Supplementary Material for:

Altered insular activation and increased insular functional connectivity during sad and happy face processing in adolescent major depressive disorder

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Participants

Healthy control (HCL) adolescents were recruited from the San Diego area with posted flyers, e-mail, and the Internet. Adolescents with major depressive disorder (MDD) were recruited from 35 adolescent psychiatric and primary care clinics throughout the San Diego county area. Although multiple clinics referred potentially depressed adolescents to our study, all diagnoses were made independently of the source clinic and all fMRI scanning took place at only one site and on one MRI scanner. Behavioral measures were conducted either at the study site or were completed self-paced at the participant's home.

Assessment

<u>All participants were administered the following tests:</u>

- Wechsler Abbreviated Scale of intelligence (WASI) (Wechsler, 1999)
- Standard Snellen Eye Chart (Hetherington, 1954)
- Ishihara Color Plates test (8 plate, 2005 ed.) (Ishihara, 1917)
- Customary Drinking and Drug Use Record (CDDR) (Brown et al., 1998)
- Family Interview for Genetics Studies (FIGS) (Maxwell, 1992)
- Multidimensional Anxiety Scale for Children (MASC) (March et al., 1997)
- Children's Depression Rating Scale- Revised (CDRS-R) (Poznanski, 1996)
- Beck Depression Inventory II (BDI-II) (Beck et al., 1996)
- Children´s Global Assessment Scale (C-GAS) (Shaffer et al., 1983)
- Hollingshead Two Factor Index of Social Position (HSP) (Hollingshead, 1957)
- Tanner Stage (Tanner, 1962)
- General medical and developmental history forms

<u>Additional assessment in the MDD group</u>
Validation of MDD diagnosis and assessment of psychiatric comorbidities in the group of depressed adolescents was done with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (KSADS-PL)

(Kaufman et al., 2000) and diagnoses were verified by a board certified child and adolescent psychiatrist (TTY).

Additional assessment in the healthy controls

All healthy controls were subjected to the Diagnostic Interview Schedule for Children (DISC; Shaffer et al., 2000) and the Diagnostic Predictive Scale (DPS; Lucas et al., 2001) instruments to rule out any psychiatric diagnosis.

Exclusion criteria for MDD and HCL:

1. IQ score lower than 80 on the WASI.
2. Color blindness as established by the Ishihara Color Plates test
3. Less then 20/40 correctible vision on Standard Snellen Eye Chart.
4. Contraindications for MRI (e.g. ferrometallic implants, braces or claustrophobia).
5. Pregnancy or the possibility thereof.
6. Evidence of drug misuse (illicit or prescription) within the previous month.
7. Two or more alcoholic drinks per week currently or within the previous month as determined by the CDDR.
8. Left-handedness.
9. Prepubertal status (Tanner stages 1 or 2).
10. Inability to comprehend and comply with study procedures.
11. Use of medications with a CNS effect in the 2 weeks prior to scanning.
12. Any history of neurologic disorder (e.g. meningitis, migraine, HIV) or head trauma
13. A learning disability
14. Serious medical health problems
15. A complicated or premature birth before 33 weeks gestation (due to the possibility of abnormal neurodevelopment).

Additional exclusion criteria for MDD

1. Children's Depression Rating Scale-Revised (CDRS-R) T-score less than 55.
2. A primary psychiatric diagnosis other than MDD.

Additional exclusion criteria for HCL:

1. Any current or lifetime DSM-IV-TR Axis I psychiatric disorders as determined by the Diagnostic Interview Schedule for Children (DISC) and Diagnostic Predictive Scale (DPS) instruments.
2. A family history of mood or psychotic disorders in first- or second-degree relatives as determined by the FIGS.
3. CDRS-R T-score greater than 54.

