Available online at:
https://cc.arcabc.ca/islandora/object/cc%3Apsycjournal

J Camosun Psyc Res. (2021). Vol. 3(1), pp. 148-157.
Submitted Fall 2020; accepted July 2021.

What Is the Biological Mechanism of Chronic Anxiety?

Authors: Tejpreet Mand* and Chelsea Mappin

Supervising Instructor: Michael Pollock, Psyc 215 ("Biological Psychology")

Department of Psychology, Camosun College, 3100 Foul Bay Road, Victoria, BC, Canada V8P 5J2

*Corresponding author email: tejpreetmand@gmail.com

ABSTRACT

In this paper, we seek to understand the causes of chronic anxiety in order to learn how to overcome this disorder. Previous research has found that decreases in anxiety are associated with decreases in amygdala activity and increases in consumption of the fatty acid DHA, while increases in anxiety are associated with having higher levels of the inflammatory protein interleukin-6. In our correlational study, we tested the strength of these relationships by examining naturalistic daily changes in their variables longitudinally over a two-week period. We measured amygdala activity by measuring the difference in heart rate before and after watching a scary video, DHA levels by calculating the amount of DHA consumed each day, levels of interleukin-6 by daily body temperature daily, and anxiety levels by ratings on a scale of 0-10. Data pooled across participants in our correlation study showed significant correlations of anxiety levels with amygdala activity and DHA intake, but not with interlueken-6.

1. Introduction

1.1 Research Problem

Understanding the biological mechanism of chronic anxiety can help identify why people experience chronic anxiety and ways to overcome it. People who have anxiety over long periods of time may experience negative related health problems and learning about what causes chronic anxiety and stress can help prevent such problems and help people live a better and more positive life. Additionally, if people understand why they experience chronic anxiety then they can implement ways to overcome or mitigate it. Anxiety is your body's natural response to stress. It orients us to danger and prepares our bodies to either challenge it or escape it. Learning about why we experience chronic anxiety can benefit people in numerous ways as chronic anxiety can leave a person feeling on edge all the time. If we learn ways to overcome this condition, many who suffer from this condition could get relief and live a more positive lifestyle.

1.2 Literature Review

One factor previously found to decrease chronic anxiety is a decrease in amygdala glutamate activity. According to Ullmann et al. (2019), levels of anxiety were decreased in rats that are engaging in active offensive response behavioral strategies to chronic predator scent stress and show lower plasma cortisol levels vs. rats engaging in passive defensive response behavioral strategies to chronic predator scent stress. Rats that are

engaging in active offensive response also have higher lactate and lower glutamate levels in amygdala. The researchers used 28 rats and divided them into two phenotypes based on their behaviour in anxiety related situations. The first phenotype was the active offensive response group which was the control group of the experiment and the second phenotype was the passive defensive response group. The cages with control groups, which were the active response rats, got clear sawdust without cat urine contamination in their cages while defensive response rats got the cages with the cat urination contaminated sawdust (20 rats were submitted to stress exposure; 8 control rats were exposed to a neutral scent). This study demonstrated decreased excitatory glutamate activity in the amygdala of active offensive response rats vs. in passive defensive response rats after chronic predator stress, suggesting a possible endogenous calming psychophysiological mechanism in the active offensive response phenotype.

The type and quantity of fatty acids a person consumes may be directly linked to the level of stress and anxiety they experience. Hashemi et al. (2020) found that higher consumption of docosahexaenoic acid (DHA) is linked to a protective effect on stress and anxiety levels. They used a case control study to measure the effects of the fatty acid profile in erythrocytes (red blood cell), which is a long-term marker for dietary fat consumption. The researchers used 45 students in each case and control group and gave them all a questionnaire that measured stress/anxiety levels, dietary intake, and general characteristics that include weight, age and physical activity; Additionally, they were given a blood test to measure the fatty acid content in their red blood cells. Hashemi et al. (2020) found that DHA levels were lower in the anxiety group. Thus, having higher DHA may reduce the risk of anxiety.

Higher levels of inflammatory proteins are found in people that experience higher levels of anxiety. According to Moriarity et al. (2018), interleukin-6 (proinflammation marker) levels were higher in the subjects that experienced anxiety. The researchers recruited 640 adolescents originally, but blood samples were only taken after 4 years into the study with 140 of the subjects participating in this part of the research. The researchers took blood samples from the 140 participants 2 times with an average time of about a year in between to measure inflammatory proteins. Moreover, they had the subjects self- report their anxiety at the second visit. The researchers found that anxiety was correlated with higher amounts of inflammatory proteins. Thus, inflammation may be a cause of anxiety.

