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Differing Amygdala Responses to Facial Expressions in Children vs. Adults with Bipolar Disorder

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Abstract

Objective—Bipolar disorder (BD) is highly debilitating in both children and adults. Child and adult BD patients show both behavioral deficits in face emotion processing and abnormal amygdala activation. However, amygdala function in pediatric vs. adult BD patients has never been compared directly.

Method—This study compared amygdala responses to emotional facial expressions in 74 subjects [pediatric (N=18) and adult (N=17) patients with BD, healthy volunteer (HV) children (N=15) and adults (N=22)]. Subjects performed a gender identification task while viewing fearful, angry, and neutral faces.

Results—In response to fearful faces, patients with BD across age-groups showed right amygdala hyperactivity relative to healthy volunteers. However, when responses to all facial expressions were combined, pediatric patients exhibited greater right amygdala activation than either adults with BD or HV children.

Conclusions—Amygdala hyperactivity in response to fearful faces is present in both youths and adults with BD. However, compared to adults with BD or healthy youths, youths with BD show amygdala hyperactivity in response to a broad array of emotional faces. Thus, abnormal amygdala activation during face processing appears to be more pervasive in children than adults with BD.

INTRODUCTION

Both children and adults with bipolar disorder (BD) exhibit deficits in face emotion processing and abnormalities in amygdala structure and activity (1-3). However, no study has compared children and adults with BD in amygdala activity during face emotion processing. Such a comparative study could facilitate developmentally-sensitive diagnosis and treatment (4, 5). In this cross-sectional fMRI study, our goal was to begin to fill this research gap.

Studies report behavioral deficits in explicit emotion processing (i.e. face emotion labeling) in children with BD (6, 7), unaffected children at risk for BD (8), and adults with BD (1, 9). Neural abnormalities during explicit emotion processing have been observed in children and adults with BD (10). However, the most consistent evidence of neural abnormalities in emotion processing in children and adults with BD is amygdala hyperactivity during implicit

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emotion processing. During such implicit tasks, emotional features are reflected in aspects of a stimulus, such as the display of emotion in a face, but task instructions focus on non-emotional features of the face, such as the gender of the person depicting the emotion. With this type of implicit task, amygdala hyperactivity has been found in children with BD in response to fearful, angry, or happy faces (3, 11), and in adults with BD in response to fearful, happy, and sad faces (12, 13). In the current study, we used a gender identification paradigm that involves implicit face emotion processing to test for abnormal amygdala activation in child and adult patients with BD.

Evidence suggests that the course of BD may be more severe in children than in adults (5, 14) and that younger patients may have greater impairment in face emotion perception than older patients (1). This, in turn, suggests that the neural circuitry mediating emotion information processing may be more impaired in youth than adults with BD. Indeed, recent meta-analyses report that decreased amygdala volume is found more consistently in youth than adults with BD (15, 16). However, these meta-analyses are based on comparing studies that include either youth or adults alone; studies are needed that include both groups in the same analysis. Similarly, amygdala function in BD has not been studied by applying identical methods to adults and children. Such a study begins the process of identifying developmental trajectories of amygdala function in BD to be pursued in future longitudinal work.

The current cross-sectional study compared amygdala activity in children and adults with BD and healthy subjects during implicit processing of angry, fearful and neutral facial expressions. We included only three facial expressions to ensure an adequate number of presentations of each stimulus type, thus maximizing statistical power while keeping the task brief enough to be tolerable for children with BD. Fearful expressions were selected because these elicit amygdala hyperactivity consistently in both children and adults with BD (3, 12). Angry and neutral expressions were included as a comparison negative emotion and a control stimulus, respectively. To compare neural activity in children and adults with BD and age-matched controls, we conducted an amygdala region-of-interest (ROI) analysis and a whole-brain analysis.

METHODS

Participants

The 72 participants included pediatric BD patients (n=18; age range 9-18), adult BD patients (n=17; age range 20-58), HV children (n=15; age range 12-17) and HV adults (n=20-56). Participants enrolled in an Institutional Review Board-approved protocol at the National Institute of Mental Health. Adult participants gave written informed consent. Parents and pediatric participants provided written informed consent and assent, respectively. BD children (ages 7-18) and adults (ages 19-60) were recruited through advertisements placed on support groups' websites and distributed to psychiatrists nationwide. HV children and adults were recruited by advertisement. No participants were biologically related.

