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

Self-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. 1*A*). 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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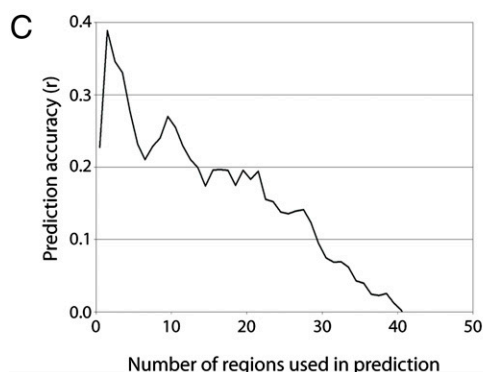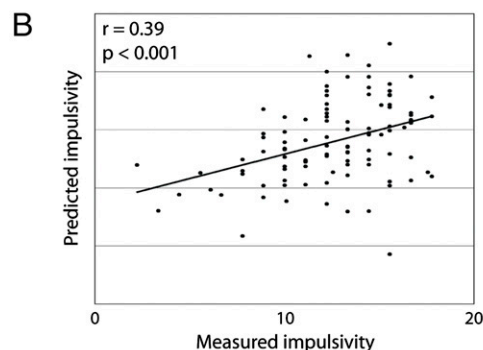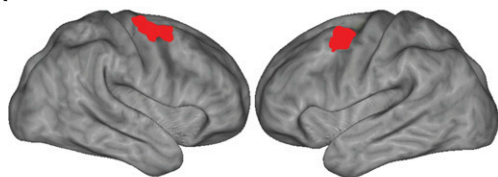
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Fig. 1. Premotor functional connectivity and impulsivity. (*A*) Bilateral dorso-rostral premotor regions (PMdr). These two regions showed the greatest correlation between resting state functional connectivity (RS-fcMRI) and impulsivity in the juvenile 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. 1*B*; $r = 0.39$, $P < 0.001$). 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. 1*C*). 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. 2*A*). 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. 2*B*).

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. 2*C*). 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:
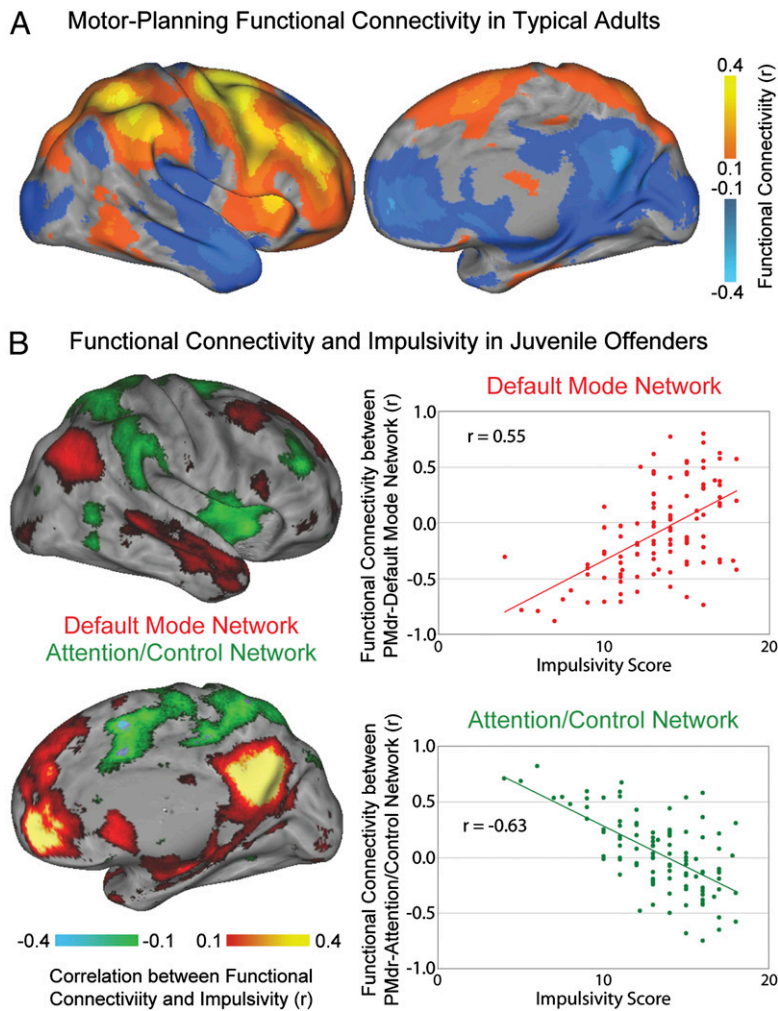
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Fig. 2. (*A*) PMdr functional connectivity in typical young adults. Images are thresholded at a value of *r* = 0.1. PMdr is positively correlated with the dorsal-attention network and the executive-control network; it is anticorrelated with the default-mode network. (*B*) Correlation between PMdr functional connectivity and impulsivity in juvenile offenders. PMdr functional connectivity in less-impulsive juveniles is similar to that of adults. However, in more-impulsive individuals its relationships reverse, such that it is positively correlated with the default-mode network and anticorrelated with the dorsal-attention and executive-control networks.

