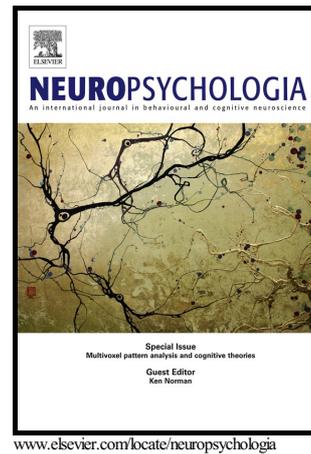


# Author's Accepted Manuscript

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Against Neural Risk for Psychological  
Vulnerability to Future Life Stress

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## Post-Secondary Maternal Education Buffers Against Neural Risk for Psychological Vulnerability to Future Life Stress

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### Abstract

We have previously reported that threat-related amygdala activity measured during a baseline fMRI scan predicts the experience of depression and anxiety associated with stressful life events years later. Here, we examine whether two broad measures of childhood environmental enrichment, namely parental educational achievement and subjective parental socioeconomic status, buffer against the effects of amygdala activity on future vulnerability to stress. Analyses of data available from 579 young adults revealed that maternal, but not paternal, educational achievement moderates the association between amygdala activity, recent life stress, and changes in mood and anxiety symptoms, even when controlling for participants' current subjective

socioeconomic status. Specifically, only participants reporting lower maternal educational achievement exhibited our previously observed interaction between amygdala activity and future life stress predicting increases in depression and anxiety. These results suggest that higher maternal educational achievement may help buffer stress sensitivity associated with heightened threat-related amygdala activity.

**Keywords:** fMRI; amygdala; socioeconomic status; depression; anxiety; stress

Accepted manuscript

## 1. Introduction

Recent research on moderators of brain-behavior associations underscores the importance of considering context in understanding how individual differences in brain function influence risk for developing psychopathology. One pattern of brain function that has emerged as an important predictor of risk for mood and anxiety problems is heightened threat-related amygdala activity (i.e., heightened amygdala activity in response to a threatening stimulus such as an angry or fearful face). Specifically, in adolescent (McLaughlin et al., 2014; Swartz, Hariri, & Williamson, 2017), young adult (Swartz, Knodt, Radtke, & Hariri, 2015), and adult samples (Admon et al., 2009), increased baseline threat-related amygdala activity has been found to predict the future emergence of mood and anxiety symptoms. However, participants' current context was found to be an important moderator of this brain-behavior association.

In all of these cases, relatively heightened threat-related amygdala activity only predicted the future emergence of mood or anxiety symptoms in stressful or negative environmental contexts, including having a first-degree relative with a history of depression, exposure to trauma, or relatively high levels of recent stressful life events. The possibility remains, however, that other environmental contexts may further moderate these brain-behavior associations. In particular, it is possible that the experience of positive or negative environments during early development may buffer or further exacerbate the risk for stress-related mood and anxiety symptoms associated with higher threat-related amygdala activity. One specific developmental context through which such modulatory effects may emerge is childhood socioeconomic status (SES).

Indeed, prior research indicates that lower childhood SES is a risk factor for the later development of mood and anxiety problems (Gilman, Kawachi, Fitzmaurice, & Buka, 2002;

Mossakowski, 2015; Park, Fuhrer, & Quesnel-Vallee, 2013; Sheikh, Abelsen, & Olsen, 2014, 2016). Childhood SES can be measured through several indicators including parents' education, income, and/or occupational level during the participant's childhood, and some research suggests that certain aspects of childhood SES may be stronger predictors of adult depression than others. For instance, in a large longitudinal survey, lower maternal education was found to be a significant predictor of the onset of major depression in young adulthood whereas paternal education was not a significant predictor (Park et al., 2013). In a different large survey, there was an association between lower maternal education and adult women's anxiety and depression symptoms (Sheikh et al., 2014), but childhood financial conditions (measured with the retrospective question: "How was your family's financial situation when you were a child?") were generally more predictive of adult mental health than parents' education (Sheikh et al., 2014, 2016).

