Proceedings of The National Conference
On Undergraduate Research (NCUR) 2016
University of North Carolina Asheville
Asheville, North Carolina
April 7-9, 2016

Physiological Measures and Genetic Predictors of Empathy

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Abstract

Over the past few decades, novel methods for measuring and quantifying empathy have been introduced to the scientific community. Many studies have used the "Reading the Mind in the Eyes" (RMET) test in order to obtain an objective empathy score for participants. While this measure may be useful, other methods have recently been introduced that allow scientists to further investigate the phenomenon of empathy in an objective manner. For example, facial electromyography (EMG) has been shown to be a valid method for measuring empathy using the Corrugator supercilii (CS) and Zygomaticus major (ZM) muscles to infer negative and positive affective states, respectively[1]. In addition, there have been several genetic determinants identified as having a relationship with empathetic responses. Chiefly, a single-nucleotide polymorphism (rs53576) of the oxytocin receptor gene (OXTR) has been found to be a significant predictor of empathetic behavior[2]. This study was designed to assess whether the presence of genetic predictors of empathetic behavior were correlated with the magnitude of EMG measures and RMET scores. DNA samples were collected for genotyping via a buccal brush and subjected to real-time polymerase chain reaction (PCR) for analysis. Facial EMG data were also collected from each participant. These data were then compared with RMET scores for each participant. It was hypothesized that individuals with a copy of the A allele at the location of interest on OXTR would show lower RMET scores, as well as lower mean EMG activation from baseline when compared to individuals that did not express this polymorphism. Results show a significant relationship between genotype and the magnitude of EMG measures in both the positive affective condition (p = .017) and negative affective condition (p = .014). The relationship between genotype and RMET scores was not found to be significant.

Keywords: Empathy, Genetics, Facial Electromyography

1. Introduction

Linking the disciplines of medicine and the humanities may enhance certain aspects of patient care such as empathy, compassion, altruism, and communication skills[3]. However, it has long been debated whether there would be a benefit in teaching empathy-related courses in healthcare programs such as nursing and medical schools due to a lack of objective, reliable data. This study aimed to understand the relationship between several different objective measures of empathy. Empathy is defined as an intellectual and emotional awareness and understanding of another's thoughts, feelings, and behavior[4]. Some studies have found that empathy contributes to higher quality patient care[5,6,7]. Adler (2002) asserts that patients' experience of feeling cared for reduces the secretion of stress hormones and allows a shift of the neuroendocrine system towards homeostasis. It is mentioned that the sociophysiological relationship between the physician and the patient provides a feedback loop, which can lead to an escalation or de-escalation of distress. Adler also suggests that a caring relationship results in economic benefits for the healthcare system. It is asserted that a setting in which the patient feels comfortable is more likely to result in a complete medical history, improved clinical judgment in regards to clinical testing, more accurate diagnoses, more cost-effective prescribing, better patient compliance, and better treatment outcomes. Additionally, Ong et al. (2000) examined physicians' patient-centeredness and communication during an oncological consultation, and assessed the patients' quality of life and satisfaction. They found that physicians' socio-emotional behaviors were related to both the visit-specific and global satisfaction of the patient. They also showed through multiple regression analyses that patients' quality of life and overall satisfaction were most clearly predicted by the quality of the affective interaction during the consultation. Additional studies have produced similar findings; for example, Zachariae et al. (2003) asked cancer patients to report satisfaction, distress, cancer-related self-efficacy, and perceived control of their disease both prior to and following a consultation at an outpatient oncology clinic. Patients were also asked to rate the physicians' communicative behaviors by responding to the patient-physician relationship inventory (PPRI). The results found that higher PPRI scores of physician empathy and attentiveness were associated with increased patient satisfaction, self-efficacy, and reduced emotional distress after the consultation.