Description of the task

The task consists of two phases encoding and recall. The encoding phase required participants to view 32 adult actors depicting four sad, happy, fear, and neutral (8

instances each). The pairings of actor with face-emotion were randomized across participants; thus, participants saw the same set of 32 actors but each actor displayed a different emotion for each participant. All together, the encoding phase constituted a 160 trial run that lasted 14min 20sec. The 160 trials were divided into four 40-trial epochs that were further subdivided into four blocks, one for each of the four instructional sets: 1) the sadness level of the face ("How sad is the face?"); 2) the participant's emotional reaction to the face ("How sad does the face make you feel?"); 3) the size of a non-emotional facial feature ("How wide is the nose?"); 4) passive viewing of the face. With the exception of the passive viewing condition, subjects made ratings according to each instruction based on a 4-point scale. Each instruction block consisted of 10 pseudo-randomly presented trials: eight of which were faces plus two fixation events. Instructions lasted 3000ms and were presented prior to each block. Each face image was presented for 4000ms, during which participants made their responses. Each event (face or fixation) was followed by a variable inter-trial interval of 750 – 1250ms. The same image of each actor was presented to each participant for each of the four viewings. Figure 1 illustrates the task. The recall phase took the form of an unannounced memory test that occurred outside the scanner at the end of the scanning session. The image set used in the test consisted of 24 previously seen actors and 24 novel actors, each depicting a neutral expression, which participants rated as old or new.

Computation of effect sizes

Effect sizes for age, WASI, BDI-II, CDRS-R and MASC were determined using Hedge's g (Hedges and Olkin, 1985). Effect sizes for Tanner stage, CGAS, and HSP were computed using the probability of superiority (PS; range 0 – 1) (Erceg-Hurn and Mirosevich, 2008). PS represents the probability that a randomly selected MDD participant reported a greater value on the corresponding measure than a randomly selected control. Confidence intervals for the PS were computed using a bootstrap method (Ruscio and Mullen, 2012).

Behavioral analyses

To calculate d', four initial measures were computed: hits (correctly recognizing a previously seen actor), false alarms (incorrectly identifying a novel actor as previously seen), misses (failure to recognize a previously seen actor), and correct rejections (correctly identifying a novel actor as novel). Thereafter, d' was calculated as the difference between the signal and the signal + noise distributions (i.e., d' = z (hits) - z (false alarms)). This approach is consistent with prior studies involving similar versions of this task that showed that participants were better at reporting novel individuals as novel whereas the faces of actors previously seen depicting an emotion but now portraying a neutral expression were more difficult to recognize (Nelson et al., 2003;

Pine et al., 2004; Roberson-Nay et al., 2006). Total d' scores and those for each face-emotion type were calculated for each subject.

Censoring of Volumes with Excessive Motion and Outliers

We censored outlier volumes and those volumes with excessive motion from the multiple linear regression analysis. Each volume where the Euclidean norm of the six motion estimates (three rotational and three translational components) was greater than 0.3 was censored from the analysis. Similarly, outlier volumes where more than 10% of voxels were greater than the median absolute deviation of the detrended time-series were also censored from the analysis.

Functional Connectivity Analysis

Functional connectivity was assessed using the method of psychophysical interaction (PPI) modeling (Friston et al., 1997) implemented in AFNI (http://afni.nimh.nih.gov/sscc/gangc/CD-CorrAna.html). Analysis was performed for the left claustrum/anterior insula seed identified by the happy-sad contrast. Using methods identical to those for the task-based analysis, the EPI time-series were slice-time and motion corrected, aligned to the T1 images, smoothed with a 4.2 FWHM Gaussian kernel, grand-mean scaled, transformed to MNI152 space at 3×3×3mm resolution, and subject to bandpass filtering ($0.009 < f < 0.08$). The average EPI time-series within the AIC ROI was extracted and then detrended with a 1^{st} order Legendre polynomial, thereafter the hemodynamic delay was removed (Friston et al., 1997), before being multiplied by the condition regressor (i.e., for the happy-sad contrast, happy was coded as 1 and sad as -1). The resultant time-series was then convolved with a γ-variate function modeling a prototypical hemodynamic response function (Boynton et al., 1996), yielding an interaction regressor. Subsequently, multiple linear regression, that accounted for the serial correlation in the noise structure using an ARMA(1, 1) model, was performed where the task-derived time-series of interest, motion regressors, seed time-series, and interaction regressor where included in the model. The same outlier and motion-contaminated volumes that were excluded from the task-based analysis were also censored from the PPI analysis. The voxel-wise coefficients of determination (R^2) for the interaction regressor were extracted and converted to a correlation coefficients (R) that were then converted to z-scores using Fisher's r-to-z transform, yielding variates that were approximately normally distributed.