Researchers have argued that from a theoretical and policy perspective, identifying the specific components of childhood SES that predict future outcomes is important in identifying mechanisms that can be targeted for intervention (Duncan & Magnuson, 2012). For example, although parental education and income levels are often highly correlated, effects of parental education may be more strongly mediated by the quality of parent-child interactions whereas effects of parent income levels may be more strongly mediated by material support and physical resources (Duncan & Magnuson, 2012; Noble et al., 2015). Indeed, in a nationally representative longitudinal study of young adults in the U.S., effects of lower parental education on young adults' depression symptoms were mediated by low self-esteem (and to a lesser extent, chronic poverty), whereas effects of lower parental occupational prestige were mediated by

chronic poverty, but not low self-esteem (Mossakowski, 2015), indicating that different aspects of parental SES may influence risk for depression through different mechanisms.

As reviewed by Johnson, Riis, and Noble (2016), prior research examining links between childhood SES, amygdala function, and mental health has primarily examined whether childhood SES influences amygdala activity, posing a mediational framework in which amygdala activity may mediate associations between childhood SES and later outcomes (e.g., Kim et al., 2013). In the current study, we considered childhood SES within a moderation framework, testing whether childhood SES influences risk for internalizing outcomes by moderating the association between higher threat-related amygdala activity and the later development of internalizing symptoms. Although both the direct effect of childhood SES on amygdala function and the moderating effect of childhood SES on the association between amygdala function and internalizing symptoms are likely important in the development of depression and anxiety, the latter process has been relatively under-examined to date. Moreover, prior neuroimaging research has generally not parsed contributions of maternal and paternal education from other measures of childhood SES. Thus, we sought to leverage data from a large multimodal study of young adult volunteers to examine a three-way interaction between threat-related amygdala activity, stress, and two different measures of childhood SES, namely parental educational achievement and subjective parental SES, in predicting the emergence of future depression and anxiety symptoms.

The current sample of 579 university students with longitudinal follow-up data, recruited as part of the Duke Neurogenetics Study, is an expansion of the original 340 participants that formed the basis of our earlier research linking baseline threat-related amygdala activity, life stress, and future internalizing symptoms (Swartz et al., 2015), including new data collected since 2015. Based on the collective findings summarized above, we hypothesized that relatively

heightened threat-related amygdala activity would predict the future emergence of mood and anxiety symptoms in the context of relatively high life stress, but that this association would be buffered for participants reporting higher maternal education levels and/or higher subjective parental SES. Finally, while some studies have shown that childhood SES predicts increased risk for depression controlling for adult SES (Gilman et al., 2002; Park et al., 2013), others have suggested that adult SES largely accounts for associations between childhood SES and adult depression (Harper et al., 2002). Therefore, we also examined whether any effects of parental SES were independent of the participants' current subjective SES.

## **2. Materials and Methods**

### *2.1 Participants*

Participants included 579 young adult university students who completed the Duke Neurogenetics Study (DNS) protocol and who also completed at least one follow-up interview to assess the future development of symptoms. All procedures were approved by the Duke University School of Medicine Institutional Review Board and participants provided informed consent before study initiation. Participants' ages ranged from 18 to 22 ( $M=19.6$ ,  $SD=1.2$ ) at baseline and 63% were female. Participants self-reported their race/ethnicity as follows: 50% Caucasian/Non-Hispanic; 26% Asian; 8% African American; 8% bi- or-multi-racial; 5% Hispanic/Latino, and 3% other. Exclusion criteria have been described in detail previously (Swartz et al., 2015); participants were excluded due to: 1) any medical diagnoses of cancer, stroke, diabetes, chronic kidney or liver disease, or lifetime history of psychotic symptoms; 2) use of psychotropic, glucocorticoid, or hypolipidemic medication; and 3) conditions affecting cerebral blood flow and metabolism (e.g, hypertension). Diagnosis of a DSM-IV Axis I or select

Axis II disorders (antisocial personality disorder and borderline personality disorder), based on the electronic M.I.N.I. Neuropsychiatric Interview (Sheehan et al., 1998) was not an exclusion criterion for the study. In the sample of 579 participants reported on here, 18% received a past or current psychiatric diagnosis. The most common diagnoses in the sample were major depression and substance use disorders. In all analyses, presence of a psychiatric diagnosis was entered as a covariate. We also re-ran all analyses excluding participants with a past or present internalizing diagnosis (major depression or an anxiety disorder) at baseline, similar to the procedures in our original study (Swartz et al., 2015) (see Supplementary Online Material).