Younger brains tend to have a "more impulsive" pattern of PMdr functional connectivity.

To confirm the correspondence between the effects of age and impulsivity, we calculated functional connectivity between PMdr and the attention/control and default-mode networks, with all regions and networks defined using the juvenile offender data. Consistent with prior reports (9, 29), we observed substantial individual variability. Nevertheless, the age/impulsivity relationship was found in typical development as well as in juvenile offenders: PMdr functional connectivity with the attention/control networks significantly increased with age (*r* = 0.20, *P* < 0.05), whereas functional connectivity with the default-mode network significantly decreased with age (r = −0.35, *P* < 0.001). These results offer an indirect validation of the algorithmic approach used on the juvenile offender data: The networks, regions, and functional connectivity relationships identified by the algorithm were recapitulated in the typically developing sample.

Discussion

We searched for functional connectivity patterns associated with impulsivity in juvenile offenders, using a unique algorithmic approach. This technique identified motor-planning regions in left and right PMdr. In healthy young adults and less-impulsive juveniles, PMdr was functionally connected with attention- and control-related networks. In more impulsive juveniles, PMdr instead was functionally connected with the default-mode network. To relate impulsivity to development, we tested PMdr functional connectivity in typically developing individuals between the ages of 7 and 31. A very similar pattern emerged as we move across the age span: PMdr shifted from a correlation with the default-mode network to a correlation with attention and control networks.

Whereas PMdr has not been a major focus of neuroimaging investigation, the cognitive operations represented in the attention, control, and default-mode networks have been well characterized. The attention and control networks are recruited by many tasks involving effortful, goal-directed cognition (30). One illustrative example is the antisaccade task, in which a light appears in the visual periphery, and subjects are asked to inhibit their natural response of looking toward the light and instead look away. Correct performance of this task recruits frontal eye fields, dorsolateral prefrontal cortex, and anterior cingulate cortex, all parts of the attention and control networks and all showing reduced functional connectivity to PMdr in impulsive juveniles (31–33). The control network is also characteristically recruited by error detection and correction, task switching, and complex problem solving and planning (34–36).

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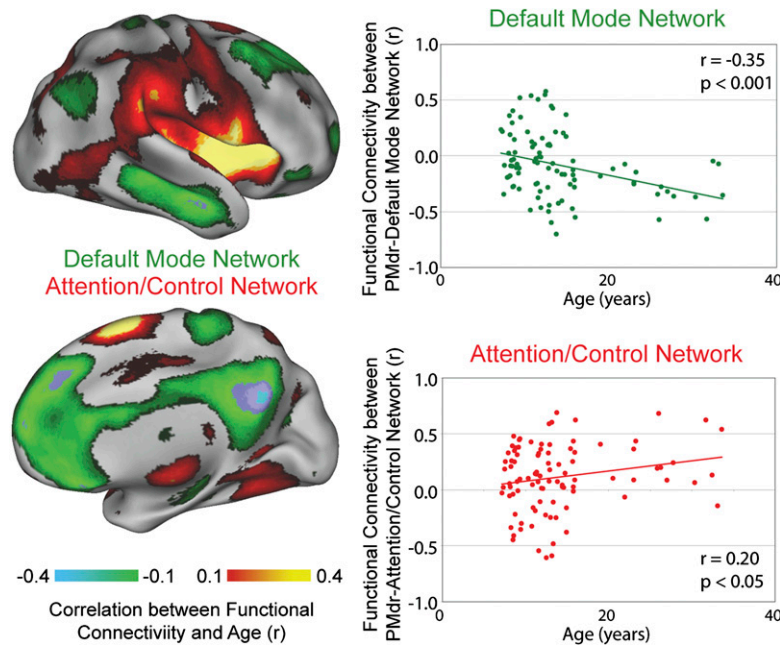## Functional Connectivity and Age in Typical Development