1.3 Hypotheses

- Hypothesis #1: If amygdala activity increases then anxiety will increase.
- Hypothesis #2: If consumption of DHA increases then anxiety will decrease
- Hypothesis #3: If levels of interleukin-6 increase then anxiety will increase

2. Methods

2.1 Participants

The two authors of this paper served as the participants in its studies. The participants ranged in age from 20 to 42 years old, with an average age of 31 years, and included two women. The participants were all undergraduate students at Camosun College who completed the current studies as an assignment for Psyc 215 (“Biological Psychology”) and were grouped together

due to their mutual interest in the causes of anxiety and stress.

2.2 Materials and Procedure

We performed a correlational study to test concurrently all of our hypotheses by examining naturalistic daily changes in their variables longitudinally. Each participant kept a study journal with them at all times over this study's two-week period in order to record self-observations of the following 4 variables: (1) amygdala activity, (2) Intake of DHA, (3) interleukin- 6 levels and (4) anxiety levels

To measure amygdala activity, each participant recorded their heart rate by checking their pulse twice a day: once before and once after watching 4:38 minutes of a scary video clip from YouTube (see Appendix for the link). The difference in heart rate between these two time points was then calculated.

To measure DHA levels, each participant calculated how much DHA they consumed at the end of each day by reading food labels and looking up DHA levels in foods without labels from the list found in the Appendix.

To measure the interleuken-6 levels, each participant took their temperature 3 times a day (morning, noon and night) and recorded their average temperature for the day.

To measure the anxiety levels, each participant rated on a 0 to 10 scale how much anxiety they felt throughout each following day of this study. Participants recorded in a study journal how much anxiety they felt three times a day (morning, noon, and night). The following response were used on the anxiety scale: 0= not feeling anxious at all to 10=feeling extremely anxious. From these records, the average level of anxiety of each participant for each day was calculated.

To assess the strength and statistical significance of associations between variables predicted by our 3 hypotheses, we performed Pearson product moment correlations of their predictor variables (amygdala, DHA, interleukin-6) with their outcome variable (anxiety). For testing Hypotheses #1, we correlated the heart rate of each participant with that participant's average anxiety score for each day. For testing Hypothesis #2, we correlated the intake of DHA of each participant with that participant's average anxiety score for each day. For testing Hypothesis #3, we correlated body temperature with the participant's anxiety score for each day. We performed all of the above correlations separately for each participant as well as using data pooled across all of the participants. For the correlations using pooled data, in addition to using the raw data, we also performed correlations after we had first transformed the data from each participant into *z*-scores in order to standardize differences in averages and variability seen between the participants in their data and thus make them more comparable. A correlation coefficient was considered statistically significant if the probability of its random occurrence (p) was $< .05$ (i.e., less than 5% of the time expected by chance alone).

3. Results

As shown in Table 1, amygdala activity and DHA were significantly correlated with anxiety levels. Although not being statistically correlated for participant #2 (r =0.43, p =0.125), amygdala activity was significantly correlated for participant #1 (r =0.64, p =0.012) and using the pooled standardized data (r =0.53, p =0.0029). DHA and anxiety levels were only significantly correlated using the pooled

standardized data (r =-0.40, p =0.035). In contrast, no statistically significant correlation was found between interleuken-6 and anxiety levels in any single participant's data (all $r \geq$ -0.26, all $p \geq 0.38$) nor using the pooled standardized data (r = -0.08, p = 0.68). Based on a comparison of the correlation coefficients using the pooled standardized data, amygdala activity levels showed the strongest correlation with anxiety.

4. Discussion

4.1 Summary of Results

Based on previous research, we hypothesized that increases in three variables would be followed by less severe anxiety experienced after checking our heart rate: amygdala activity (Hypothesis #1), intake of DHA (Hypothesis #2), and interleukin-6 levels (Hypothesis #3). Data pooled across participants in our correlational study supported the predicted relationship of anxiety with amygdala activity and intake of DHA (Hypotheses #1&2) but not with interleukin-6 levels (Hypothesis #3).

4.2 Relation of Results to Past Research

The ability of our correlational study to predict anxiety severity based on amygdala glutamate activity is in line with previous research. Ullmann et al. (2019) found that decreases in amygdala glutamate activity reported by active offensive response rats was associated with a decrease in anxiety levels. While Ullmann et al. (2019) experimented on 28 male Sprague-Dawley rats, assessing their amygdala activity and anxiety levels, we longitudinally assessed these variables in students. The similarity of both our conclusions despite using different research designs suggests a generalized relationship exists between decreased amygdala glutamate activity and decrease anxiety levels.

