

Selected references – Catherine Sebastian

Lockwood, P. L., Sebastian, C. L., McCrory, E. J., Hyde, Z. H., Gu, X., De Brito, S. A. et al. (2013). Association of callous traits with reduced neural response to others' pain in children with conduct problems. *Current Biology*, 23, 901-905.

Notes: Children with conduct problems (CP) persistently violate others' rights and represent a considerable societal cost. These children also display atypical empathic responses to others' distress, which may partly account for their violent and antisocial behavior. Callous traits index lack of empathy in these children and confer risk for adult psychopathy. Investigating neural responses to others' pain is an ecologically valid method to probe empathic processing, but studies in children with CP have been inconclusive. Using functional magnetic resonance imaging (fMRI), we measured neural responses to pictures of others in pain (versus no pain) in a large sample of children with CP and matched controls. Relative to controls, children with CP showed reduced blood oxygen level-dependent responses to others' pain in bilateral anterior insula (AI), anterior cingulate cortex (ACC), and inferior frontal gyrus, regions associated with empathy for pain in previous studies. In the CP group, callous traits were negatively associated with responses to others' pain in AI and ACC. We conclude that children with CP have atypical neural responses to others' pain. The negative association between callous traits and AI/ACC response could reflect an early neurobiological marker indexing risk for empathic deficits seen in adult psychopathy

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Sebastian, C. L., Fontaine, N. M., Bird, G., Blakemore, S. J., Brito, S. A., McCrory, E. J. et al. (2012). Neural processing associated with cognitive and affective Theory of Mind in adolescents and adults. *Social Cognitive and Affective Neuroscience*, 7, 53-63.

Notes: Theory of Mind (ToM) is the ability to attribute thoughts, intentions and beliefs to others. This involves component processes, including cognitive perspective taking (cognitive ToM) and understanding emotions (affective ToM). This study assessed the distinction and overlap of neural processes involved in these respective components, and also investigated their development between adolescence and adulthood. While data suggest that ToM develops between adolescence and adulthood, these populations have not been compared on cognitive and affective ToM domains. Using fMRI with 15 adolescent (aged 11-16 years) and 15 adult (aged 24-40 years) males, we assessed neural responses during cartoon vignettes requiring cognitive ToM, affective ToM or physical causality comprehension (control). An additional aim was to explore relationships between fMRI data and self-reported empathy. Both cognitive and affective ToM conditions were associated with neural responses in the classic ToM network across both groups, although only affective ToM recruited medial/ventromedial PFC (mPFC/vmPFC). Adolescents additionally activated vmPFC more than did adults during affective ToM. The specificity of the mPFC/vmPFC response during affective ToM supports evidence from lesion studies suggesting that vmPFC may integrate affective information during ToM. Furthermore, the differential neural response in vmPFC between adult and adolescent groups indicates developmental changes in affective ToM processing

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Sebastian, C. L., McCrory, E. J., Cecil, C. A., Lockwood, P. L., De Brito, S. A., Fontaine, N. M. et al. (2012). Neural responses to affective and cognitive theory of mind in children with conduct problems and varying levels of callous-unemotional traits. *Archives of General Psychiatry*, 69, 814-822.

