D., Happaney, K. R., Lee, W. S., & Zelazo, P. D. (2005). Assessment of hot and cool executive function in young children: Age-related changes and individual differences. *Developmental Neuropsychology*, 28, 617–644.
- Kelley, W. M., Marace, C. N., Wyland, C. L., Cagler, S., Inati, S., & Heatherton, T. F. (2002). Finding the self? An event-related fMRI study. *Journal of Cognitive Neuroscience*, 14, 785–794.
- Kohlberg, L. (1964). Development of moral character and moral ideology. In M. L. Hoffman & L. W. Hoffman (Eds.), *Review of child development research* (Vol. 1, pp. 381–431). New York: Russell Sage Foundation.
- Kohlberg, L., & Candee, D. (1984). The relationship of moral judgment to moral action. In W. Kertines & J. Gewirtz (Eds.), *Morality, moral behavior and moral* development (pp. 52–73). New York: Wiley.

- LeDoux, J. E. (2000). Emotion circuits in the brain. *Annual Review of Neuroscience*, 23, 155–184.
- Marlowe, W. (1992). The impact of right prefrontal lesion on the developing brain. *Brain and Cognition*, 20, 205–213.
- Mateer, C. A., & Williams, D. (1991). Effects of frontal lobe injury in childhood. *Developmental Neuropsychology*, 7, 359–376.
- Moll, J., Eslinger, P. J., & Oliveira-Souza, R. (2001). Frontopolar and anterior temporal cortex activation in a moral judgment task: Preliminary functional MRI results in normal subjects. Arquivos de Neuro-Psiquiatria, 59, 667–664.
- Moll, J., Krueger, F., Zahn, R., Pardini, M., Oliveira-Souza, R., & Grafman, J. (2006). Human frontomesolimbic networks guide decisions about charitable donation. *Proceedings of the National Academy of Sciences*, 103, 15623–15628.
- Moll, J., Oliveira-Souza, R., & Eslinger, P. (2003).
 Morals and the human brain: A working model.
 Neuroreport, 14, 299–305.
- Moll, J., Oliveira-Zouza, R., Eslinger, P., Bramati, I., Miranda, J., Andreiuolo, P., et al. (2002). The neural correlates of moral sensitivity: A functional magnetic resonance imaging investigation of basic and moral emotions. *The Journal of Neuroscience*, 22, 2370–2736.
- Moll, J., Zahn, R., Oliveira-Zouza, R., Kruger, F., & Grafman, J. (2005). Opinion: The neural basis of human moral cognition. *Nature Review of Neuro*science, 6, 799–809.
- Moll, J., Oliveira-Souza, R., Garrido, G., Bramati, I., Caparelli-Daquer, E., Paiva, M., et al. (2007). The self as a moral agent: Linking the neural bases of social agency and moral sensitivity. *Social Neuro*science, 2(3–4), 336–352.
- Piaget, J. (1968). Six psychological studies (A. Tenzer, Trans.). New York: Vintage Books.
- Powell, K. B., & Voeller, K. K. (2004). Prefrontal executive function syndromes in children. *Journal of Child Neurology*, 19, 785–797.
- Price, B. H., Daffner, K. R., Stowe, R. M., & Lesulam, M.-M. (1990). The comportmental learning disabilities of early frontal lobe damage. *Brain*, 113, 1383–1393.
- Saleem, K. S., Kondo, H., & Price, J. L. (2008). Complementary circuits connecting orbital and medial prefrontal networks with the temporal, insular, and opercular cortex in the macaque monkey. *Journal of Comparative Neurology*, 506, 659–693.
- Seger, C. A., Stone, M., & Keenan, J. P. (2004). Cortical activations during judgments about the self and an other person. *Neuropsychologia*, 42, 1168–1177.
- Seitz, R. J., Nickel, J., & Azari, N. P. (2006). Functional modularity of the medial prefrontal cortex: Involvement in human empathy. *Neuropsychology*, 20, 743–751.
- Stams, G., Brugman, D., Dekovic, M., Rosmalen, L., Laan, P., & Gibbs, J. (2006). The moral judgment of juvenile delinquents: A meta-analysis. *Journal of Abnormal Child Psychology*, 34, 697–713.
- Young, L., Cushman, F., Hauser, M., & Saxe, R. (2007). The neural basis of the interaction between theory of mind and moral judgment. *Proceedings of the National Academy of Sciences*, 104, 8235–8240.
- Zahn, R., Moll, R., Krueger, F., Huey, E. D., Garrido, G., & Grafman, J. (2007). Social concepts are represented in the superior anterior temporal cortex. *Proceedings of the National Academy of Sciences*, 104, 6430–6435.