

# Premotor functional connectivity predicts impulsivity in juvenile offenders

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Teenagers are often impulsive. In some cases this is a phase of normal development; in other cases impulsivity contributes to criminal behavior. Using functional magnetic resonance imaging, we examined resting-state functional connectivity among brain systems and behavioral measures of impulsivity in 107 juveniles incarcerated in a high-security facility. In less-impulsive juveniles and normal controls, motor planning regions were correlated with brain networks associated with spatial attention and executive control. In more-impulsive juveniles, these same regions correlated with the default-mode network, a constellation of brain areas associated with spontaneous, unconstrained, self-referential cognition. The strength of these brain-behavior relationships was sufficient to predict impulsivity scores at the individual level. Our data suggest that increased functional connectivity of motor-planning regions with networks subserving unconstrained, self-referential cognition, rather than those subserving executive control, heightens the predisposition to impulsive behavior in juvenile offenders. To further explore the relationship between impulsivity and neural development, we studied functional connectivity in the same motor-planning regions in 95 typically developing individuals across a wide age span. The change in functional connectivity with age mirrored that of impulsivity: younger subjects tended to exhibit functional connectivity similar to the more-impulsive incarcerated juveniles, whereas older subjects exhibited a less-impulsive pattern. This observation suggests that impulsivity in the offender population is a consequence of a delay in typical development, rather than a distinct abnormality.

self-control | psychopathy | functional MRI

**S**elf-control is an important cognitive ability that develops with age. Individual variability in self-control has been linked to a wide variety of life outcomes, ranging from educational and economic achievement to likelihood of incarceration (1, 2).

Clinical disorders of self-control can take several forms, including attention-deficit/hyperactivity disorder (ADHD), antisocial personality disorder, psychopathy, and conduct disorder. Each has received attention from neuroscientists, often focused on structural MRI or functional activation experiments (3, 4), although several studies also examine resting functional connectivity (5). Of particular relevance to the present results are theories that emphasize the role of attentional processes in these disorders. For example, Newman identified differences in attentional abilities in juveniles and adults with psychopathic traits, suggesting that an inability to properly focus on relevant stimuli contributed to their disorder (6, 7).

The etiology of these disorders remains cloudy. We know that young children lack self-control but gradually acquire it over the course of development (8). At what point does pathological impulsivity deviate from typical developmental trajectories? Clues may be found by comparing functional brain activity associated with impulsivity with that seen in development. A growing body of neuroscientific evidence indicates that developing brains exhibit important differences in functional activity

and organization. The functional organization of children's brains is quite different from that of adults, displaying stronger short-distance connections and weaker long-distance connections (9, 10). Adult functional connectivity patterns develop gradually over the course of many years.

In this study we sought evidence for a neural basis of impulsivity, a critical component of self-control. To this end, we evaluated resting-state functional (f)MRI activity in a population of juvenile offenders, as well as two additional cohorts of typical individuals across a broad age range.

All subjects were evaluated using resting-state functional connectivity magnetic resonance imaging (RS-fcMRI). RS-fcMRI studies of functional connectivity are rapidly emerging as a major theme of human imaging research. In this context, functional connectivity refers to spatial patterns of coherence in the spontaneous fluctuations of the fMRI blood-oxygen-level-dependent (BOLD) signal observed during quiet wakefulness (11). These patterns change during the course of typical childhood and adolescent development (9, 10) and during healthy aging (12). Departures from typical functional connectivity have been described in a wide variety of diseases, including Alzheimer's, Parkinson's, schizophrenia, autism, and ADHD (13). Here we investigate the relationship between functional connectivity, impulsivity, and development.

## Results

We analyzed RS-fcMRI measures, along with behavioral assessments of impulsivity, in a group of 122 juvenile offenders who were incarcerated in a high-security prison facility. We used a unique, data-driven algorithm (*Methods*) to search throughout the brain for patterns of functional connectivity associated with impulsivity. This algorithm identified two bilaterally symmetric regions whose functional connectivity patterns changed substantially in relation to individuals' impulsivity ratings (Fig. 1A). These regions were located in the left and the right rostral aspect of the dorsolateral premotor cortex (PMdr) in Brodmann area 6 (Talairach coordinates  $[-33, -1, 50]$  and  $[36, -4, 56]$ ). They border the frontal eye fields (FEF), but are anatomically distinct, being situated medial and dorsal to FEF. Functional activation experiments have shown that these regions are recruited primarily by tasks requiring complex motor planning and motor execution (14, 15).