Pediatric patients were assessed with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) (17), administered separately to children and parents by clinicians with established inter-rater reliability ($\kappa = 0.9$). To evaluate mood state in children with BD, clinicians administered the Children's Depression Rating Scale (CDRS) (18) and the Young Mania Rating Scale (YMRS) (19) within 48 hours of scanning. Pediatric patients met criteria for "narrow phenotype" BD (20), with at least one full-duration (hypo)manic episode characterized by abnormally elevated mood and at least three DSM-IV-TR "B" mania symptoms. Adult patients were assessed with the Structured Clinical Interview for DSM-IV-TR Axis I

Disorders-Patient Edition (SCID-I/P) (21) or the Diagnostic Interview for Genetic Studies (DIGS) (22) by clinicians with established inter-rater reliability ($\kappa = 0.85$). Structural Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders Version (SIGH-SAD) (23) and YMRS (19) were used to evaluate mood state in adult patients.

HV participants were medication-free and had no lifetime psychiatric diagnoses and no first-degree relatives with a mood disorder. HV participants were assessed using the same diagnostic interviews as patients.

Participants had IQ >70 (determined by the Wechsler Abbreviated Scale of Intelligence (24)) with no history of neurological disorder, pervasive developmental disorder, chronic medical illness, or substance abuse/dependence in the past three months. After scanning, 28 of the 100 scanned participants were excluded due to scanner malfunction (N=19), excessive movement (N=1), poor image alignment (N=1) or behavioral accuracy below 65% (N=7).

Behavioral paradigm

The paradigm has been used previously (25, 26). Participants viewed grey-scale images of fearful, angry, and neutral expressions from 10 men and 10 women from the Pictures of Facial Affect series (27). For fearful and angry faces, in addition to standard (100%) expressions, lower (50%) and higher (150%) expressions were created by morphing with that person's neutral expression picture. This was done to enhance ecological validity, since participants normally encounter different face expression intensity levels (25). To create neutral faces, neutral and happy faces were morphed to obtain 25% happy, since studies suggest that children (28) and adults (29) perceive such expressions as neutral.

Using a two-button box, participants indicated whether the face was male or female. Faces were presented for 2500ms followed by a 500ms fixation cross. Each of the 4 runs included 80 face trials (20 neutral and 10 of each intensity of fearful and angry) and 25 fixation trials. Trial order was randomized within each run.

Image acquisition

Scanning was in a General Electric 1.5 Tesla magnet scanner (Milwaukee, WI). Functional data were acquired using multi-slice gradient echo-planar sequence (31 axial slices, 4mm thick, voxels = $3.75 \times 3.75 \times 4$ mm, TR = 3000 ms, TE = 30ms, flip angle = 90, field of view = 240mm, matrix size 64×64). Anatomical T1-weighted three-dimensional spoiled-gradient-recalled acquisition in the steady state (GRASS) images with inversion recovery prep pulse (128 axial slices, 1.5mm thick, TR = 8.1 ms, TE = 3.2 ms, flip angle = 20, field of view = 240mm, matrix size 256×256) were acquired to be coplanar with the functional scans for spatial registration.

Data Analysis

Behavioral data—A three-way repeated-measure analysis of covariance (ANCOVA) with age-group (child, adult) and diagnosis (BD, HV) as between-subject factors and emotion (fearful, angry, neutral) as a within-subject factor compared accuracy and reaction time (RT) using SPSS (SPSS, Inc., Chicago, Ill). Since there was a trend difference in IQ between groups, IQ was included as a covariate. Post-hoc ANCOVAs were performed using SPSS.

fMRI data

Data Preprocessing: Functional imaging data were preprocessed and analyzed using AFNI (Analysis of Functional NeuroImages) (30). The first four images of each run were discarded to account for magnetic equilibrium. After slice time correction, images within

each run were realigned to the fifth image to correct for movement. Images with motion greater than 2mm in any direction were censored. If more than 5% of the total images were censored, a participant was excluded. After motion correction, realigned functional images were coregistered to anatomical images, and functional images were anatomically normalized to Talairach space. Images were spatially smoothed with 6 mm root-mean-square (RMS) deviation Gaussian blur.