## 2.2 *Amygdala activity*

Threat-related amygdala activity was measured with an emotional face-matching challenge paradigm that has been described in detail in previous research (Swartz et al., 2015). Details regarding fMRI data acquisition, pre-processing, quality control criteria, and the first-level model are provided in the Supplemental Online Material. As in our prior research (Swartz et al., 2015), for the current analysis we focused on the contrast of Angry and Fearful Faces > Shapes as a measure of threat-related amygdala activity. To obtain a measure of amygdala activity to submit to statistical analyses, first we identified functional clusters that were significantly activated at the group level for this condition (Angry and Fearful Faces > Shapes) at  $p < .05$ , family-wise error (FWE) corrected for the search regions of the left and right amygdala, defined with the Automated Anatomical Labeling Atlas. Next, mean contrast values were extracted from the left and right functional clusters and averaged to obtain a mean measure of threat-related amygdala activity in response to angry and fearful faces. When significant effects were observed for the whole amygdala, we conducted post hoc analyses to determine whether effects were driven by

the centromedial or basolateral amygdala subregions, defined based on cytoarchitectonic mapping (Amunts et al., 2005). Similar to procedures for the whole amygdala, when examining effects by amygdala subregion, we first identified clusters that were significantly activated at  $p < .05$  FWE-corrected within each subregion, extracted a mean contrast value from the left and right cluster, and then averaged these to obtain a mean measure of threat-related basolateral and centromedial amygdala activity.

### 2.3 Childhood SES

As part of the DNS protocol, at baseline participants reported on their parents' SES through two questions. First, they were asked to place their parents on a subjective socioeconomic ladder (Adler, Epel, Castellazzo, & Ickovics, 2000) with the following question: Where, during your childhood and adolescence, would you have placed your biological father on this ladder relative to other people in the United States (or your country of origin)? If you did not know your biological father, please think of the male that was most like a father figure to you (0 = lowest, 10 = highest). A similar question asked this information for mothers.

Second, participants were asked to report on their parents' highest education level achieved or completed before the participant had turned 18 (see Table 1 for the distribution of education levels in the sample). Parents' education was collapsed into groups in line with prior research (Ursache, Noble, & Blair, 2015); however, given the relatively affluent sample and the small number of participants at the lower end of the distribution, we collapsed across groups with less than high school education or a high school diploma to create the following groups: 1) Technical training or less (no high school diploma, high school diploma or GED, or technical training); 2) Some college or Associate's degree, 3) Bachelor's degree or post-bachelor degree

coursework; 4) Graduate degree (Master's degree or MD/PhD/JD/PharmD). Each question was reported separately for participants' fathers and mothers. After responding to each education question, participants were asked if their response referred to their biological father and mother; 98% reported that they had responded about their biological father and 99% reported that they had responded about their biological mother. Responses of "unknown" were coded as missing. Four participants were missing data for father's education and one participant was missing data for mother's education.

**Table 1. Distribution of highest education achieved by fathers and mothers in the current sample**

<b>Education</b>	<b>Father (n)</b>	<b>Mother (n)</b>
No High School Diploma	13	11
GED or High School Diploma	33	27
Technical Training	18	12
Some college, no degree	33	35
Associate degree	22	39
Bachelor's degree or post-bachelor coursework	129	210
Master's degree	154	156
MD/PhD/JD/PharmD	173	88

In addition, participants reported on their current subjective SES by placing themselves on the subjective socioeconomic scale (Adler et al., 2000) with the following question: "Where would you place yourself on this ladder, compared to all the other people in the United States? Please select the number that you think represents the rung where you stand." (0 = lowest, 10 =