The iterative approach used here employs a very large number of comparisons to arrive at a final set of regions. It was therefore

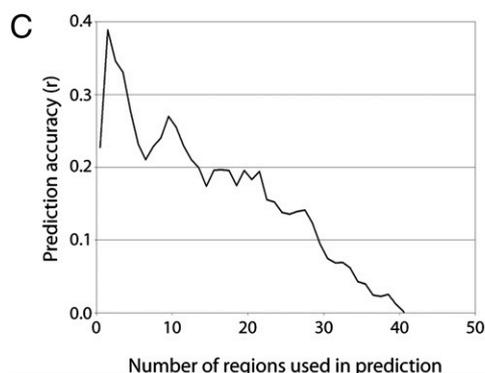
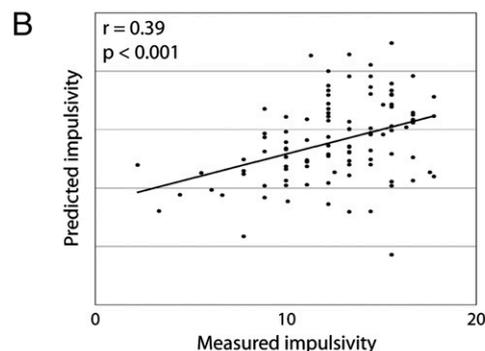
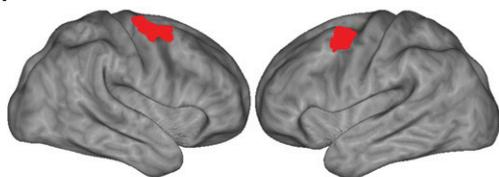
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**A** Motor-Planning Regions Implicated in Impulsivity

**Fig. 1.** Premotor functional connectivity and impulsivity. (A) Bilateral dorsorostral premotor regions (PMdr). These two regions showed the greatest correlation between resting state functional connectivity (RS-fcMRI) and impulsivity in the juvenile offender cohort. (B) Predicted vs. measured impulsivity evaluated in juvenile offenders using the leave-one-out procedure. Impulsivity (arbitrarily scaled; *SI Text*) was predicted on the basis of bilateral PMdr RS-fcMRI. The correlation between predicted and measured impulsivity is highly significant ( $n = 106$ ,  $r = 0.39$ ;  $P < 0.001$ ). (C) Dependence of prediction accuracy on selection of regions of interest (ROIs) used to compute the prediction. The IDEA algorithm identifies many regions sorted by decreasing power to discriminate high vs. low impulsivity. The plot shows the effect of including progressively more ROIs from the sorted list. Predictive accuracy peaked with two regions (left and right PMdr), suggesting that the relation of RS-fcMRI to impulsivity is highly focal.

important to assess the reliability of the algorithm. To that end, we used leave-one-out cross-validation to test whether our method could predict the impulsivity scores of individuals whose data did not contribute to the generated model (16). We repeated our analysis 107 times, each time leaving out a different subject. On the basis of the identified regions and connectivity changes, we made a prediction for the left-out subject's impulsivity rating (*SI Text*). These predictions were then compared against the subjects' actual ratings. This strategy addresses the issue of multiple comparisons: If the results that have been found on 106 subjects are indeed false positives due to multiple comparisons, then the impulsivity rating predicted from the left-out subject's scan data will not correlate with the left-out subject's actual impulsivity score.

In every one of the 107 leave-one-out instances, the left and the right PMdr were the two top-ranked regions identified by the al-

gorithm; their functional connectivity maps varied systematically with impulsivity ratings. Critically, our process was able to predict individual impulsivity scores with accuracy far above chance (Fig. 1B;  $r = 0.39$ ,  $P < 0.001$ ). Because these predictions were made using the rigorous leave-one-out procedure, we expect that our model should maintain its accuracy in an independent sample.

