INVESTIGATION OF THE RELATIONSHIP BETWEEN THE NEGATIVE AFFECT IN YOUNG ADULTS AND DEPRESSION

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INVESTIGATION OF THE RELATIONSHIP BETWEEN THE NEGATIVE AFFECT IN YOUNG ADULTS AND DEPRESSION

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ABSTRACT

Young adults display the negative affect where they pay attention to and remember negative information better than positive information. A similar affect is in observed in individuals with depression. Since depression is prevalent in young adults, this bring into question whether there is a connection between the negative affect in young adults and depression. This study explores this phenomenon by using fMRI imaging to identify any patterns of activation involved in the relationship between depression and the negative affect in young adults. To achieve this, 13 young adults between the ages of 18 and 34 years old were recruited. After confirming that they are fMRI safe, a set of neuropsychological assessments and depression questionnaires were carried out, followed by an fMRI Encoding Task. During the Encoding Task participants are presented with a positive, negative, or neutral auditory cue and an imaging matching its emotional valence. They were then asked to evaluate the emotional intensity of the picture. After the fMRI a Retrieval Task where individuals asked if the image is new or old and then how confident they are in their decision. Behavioral analysis of memory accuracy with a repeated measures ANOVA resulted in no significant differences in the memory for any of the conditions. ANOVA analysis of the fMRI images with an uncorrected voxel threshold of .001 also showed no significant activation patterns. Overall, this study was not able to achieve its goal due to time restrains. As this is an ongoing project, greater analysis will be utilized to identify a relationship between the experimental conditions and brain activity.

INTRODUCTION

Repetitive exposure to stressful events can release cortisol, lead to depression, and eventually cause cognitive damage. After the first episode of Major Depression Disorder (MDD), significant deficits in psychomotor speed, visual learning, memory encoding and retrieval, executive function, and attention can be observed (Brand, Jolles, & Gispen-de Wied, 1992; J. Douglas Bremner, Meena Vythilingam, Eric Vermetten, Viola Vaccarino, & Dennis S. Charney, 2004; Lee, Hermens, Porter, & Redoblado-Hodge, 2012). Included in the memory impairments is a negative affect where individuals pay more attention to and recall more negative information than positive or neutral information (Dalgleish & Watts, 1990). A similar negative affect is found in young adults, an age group that is more likely to develop depression (Shim, Baltrus, Ye, & Rust, 2011). There is yet to be any study examining whether this negative affect presented in young adults is actually linked to depressive symptomology.

A previous study conducted in my lab was able to attribute the positive bias in older adults where they focus more on and recall more positive information by suppressing their emotional response in anticipation of negative stimuli (Corbett, Rajah, & Duarte, 2018). While the negative affect was observed, a mechanism for it was not uncovered. The study did not consider that the negative affect in young adults may be due to the prevalence of depressive symptoms that is common in the age group (The National Institute of Mental Health, 2019, February). This study seeks to fill in the gap and examine if the negative affect in young adults is due to depressive symptomology by observing different brain activation patterns in young adults during functional Magnetic Resonance Imaging (fMRI) while they encode or process emotional stimuli. During the fMRI, participants were asked to rate the emotional intensity of positive, negative, and neutral images and later underwent a retrieval task based on the pictures

they saw in the fMRI. The pattern of activity during encoding can affect how well one may be able to retrieve certain stimuli, therefore, by comparing the brain activity patterns between normal young adults and depressed young adults, we can understand the underlying mechanism of the negative affect found in the age group and analyze whether it is actually due to depressive symptomology.

With neuroimaging techniques such as fMRI, we are able to see the structural and function changes in the brain as a result of depression in young adults. The hippocampus is involved in memory formations, but with persistent depressive feelings, its structure can be atrophied and thus lead to memory impairments (Taylor et al., 2014). There is also a significant decrease in activity of the hippocampus and prefrontal cortex during encoding of emotional stimuli, which is when information is processed for the brain to later recall (J. Douglas Bremner et al., 2004). MDD is also known to result in an increase in amygdala volume and white matter abnormalities in the frontal–subcortical circuit which may explain the mood congruent behavior in depressed individuals (Ning Ma et al., 2007).

