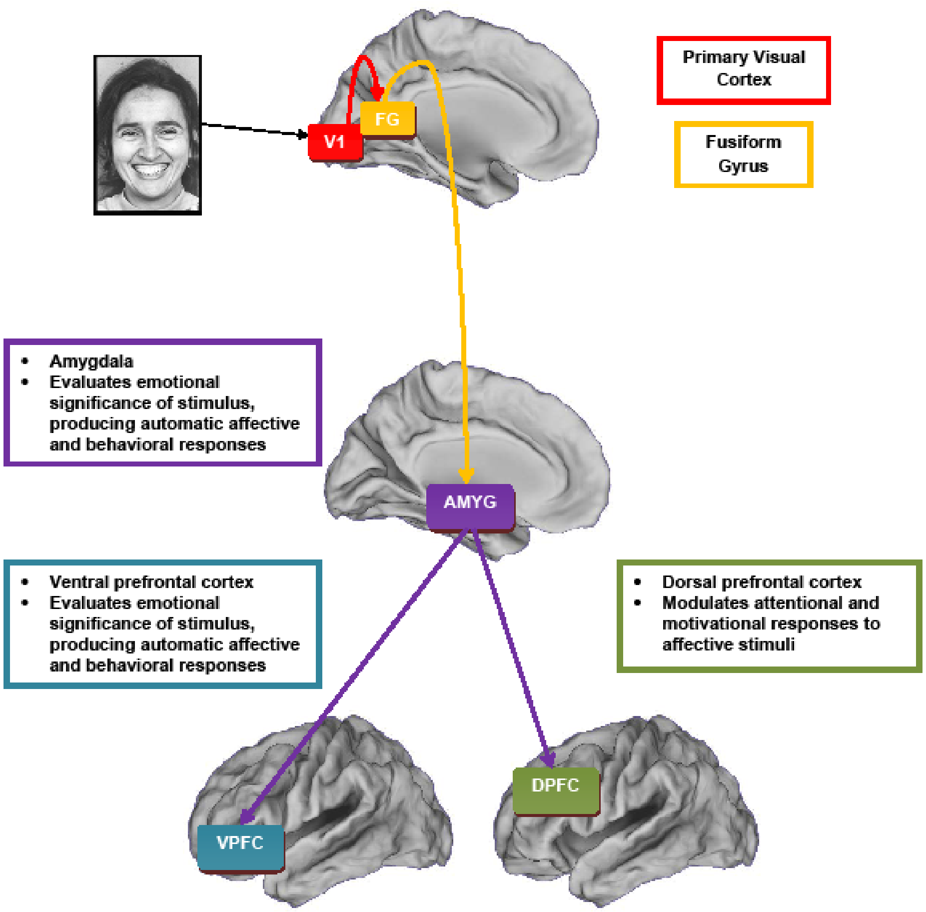
Supplementary Online Content

Diwadkar VA, Wadehra S, Pruitt P, Keshavan MS, Rajan U, Zajac-Benitez C, Eickhoff SB. Disordered corticolimbic interactions during affective processing in children and adolescents at risk for schizophrenia revealed by functional magnetic resonance imaging and dynamic causal modeling. *Arch Gen Psychiatry*. 2012;69(3):231-242.

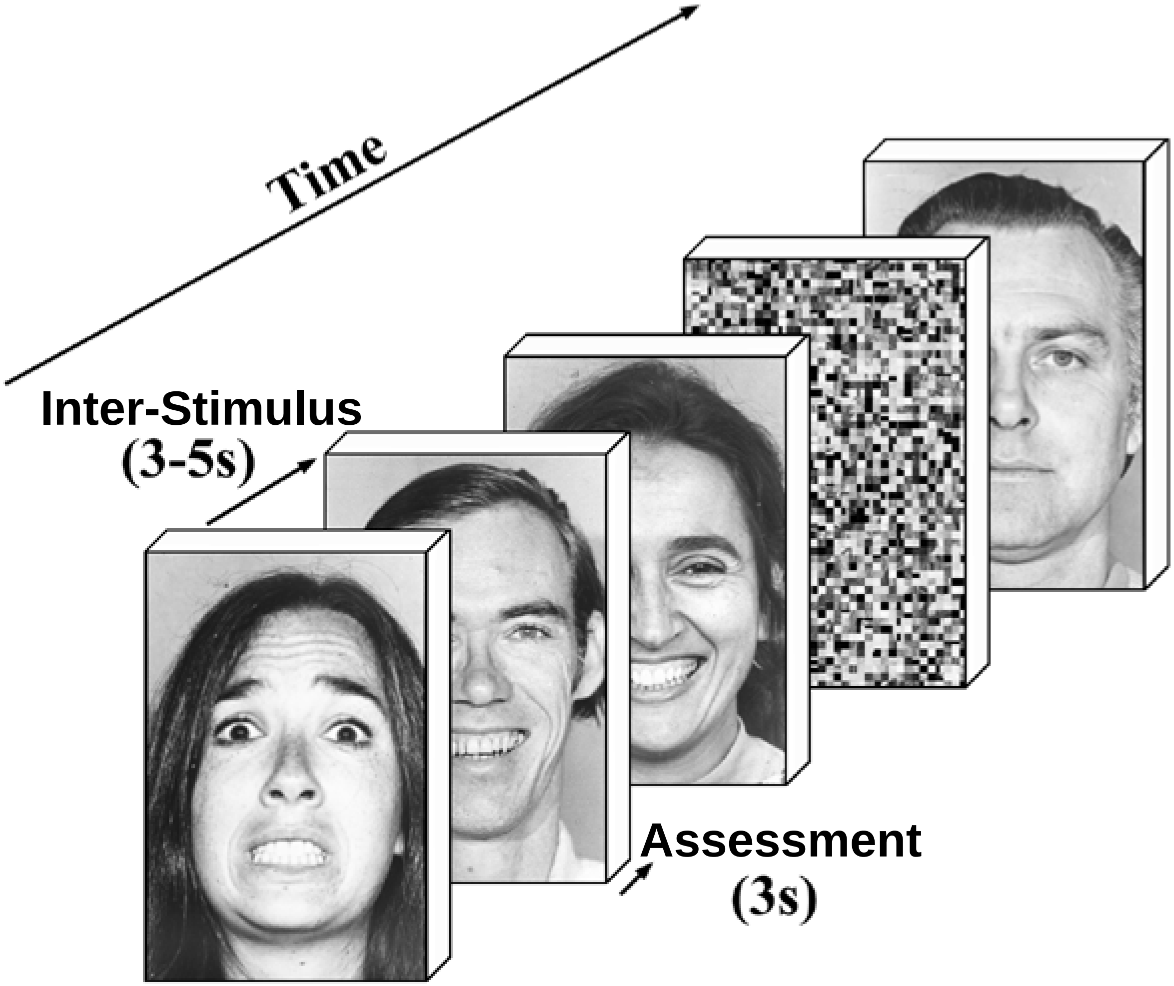
This supplementary material has been provided by the authors to give readers additional information about their work.