The algorithm identifies a large number of regions and rates the degree to which each region's functional connectivity may potentially be predictive of impulsivity. We examined the effect of varying the number of regions contributing to the impulsivity-predictive model, starting with the highest-rated region and adding additional regions in descending order of rating (Fig. 1C). Predictive accuracy peaked using the two most discriminating regions (left and right PMdr). Adding additional regions reduced predictive accuracy. We therefore focus on left and right PMdr as key components in the neural correlates of impulsivity.

To understand the relationship between impulsivity and altered PMdr functional connectivity in juvenile offenders, it is instructive to compare the same measures in typical juveniles and young adults. We first examined the functional connectivity of these regions in a previously acquired dataset of RS-fcMRI in 17 healthy young adults (17). We lack impulsivity measures for these subjects, but individuals from the general population typically score in a range similar to the least-impulsive individuals in the incarcerated group (18).

In the typical young adult cohort, the resting-state BOLD signal from PMdr was positively correlated with signals from the dorsal attention and executive-control networks (19–22) and negatively correlated with the default-mode network signal (23, 24) (Fig. 2A). A very similar pattern is seen in less-impulsive juvenile offenders. However, in more-impulsive juvenile offenders, the network associations were reversed: PMdr correlated positively with the default-mode network and negatively with the attention and control networks (Fig. 2B).

We defined dorsal-attention, executive-control, and default-mode networks on the basis of interactions with PMdr and impulsivity (*SI Text*). The correlation between PMdr and the default-mode network ranged in value from  $-0.8$  for the least impulsive individual to  $0.25$  for the most impulsive individual (Fig. 2C). Correlations between PMdr and the attention and control networks ranged in value from  $0.75$  to  $-0.3$ . These impulsivity-related differences are quite large in comparison with changes in functional connectivity achieved by varying task performance, sleep state, and even anesthesia (25–28). Hence, it is unlikely that the presently observed functional connectivity differences are attributable to ongoing cognition. It appears more likely that these differences reflect aspects of intrinsic brain organization.

The findings described above were obtained in a population in which impairment to self-control has frequently reached a level that might be described as pathological—in many cases it has contributed to criminality and often interferes with individuals' ability to interact appropriately with others. However, it is well known that self-control is not an ability we are born with, but one that continues to develop well into the late teens and early twenties. Can the neural correlates of impulsivity in the juvenile offender population be observed as an effect of age during typical development?

To answer this question, we examined PMdr functional connectivity in a cohort of 95 typically developing individuals between the ages of 7 and 31. We computed functional connectivity maps for PMdr for each subject. We then tested the correlation between features of these maps and chronological age. In Fig. 3, we calculated the voxelwise correlation across subjects between PMdr functional connectivity and age. As age increases, PMdr functional connectivity shifts from the default-mode network to the attention and control networks. This finding strikingly parallels the impulsivity-related result in the juvenile offenders:





commonly subdivided into two groups: Factor 1 is associated with poor empathy (we did not identify consistent effects of factor 1 on functional connectivity; *SI Text*), whereas factor 2 is associated with impulsivity and a need for stimulation (50). This report focuses on neural correlates of impulsivity as measured by factor 2.

A unique algorithm [termed "iterative data-driven evolutionary algorithm" (IDEA)] was used to identify regions whose correlation maps were consistently altered in relation to impulsivity. IDEA begins with a set of 36 regions representing nodes of several networks throughout the brain. For each region, it generates a map of functional connectivity to all voxels in the brain for each subject and searches for areas whose functional connectivity systematically increases or decreases as a function of subjects' impulsivity. These areas are themselves possible sites of interest, so IDEA investigates them in the same way it investigates the original 36. This process continues iteratively until IDEA has settled on regions whose functional connectivity is most diagnostic of impulsivity (additional details can be found in *SI Text*).

In our study of typical development, we obtained 7–10.5 min of RS-fMRI from a cohort of 95 individuals between the ages of 7 and 31. Participants were recruited from the community with a combination of advertisements

and mailings. All subjects were scanned using a 3.0-T Siemens Magnetom Tim Trio scanner with a 12-channel head coil at the Oregon Health and Science University Advanced Imaging Research Center. During the resting-state scans, subjects were simply asked to remain still and maintain fixation on a central crosshair. Seven subjects were excluded from the analysis due to excess movement and to ensure that there was no age relationship with movement (*SI Text*). As with the juvenile offender sample, to further reduce the effect of movement on functional connectivity calculations, individual fMRI volumes exhibiting excessive movement were identified and excluded from analysis (*SI Text*).