Notes: CONTEXT Reduced neural responses to others' distress is hypothesized to play a critical role in conduct problems coupled with callous-unemotional traits, whereas increased neural responses to affective stimuli may accompany conduct problems without callous-unemotional traits. Heterogeneity of affective profiles in conduct problems may account for inconsistent neuroimaging findings in this population. OBJECTIVES To broaden understanding of neural processing in conduct problems using an affective processing task including an empathy component as well as to explore dimensional contributions of conduct problems symptoms and callous-unemotional traits to variance in affective neural responses. DESIGN Case-control study. SETTING On-campus neuroimaging facility. PARTICIPANTS Thirty-one boys with conduct problems (mean age, 14.34 years) and 16 typically developing control subjects (mean age, 13.51 years) matched for age (range, 10-16 years), IQ, socioeconomic status, handedness, and race/ethnicity. Participants were recruited using screening questionnaires in a community-based volunteer sample. MAIN OUTCOME MEASURES Functional magnetic resonance imaging of a task contrasting affective and cognitive theory of mind judgments. RESULTS Relative to typically developing children, children with conduct problems showed reduced activation in right amygdala and anterior insula for affective vs cognitive theory of mind judgments. Furthermore, in the right amygdala, regression analysis within the conduct-problems group showed suppressor effects between ratings of conduct problems and callous-unemotional traits. Specifically, unique variance associated with conduct problems was positively correlated with amygdala reactivity, whereas unique variance associated with callous-unemotional traits was negatively correlated with amygdala reactivity. These associations were not explained by hyperactivity, depression/anxiety symptoms, or alcohol use ratings. CONCLUSIONS Childhood conduct problems are associated with amygdala and anterior insula hypoactivity during a complex affective processing task including an empathy component. Suppressor effects between conduct problems and callous-unemotional traits in the amygdala suggest a potential neural substrate for heterogeneity in affective profiles associated with conduct problems

Viding, E., Sebastian, C. L., Dadds, M. R., Lockwood, P. L., Cecil, C. A., De Brito, S. A. et al. (2012). Amygdala response to preattentive masked fear in children with conduct problems: the role of callous-unemotional traits. *American Journal of Psychiatry*, 169, 1109-1116.

Notes: OBJECTIVE In children with conduct problems, high levels of callous-unemotional traits are associated with amygdala hypoactivity to consciously perceived fear, while low levels of callous-unemotional traits may be associated with amygdala hyperactivity. Behavioral data suggest that fear processing deficits in children with high callous-unemotional traits may extend to stimuli presented below conscious awareness (preattentively). The authors investigated the neural basis of this effect.

Amygdala involvement was predicted on the basis of its role in preattentive affective processing in healthy adults and its dysfunction in previous studies of conduct problems. METHOD Functional MRI was used to measure neural responses to fearful and calm faces presented preattentively (for 17 ms followed by backward masking) in boys with conduct problems and high callous-unemotional traits (N=15), conduct problems and low callous-unemotional traits (N=15), and typically developing comparison boys (N=16). Amygdala response to fearful and calm faces was predicted to differentiate groups, with the greatest response in boys with conduct problems and low callous-unemotional traits and the lowest in boys with conduct problems and high callous-unemotional traits. RESULTS In the right amygdala, a greater amygdala response was seen in boys with conduct problems and low callous-unemotional traits than in those with high callous-unemotional traits. The findings were not explained by symptom levels of conduct disorder, attention-deficit hyperactivity disorder, anxiety, or depression. CONCLUSIONS These data demonstrate differential amygdala activity to preattentively presented fear in children with conduct problems grouped by callous-unemotional traits, with high levels associated with lower amygdala reactivity. The study's findings complement increasing evidence suggesting that callous-unemotional traits are an important specifier in the classification of children with conduct problems

Burnett, S., Sebastian, C., Cohen, K. K., & Blakemore, S. J. (2011). The social brain in adolescence: evidence from functional magnetic resonance imaging and behavioural studies. *Neuroscience and Biobehavioral Reviews*, *35*, 1654-1664.
Notes: Social cognition is the collection of cognitive processes required to understand and interact with others. The term 'social brain' refers to the network of brain regions that underlies these processes. Recent evidence suggests that a number of social cognitive functions continue to develop during adolescence, resulting in age differences in tasks that assess cognitive domains including face processing, mental state inference and responding to peer influence and social evaluation. Concurrently, functional and structural magnetic resonance imaging (MRI) studies show differences between adolescent and adult groups within parts of the social brain. Understanding the relationship between these neural and behavioural observations is a challenge. This review discusses current research findings on adolescent social cognitive development and its functional MRI correlates, then integrates and interprets these findings in the context of hypothesised developmental neurocognitive and neurophysiological mechanisms

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Sebastian, C. L. & Blakemore, S. J. (2011). Understanding the neural response to social rejection in adolescents with autism spectrum disorders: a commentary on Masten et al., McPartland et al. and Bolling et al. *Dev.Cogn.Neurosci.*, *1*, 256-259.
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Sebastian, C. L., Tan, G. C., Roiser, J. P., Viding, E., Dumontheil, I., & Blakemore, S. J. (2011). Developmental influences on the neural bases of responses to social rejection: Implications of social neuroscience for education. *NeuroImage*, *57*,

686-694.