Our correlational study confirmed the relationship between DHA intake and anxiety levels, reported by previous research. Hashemi et al. (2020), found that higher levels of consumption of DHA had a protective effect on anxiety levels. The methodology of our correlational study differed from that of Hashemi et al. (2020), in that our correlational study measured DHA intake by reading labels and estimating how much DHA we had consumed throughout the day, while Hashmi et al. (2020) measured the fatty acid profile of the participants red blood cells. Despite these differences in methodology, the previous results were replicated.

Our correlational study failed to confirm the relationship between interleukin-6 levels and anxiety level as reported by previous research. Moriarty et al. (2018) found that higher levels of interleukin-6 were found in subjects that experienced a variety of mental health challenges, including anxiety. The methodology of our correlational study differed from that of Moriarty et al. (2018) in that we measured interleukin-6 levels by taking our temperature daily while Molarity et al. (2018) measured interleukin-6 levels by taking blood samples. This could be the reason for the difference in results between the two studies.

References

Hashemi, S., Amani, R., Cheraghian, B., & Neamatpour, S. (2020). Stress and anxiety levels are associated with erythrocyte fatty acids content in young women. *Iranian Journal of Psychiatry, 15*(1), 47–54.

Moriarity, D. P., McArthur, B. A., Ellman, L. M., Coe, C. L., Abramson, L. Y., & Alloy, L. B. (2018). Immunocognitive model of depression secondary to anxiety in adolescents. *Journal of Youth and Adolescence*, *47*(12), 2625–2636. https://doi-org.libsecure.camosun.bc.ca:2443/10.1007/s10964-018-0905-7

Ullmann, E., Perry, S. W., Licinio, J., Wong, M. L., Dremencov, E., Zavjalov, E. L., ... & Tseilikman, V. (2019). From allostatic load to allostatic state—an endogenous sympathetic strategy to deal with chronic anxiety and stress?. *Frontiers in Behavioral Neuroscience, 13*, 47. doi:10.3389/fnbeh.2019.00047

Table 1

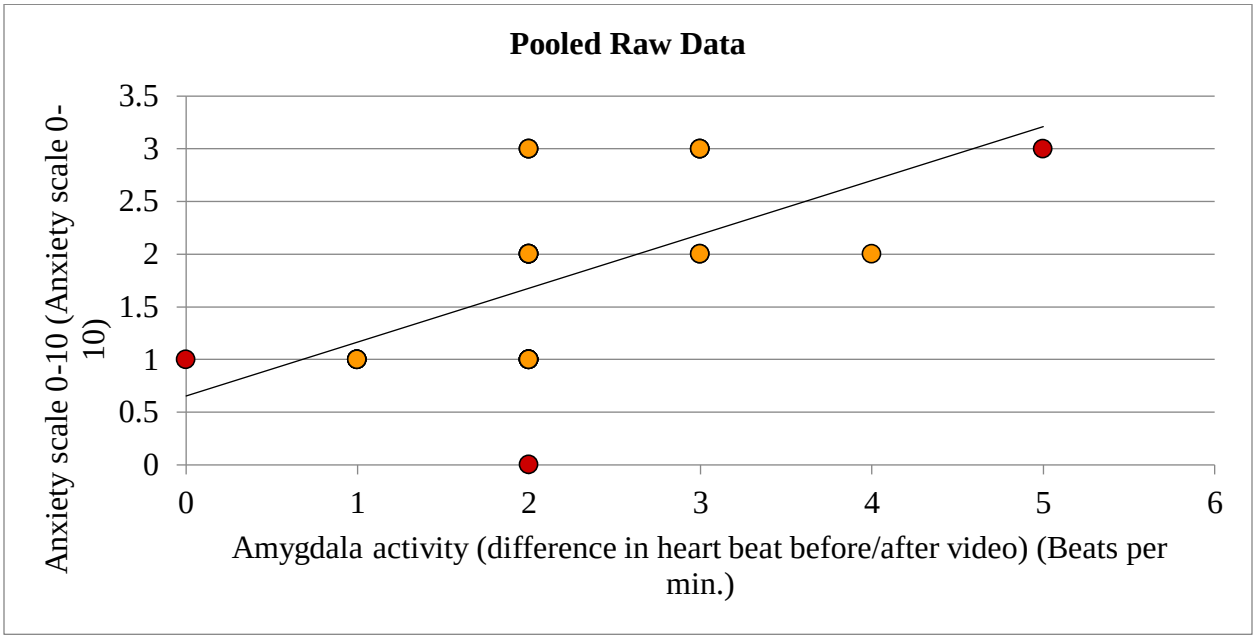
Correlation coefficient (r) values, with number of daily trials (n) per correlation in brackets.