Between-group analyses on the resultant z-score maps was accomplished using linear mixed effects models implemented in R (R Development Core Team, 2012) where participant was treated as a random effect. Significant voxels were required to pass a voxel-wise statistical threshold ($F_{(1, 65)} = 3.99$, $p<0.05$ uncorrected) and to correct for multiple comparisons were required to be part of a cluster of no fewer than 62 voxels (1669 μL). As with the task-based analysis, the volume threshold was determined using

a Monte-Carlo simulation (10,000 iterations) that in combination with the voxel-wise threshold resulted a 5% probability of a cluster surviving due to chance (i.e., $p<0.05$).

Processing of fearful faces in adolescent depression

Our task included fearful faces in addition to sad, happy and neutral faces; however, we chose to focus only on the happy-sad continuum in our main analyses due to its specific relevance for major depressive disorder (Arce et al., 2009; Joormann and Gotlib, 2006; Schepman et al., 2012). Here, we report all results from the fMRI task analysis involving the fearful face condition using the methods described in the main manuscript (see Table S1). We replicate the results of differential amygdalar activation to fearful versus neutral faces (see Figure S1) that has been previously reported in the literature (Guyer et al., 2008; Ho et al., 2014; Tao et al., 2012; Yang et al., 2010). For reviews on fMRI studies in adolescent depression during face processing tasks more generally (see Hulvershorn et al., 2011; Kerestes et al., 2010).

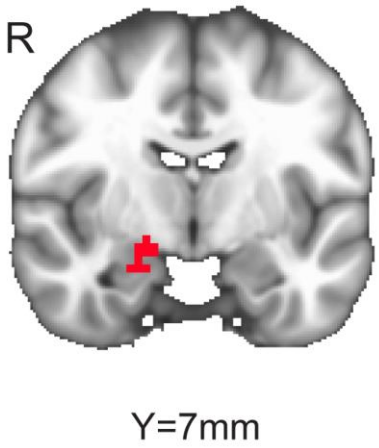

Figure S1. Differential right amygdala/parahippocampal activation elicited by the fearful-neutral contrast.

Table S1: Description of brain regions showing significant differences between depressed adolescents and healthy controls in the various face-emotion contrasts.

			Center of mass			Average	Average Contrast	
Structure	**Hemisphere**	**Volume (μL)**	**X**	**Y**	**Z**	**F value [a]**	**MDD [b]**	**NCL [b]**
Fearful-Happy								
Thalamus	R	10,368	-8	11	-7	6.51	-5.39	6.75
Middle Temporal Gyrus	L	2,835	53	38	-7	6.86	5.5	-9.47
Cuneus	R	1,809	-4	73	2	5.77	4.39	-7.56
Fearful-Neutral								
Medial Frontal Gyrus	R	3,375	-17	4	55	6.23	-4.96	2.05
Amygdala/Parahippocampal Gyrus	R	2,295	-20	11	-13	6.35	-9.4	3.81
Fearful-Sad								
Lingual Gyrus	R	4,050	-15	86	-14	6.06	-1.94	17.42
Cingulate Gyrus	L	2,565	3	53	26	5.9	-10.63	2.78
Medial Frontal Gyrus	L	2,214	0	-52	-12	6.38	-15.68	3.36
Culmen	R	2,106	-6	32	-14	6.12	-7.65	4.83
Superior Frontal Gyrus	R	1,971	-32	-56	-2	5.72	10.58	-4.44
Happy-Neutral								
Cuneus	L	2,700	20	97	-5	6.23	-5.13	10.18
Lingual Gyrus	R	2,322	-22	93	-7	6.11	-7.55	13.56
Inferior Frontal Gyrus	L	1,836	31	-34	18	5.46	-5.58	1.08
Superior Frontal Gyrus	L	1,674	18	-63	4	6.4	-6.82	5.83
Happy-Sad								
Lingual Gyrus	R	5,886	-15	86	-20	6.08	-11.14	21.14

Fusiform Gyrus	L	3,402	33	82	-21	5.95	-16.29	7.89
Fusiform Gyrus	L	2,538	47	54	-19	6.91	-15.85	9.34
Claustrum/Anterior Insular Cortex	L	2,322	31	-7	0	6	2.48	-5.22
Thalamus	R	2,079	-11	14	0	5.59	3.93	-6.08
Declive	R	1,917	-44	53	-26	6.47	-11.54	6.14
Neutral-Sad								
Culmen	R	2,160	-8	34	-18	6.45	-5.65	6.93
Superior Frontal Gyrus	L	2,106	30	-48	27	6.12	6.05	-1.28
Middle Frontal Gyrus	L	1,701	37	-20	23	6.74	5.96	-2.6

[a] $F_{(1, 65)}$

[b] Mean contrast value within the cluster

Table S2: Follow-up tests examining the source of differences within regions identified by the between-group task-related analysis.