At the individual subject level, general linear models (GLMs) estimated the shape of the hemodynamic response for each event type. To account for baseline drift and residual motion artifact, regressors included six motion parameters obtained during coregistration and a third-order baseline drift function. Regressors were created for each event type i.e., fearful, angry and neutral expressions. Regressors of fearful and angry expressions were weighted according to emotional intensity (1 for 50%, 2 for 100%, and 3 for 150%). Trials with wrong answers were analyzed separately, by including a regressor that accounted for incorrect behavioral responses. All regressors were convolved with a gamma-variate hemodynamic response function. Beta coefficients from the individual subject level were oriented to the standard space of Talairach and Tournoux, then re-sampled to resolution of 3 mm³.

Region of interest (ROI) analysis: Anatomic masks of right and left amygdala were created based on the Talairach-Tournoux Daemon. The masks were re-sampled to match their resolution to the fMRI images. BOLD signal change from each event type vs. fixation was averaged across all amygdala voxels and entered in SPSS for the group-level analysis. An omnibus three-way repeated-measure ANCOVA with age-group (child, adult) and diagnosis (BD, HV) as between-subject factors and emotion (fearful, angry, neutral) as a within-subject factor was performed in right and left amygdala. Since RT differed between groups, it was included as a covariate in addition to IQ. Post-hoc univariate ANCOVAs were performed to identify differences between groups in SPSS.

Whole-brain analysis: A group-level linear mixed-effects (LME) model was conducted with 3dLME in AFNI to examine between-group differences in response to the face emotions. The model included age-group (child, adult) and diagnosis (BD, HV) as between-subject factors and emotion (fearful, angry, neutral) as a within-subject factor, with IQ and RT as covariates. Using the 3dClustSim program in AFNI (http://afni.nimh.nih.gov/pub/dist/doc/program_help/3dClustSim.html), Monte Carlo simulation (10000 iterations, 54 64 50 dimensions, 3 3 3 voxels, 9 9 8 mm smoothness) indicated that an initial, voxel-wise threshold of $p < 0.001$ and a minimum cluster size of 22 voxels gave a corrected p value of 0.05. Post-hoc univariate ANCOVAs were performed to identify differences between groups and conditions in SPSS. Post-hoc analyses on effects of mood state, medication, comorbid illnesses, and BD subtype

We conducted post-hoc exploratory univariate ANCOVAs in SPSS to test potentially confounding effects of mood state, medication, comorbid illnesses, and BD subtype on the ROI results (see Supplementary Materials). Because these exploratory analyses included relatively small subsets of BD patients, we report significant results as well as those at a trend level, $p < .10$.

RESULTS

Demographic and clinical characteristics

Within each age group, patients and controls did not differ in age ($p > .10$) (Table 1). Between groups, participants did not differ in gender ($p = .54$). There was a trend toward

higher IQ among adults relative to children ($p=.07$), so IQ was included as a covariate in all analyses.

Compared to adult patients, child patients were more likely to have an earlier age of BD onset ($p<.001$), be euthymic ($p=.05$), and have higher YMRS scores ($p=.001$). Child patients also had higher rates of attention deficit hyperactivity disorder (ADHD) ($p=.003$), stimulant treatment ($p=.02$), and, at trend level, oppositional defiant disorder (ODD) ($p=.08$) (Table 1). Child patients also tended to be more likely than adult patients to be unmedicated ($p=.08$). Adult patients were more likely to be depressed ($p=.02$) and to be receiving antiepileptic medication ($p=.02$).

Behavioral data

For accuracy, no three-way or two-way interactions were found. The only main effect was that of age-group ($F=23.98$, $df=1,67$, $p<.001$), indicating children were less accurate than adults. Since only correct trials were included in the fMRI analysis, this was accounted for in the analysis of fMRI data.

For RT, no three-way or two-way interactions were found. There were main effects of diagnosis (BD slower than HV; $F=5.64$, $df=1,67$, $p=.02$) and age-group (children slower than adults; $F=13.63$, $df=1,67$, $p<.001$). Because of these between-group differences, RT was included as a covariate in the fMRI analyses.

fMRI data

ROI analysis—In the right amygdala (Figure 1A), the age-group X diagnosis X emotion interaction was not significant, but both two-way interactions were: age-group X diagnosis ($F=4.30$, $df=1,64$, $p=.04$) and diagnosis X emotion ($F=4.52$, $df=2,128$, $p=.01$).