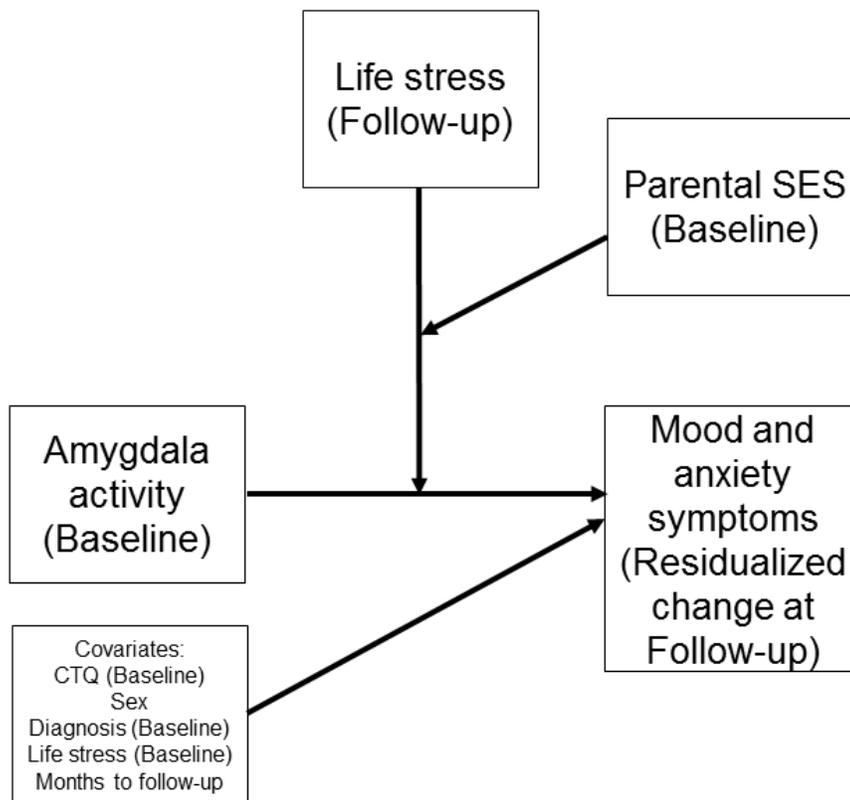
highest). As expected, parental subjective SES, parental education, and current subjective SES were all significantly, although not perfectly, correlated (Table S1).

#### *2.4 Life stress*

As part of the DNS, all participants having successfully completed the baseline protocol are invited to complete a follow-up survey online every 3 months. For the present analyses, the most recent follow-up available for each participant was used to obtain measures of stress and symptoms reported post-scanning. The mean time between scanning and the follow-up questionnaire was 477 days (SD=363, range = 90 to 1706 days). Life stress was measured at baseline and in the follow-up online survey with the Life Events Scale for Students (LESS; Clements & Turpin, 1996). Similar to our prior work (Swartz et al., 2015), we summed the severity ratings of life events to obtain a total life stress score that encompassed both a higher number and severity of life events. As life stress scores were skewed at baseline and follow-up, a square root transformation was applied to each measure to achieve a more normal distribution.

#### *2.5 Internalizing symptoms*

Internalizing symptoms were measured at baseline and follow-up with the Mood and Anxiety Symptom Questionnaire Short Form (MASQ; Watson et al., 1995). As in our prior research (Swartz et al., 2015; Swartz, Prather, Di Iorio, Bogdan, & Hariri, 2017), we standardized scores on each subscale and summed them to obtain a total measure of mood and anxiety symptoms. To assess change in total MASQ symptoms from baseline to follow-up, we calculated a residualized change score (Swartz, Hariri, et al., 2017). The statistical model tested is shown in Figure 1. Full details on all statistical analyses conducted are reported in the Supplement.



**Figure 1. Statistical model.** Statistical analyses examined a three-way interaction between amygdala activity, parental SES, and life stress measured at follow-up in predicting changes in mood and anxiety symptoms from baseline to follow-up.

### 2.6 Covariates

Total scores on the Childhood Trauma Questionnaire (CTQ; Bernstein et al., 2003) were included as a covariate to control for potential parental SES effects mediated by child maltreatment. Because CTQ scores were skewed, they were log transformed. Participant sex, presence of a psychiatric diagnosis at baseline (coded 0 = no diagnosis, 1 = diagnosis), life stress at baseline, and months between imaging and follow-up were also included as covariates in all

analyses. MASQ symptoms at baseline were controlled for by using the residualized change score as the dependent variable, which reflects MASQ symptoms at follow-up controlling for MASQ symptoms at baseline.

### *2.7 Attrition*

Of the 1,210 participants with fMRI data meeting quality control criteria, 579 completed at least one follow-up questionnaire (see Figure S1 for a flow chart depicting participant data loss and attrition). Attrition analyses indicated that participants included in the present sample were more likely to be female,  $\chi^2(1)=17.35$ ,  $p<.001$  and younger at baseline,  $t(1208)=2.60$ ,  $p=.009$ . Participants who completed a follow-up were also less likely to have a psychiatric diagnosis at baseline,  $\chi^2(1)=5.45$ ,  $p=.020$ . The present sample did not differ from the excluded sample in terms of any of the measures of SES or stress or internalizing symptoms reported at baseline.