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- Mischel W, Shoda Y, Rodriguez MI (1989) Delay of gratification in children. *Science* 244:933–938.
- Moffitt TE, et al. (2011) A gradient of childhood self-control predicts health, wealth, and public safety. *Proc Natl Acad Sci USA* 108:2693–2698.
- Crowe SL, Blair RJ (2008) The development of antisocial behavior: What can we learn from functional neuroimaging studies? *Dev Psychopathol* 20:1145–1159.
- Blair RJ (2010) Neuroimaging of psychopathy and antisocial behavior: A targeted review. *Curr Psychiatry Rep* 12:76–82.
- Konrad K, Eickhoff SB (2010) Is the ADHD brain wired differently? A review on structural and functional connectivity in attention deficit hyperactivity disorder. *Hum Brain Mapp* 31:904–916.
- Kosson DS, Newman JP (1986) Psychopathy and the allocation of attentional capacity in a divided-attention situation. *J Abnorm Psychol* 95:257–263.
- Vitale JE, et al. (2005) Deficient behavioral inhibition and anomalous selective attention in a community sample of adolescents with psychopathic traits and low-anxiety traits. *J Abnorm Child Psychol* 33:461–470.
- Arnett J (1992) Reckless behavior in adolescence: A developmental perspective. *Dev Rev* 12:339–373.
- Fair DA, et al. (2008) The maturing architecture of the brain's default network. *Proc Natl Acad Sci USA* 105:4028–4032.
- Supekar K, Musen M, Menon V (2009) Development of large-scale functional brain networks in children. *PLoS Biol* 7:e1000157.
- Fox MD, Raichle ME (2007) Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging. *Nat Rev Neurosci* 8:700–711.
- Andrews-Hanna JR, et al. (2007) Disruption of large-scale brain systems in advanced aging. *Neuron* 56:924–935.
- Zhang D, Raichle ME (2010) Disease and the brain's dark energy. *Nat Rev Neurol* 6:15–28.
- Hanakawa T, et al. (2002) The role of rostral Brodmann area 6 in mental-operation tasks: An integrative neuroimaging approach. *Cereb Cortex* 12:1157–1170.
- Abe M, Hanakawa T (2009) Functional coupling underlying motor and cognitive functions of the dorsal premotor cortex. *Behav Brain Res* 198:13–23.
- Hastie T, Tibshirani R, Friedman J (2009) *The Elements of Statistical Learning: Data Mining, Inference, and Prediction* (Springer, New York), 2nd Ed.
- Fox MD, Snyder AZ, Vincent JL, Raichle ME (2007) Intrinsic fluctuations within cortical systems account for intertrial variability in human behavior. *Neuron* 56:171–184.
- Forth AE, Kosson DS, Hare RD (2003) *Hare Psychopathy Checklist: Youth Version* (Multi-Health Systems, Toronto), pp 1–52.
- Corbetta M, Shulman GL (2002) Control of goal-directed and stimulus-driven attention in the brain. *Nat Rev Neurosci* 3:201–215.
- Fox MD, et al. (2005) The human brain is intrinsically organized into dynamic, anticorrelated functional networks. *Proc Natl Acad Sci USA* 102:9673–9678.
- Seeley WW, et al. (2007) Dissociable intrinsic connectivity networks for salience processing and executive control. *J Neurosci* 27:2349–2356.
- Dosenbach NU, Fair DA, Cohen AL, Schlaggar BL, Petersen SE (2008) A dual-networks architecture of top-down control. *Trends Cogn Sci* 12:99–105.
- Raichle ME, et al. (2001) A default mode of brain function. *Proc Natl Acad Sci USA* 98:676–682.
- Buckner RL, Andrews-Hanna JR, Schacter DL (2008) The brain's default network: Anatomy, function, and relevance to disease. *Ann N Y Acad Sci* 1124:1–38.
- Fransson P (2006) How default is the default mode of brain function? Further evidence from intrinsic BOLD signal fluctuations. *Neuropsychologia* 44:2836–2845.
- Horowitz SG, et al. (2008) Low frequency BOLD fluctuations during resting wakefulness and light sleep: A simultaneous EEG-fMRI study. *Hum Brain Mapp* 29:671–682.