A post-hoc ANCOVA of the age-group X diagnosis interaction revealed that, across expressions, BD children exhibited greater amygdala activation than both BD adults ($F=5.66$, $df=1,29$, $p=.02$) and HV children ($F=8.99$, $df=1,27$, $p=.006$) whereas BD adults and HV adults did not differ (Figure 1B).

A post-hoc ANCOVA of the emotion X diagnosis interaction showed that patients had greater amygdala responses to fearful expressions than HV's ($F=12.49$, $df=1,68$, $p<.001$; Figure 1C). Amygdala activity did not differ between patients and healthy subjects for angry or neutral expressions.

In the left amygdala, no interactions were significant. A main effect of age indicated that amygdala activation was greater among children than adults ($F=7.75$, $df=1,64$, $p=.007$).

Whole-brain analysis—Age-group X diagnosis X emotion interaction was found in left posterior cingulate cortex (PCC) [$F=12.34$, $df=2,128$; $x,y,z = -7, -28, 38$; 38 voxels], $p<.05$ (corrected). In left PCC, age-group X diagnosis interaction was observed only for angry expressions ($F=4.61$, $df=1,68$, $p=.04$). Specifically, BD children showed less activity to angry expressions than HV children ($F=5.81$, $df=1,31$, $p=.02$).

Effects of mood state, medication, comorbid illnesses, and BD subtype

Post-hoc analyses examined whether the age-group X diagnosis interaction in the right amygdala could be driven by differences between child and adult patients in mood state, medication, comorbid illnesses or BD subtype (see Supplementary Materials). The difference in the right amygdala between child and adult patients was either significant or a trend after controlling for most clinical differences, $p's < .07$ (Table s1). The exceptions

were antiepileptic medication and comorbid ODD, whose confounding effects could not be ruled out.

Data indicate that, relative to HVs, patients with anxiety disorders have amygdala hyperactivity to fearful faces (31). Therefore, we tested whether amygdala hyperactivity in response to fearful faces in BD patients vs. controls could be due to comorbid anxiety disorders. BD patients without comorbid anxiety disorders showed greater amygdala activity ($p=.003$) in response to fearful expressions than HV's (Table s1).

DISCUSSION

We compared amygdala activity in children and adults with BD and age-matched healthy participants while they performed an implicit face emotion processing task that included fearful, angry, and neutral faces. Compared to healthy subjects, both children and adults with BD exhibit amygdala hyperactivity in response to fearful expressions. However, compared to adults with BD, children with the illness exhibit amygdala abnormalities in response to a greater array of face expressions. The results of this cross-sectional study suggest potential developmental differences in amygdala activity in BD patients. Longitudinal studies are needed to test the hypothesis that amygdala abnormalities persists in response to fear, but not angry and neutral expressions, as children with BD age.

In response to fearful faces, both children and adults with BD had increased right amygdala activity relative to their similarly-aged healthy volunteer group. This is consistent with previous studies that included only children or adults (3, 10, 12). However, in the current study, when amygdala response was considered across all emotions, including angry and neutral as well as fearful, pediatric patients exhibited amygdala hyperactivity relative to both adults with BD and healthy children. Observation of amygdala hyperactivity across expressions in pediatric BD suggests a more general form of face-emotion dysfunction in pediatric than in adult BD. Such an observation is consistent other data, including behavioral results; a recent meta-analysis suggests that explicit face emotion processing deficits (i.e., deficits in face emotion labeling across expressions) are observed more consistently in youth than adults with BD (1). However, it is important to note that abnormalities in implicit and explicit emotion processing may not necessarily be linked (32). Thus, more fMRI studies are needed to understand the relevance of implicit processing deficits to behavioral explicit processing deficits, as well as to examine brain activity during explicit emotion processing in both pediatric and adult BD patients.

Greater cumulative lifetime medication exposure in adult vs. pediatric patients may explain the amygdala activity differences between the two patient groups. In our study, the two groups did not differ on current rates of antidepressant and antipsychotic use. Nonetheless, cross-sectional research suggests that such medications may normalize amygdala activity in adults with BD (33). Although this has not yet been tested, it is likely that cumulative exposure to medication may affect amygdala activity. In addition, the developmental differences in amygdala activity that we observed may be associated with differences in clinical course between adults and youths with BD. Although few studies have compared clinical course between the two groups directly, evidence suggests that pediatric patients with BD may be more likely than adult patients to experience rapid cycling and/or mixed states (14). These clinical features, along with early age of onset, tend to be associated with poor longitudinal outcomes (14, 34). In the current study, detailed information about mood cycling or global functioning is not available to test the hypothesis that amygdala hyperactivity across emotions may be linked with worse clinical outcome among pediatric vs. adult BD patients; however, it is an important question for future research.