Several studies have discovered a trend of declining empathy in healthcare professionals and students as they progress through their careers[8,9,10,11,12,13,14]. Hojat et al. (2004) examined changes in empathy in medical students by administering the Jefferson Scale of Physician Empathy (JSPE) at the beginning and end of their third year. The study found that there were statistically significant declines for 5-items on the scale, as well as significant declines in total scores after the post-test. They suggest that the downward trend indicates that empathy may be amendable to change during medical school. Likewise, Chen et al. (2007) found that there were significant declines in empathy from students in their preclinical years to students in the clinical years, using the same scale. Additionally, Nunes et al. (2011) used the JSEP to observe changes in first year students studying dentistry, pharmacy, medicine, veterinary medicine, and nursing. Following the post-test procedures, results showed mean empathy scores declined in all 5 groups—with medical, dental, and nursing students showing a statistically significant decline in empathy scores. Thomas et al. (2007) suggest that distress and well-being are factors that may have a role in the decline in empathetic behavior in healthcare students. Their study found that burnout had a negative correlation, and well-being had a positive correlation with student empathy scores. They suggest that efforts should be made to reduce distress in students in order to promote student well-being—which may enhance aspects of medical professionalism. Despite the existing data regarding the trend of declining empathy in healthcare students, the debate continues whether empathy-related coursework should be implemented into curriculum. Some research argues that empathy decline is not as common as the data suggests[15]. Colliver et al. (2010) reviewed 11 studies that suggest empathy declines during healthcare training. They bring the methodology of these studies into question; particularly, they assert that instruments used to measure empathy are primarily self-reports and are too subjective. It is also noted that there is a lack of clarity in what these reports are actually measuring. Additionally, data suggesting that empathy-related coursework may result in increased empathetic behavior in healthcare professionals is limited. Spiro (1992) provides a commentary on this issue, and argues for the importance of empathy education in medical school[16]. He argues that strengthening empathy relies on experience; and, for students, this experience can be attained through novels, fiction, stories, and paintings. However, experimental evidence to support this claim is lacking. Brunero et al. (2010), however, examined the effectiveness of empathy training in postgraduate and/or undergraduate nurses. They reviewed evidence from 17 studies that met the exclusion criteria and found that 11 of which showed statistically significant improvements in empathy scores[17]. They suggest these findings demonstrate that it is possible to increase empathetic behavior through education.

In order to overcome objections regarding empathy training in healthcare, it is necessary to have a means of empirically collecting empathy-related data objectively and reliably. Several methods for measuring empathy objectively in test subjects have been proposed—including both perception-based cognitive measures as well as physiological measures. The "Reading the Mind in the Eyes" test (RMET) is one cognitive measure that has been used in several research studies in order to obtain an objective empathy score in participants[18,19,20,21,22]. Baron-Cohen and Wheelwright (2001) have found that this test was successful in differentiating adults with Asperger syndrome or high-functioning autism from controls; asserting that because these individuals were not impaired on the control tests that this measure is valid for identifying subtle impairments in social intelligence in otherwise normally intelligent adults. It has also been found that individuals with borderline personality disorder score higher on the RMET than healthy controls[23]. This is in-line with previous research suggesting individuals with borderline personality disorder have heightened sensitivity to negative emotional cues[24]. These findings highlight the potential medical applications of this test.

Physiological measures may also be used to measure empathy objectively. This may be done using fMRI equipment; however this method is prohibitive due to cost and time constraints. Another method that has been shown to be a valid measure of empathy is facial electromyography (EMG). It has been noted that the measurement of facial muscle activity is relevant for empirical research on empathy because of the association between these muscles and the expression of emotion[25,26]. Additionally, Neumann and Westbury (2011) provide an exhaustive review of the psychophysiological methods for measuring empathy, among which is facial EMG. They assert that activity of the Corrugator supercilii muscle (CS) is indicative of a negative affective state, while activity of the Zygomaticus major muscle (ZM) is indicative of a positive affective state. This literature also discusses the Perception-Action Model (PAM), which is a proposed model for interpreting results in psychophysiological studies of empathy. In the PAM, the target's affective state is perceived by the viewer and thus activates representations in the individual that are relevant to the target's situation and affective state. This response primes the associated autonomic and somatic responses in the individual as they view the target. Therefore, empathy-inducing stimuli should produce autonomic and somatic responses in the viewer that reflect their interpretation of the target's affective state. These responses can be measured using facial EMG[1]. Indeed, it has been found that individuals who score high on measures of emotional empathy show higher CS activation when viewing faces that displayed a negative affective state, and higher ZM activation when viewing faces that displayed a positive affective state[27].