Region	Variable	Statistic	p value	Significance	Direction of Difference
Fearful vs. Happy					
R Thalamus	MDD	t(59.48)=-2.04	0.046	*	Fearful < Happy
L Middle Temporal Gyrus	NCL	t(64.76)=-3.32	0.001	**	Fearful < Happy
R Thalamus	NCL	t(69.83)=2.93	0.005	**	Fearful > Happy
L Middle Temporal Gyrus	Happy	t(51.60)=-2.72	0.009	**	MDD < NCL
R Thalamus	Happy	t(60.25)=3.10	0.003	**	MDD > NCL
Fearful vs. Neutral					
R Medial Frontal Gyrus	MDD	t(58.61)=-3.08	0.003	**	Fearful < Neutral
R Parahippocampal Gyrus	MDD	t(59.17)=-2.52	0.015	*	Fearful < Neutral
R Medial Frontal Gyrus	Neutral	t(64.77)=2.72	0.008	**	MDD > NCL
R Parahippocampal Gyrus	Fearful	t(62.74)=-2.18	0.033	*	MDD < NCL
Fearful vs. Sad					
R Superior Frontal Gyrus	MDD	t(59.75)=2.60	0.012	*	Fearful > Sad
L Cingulate Gyrus	MDD	t(59.95)=-2.53	0.014	*	Fearful < Sad
L Medial Frontal Gyrus	MDD	t(59.97)=-3.07	0.003	**	Fearful < Sad
R Culmen	MDD	t(59.95)=-2.59	0.012	*	Fearful < Sad
R Lingual Gyrus	NCL	t(69.30)=2.85	0.006	**	Fearful > Sad
L Cingulate Gyrus	Sad	t(64.92)=2.02	0.047	*	MDD > NCL
L Medial Frontal Gyrus	Sad	t(63.42)=2.07	0.043	*	MDD > NCL
R Culmen	Sad	t(64.89)=2.87	0.006	**	MDD > NCL
R Superior Frontal Gyrus	Fearful	t(62.16)=2.49	0.016	*	MDD > NCL
Happy vs. Neutral					
L Inferior Frontal Gyrus	MDD	t(59.15)=-3.01	0.004	**	Happy < Neutral

L Superior Frontal Gyrus	MDD	t(58.15)=-2.25	0.028	*	Happy < Neutral
L Cuneus	NCL	t(68.36)=2.02	0.047	*	Happy > Neutral
R Lingual Gyrus	NCL	t(69.98)=2.15	0.035	*	Happy > Neutral
R Lingual Gyrus	Happy	t(64.37)=-3.28	0.002	**	MDD < NCL
L Cuneus	Happy	t(64.37)=-2.05	0.044	*	MDD < NCL
L Superior Frontal Gyrus	Neutral	t(64.31)=2.25	0.028	*	MDD > NCL
Happy vs. Sad					
L Fusiform Gyrus	MDD	t(59.99)=-2.49	0.016	*	Happy < Sad
L Claustrum	NCL	t(69.67)=-2.90	0.005	**	Happy < Sad
R Thalamus	NCL	t(69.86)=-2.57	0.012	*	Happy < Sad
R Declive	MDD	t(53.48)=-2.15	0.036	*	Happy < Sad
L Fusiform Gyrus	MDD	t(54.94)=-2.77	0.008	**	Happy < Sad
R Lingual Gyrus	NCL	t(66.00)=2.68	0.009	**	Happy > Sad
R Lingual Gyrus	Happy	t(63.98)=-2.81	0.007	**	MDD < NCL
L Fusiform Gyrus	Happy	t(64.05)=-2.22	0.03	*	MDD < NCL
L Fusiform Gyrus	Happy	t(64.67)=-2.37	0.021	*	MDD < NCL
L Claustrum	Sad	t(54.36)=-2.15	0.036	*	MDD < NCL
R Declive	Happy	t(65.00)=-3.53	0.001	***	MDD < NCL
R Thalamus	Happy	t(58.62)=3.05	0.003	**	MDD > NCL
Neutral vs. Sad					
R Culmen	MDD	t(59.89)=-2.14	0.036	*	Neutral < Sad
R Culmen	NCL	t(70.00)=2.40	0.019	*	Neutral > Sad
L Superior Frontal Gyrus	MDD	t(58.53)=2.19	0.032	*	Neutral > Sad
L Middle Frontal Gyrus	MDD	t(57.63)=2.22	0.03	*	Neutral > Sad
L Middle Frontal Gyrus	Sad	t(63.50)=-2.31	0.024	*	MDD < NCL
R Culmen	Sad	t(65.00)=3.88	<0.001	***	MDD > NCL