It is important to understand the different aspects of depressive symptomology to be able to develop and provide better treatments to those individuals suffering from it and to help foster a more positive functioning society. A 2017 National Survey on Drug Use and Healthy (NSDUH) found about 7.1% of all U.S. adults to have experienced at least one major depressive episode (MDD). While it seems like a relatively small percentage, it makes up to be about 17.3 million adults. 64% of these adults have had severe impairments due to depression. Moreover, depressive symptomology is even more prevalent than MDD in the United States, especially in young adults, but the lack of severity makes individuals ineligible for traditional depression treatments such as antidepressants (Shim et al., 2011; The National Institute of Mental Health,

2019, February). Young adults who showed depressive symptomology but did not meet the threshold for Major Depression Disorder (MDD) are not only more likely to have early-adulthood depression but are also likely to abuse substances and have adverse social and psychological functioning later in life (Terhi Aalto-Setälä, Mauri Marttunen, Annamari Tuulio-Henriksson, Kari Poikolainen, & Jouko Lönnqvist, 2002). The positive affect seen in older adults is known to lead to a greater self-evaluation of wellbeing and inducing a similar positive affect or decreasing the negative affect in young adults may lead to the same sense of wellbeing for the youth (Susan T. Charles & Luong, 2013; Susan Turk Charles, Reynolds, & Gatz, 2001)

LITERATURE REVIEW

Major Depressive Disorder (MDD) is a leading mental issue in the United states as it is underdiagnosed or left untreated by primary care physicians (The National Institute of Mental Health, 2019, February). Moreover, depressive symptomology is even more prevalent in the United States than MDD, but individuals are ineligible for traditional depression treatments due to lack of severity. Prolonged depressive symptoms can lead to many cognitive and motor deficits such as the negative affect where the individual pays more attention to and remembers negative information better than positive information (Brand et al., 1992; J. Douglas Bremner et al., 2004; Lee et al., 2012) This mood congruent effect is known to induce a positive feedback loop which makes it hard to escape the depressive state individuals experience (Dalgleish & Watts, 1990). This negative bias is also commonly seen in young adults. This brings into question if there is a relationship between the negative affect in young adults, who historically tend to have depressive symptomology, and the negative affect in depression (Shim et al., 2011). This study examines the possible relationship by using functional Magnetic Resonance Imaging (fMRI) to identify patterns of brain activation that may be significant in causing this bias.

Aging Effect:

There are few theories that explain why younger adults the negative affect have, but the most prevalent theory is the Socioemotional Selectivity Theory (SST). The theory attributes the negativity bias in younger adults to how individuals regulate emotions and what motivations they have. It also explains a phenomenon that is studied more in depth, the positive affect in older adults. The positive affect is the exact opposite of the negative affect, in which they tend to have a bias to more positive information. The SST's justification for the affects is that when one is young, time is thought to be endless and therefore interests surround exploration and learning,

giving importance to negative information. However, in old age, life is considered to be near its end and therefore goals shift more towards emotional balance and satisfaction with oneself inducing the positive affect (Carstensen, Isaacowitz, & Charles, 1999).

Some other theories provide an alternative reason for the negative/positive affect such as the Dynamic Integration Theory (DIT) which explains that with age there is decline in processing skills, the ability to process complex negative information is more difficult, and the dysfunctional nervous system allows for more positive information to be remembered (Labouvie-Vief, 2009). This theory is false since if a positive affect is due to dysregulation, then the negative affect in young adults has to be due to normal brain function, however; during a dysregulated depressed state the same negative affect. This was theory is further negated by the fact that a positivity effect is still observed in older adults with high executive function, regardless of cognitive load (Mather & Knight, 2005). Overtime, theories like the DIT that attribute the positive affect to age-related decline have been falsified. Instead, the SST has gained a lot of support and is considered to be the root of the negative affect in young adults and the positive affect in old adults.

     While the SST accounts for the negative affect, most studies and theories put a greater emphasis on the positive affect in adults, and therefore most literature focuses on the positive affect. Even though research is conducted to study both affects, conclusions are typically derived from the significant results from older adults, contributing to the lack of literature on the negative bias. Regardless, many inferences can be drawn on the negative affect by studying the source of the positive affect in older adults.