Figure 1 (Supplementary)



eFigure 1. Conceptual model of information flow in response to an affective face stimulus. As noted in the text, visually driven affective appraisal is initiated by sensory stimulus processing and feature extraction in the early visual cortex and subsequently the face-sensitive cortex on the fusiform gyrus.[1,2] This region feeds into core limbic circuitry, including the amygdala and its functionally differentiated nuclei.[3] Amygdala projections to ventral and dorsal prefrontal regions may be essential to transmitting affective information to higher-order heteromodal cortex. In turn, frontal control of the amygdala[4] may be essential in modulating the deliberative (as opposed to the automatic) responses driven by corticoamygdala interactions.[5] Importantly, the degree of this modulation may be top-down mediated by the context of the task or bottom-up driven by the stimulus itself. Intricate interplay between relatively specialized and distinct regions of corticolimbic pathways is supposed to be maturing during adolescence.[6]

Figure 2 (Supplementary)



eFigure 2. Example of the experimental paradigm used.

Note: A conservative Bonferroni correction was applied taking into account 17 statistical tests conducted on all coupling pairs (driving, intrinsic, and modulation: Figures 4-6). The overall α level was set to $P = .01$ and the effective degrees of freedom for each test were approximated based on the Welch-Satterthwaite equation for independent samples with unequal sample sizes and assuming unequal variances. The resultant Bonferroni-corrected α level for each individual test was fixed at $P < .005$. Only pairwise tests of parameter estimates that were significant at this Bonferroni corrected level were considered to be significantly different.

eTable 1. *t* Statistics for the Winning Model for Comparison of Driving Inputs[a]

V1	FG	Amygdala
18.34*	4.44	3.95

Abbreviations: FG, fusiform gyrus; V1, primary visual cortex.
[a]Indicates comparison between control group and children and adolescent offspring of patients with schizophrenia (Figure 4). Indicated values were significant ($P < .01$, Bonferroni correction). Columns indicate regions driven by inputs.

eTable 2. *t* Statistics Across Comparison of Intrinsic Connections[a]

V1→ FG	FG→ Amygdala	Amygdala → VPFC	Amygdala → DPFC	VPFC→ Amygdala	VPFC→ DPFC	DPFC→ Amygdala	DPFC→ VPFC
4.93*	20.29*	39.42*	43.00*	49.04*	48.23*	44.86*	42.44*

Abbreviations: DPFC, dorsal prefrontal cortex; FG, fusiform gyrus; V1, primary visual cortex; VPFC, ventral prefrontal cortex.
[a]Indicates comparison between control group and children and adolescent offspring of patients with schizophrenia (Figure 5). * *P* = .01, Bonferroni correction. Columns indicate directional connections across the network in the winning model.

eTable 3. *t* Statistics for Comparison of Contextual Modulation of Frontolimbic Connections[a]

	VPFC→Amygdala	DPFC→Amygdala
Negative	4.85*	12.8*
Neutral	0.31	4.8*
Positive	0.24	0.21

[a]Indicates comparison between control group and children and adolescent offspring of patients with schizophrenia (Figure 6). * *P* = .01, Bonferroni correction.

eReferences

1. Ishai A. Let’s face it: it’s a cortical network. *Neuroimage*. 2008;40(2):415-419.
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3. Pitkänen A, Amaral DG. Organization of the intrinsic connections of the monkey amygdaloid complex: projections originating in the lateral nucleus. *J Comp Neurol*. 1998;398(3):431-458.
4. Likhtik E, Pelletier JG, Paz R, Paré D. Prefrontal control of the amygdala. *J Neurosci*. 2005;25(32):7429-7437.
5. Phelps EA, LeDoux JE. Contributions of the amygdala to emotion processing: from animal models to human behavior. *Neuron.* 2005;48(2):175-187.
6. Hare TA, Tottenham N, Galvan A, Voss HU, Glover GH, Casey BJ. Biological substrates of emotional reactivity and regulation in adolescence during an emotional go-nogo task. *Biol Psychiatry*. 2008;63(10):927-934.