* p<0.05, ** p<0.01, *** p<0.001

References

Arce, E., Simmons, A.N., Stein, M.B., Winkielman, P., Hitchcock, C., Paulus, M.P., 2009. Association between individual differences in self-reported emotional resilience and the affective perception of neutral faces. J Affect Disord 114, 286–293. doi:10.1016/j.jad.2008.08.015

Beck, A.T., Steer, R.A., Brown, G.K., 1996. Beck Depression Inventory-Second Edition Manual. The Psychological Corporation, San Antonio, Texas.

Boynton, G.M., Engel, S.A., Glover, G.H., Heeger, D.J., 1996. Linear systems analysis of functional magnetic resonance imaging in human V1. J Neurosci 16, 4207–4221.

Brown, S.A., Myers, M.G., Lippke, L., Stewart, D.G., Vik, P.W., 1998. Psychometric evaluation of the customary drinking and drug use record (CDDR): A measure of adolescent alcohol and drug involvement. J Stud Alcohol 59, 427–438.

Erceg-Hurn, D.M., Mirosevich, V.M., 2008. Modern robust statistical methods: an easy way to maximize the accuracy and power of your research. Am Psychol 63, 591–601. doi:10.1037/0003-066X.63.7.591

Friston, K.J., Buechel, C., Fink, G.R., Morris, J., Rolls, E., Dolan, R.J., 1997. Psychophysiological and modulatory interactions in neuroimaging. NeuroImage 6, 218–229. doi:10.1006/nimg.1997.0291

Guyer, A.E., Monk, C.S., McClure-Tone, E.B., Nelson, E.E., Roberson-Nay, R., Adler, A.D., Fromm, S.J., Leibenluft, E., Pine, D.S., Ernst, M., 2008. A developmental examination of amygdala response to facial expressions. J Cognitive Neurosci 20, 1565–1582. doi:10.1162/jocn.2008.20114

Hedges, L.V., Olkin, I., 1985. Statistical Methods for Meta-Analysis. Academic Press, New York.

Hetherington, R., 1954. The Snellen chart as a test of visual acuity. Psychol Forsch 24, 349–357.

Ho, T.C., Connolly, C.G., Blom, E.H., LeWinn, K.Z., Strigo, I.A., Paulus, M.P., Frank, G., Max, J.E., Wu, J., Chan, M., Tapert, S.F., Simmons, A.N., Yang, T.T., 2014. Emotion-dependent functional connectivity of the default mode network in adolescent depression. Biol Psychiatry. doi:10.1016/j.biopsych.2014.09.002

Hollingshead, A. de B., 1957. *Two factor index of social position*. New Haven, CT.

Hulvershorn, L.A., Cullen, K., Anand, A., 2011. Toward dysfunctional connectivity: a review of neuroimaging findings in pediatric major depressive disorder. Brain Imaging Behav 5, 307–328. doi:10.1007/s11682-011-9134-3

Ishihara, S., 1917. Tests for colour-blindness. Hongo Harukicho, Handaya, Tokyo.

Joormann, J., Gotlib, I.H., 2006. Is this happiness I see? Biases in the identification of emotional facial expressions in depression and social phobia. J Abnorm Psychol 115, 705–714. doi:10.1037/0021-843X.115.4.705

Kaufman, J., Birmaher, B., Brent, D.A., Ryan, N.D., Rao, U., 2000. K-SADS-PL. Journal of the American Academy of Child and Adolescent Psychiatry 39, 1208. doi:10.1097/00004583-200010000-00002

Kerestes, R., Davey, C.G., Stephanou, K., Whittle, S., Harrison, B.J., 2010. Functional brain imaging studies of youth depression: A systematic review. NeuroImage: Clinical 4, 209–231. doi:10.1016/j.nicl.2013.11.009