     Inspecting the structural changes in the amygdala of an aging brain gives insight into what changes may influence the changes from the positive affect. The amygdala is an important

subcortical structure to analyze due its central role in emotional. The Aging-Brain Model predicts that the positive affect is to be due to a decrease in amygdala volume (Todorov, Fiske, & Prentice, 2011); however, a postmortem study shows less decline in amygdala volume than in other brain structures, deeming the change in amygdala volume to not be the cause of the positive affect (Brabec et al., 2010). It has also been demonstrated that older adults have greater connectivity between the amygdala and ventral anterior cingulate cortex than young adults, allowing for greater regulation of emotions in a way that is consistent with the Cognitive Control Model (Bush, Luu, & Posner, 2000). The Cognitive Control Model attributes a decrease emotional response to stimuli due to PFC modulation of the amygdala through top-down downstream (Jackson & Moghaddam, 2001). It is therefore no surprise that there is greater activation in the PFC in response to negative stimuli in older adults than younger adults to suppress emotional appraisal (Tessitore et al., 2005). The amygdala's connections with the frontal lobe may provide a route for the mechanism of the positive affect or the lack of negative affect to take place.

Other studies have shown the functional changes in the amygdala with age. There is still a significant decrease in amygdala activation in older adults after the presentation of negative stimuli, and an increase activation for positive stimuli (Mather et al., 2004). This is not true young adults who instead have an increase in activation to stimuli with high intensities (very positive or very negative stimuli). This functional change in the pattern of amygdala activation may be a cause of the different emotional biases (Lin et al., 2016).

Along with changes in the amygdala, there are changes in the hippocampus with age. The famous case study of H.M. showed the relevance of the hippocampus in the formation of episodic memories (Corkin, 1984). With reduced hippocampus volume, as observed in old

adults, there is a decrease in episodic memory and working memory (Head, Rodrigue, Kennedy, & Raz, 2008). Such impairments can also be due to other factors such as physical frailty, ethnicity, lower levels of education, poor health, but depression is one of leading cause of this reduction (Taylor et al., 2014). Since the hippocampus reduction is seen with individuals who have the positive affect and with individuals with depression, it is likely that it is not the cause of the negative affect. The hippocampus' significance in episodic memory still makes it an important structure to examine.

Effects of Depression:

The effects of depressive symptomology are similar to the effects to depression which is studied more in depth. Neuroimaging techniques have been used to show the structural changes in the brain as a result of depression, many of which may has parallels to the changes in young adults. Long-term, persistent depression can lead to hippocampal atrophy and lead to memory impairments (Taylor et al., 2014). Depression can also increase amygdala volume, changing mood regulation, allowing the amygdala's impact to surpass the PFC's down regulation. Individuals with MDD also have white matter abnormalities in the frontal–subcortical circuitry. The circuitry was previously mentioned to be in important in mood regulation (Ning Ma et al., 2007). Since the connection seen in old adults with the positive affect, lack of integration in depressed individuals may be response for the negative affect. These structural changes can affect episodic and semantic memory, processing speed, emotion regulation and induce the similar negative affect as the one seen in young adults (Herrmann, Goodwin, & Ebmeier, 2007).

Significance:

fMRI data can help assess similarities in brain activation patterns and structural changes in young adults and depression and can aid identify the relationship between the negative affect

in young adults and depressive symptomology. It is important to understand this interaction to help younger adults cope with depressive symptomology. Young adults with such symptomology are more likely to make dangerous, unhealthy decisions and have substance abuse issues along with adverse social and psychological functioning (Terhi Aalto-Setälä et al., 2002).This study's results can inspire treatments that can help not only decrease the negative affect in young adults but also help ensure their wellbeing.

METHODS

Participants

Participants included 23 adults between the ages of 18 to 35 with no depression,

subthreshold depression, or diagnosed MDD. Ten participants were excluded from the analysis:

four participants wished to stop the experiment, four had imaging issues, one had technical

issues, and another one misunderstood the procedure, therefore leading to a final sample size of

13 adults (6 females; mean age of 26.92 years; mean education of 15.19 years). Participants

were recruited from Georgia Institute of Technology (Georgia Tech) and the greater Atlanta area.