## **3. Results**

### *3.1 Bivariate Correlations and Group Differences*

Bivariate correlations between parental subjective SES, parental education, current subjective SES, life stress, amygdala activity, and mood and anxiety symptoms are reported in Table S1. Maternal and paternal subjective SES were both negatively associated with subjective stress and mood and anxiety symptoms at baseline, although not with change in MASQ symptoms at follow-up. Additionally, current subjective SES was negatively associated with life stress and mood and anxiety symptoms at both baseline and follow-up. Amygdala activity was positively associated with parental subjective SES.

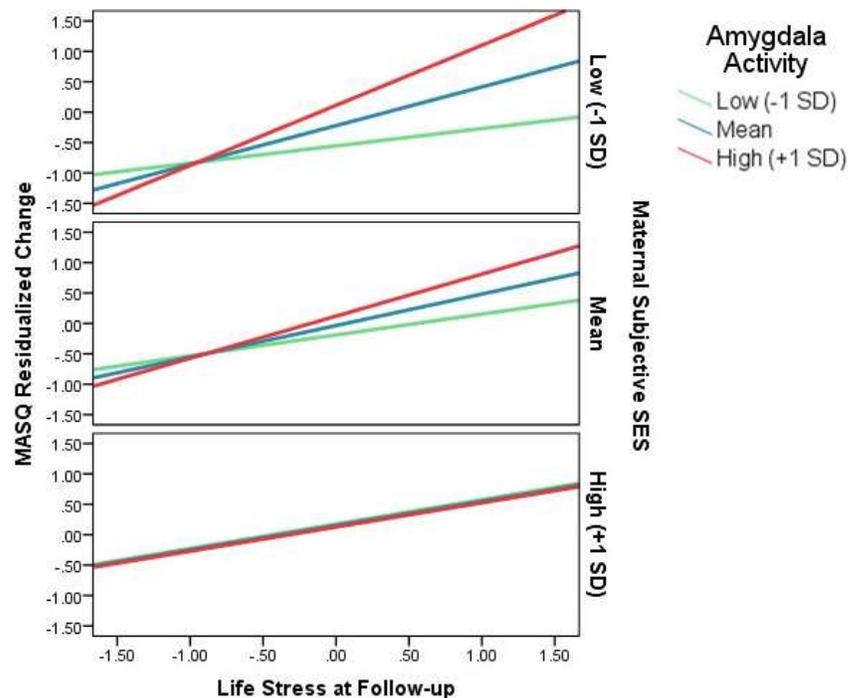
Differences by maternal and paternal educational group are reported in Table S2. There was a significant difference in childhood trauma scores, with the maternal and paternal high school diploma/technical training groups reporting higher childhood trauma scores relative to the other groups. The paternal high school diploma/technical training group also reported higher levels of recent life stress at baseline and follow-up.

### *3.2 Parental subjective SES as a moderator of the association between amygdala activity, stress, and future changes in mood and anxiety symptoms*

As reported in our prior research, perceptual matching of threatening facial expressions (Angry and Fearful Faces > Shapes) elicited significant bilateral amygdala activation (Swartz et al., 2015; Swartz, Prather, et al., 2017). Contrast values were extracted from functional clusters significant at  $p < .05$  family-wise error corrected for the search volumes of the amygdala regions of interest, averaged between the left and right amygdala to obtain a measure of mean threat-related amygdala activity, and submitted to statistical analyses in SPSS.

The three-way interaction between maternal subjective SES, amygdala activity, and recent life stress at follow-up was significant,  $B = -.27$ ,  $SE = .11$ ,  $p = .012$ ,  $\Delta r^2 = .01$ . The significant three-way interaction was probed using simple slopes analysis with the PROCESS macro for SPSS. As illustrated in Figure 2, simple slopes analysis indicated that the amygdala x stress interaction was significant at low levels of maternal subjective SES ( $p = .002$ ), and at mean levels of maternal subjective SES ( $p = .032$ ), but not at high levels of maternal subjective SES ( $p = .986$ ). Post hoc dissection revealed the interaction was significant for the basolateral amygdala,  $B = -.32$ ,  $SE = .16$ ,  $p = .047$ , and marginally significant for the centromedial amygdala,  $B = -.36$ ,  $SE = .19$ ,  $p = .060$ . This interaction remained significant,  $B = -.39$ ,  $SE = .15$ ,  $p = .009$ , when including