Lucas, C.P., Zhang, H., Fisher, P.W., Shaffer, D., Regier, D.A., Narrow, W.E., Bourdon, K., Dulcan, M.K., Canino, G., Rubio-Stipec, M., Lahey, B.B., Friman, P., 2001. The DISC Predictive Scales (DPS): efficiently screening for diagnoses. Journal of the American Academy of Child and Adolescent Psychiatry 40, 443–449. doi:10.1097/00004583-200104000-00013

March, J.S., Parker, J.D., Sullivan, K., Stallings, P., Conners, C.K., 1997. The Multidimensional Anxiety Scale for Children (MASC): factor structure, reliability, and validity. Journal of the American Academy of Child and Adolescent Psychiatry 36, 554–565. doi:10.1097/00004583-199704000-00019

Maxwell, M.E., 1992. Family Interview for Genetic Studies (FIGS): A manual for FIGS. National Institute of Mental Health, Bethesda, MD.

Nelson, E.E., McClure, E.B., Monk, C.S., Zarahn, E., Leibenluft, E., Pine, D.S., Ernst, M., 2003. Developmental differences in neuronal engagement during implicit encoding of emotional faces: an event-related fMRI study. J Child Psychol & Psychiat 44, 1015–1024. doi:10.1111/1469-7610.00186

Pine, D.S., Lissek, S., Klein, R.G., Mannuzza, S., Moulton, J.L., Guardino, M., Woldehawariat, G., 2004. Face-memory and emotion: associations with major depression in children and adolescents. J Child Psychol Psychiatry 45, 1199–1208. doi:10.1111/j.1469-7610.2004.00311.x

Poznanski, E.O., 1996. Children's Depression Rating Scale-Revised (CDRS-R). Western Psychological Services, Los Angeles.

R Development Core Team, 2012. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria.

Roberson-Nay, R., McClure, E.B., Monk, C.S., Nelson, E.E., Guyer, A.E., Fromm, S.J., Charney, D.S., Leibenluft, E., Blair, J., Ernst, M., Pine, D.S., 2006. Increased amygdala activity during successful memory encoding in adolescent major depressive disorder: An FMRI study. Biol Psychiatry 60, 966–973. doi:10.1016/j.biopsych.2006.02.018

Ruscio, J., Mullen, T., 2012. Confidence Intervals for the Probability of Superiority Effect Size Measure and the Area Under a Receiver Operating Characteristic Curve. Multivariate Behavioral Research 47, 201–223. doi:10.1080/00273171.2012.658329

Schepman, K., Taylor, E., Collishaw, S., Fombonne, E., 2012. Face emotion processing in depressed children and adolescents with and without comorbid conduct disorder. J Abnorm Child Psych 40, 583–593. doi:10.1007/s10802-011-9587-2

Shaffer, D., Fisher, P., Lucas, C.P., Dulcan, M.K., 2000. NIMH Diagnostic Interview Schedule for Children Version IV (NIMH DISC-IV): description, differences from previous versions, and reliability of some common diagnoses. Journal of the American Academy of Child and Adolescent Psychiatry 39, 28–38. doi:10.1097/00004583-200001000-00014

Shaffer, D., Gould, M.S., Brasic, J., Ambrosini, P., Fisher, P., Bird, H., Aluwahlia, S., 1983. A Childrens Global Assessment Scale (Cgas). Arch Gen Psychiatry 40, 1228–1231.

Tanner, M.J., 1962. Growth and Adolescence. Blackwell Publishing Inc, Oxford.
Tao, R., Calley, C.S., Hart, J., Mayes, T.L., Nakonezny, P.A., Lu, H., Kennard, B.D., Tamminga, C.A., Emslie, G.J., 2012. Brain activity in adolescent major depressive disorder before and after fluoxetine treatment. Am J Psychiatry 169, 381–388. doi:10.1176/appi.ajp.2011.11040615
Wechsler, D., 1999. Wechsler Abbreviated Scale of Intelligence Administration and Scoring Manual. The Psychological Corporation, San Antonio.
Yang, T.T., Simmons, A.N., Matthews, S.C., Tapert, S.F., Frank, G.K., Max, J.E., Bischoff-Grethe, A., Lansing, A.E., Brown, G., Strigo, I.A., Wu, J., Paulus, M.P., 2010. Adolescents with major depression demonstrate increased amygdala activation. Journal of the American Academy of Child and Adolescent Psychiatry 49, 42–51. doi:10.1016/j.jaac.2009.09.004