Notes: Relational aggression such as social rejection is common within school peer groups. Converging evidence suggests that adolescent females are particularly sensitive to social rejection. We used a novel fMRI adaptation of the Cyberball social rejection paradigm to investigate the neural response to social rejection in 19 mid-adolescent (aged 14-16) and 16 adult female participants. Across all participants, social exclusion (relative to inclusion) elicited a response in bilateral medial prefrontal cortex (mPFC) extending into ventral and subgenual anterior cingulate cortex and medial orbitofrontal cortex; and the left ventrolateral PFC (vlPFC); regions that have been associated in previous studies with social evaluation, negative affective processing, and affect regulation respectively. However, the exclusion-related response in right vlPFC, a region associated in previous studies with the regulation of rejection-related distress, was attenuated in adolescents. Within mPFC, greater activation during exclusion vs. inclusion was associated with greater self-reported susceptibility to peer influence in adolescents but not in adults. This suggests that the brain's response to experimentally-induced social rejection relates to adolescent behaviour in real-world social interactions. We speculate about the potential implications of these findings for educational settings. In particular, functional development of affective circuitry during adolescence may influence social interaction within the school peer group

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Sebastian, C., Viding, E., Williams, K. D., & Blakemore, S. J. (2010). Social brain development and the affective consequences of ostracism in adolescence. *Brain and Cognition*, 72, 134-145.

Notes: Recent structural and functional imaging studies have provided evidence for continued development of brain regions involved in social cognition during adolescence. In this paper, we review this rapidly expanding area of neuroscience and describe models of neurocognitive development that have emerged recently. One implication of these models is that neural development underlies commonly observed adolescent phenomena such as susceptibility to peer influence and sensitivity to peer rejection. Experimental behavioural evidence of rejection sensitivity in adolescence is currently sparse. Here, we describe a study that directly compared the affective consequences of an experimental ostracism manipulation (Cyberball) in female adolescents and adults. The ostracism condition led to significantly greater affective consequences in the adolescents compared with adults. This suggests that the ability to regulate distress resulting from ostracism continues to develop between adolescence and adulthood. The results are discussed in the context of models of neurocognitive development

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Sebastian, C., Blakemore, S. J., & Charman, T. (2009). Reactions to ostracism in adolescents with autism spectrum conditions. *Journal of Autism and Developmental Disorders*, 39, 1122-1130.

Notes: Little is known about how adolescents with autism spectrum conditions (ASC) experience the initial impact of ostracism. This study investigated whether a mild, short-term episode of experimentally induced ostracism (Cyberball) would affect self-reported anxiety, mood, and the extent to which four social needs (self-esteem, belonging, control and meaningful existence) were threatened in adolescents with ASC and matched controls. Anxiety and the four needs were negatively affected by ostracism in both groups. However, ostracism did not modulate mood in the ASC group, and a number of possible interpretations of this group difference are discussed. In general, the results of this study suggest that normative models of ostracism are applicable to ASC
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Sebastian, C., Burnett, S., & Blakemore, S. J. (2008). Development of the self-concept during adolescence. *Trends in Cognitive Sciences*, 12, 441-446.

Notes: DA - 20090309

Adolescence is a period of life in which the sense of 'self' changes profoundly. Here, we review recent behavioural and neuroimaging studies on adolescent development of the self-concept. These studies have shown that adolescence is an important developmental period for the self and its supporting neural structures. Recent neuroimaging research has demonstrated that activity in brain regions associated with self-processing, including the medial prefrontal cortex, changes between early adolescence and adulthood. These studies indicate that neurocognitive development might contribute to behavioural phenomena characteristic of adolescence, such as heightened self-consciousness and susceptibility to peer influence. We attempt to integrate this recent neurocognitive research on adolescence with findings from developmental and social psychology
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