regressors for paternal subjective SES and its interactions with stress and amygdala activity. This interaction also remained significant when excluding participants with current or prior internalizing diagnoses at baseline (see Supplementary Analyses). However, this interaction did not remain significant,  $B=-.22$ ,  $SE=.15$ ,  $p=.150$ , when including regressors for participants' current subjective SES and its interactions with stress and amygdala activity. In contrast to maternal subjective SES, the interaction between paternal subjective SES, amygdala activity, and stress was not significant,  $B=-.14$ ,  $SE=.10$ ,  $p=.130$ ; nor were any two-way interactions significant.



**Figure 2. Maternal subjective SES moderates the association between amygdala activity, stress, and future internalizing symptoms.** Three-way interactions were tested with the PROCESS macro for SPSS. Life stress at follow-up is mean-centered. MASQ scores are standardized so that a value of 1 indicates a 1 SD increase in symptoms.

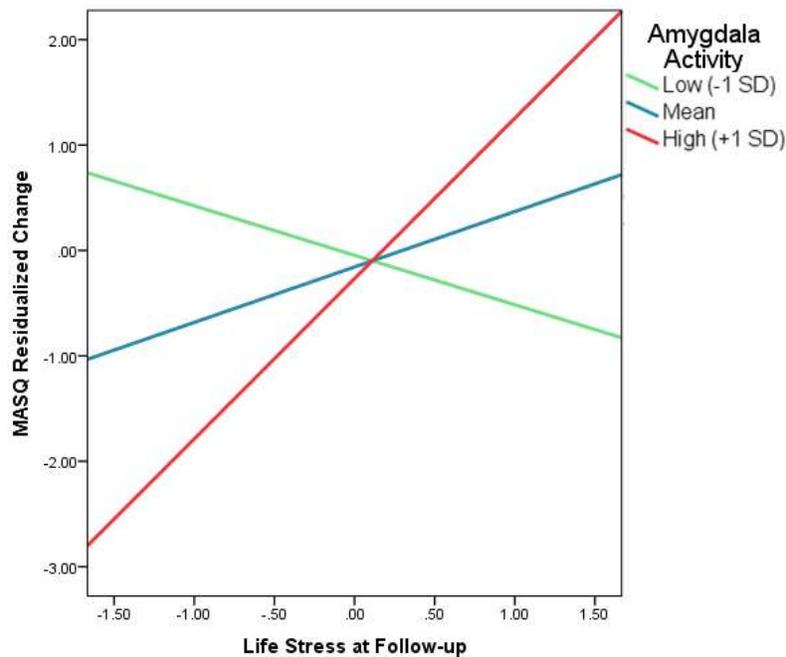
### *3.3 Current subjective SES as a moderator of the association between amygdala activity, stress, and future changes in mood and anxiety symptoms*

Additionally, we examined an interaction between current subjective SES, amygdala activity, and stress, controlling for main effects of maternal and paternal subjective SES. The three-way interaction was significant,  $B=-.34$ ,  $SE=.14$ ,  $p=.016$ ,  $\Delta r^2=.01$ . Simple slopes analysis indicated that the amygdala x stress interaction was significant at low levels of current subjective SES ( $p=.005$ ) but not at mean ( $p=.155$ ) or high levels of current subjective SES ( $p=.638$ ). Notably, however, when controlling for interactions between maternal subjective SES, stress, and amygdala activity, the interaction of current subjective SES x stress x amygdala activity was no longer significant ( $p=.733$ ), suggesting that maternal subjective SES and current subjective SES explain overlapping variance in this risk pathway.