Each participant was compensated $15 an hour and $5 for any travel costs, and if the individual

were a student at Georgia Tech, they had the option to receive SONA credit for a psychology-

based class. All participants were screened to be right-handed, English speakers, with normal or

corrected to normal vision. Individuals were excluded from the study if they had the following

characteristics: Epilepsy, Parkinson's disease, a history of stroke or seizure, Attention Deficit

Disorder, Multiple Sclerosis, untreated hyper- or hypotension, untreated Diabetes, Sickle Cell

Anemia, alcoholism and regular use of illegal drugs. All participants signed Georgia Tech

Institutional Review Board approved consent forms. Demographic information and mean scores

for each of the neuropsychological tests and questionnaires are presented in Table 1.

Measures	Mean (n=13)	SD
Age	26.92	4.99
Sex	F = 6	
Years of Education	15.19	1.75
CES-D	28.54	12.93
DASS-12	18.31	9.96

MMSE		29.85	0.38
MoCA		27.38	2.18
GPAQ (min)		2819.23	2121.49
PANAS 1	Positive	30.00	8.14
	Negative	14.77	3.35
PANAS 2	Positive	25.69	7.93
	Negative	14.85	4.39
ERQ	Reappraisal	28.38	6.55
	Suppression	14.00	5.12
Logical Memory I Immediate Recall	Story A	10.46	1.90
	Story B	14.38	3.62
Logical Memory II Delayed Recall	Story A	6.85	3.63
	Story B	11.69	3.86
Logical Memory II Recognition	Story A	6.23	1.48
	Story B	12.23	1.92

Table 1. Demographic Information and mean scores of neuropsychological tests and questionnaires. SDs are reported in the parenthesis.

General Procedure

Participants were screened over the phone for exclusionary criteria mentioned before and their level of depressive, stress, and anxiety symptomology was evaluated. If the criteria were met, an appointment was scheduled during which assessments on neuropsychological competence and depressive, stress, and anxiety symptomology were conducted. The fMRI task was then conducted during which participants had to complete four blocks of the Encoding Task.

Last, the participant was asked to complete the Retrieval Task on a computer. Practice trials were repeated prior to the Encoding Task and Retrieval task and were not included in the analysis.

Neuropsychological Assessments

Participants were given a series of neuropsychological assessments to identify if there are any individual differences in cognitive abilities. The evaluation included: The Positive and Negative Affect Schedule (PANAS), Logical Memory Test (Part 1 and 2), Mini Mental State Examination (MMSE), and Montreal Cognitive Assessment (MoCA). Participants' scores were adjusted based on age.

Symptomology Assessments

Depressive symptomology was assessed with the Center for Epidemiologic Studies Depression Scale (CES-D). Stress and anxiety symptomologies were also measured with the 21-item Depression, Anxiety and Stress Scale (DASS-21). Differences in symptomology levels were not analyzed in this thesis but analysis is still in progress at Georgia Tech's Memory and Aging Lab.

fMRI Encoding Task

During the encoding task, participants communicated their answers with two button boxes, one for each hand. The left-hand box included the numbers "1" and "2" and the right-hand box included the numbers "3" and "4". The task began with a sub-task known as the Cue Task (Figure 1A), during which participants responded to an arrows task and heard positive, neutral, and negative auditory cues to certify that the sound and the buttons were working. First there was a 500 ms central fixation cross and then a 1 s auditory cue was given. The arrows task asked participants to indicate which way the arrow on the screen (2-6 s) was pointing. If the arrow is pointing to the left (<), the participant would have to press 1 or 2, and if the arrow is

pointing to the right (>), the participant would have to press 3 or 4. The arrow task was implemented to identify an active baseline of brain activation.