- Mhuirheartaigh RN, et al. (2010) Cortical and subcortical connectivity changes during decreasing levels of consciousness in humans: A functional magnetic resonance imaging study using propofol. *J Neurosci* 30:9095–9102.
- Boveroux P, et al. (2010) Breakdown of within- and between-network resting state functional magnetic resonance imaging connectivity during propofol-induced loss of consciousness. *Anesthesiology* 113:1038–1053.
- Fair DA, et al. (2007) Development of distinct control networks through segregation and integration. *Proc Natl Acad Sci USA* 104:13507–13512.
- Duncan J, Owen AM (2000) Common regions of the human frontal lobe recruited by diverse cognitive demands. *Trends Neurosci* 23:475–483.
- Hallett PE (1978) Primary and secondary saccades to goals defined by instructions. *Vision Res* 18:1279–1296.
- Munoz DP, Everling S (2004) Look away: The anti-saccade task and the voluntary control of eye movement. *Nat Rev Neurosci* 5:218–228.
- Ford KA, Goltz HC, Brown MR, Everling S (2005) Neural processes associated with antisaccade task performance investigated with event-related fMRI. *J Neurophysiol* 94:429–440.
- Koechlin E, Basso G, Pietrini P, Panzer S, Grafman J (1999) The role of the anterior prefrontal cortex in human cognition. *Nature* 399:148–151.
- Braver TS, Barch DM (2006) Extracting core components of cognitive control. *Trends Cogn Sci* 10:529–532.
- Crone EA, Wendelken C, Donohue SE, Bunge SA (2006) Neural evidence for dissociable components of task-switching. *Cereb Cortex* 16:475–486.
- Shulman GL, et al. (1997) Common blood flow changes across visual tasks: II. Decreases in cerebral cortex. *J Cogn Neurosci* 9:648–663.
- Mason MF, et al. (2007) Wandering minds: The default network and stimulus-independent thought. *Science* 315:393–395.
- Andrews-Hanna JR, Reidler JS, Sepulcre J, Poulin R, Buckner RL (2010) Functional-anatomic fractionation of the brain's default network. *Neuron* 65:550–562.
- Simpson JR, et al. (2000) The emotional modulation of cognitive processing: An fMRI study. *J Cogn Neurosci* 12(Suppl 2):157–170.
- Dolan RJ (2002) Emotion, cognition, and behavior. *Science* 298:1191–1194.
- Gusnard DA, Akbudak E, Shulman GL, Raichle ME (2001) Medial prefrontal cortex and self-referential mental activity: Relation to a default mode of brain function. *Proc Natl Acad Sci USA* 98:4259–4264.
- Kelley WM, et al. (2002) Finding the self? An event-related fMRI study. *J Cogn Neurosci* 14:785–794.
- Kjaer TW, Nowak M, Lou HC (2002) Reflective self-awareness and conscious states: PET evidence for a common midline parietofrontal core. *Neuroimage* 17:1080–1086.
- Brown TT, et al. (2005) Developmental changes in human cerebral functional organization for word generation. *Cereb Cortex* 15:275–290.
- Lewis CM, Baldassarre A, Committeri G, Romani GL, Corbetta M (2009) Learning sculpts the spontaneous activity of the resting human brain. *Proc Natl Acad Sci USA* 106:17558–17563.
- Smyser CD, Snyder AZ, Neil JJ (2011) Functional connectivity MRI in infants: Exploration of the functional organization of the developing brain. *Neuroimage* 56:1437–1452.
- Corrado RR, Vincent GM, Hart SD, Cohen IM (2004) Predictive validity of the Psychopathy Checklist: Youth Version for general and violent recidivism. *Behav Sci Law* 22:5–22.
- Vincent GM, Ogdens CL, McCormick AV, Corrado RR (2008) The PCL: YV and recidivism in male and female juveniles: A follow-up into young adulthood. *Int J Law Psychiatry* 31:287–296.
- Harpur TJ, Hakstian AR, Hare RD (1988) Factor structure of the Psychopathy Checklist. *J Consult Clin Psychol* 56:741–747.