### *3.4 Parental educational achievement as a moderator of the association between amygdala activity, stress, and future changes in mood and anxiety symptoms*

The three-way interaction between maternal educational achievement, amygdala activity, and recent life stress at follow-up was a significant predictor of change in mood and anxiety symptoms from baseline,  $F(3, 556)=6.05$ ,  $p<.001$ , partial  $\eta^2=.03$ . Post hoc analyses conducted with the PROCESS macro to probe this interaction indicated that the amygdala x stress interaction was significant for participants whose mothers were in the technical training or less group (i.e., completed less than high school, a high school diploma, or technical training),  $B=3.49$ ,  $SE=.86$ ,  $p<.001$ ,  $\Delta r^2=.22$ , but not in participants whose mothers had received some college or an Associate's degree ( $p=.238$ ), a Bachelor's degree ( $p=.167$ ) or graduate degree ( $p=.303$ ). For participants with mothers in the technical training or less group, higher recent life

stress predicted significant increases in mood and anxiety symptoms in participants with high levels of amygdala activity ( $p < .001$ ), but not in individuals with mean ( $p = .074$ ) or low levels of amygdala activity ( $p = .262$ ) (Figure 3). Post hoc analyses indicated the interaction between maternal education, life stress, and amygdala activity was significant for both the basolateral,  $F(3, 556) = 5.31, p = .001$  and centromedial amygdala,  $F(3, 556) = 6.89, p < .001$ . This interaction also remained significant when excluding participants with current or prior internalizing diagnoses at baseline (see Supplementary Analyses). Finally, the interaction between maternal education, amygdala activity, and stress remained significant when entering covariates for paternal education and its interactions with amygdala activity and stress,  $F(3, 541) = 6.76, p < .001$ , as well as when entering covariates for current subjective SES and interactions with amygdala activity and stress,  $F(3, 552) = 3.65, p = .013$ , suggesting that maternal education may have a unique influence on the future emergence of mood and anxiety symptoms above and beyond paternal education and current subjective SES. For paternal education, the three-way interaction was not significant,  $F(3, 553) = 1.60, p = .188$ , nor were the two-way interactions of paternal education x amygdala activity and paternal education x stress.



**Figure 3. Amygdala activity x recent life stress interaction in participants whose mothers had completed technical training or less.** The interaction between amygdala activity and recent life stress in predicting changes in internalizing symptoms was only significant for participants whose mothers had completed technical training or less ( $p < .001$ ).

#### 4. Discussion

Consistent with a larger emerging literature, we previously reported that young adults with relatively higher threat-related amygdala activity are more likely to subsequently experience depression and anxiety in response to life stress (Swartz et al., 2015). Here, we provide novel evidence that the expression of this neural risk pathway is uniquely mitigated by post-secondary maternal education but not paternal education. It is first notable that while our observed effects were generally consistent across the two measures of maternal SES, the measure of maternal subjective SES was no longer a significant moderator of the amygdala x stress interaction when

controlling for current subjective participant SES. This suggests that to some degree, maternal SES may indirectly influence future risk for psychopathology by influencing an individual's current subjective SES. Indeed, we found that current subjective SES was also a moderator of the amygdala x stress interaction, with individuals reporting lower current subjective SES driving the significant amygdala x stress interaction.

Nevertheless, even when controlling for current subjective SES and its interactions with stress and amygdala activity, maternal educational achievement remained a significant moderator of the amygdala x stress interaction. This specificity of effects to maternal education aligns with prior research that has shown that maternal, but not paternal, educational achievement is a significant predictor of risk for depression and anxiety in adulthood (Park et al., 2013; Sheikh et al., 2014). It has been suggested that maternal education may have a stronger direct influence on children's mental health outcomes because education levels may influence the quality of parent-child interactions and many mothers spend more time on childrearing compared to fathers (Duncan & Magnuson, 2012; Park et al., 2013).

Indeed, paternal SES was not a significant moderator of the amygdala x stress interaction in this study. Interestingly, paternal educational achievement was significantly associated with stressful life events reported at both baseline and follow-up. This suggests that paternal SES may have a more indirect influence on risk for mood and anxiety problems through its association with access to resources that reduce or help students cope with the life stressors that in turn seem to have a direct influence on the emergence of mood and anxiety symptoms. It is also important to note that there was still a significant main effect of stress in all groups regardless of maternal educational achievement. Thus, it is not the case that students with higher maternal educational achievement are completely immune to the effects of stress, but higher

maternal education helps to buffer the increased stress sensitivity associated with heightened amygdala activity.