Once any technical issues were resolved, the true Encoding Task (Figure 1B) with the auditory cues, respective images, and the arrows task began. Each trial started with 500 ms of a central fixation cross on the screen. Next, a full trial where a 1 s auditory cue signifying the emotional valence of the upcoming picture (slot machine for positive, tire screeching for negative, or whistling for neutral) was presented, followed by its respective image stimulus. The participant then had 3 s to rate the emotional intensity of the image on a scale of 1 to 4, 1 being least intense and 4 being most intense. Catch trials where a sound is played but no image is displayed was included to isolate any cue-related activity from stimulus-related activity. The fixation cross, arrows task, the sound with their respective images, and catch tails were alternated at random throughout each encoding block. Four blocks of the encoding task are carried out, each lasting 11 minutes with a brief break for the participant in between (2-3 minutes).
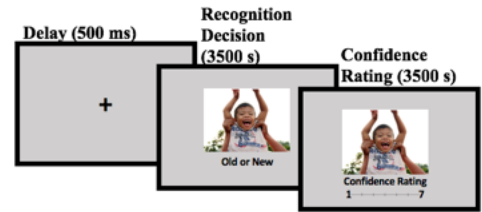
Retrieval Task

The Retrieval Task (Figure 1C) takes place on a computer after the fMRI Encoding Task. A 500 ms fixation cross was displayed on the screen followed by an image that may or may not have been included in the Encoding Task. The participant is asked to identify if the image is a "new image," as in they did not see it during the Encoding Task, or an "old image," as in they did recognize it from the Encoding Task. The image is presented for 3500 s and then have another 3500 s to give a confidence rating on their decision on a scale of 1 to 7. 1 indicated that they are not confident that the image is new or old, and 7 indicated that they were very confident that the image is new or old.
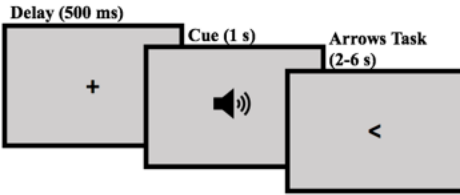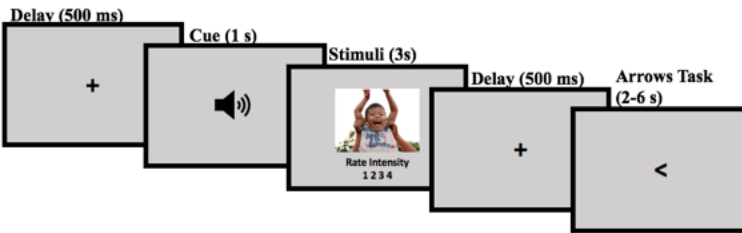
Figure 1. Design for tasks. (A) Design of Cue Task conducted prior to Encoding Task. (B) Design of Encoding Task conducted with a fMRI. (C) Design of Retrieval Task conducted after the fMRI Encoding Task.

fMRI Acquisition

A cue task and 4 encoding tasks with the images were ran with these parameters. Participants were scanned in CABI's 3-T Siemens TIM Trio system. A gradient echo pulse sequence of 38 transverse slices along the anterior posterior commissural axis at a 30-degree tilt, was utilized to create 3x3x3.5 mm voxels with 0.8 mm interslice gaps. Scans were repeated every 2s with an echo time of 30ms. The first 2 slices of each block were discarded to allow equilibration effects. A high-resolution T1-weighted magnetization-prepared rapid acquisition gradient echo (MPRAGE) image was conducted and later used for normalization of brain activity.

Materials fMRI Encoding Task

There were four encoding blocks, each consisted of 84 trials: 63 full trials and 21 catch trials. 252 pictures from the International Affective Picture System (IAPS) (Lang, Bradley, & Cuthbert, 2008) were used for stimuli. There were equivalent number of positive, negative, and neutral images that were determined by the Self-Assessment Manikan (SAM) Scale. Three 1s long auditory stimuli were delivered prior to the images indicating emotional valence of the image. The sounds were picked from the International Affective Digital Sounds (IADS) (Bradley & Lang, 2007). A tire screeching sound indicated negative image, a whistling sound indicated neutral image, and a slot machine sound indicated a positive image.