Additionally, studies that pair facial EMG data with functional MRI data have shown that facial EMG is a valid measure for inferring emotional states based on the mirror-neuron system (MNS) theory of empathy[28,29]. Likowski et al. (2012) have found that ZM responses to positive affective expressions, as well as CS responses to negative affective expressions had a significant correlation with activations in the right inferior frontal gyrus (IFG), right supplementary motor area (SMA), and the left cerebellum. Furthermore, strong ZM reactions to happy faces were associated with increased activity in the right caudate, right middle temporal gyrus (MTG), and the left posterior cingulate cortex (PCC). Additionally, CS responses to angry facial expressions were correlated with the right hippocampus, the right insula, and the right superior temporal sulcus (STS). The researchers note that the correlated regions are areas involved in the perception and execution of facial movements and their associated action representations. The researchers also found associations between mimicry and brain regions involved with emotional processing. The study showed co-activations in the insula—which connects action representation regions with the limbic system[30]. Additionally, the study found a connection between the caudate and the cingulate cortex—which are involved in the processing of positive and negative emotional content[31,32]. These results are in-line with the MNS theory of empathy. Existing literature suggests that the function of the MNS is to decode and understand other people's actions[30,33,34]. Carr et al. (2003) suggest that the activation of brain areas involved with emotional content and action representation allow the individual to simulate and recognize emotional content; and therefore empathize with the target.

There have also been several genetic determinants identified as having a relationship with empathetic responses. Chiefly, a single-nucleotide polymorphism (rs53576) of the oxytocin receptor gene (OXTR) has been found to have a significant relationship with empathetic behavior[2,35]. Using the RMET and a self-report measure, Rodrigues et al. (2009) found that individuals with one or two copies of the A allele (AG/AA) display lower behavioral and dispositional empathy when compared to individuals with a homozygous G allele (GG). Likewise, Smith et al. (2014) examined differences in empathic concern based on OXTR genotype. Their study genotyped 51 male participants for rs53576 in OXTR, and had them view a social interaction which contained high levels of individual distress and apparent physical pain. The results found that individuals with the homozygous G allele showed increased sympathetic arousal in response to the media when compared to individuals who were A allele carriers. Results also showed that GG homozygotes expressed greater levels of empathic concern. Additionally, Domes et al. (2007) have found that individuals who receive administration of intranasal oxytocin show improved scores on the RMET when compared with a placebo-control[36]. This finding further supports the theory that oxytocin may play a role in producing empathetic behavior.

With the accuracy and reliability of self-report measures coming into question with regards to studying empathy, it is imperative that the efficacy of the proposed objective measures be tested. In theory, individuals who express the homozygous G allele in rs53576 should show higher mean EMG activation from baseline, as well as higher scores on the RMET. Conversely, individuals who are carriers for an A allele in rs53576 should show lower mean EMG activation from baseline, as well as lower scores on the RMET. The use of objective measures allows for decreased response bias, and would assist in formulating a more complete and convincing model for studying empathy empirically. With no end in sight to the continuing debate on the role of empathy in healthcare and the effectiveness of empathy training in healthcare professionals, it is of the utmost importance to develop an empirical model for studying empathy objectively in order to dispel objections from opponents. This study assesses the relationship between the proposed objective measures of empathy; and the results may be useful in determining the validity of said measures in future empathy studies.

2. Methods

2.1. Participants

Participants were recruited from a large urban university in the western United States. Many of the subjects participated in order to earn credit for an introductory psychology course, however all students had the opportunity to participate in various other studies or alternative activities in order to receive research participation credit. Data were collected from 71 students for analysis (31 males, 40 females). However, only data from 61 participants were able to be used in the analyses (28 males, 33 females) due to incomplete data sets and/or errors during the collection process. All participants were treated in accordance with the American Psychological Association's guidelines for human research[37].