Variables correlated	Participant #1	Participant #2	Pooled raw data	Pooled standardized data
Amygdala activity & Anxiety Scale	0.64(14)	0.43(14)	0.56(28)*	0.53(28)*
Intake of DHA & Anxiety Scale	-0.43(14)	-0.37(14)	-0.32(28)	-0.40(28)*
Interleuken-6 levels & Anxiety Scale	0.09(14)	-0.26(14)	-0.03(28)	-0.08(28)

* $p < .05$.

Figure 1

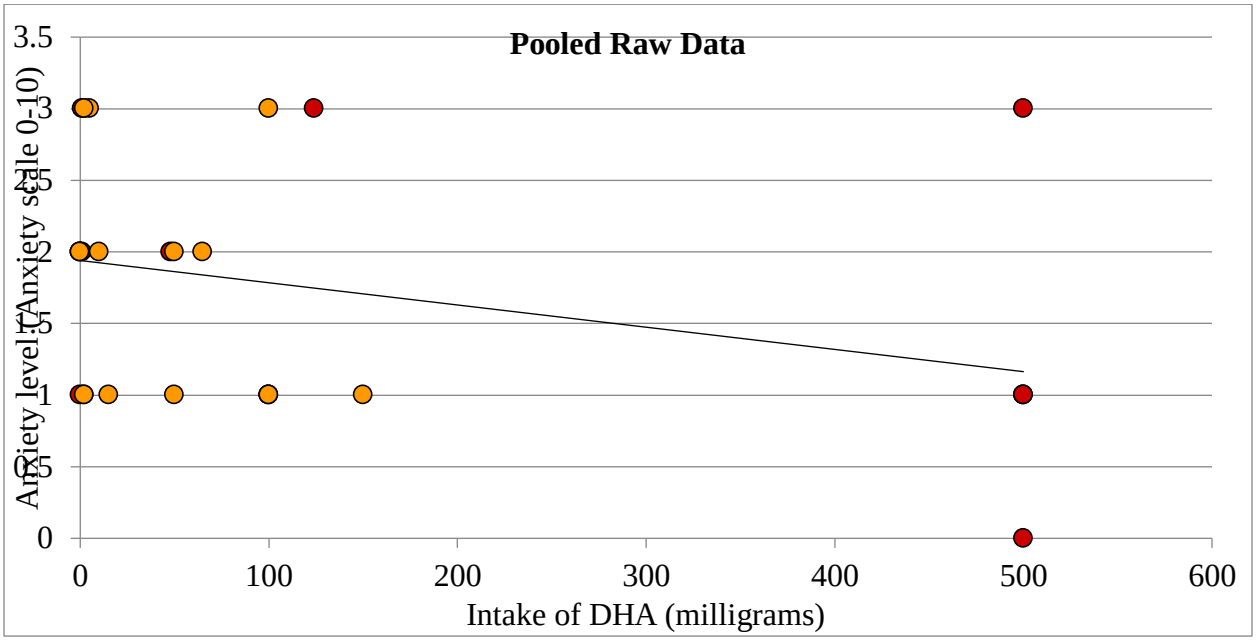
Scatterplot of Amygdala Activity and Anxiety Scale using pooled raw data across participants.



Marker color indicates which participant data is from: red = participant #1 and orange = participant #2. Some data might not be visible in the figure due to overlapping markers.