Preprocessing

Statistical Parametric Mapping 12 (SPM12) was used to analyze the fMRI data. The middle slice of each volume was used as a reference to correct the images for differences in slice timing acquisition. The first volume of the first block served as a reference to spatially realign and reslice the images. The MPRAGE images were coregistered to mean echo planar imaging (EPI) images, produced from spatial realignment. Each coregistered structural scan was then segmented using the diffeomorphic anatomical registration through exponentiated lie algebra (DARTEL) SPM 12 toolbox. Each coregistered structural scan was then segmented using the diffeomorphic anatomical registration through exponentiated lie algebra (DARTEL) SPM 12 toolbox (Ashburner, 2007). DARTEL is a suite of tools fully integrated with SPM 12, which the SPM12 manual recommends over optimized normalization, to achieve sharper nonlinear registration, for intersubject alignment. This method also achieves better localization of fMRI activations in Montreal Neurological Institute (MINI) space. It has also been used successfully in several previous studies with various healthy and neurological populations (Pereira et al., 2010;

Yassa & Stark, 2009). Briefly, the gray and white matter segmented images were used to create a study-specific template using the DARTEL toolbox and the flow fields containing the deformation parameters to this template for each subject were used to normalize each participant's realigned and resliced EPIs to MINI space. Normalized EPI images were written to 3 x 3 x 3 mm and smoothed with an 8 mm full width at half-maximum isotropic Gaussian kernel. The EPI data were then high pass filtered to a minimum of 1/128 Hz and grand mean scaled to 100.

Statistical Analyses

Statistical analysis was performed in two stages. In the first stage, neural activity was modeled as a series of 4 s epochs at study (delta functions) of various even types and convolved with a canonical hemodynamic response function. The time courses were down sampled to the middle slice to form the covariates for the General Linear Model. Temporal autocorrelations within a session were corrected. For each participant and block, six covariates representing residual movement-related artifacts, determined by the spatial realignment step, were included in the first-level model to capture residual (linear) movement artifacts. Voxel-wise parameter estimates for these covariates were obtained by restricted maximum-likelihood estimation, using a temporal high-pass filter with a cutoff of 128 s to remove low frequency drifts and modeling temporal autocorrelation across scans with an AR (1) process.

Contrasts of the parameter estimates for each participant were submitted to the second stage of analysis (treating participants as a random effect). Repeated measures ANOVA models were created for the study period that allowed us to examine both within-group effects and group interactions.

RESULTS

Neuropsychological and Depression Assessment Results

Mean scores and respective SDs for the neuropsychological assessments are shown in Table 1. The table also includes mean CES-D and DASS-12 scores and their SDs. CES-D scores identified depressive symptomology while DASS-12 evaluated stress, anxiety, and depressive symptoms, only depressive symptoms were accounted for in the analysis. We found one individual to have normal symptoms, another one to have possible depression, and another one to have probably depression. Eight individuals displayed subthreshold symptomology and two had symptoms that can be classified as Major Depressive Disorder. Overall, majority of the individuals had subthreshold depression, but there were individuals displaying diverse symptomology. Due to lack of resources and time amidst the Covid-19 Pandemic, analysis on the effects of depression on the Encoding Task were *not* evaluated.

Behavioral Results: Memory Accuracy

The mean proportions of hits and false alarms (FA) for positive, neutral, and negative groups are shown in Table 2. High confidence memory accuracy (d') was analyzed based on the signal detection theory [z (hit rate) $- z$ (FA rate)]. The d' data is visualized in Figure 2. The d' data was further analyzed with a repeated measures ANOVA resulting in no significance effects [$F(2, 13) = 0.645$, $p = 0.05$, $\eta_2 = .005$]. While negative information had a greater memory accuracy than any other emotional stimuli, there is still no significant difference in memory bias for emotional stimuli.