The whole-brain analysis revealed that neural activity differences between pediatric and adult BD patients, and between patients with BD and healthy participants, were not limited to the amygdala. Replicating a previously reported finding, children with BD exhibited less activation than healthy subjects to angry expressions in left PCC (11). The PCC has been suggested to be involved in top-down control of attention (35) as well as in integrating information about emotional expressions, particularly anger (36). Thus, the abnormal PCC activity in pediatric BD may be associated with impaired attentional and information processing for angry expressions.

Limitations of the study include its cross-sectional design; only longitudinal data can support firm conclusions about associations between development and brain activation in BD. First, we cannot disambiguate two relevant hypotheses: 1) abnormal amygdala activity in children with BD becomes specific to fearful expressions as they age, vs. 2) throughout a patient's life, pediatric-onset BD is associated with more severe amygdala abnormalities than is adult-onset BD. While children and adults with BD differed on some clinical characteristics, post-hoc exploratory analyses suggest that these variables largely do not account for the age-related differences we observed. Second, to ascertain whether differences in amygdala activity between patients and healthy volunteers represent dysfunction, as opposed to compensatory mechanisms in response to dysfunction in other brain regions, future studies should examine associations among neural activity during emotional information processing, behavior, and clinical characteristics. For example, if amygdala hyperactivity in patients reflects amygdala dysfunction, one would expect elevated amygdala activity to be associated with behavioral deficits and poor clinical course. In contrast, if such hyperactivation is compensatory to dysfunction in other brain regions, one might expect elevated amygdala activity to predict relatively intact behavior and a relatively benign clinical course. Such work to examine the compensatory process ideally would follow children prospectively after acquisition of imaging data. In addition, while we were unable here to identify aberrant activity in other brain regions to which the amygdala hyperactivation might be compensatory, future studies in larger samples, along with connectivity analyses, could be informative in that regard.

The current study provides the first evidence of age-related differences in amygdala activity in response to facial expressions among bipolar patients. Although BD patients across age-groups show amygdala hyperactivity in response to fearful faces, the abnormal amygdala activation is present in response to more emotions in child than adult BD patients. These findings provide support and guidance for future longitudinal work examining the developmental trajectory of amygdala function, from the asymptomatic risk state through the course of the illness. Knowledge about this trajectory could help in early detection of BD and the development of age-appropriate treatments.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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A.

B.

C.

Figure 1.

Findings of right amygdala ROI analysis

A. Right amygdala mask

B. Age-group X diagnosis interaction ($F=4.30$, $df=1,64$, $p=.04$). BOLD responses across expressions in right amygdala. The error bars represent the standard deviation of the mean % signal change BOLD response.

C. Emotion X diagnosis interaction ($F=4.52$, $df=2,128$, $p=.01$). BOLD responses to fearful, angry and neutral expressions across age groups in right amygdala. The error bars represent the standard deviation of the mean % signal change BOLD response.

Demographic and Clinical Characteristics of Children and Adults with Bipolar Disorder (BD) and Healthy Volunteer (HV) Children and Adults

Table 1

Characteristic	Pediatric BD (N=18)		Adult BD (N=17)		Pediatric HV (N=15)		Adult HV (N=22)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age	14.29	2.54	40.04	10.06	14.98	2.03	34.91	12.27
WASI Full-scale IQ ^a	107.83	13.83	114.53	12.71	108.27	15.35	118.05	15.51
YMRS ^b	6.83	3.73	3.77	4.55	--	--	--	--
CDRS ^c	26.53	7.41	--	--	--	--	--	--
SIGH-SAD	--	--	17.47	15.59	--	--	--	--
Age of onset ^d	9.77	3.49	20.85	8.59	--	--	--	--
Number of medications	2.83	1.89	3.00	1.06	--	--	--	--
<hr/>								
Male	N	%	N	%	N	%	N	%
Bipolar Type	10	55.6	5	29.4	5	33.3	9	40.9
Bipolar I	14	77.8	9	52.9	--	--	--	--
Bipolar II	4	22.2	8	47.1	--	--	--	--
Mood State ^e								
Euthymic ^f	15	83.3	9	52.9	--	--	--	--
Depressed ^g	2	11.1	8	47.1	--	--	--	--
Hypomanic	1	5.6	0	0	--	--	--	--
Manic	0	0	0	0	--	--	--	--
Mixed	0	0	0	0	--	--	--	--
Comorbid Conditions								
ADHD ^h	12	66.7	2	11.8	--	--	--	--
ODD ⁱ	3	16.7	0	0	--	--	--	--
Anxiety Disorder ^j	8	44.4	7	41.2	--	--	--	--
Medication								