Figure 2

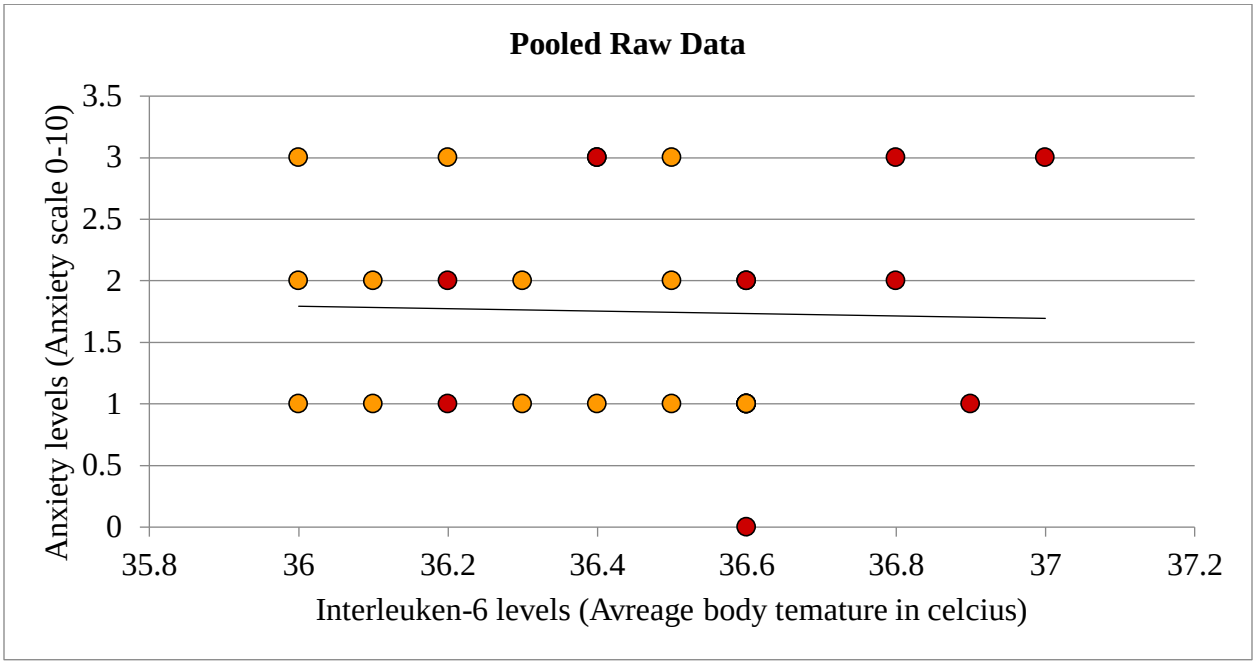
Scatterplot of intake of DHA and Anxiety level using pooled raw data across participants.



Marker color indicates which participant data is from: red = participant #1 and orange = participant #2. Some data might not be visible in the figure due to overlapping markers.

Figure 3

Scatterplot of Interleuken-6 levels and Anxiety Level using pooled raw data across participants.



Marker color indicates which participant data is from: red = participant #1 and orange = participant #2. Some data might not be visible in the figure due to overlapping markers.

Appendix

Table for measuring DHA levels in food

Table 2: Selected Food Sources of ALA, EPA, and DHA [29]

Food	Grams per serving		
	ALA	DHA	EPA
Flaxseed oil, 1 tbsp	7.26		
Chia seeds, 1 ounce	5.06		
English walnuts, 1 ounce	2.57		
Flaxseed, whole, 1 tbsp	2.35		
Salmon, Atlantic, farmed cooked, 3 ounces		1.24	0.59
Salmon, Atlantic, wild, cooked, 3 ounces		1.22	0.35
Herring, Atlantic, cooked, 3 ounces*		0.94	0.77
Canola oil, 1 tbsp	1.28		
Sardines, canned in tomato sauce, drained, 3 ounces*		0.74	0.45
Mackerel, Atlantic, cooked, 3 ounces*		0.59	0.43
Salmon, pink, canned, drained, 3 ounces*	0.04	0.63	0.28
Soybean oil, 1 tbsp	0.92		
Trout, rainbow, wild, cooked, 3 ounces		0.44	0.40
Black walnuts, 1 ounce	0.76		
Mayonnaise, 1 tbsp	0.74		
Oysters, eastern, wild, cooked, 3 ounces	0.14	0.23	0.30
Sea bass, cooked, 3 ounces*		0.47	0.18
Edamame, frozen, prepared, ½ cup	0.28		
Shrimp, cooked, 3 ounces*		0.12	0.12
Refried beans, canned, vegetarian, ½ cup	0.21		
Lobster, cooked, 3 ounces*	0.04	0.07	0.10
Tuna, light, canned in water, drained, 3 ounces*		0.17	0.02
Tilapia, cooked, 3 ounces*	0.04	0.11	
Scallops, cooked, 3 ounces*		0.09	0.06
Cod, Pacific, cooked, 3 ounces*		0.10	0.04

Tuna, yellowfin, cooked 3 ounces*		**0.09**	**0.01**
Kidney beans, canned ½ cup	**0.10**		
Baked beans, canned, vegetarian, ½ cup	**0.07**		
Ground beef, 85% lean, cooked, 3 ounces**	**0.04**		
Bread, whole wheat, 1 slice	**0.04**		
Egg, cooked, 1 egg		**0.03**	
Chicken, breast, roasted, 3 ounces		**0.02**	**0.01**
Milk, low-fat (1%), 1 cup	**0.01**		

Found on website https://ods.od.nih.gov/factsheets/Omega3FattyAcids-HealthProfessional/

Scary video https://www.youtube.com/watch?v=uZpMmP5EUEI