Positive Hit	Neutral Hit	Negative Hit
0.81 (.12)	0.81 (.14)	0.85 (.10)

Positive FA	Neutral FA	Negative FA
0.09 (.07)	0.09 (.07)	0.09 (.08)

Table 2. Mean proportions of hits and false alarms for each valence category (positive, neutral, and negative) with SD in parenthesis.
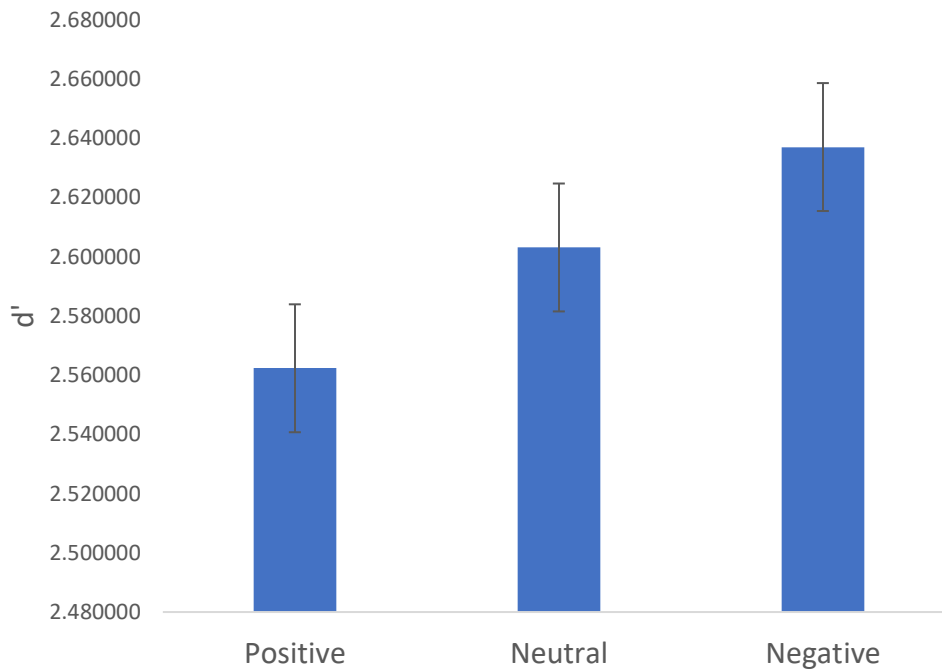
Figure 2. Mean high confidence memory accuracy (d') for positive, neutral, and negative information. Error bars represent SD.

fMRI Results

It was hypothesized that there would be greater activation of the amygdala in response to negative stimuli; however, no significant activation patterns were observed through ANOVA analysis of the hit accuracy of positive, neutral, and negative stimuli. Follow up of possible errors during analysis process was not possible, leading to no further results.

DISCUSSION

The goal of this study was to investigate the effects of depression on the negative affect observed in young adults. The effects of depression on the negative affect was not analyzed therefore there was a greater focus on the examination of pattern of activation due to the negative affect of young adults as the main purpose of the experiment. As greater amygdala activation is observed in response to negative information, we expected to see greater amygdala activation in response to negative stimuli than neutral stimuli (Beyeler et al., 2016). Older adults that have an opposite, positive affect have greater activation of vmPFC to reduce amygdala activity in anticipation of negative stimuli than neutral, therefore it was hypothesized that young adults would have a contrasting pattern and there would be greater amygdala activation in response to negative images than neutral image (Corbett et al., 2018). Similarly, the previously studied negative affect expected young adults in this study to have a greater memory accuracy for negative information than neutral or positive information.

This study was unable to demonstrate both, significant activity in the amygdala in association to negative stimuli and the negative affect commonly observed in young adults. This experiment's main purpose to compare the effect of depression on the negative affect fell short on analysis and no results were formulated in regard to the effects of depression. This project was severely limited in time and could not provide a deeper analysis than an Univariant analysis. Greater means of analysis would be required to identify a relationship between the experimental conditions and brain activity.

CONCLUSION AND FUTURE DIRECTION

In conclusion, this study hoped to investigate a relationship between the negative affect in young adults and depression that is commonly seen in that age group. However, we were unable to analyze the effects of depression on the negative affect and therefore the goal of the project shifted to identifying a pattern of activation in response to negative stimuli to observe the underlying mechanism for the negative affect. The lack of significant data in this study suggests a need for greater means of analysis would be required to identify a relationship between the experimental conditions and brain activity. This includes Region of Interest analysis and Multivoxel pattern analysis (MVPA) which is currently being conducted by graduate students in the lab.

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