Of note, we did not observe evidence that lower SES directly predicts higher amygdala activity in this study, which would be predicted by the mediational framework supported by previous research. Indeed, counter to expectations, we found that there was a positive association between both maternal and paternal subjective SES and amygdala activity, and no association between parental education and amygdala activity. Differences in the sample composition across studies may explain these results, as prior studies that have found a negative association between parental SES and amygdala activity have often over-sampled for low-income families (Kim et al., 2013), whereas the current sample came from relatively affluent families. This unexpected effect is similar to recent work in adolescents finding that more contextually appropriate expression of emotion within families is positively correlated with amygdala activity to angry faces (Farber et al., under review). The authors suggested that this effect may be driven by less frequent exposure to angry faces in adolescents from families that express emotion in more contextually-appropriate ways, making them more sensitive to these expressions. It is possible that a similar process may underlie the finding reported here, if higher parental SES is associated with more contextually appropriate affective responsiveness within families.

Of course, our work is not without limitations. First, although we examined parental education and subjective parental SES separately, it is likely that the subjective parental SES measure was strongly influenced by parental educational achievement, such that these measures could not fully separate out influences of parental education from influences of parental financial resources. Additionally, both SES measures were retrospective, self-report measures and, particularly for the measure of parental subjective SES, were likely subject to retrospective bias.

Future research with prospective and, if possible, objective measures of parental SES that can more fully separate parental education from parental income will be important in disentangling influences of parents' SES on their children's mental health. Likewise, given that maternal and paternal education were correlated, there is no ideal way to control for the influence of one while examining the effects of the other. We therefore tested for interactions in two ways: first, while not controlling for interactions with the other parent's SES and, second, while controlling for interactions with the other parent's SES. The interactions with maternal SES measures were also significant without including any covariates in the models (results not shown). That effects were significant with and without a number of covariates in the model helps to increase our confidence in these results, but we cannot completely control for these confounds given the observational nature of the study. Also, as noted above, our sample of young adult university students was generally affluent and not representative of the larger population, particularly in terms of the number of parents with graduate or professional degrees. Therefore, these results may not generalize to other populations. Indeed, an additional limitation of our study is that sample sizes were generally too small to compare across groups with no high school diploma, with a high school diploma, and with some post-high school training. Further research is needed in larger, more representative samples to allow for additional fine-grained analyses of the effects of parents' education on moderating children's risk for mood and anxiety problems. We nevertheless believe this is an important sample to study, as depression and anxiety are highly prevalent on college campuses, and identifying factors that moderate the development of depression and anxiety symptoms will be useful for helping to reduce rates of these common psychological problems in college students.

These limitations notwithstanding, our current study reveals novel moderators of the interaction between threat-related amygdala activity and recent life stress in predicting future mood and anxiety symptoms. While maternal education, maternal subjective SES, and current subjective SES were all found to moderate this association, the presence of post-secondary maternal education was uniquely associated with buffering the expression of threat-related amygdala activity as future psychological vulnerability to life stress. The mechanisms through which maternal education mitigates this neural risk remain to be determined. Investigators have proposed that the quality of parent-child relationships are important mediators of the effects of parental education on children's development (Duncan & Magnuson, 2012). Although much of this research has been conducted in the context of understanding parenting influences on children's cognitive development, some of the parenting qualities influenced by parental education are likely important predictors of children's emotional development as well. In the present study, we observed an association between lower maternal educational achievement and higher childhood trauma scores, which suggests there were higher amounts of harsh or neglectful parenting in the group with lower maternal education, which may further increase stress sensitivity in individuals with relatively heightened amygdala activity. However, even when controlling for childhood trauma, we observed a moderating effect of maternal education, suggesting that other factors may be at play, such as differences in maternal warmth (Davis-Kean, 2005; Klebanov, Brooks-Gunn, & Duncan, 1994). It is also possible that mothers with higher educational levels provide more current social support to their children while at university, which also may help buffer the risk associated with heightened amygdala activity and stress (Hyde, Gorka, Manuck, & Hariri, 2011).

More generally, the patterns we observe suggest that we are unlikely to observe strong main effects of individual differences in brain function in predicting the future emergence of psychopathology, and that careful consideration of environmental moderators conferring both relative risk and resilience will be required. Our current results suggest that maternal educational achievement is an important moderator of neural risk for stress-related psychopathology. Determining the precise mechanisms at play promises to inform the development of strategies to mitigate stress sensitivity associated with relatively heightened threat-related amygdala activity.

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**Highlights**

- Amygdala activity predicts stress-related increases in internalizing symptoms
- We tested whether this effect is moderated by parental socioeconomic status
- Maternal education, but not paternal education, moderates this effect
- Higher maternal education buffers the effect of amygdala activity on symptoms

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