Characteristic	Pediatric BD (N=18)		Adult BD (N=17)		Pediatric HV (N=15)		Adult HV (N=22)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Unmedicated ^k	3	16.7	0	0	15	100	22	100
Atypical Antipsychotic	11	61.1	8	47.1	--	--	--	--
Lithium	6	33.3	5	29.4	--	--	--	--
Antiepileptic ^l	9	50.0	15	88.2	--	--	--	--
Antidepressant	8	44.4	9	52.9	--	--	--	--
Stimulants ^m	5	27.8	0	0	--	--	--	--

YMRS = the Young Mania Rating Scale; CDRS = Children's Depression Rating Scale; SIGH-SAD = Seasonal Affective Disorders Version; HAM-D = the Hamilton Depression Rating Scale, ADHD = Attention deficit hyperactivity disorder; ODD = Oppositional defiant disorder

^aF=2.46, df=3,68, p=.07

^bt=3.70, df=33, p=.001

^cmissing from 1 pediatric BD patient

^dt=-4.93, df=31, p<.001; missing data from 1 pediatric and 1 adult BD patients

^eEuthymia was defined as: CDRS < 40 and YMRS 12 in children, YMRS 12, SIGH-SAD 20 in adults. Depression was defined as: CDRS > 40 and YMRS 12 in children; SIGH-SAD > 20 and YMRS 12 in adults; hypomania/mania as: CDRS 40 and YMRS > 12 in children; SIGH-SAD 20 and YMRS > 12 in adults; and mixed state as: SIGH-SAD > 20 and YMRS > 12.

^f $\chi^2=3.75$, df=1, p=.05

^g $\chi^2=5.54$, df=1, p=.02

^h $\chi^2=8.78$, df=1, p=.003; missing data from 3 adult BD patients

ⁱ $\chi^2=3.10$, df=1, p=.08

^jincludes generalized anxiety disorder, separation anxiety disorder, social phobia, panic disorder, post-traumatic stress disorder, and obsessive compulsive disorder

^k $\chi^2=3.10$, df=1, p=.08

^l $\chi^2=5.93$, df=1, p=.02

^m $\chi^2=5.51$, df=1, p=.02

Table 2

Behavioral performance of Children and Adults with Bipolar Disorder (BD) and Healthy Volunteer (HV)
Children and Adults

Condition	Pediatric BD (N=18)	Adult BD (N=17)	Pediatric HV (N=15)	Adult HV (N=22)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Percent Correct ^a				
Angry Expressions	86.05 ± 10.13	95.67 ± 3.33	90.92 ± 8.82	96.00 ± 3.20
Fear Expressions	86.07 ± 9.23	98.23 ± 1.87	91.49 ± 9.51	97.89 ± 2.57
Neutral Expressions	87.39 ± 11.50	98.27 ± 1.79	93.25 ± 7.45	98.26 ± 1.83
Reaction Time ^b				
Angry Expressions	933.94 ± 110.46	788.85 ± 127.67	843.52 ± 152.43	749.14 ± 86.91
Fear Expressions	932.26 ± 112.78	780.10 ± 127.18	830.77 ± 161.30	749.14 ± 87.31
Neutral Expressions	935.19 ± 119.55	760.77 ± 121.09	827.35 ± 154.40	739.73 ± 91.83

^a main effect of age-group ($F=23.98$, $df=1,67$, $p<.001$)

^b main effects of age-group ($F=13.63$, $df=1,67$, $p<.001$); main effects of diagnosis ($F=5.64$, $df=1,67$, $p=.02$)