Fig. 3. Relationship between PMdr functional connectivity and chronological age. In younger subjects, PMdr is correlated with the default-mode network and anticorrelated with the dorsal-attention and executive-control networks. In older subjects, these relationships are reversed. Thus, with respect to PMdr RS-fcMRI, the effect of youth in typically developing individuals is strikingly similar to the effect of measured impulsivity in the juvenile offenders.

In contrast, the default-mode network is generally associated with spontaneous, unconstrained, self-referential cognitive processes. Operationally, default-mode network activity is highest during quiet rest; goal-directed tasks that activate the attention and control networks usually reduce activity in the default-mode network (23, 37). Similarly, momentary lapses of cognitive focus during task performance (mind wandering) correlate with transient increases in default-mode network activity (38).

Certain tasks do recruit portions of the default-mode network: memory retrieval, social cognition, affective valuation, and self-referential processing (39). These latter two processes may be of particular relevance to the present findings. During affective valuation tasks, activity in the orbitofrontal aspect of the default-mode network increases when subjects see emotionally negative stimuli (40, 41). Moreover, both medial frontal and medial parietal regions of the default-mode network exhibit greater activation when subjects are asked to think about themselves as opposed to others (42–44). Although we remain cautious in advancing a precise cognitive interpretation of the presently observed RS-fcMRI effects, we speculate that these effects represent the neural mechanism by which impulsive individuals give greater weight to immediate gratification than to the long-term consequences of their actions.

Typical young individuals and impulsive juvenile offenders both exhibited similar patterns of PMdr functional connectivity. One obvious possibility is that this finding reflects greater impulsivity in younger subjects compared with older subjects. Alternately, functional connectivity of PMdr may develop along with that in other regions as part of a larger maturational process. The development of self-control is an important component and marker of maturation, but of course many other components contribute as well. As noted above, children display different functional connectivity patterns than adults. Perhaps as a consequence of this difference, children also exhibit differences in task-related functional responses. For example, tasks that reduce activity in the default-mode network in adults may increase activity

in children (45). Whatever the mechanism, the similarity of the dependence of PMdr functional connectivity on age on impulsivity is quite striking. We suggest that PMdr functional connectivity in impulsive juvenile offenders develops along a typical trajectory, but does so in a delayed pattern.

Our results suggest the possibility that intervention might accelerate functional maturation in impulsive individuals. Functional connectivity can be altered by intensive training on a task (46). This result suggests the possibility that our findings may have practical application in the remediation of criminal impulsivity. First, we note that the functional connectivity changes associated with high impulsivity scores in juveniles are quite focal. Thus, whereas many psychiatric diseases are associated with widespread RS-fcMRI changes (13), our analysis identified only two regions with impulsivity-dependent functional connectivity differences. Consequently, these regions offer an attractive therapeutic target. Speculatively, extensive practice of an appropriately designed task, which coactivates PMdr and attention/control networks, could rebalance PMdr functional connectivity and thereby improve behavior.

Methods

In our study of juvenile offenders, we used a mobile Siemens 1.5-T Avanto fMRI scanner to image 122 juveniles who were incarcerated in a high-security prison facility for a variety of crimes ranging from drug offenses to assault and sexual assault. In each subject, we obtained a high-resolution structural scan and a single 5-min RS-fcMRI scan. During the resting-state scans, subjects were simply asked to remain still and maintain fixation on a central crosshair. Fifteen participants were excluded from further study due to excessive movement (*SI Text*), leaving 107 individuals in the final analysis (age 14–19, mean 17.0; 78 male). There was no relationship between movement and personality scores before or after these exclusions. To further reduce the effect of movement on functional connectivity calculations, individual fMRI volumes exhibiting excessive movement within each 5-min scan were identified and excluded from analysis (47) (*SI Text*).

We assessed the juvenile offenders using the youth version of the Hare Psychopathy Checklist (PCL-YV) (18). The PCL-YV is a strong predictor of propensity to commit crimes (48, 49). The items composing the PCL-YV are

Shannon et al.

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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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