2.2. Materials

Participants were provided with forms to collect demographic information such as age, ethnicity, gender, handedness, as well as the date and time of day that the study was conducted. A DNA sample was collected from each participant using a buccal brush. DNA samples were then purified and subjected to real-time polymerase chain reaction (PCR) for amplification and analysis. TaqMan® SNP genotyping assays (Applied Biosystems, Foster City, CA, http://www.appliedbiosystems.com) were used to genotype the SNP marker rs53576 [Celera ID: C_3290335_10] on OXTR. All real-time PCR reactions were performed using an Eppendorf Mastercycler® ep *realplex* system (SABiosciences™).

Facial EMG data were collected using BIOPAC® physiological data acquisition units. EL254s reusable gel-electrodes were connected to each facial muscle and SS1LA adapters in order to collect EMG data from the ZM and CS muscles using the BIOPAC® units. An additional EL254s electrode was used as a ground reference. Physiological data were recorded and analyzed using Acq*knowledge*® software (v 4.0.3).

In order to elicit an emotional response in participants during the facial EMG task, several media clips were shown during this phase. First, participants viewed a clip of a man at a bus stop that starts laughing uncontrollably and makes the others around him laugh as well (Video A). This clip was selected because it is designed to produce a positive affective state in the viewers, and it clearly displays several individuals' facial expressions as they laugh and smile. This segment was followed by showing the participant a relaxing video of ocean scenery in order to allow the individual to recover from the positive affective state before moving on to the next segment (Video B). The final segment included a short clip of a depressed teenager and an interaction with her mother (Video C). This clip was selected because it is designed to produce a negative affective state in the viewer, and also clearly displays the negative facial expressions of the actors. Electrode connections were assessed between each video clip to ensure proper signal transmission. This method follows a similar protocol to those used in previous empathy studies using film clips and facial EMG[38]. Although this method follows the protocol set forth by De Wied et al. (2012), it is important to note that alternative film clips were used in the current study, because the clips used by De Wied et al. could not be obtained. Therefore, the resulting data should be interpreted with caution.

Objective empathy data were also acquired using the RMET. This measure is a 36-item test designed to assess participants' ability to infer the affective state of a pictured individual by viewing only their eyes. For each question, participants were shown a picture of an individual's eyes as they expressed a specific emotion. Each participant then selected one response from the four options given. A higher score on the RMET is believed to be indicative of higher empathetic responding. This measure has commonly been used in previous empathy studies; and has been shown to have good test-retest reliability[39].

2.3. Procedure

Students were greeted and given a copy of the informed consent and demographic forms upon arrival to the research location; and the expectations of the study were explained to them. Participants had the right to withdraw from the study at any time with no penalty. Once each participant read and signed the informed consent form, they were given a copy to keep with them.

Facial EMG data were collected from each participant by placing 4 mm electrodes on the CS and ZM muscles to measure negative affective responses and positive affective responses, respectively. Participants were then shown the three short clips that are designed to elicit emotional responses during this phase of the experiment. First, participants viewed video A. This segment was followed by viewing video B, in order to allow the participant to recover from the positive affective state before moving on to the next segment. Participants then viewed video C. Upon completion of this phase, participants were detached from the physiological recording equipment and allowed to remove any excess gel left on their skin by the electrodes. Each participant was then escorted into a separate room and asked to complete the RMET.

Upon completion of the objective measures of empathy, DNA data were collected from each participant via a buccal brush sample. Each subject was instructed on how to properly obtain a DNA sample using the buccal brush, and a researcher supervised each DNA collection process to ensure accuracy of the procedure. Following completion of all testing, participants were debriefed as to the purpose of the study and were encouraged to ask any questions. A copy of the informed consent form with the researchers' contact information was made available to each participant so that they could follow up on the results of the study if they desired.

Each DNA sample was purified and refrigerated for storage, and then subjected to TaqMan® genotyping assays and real-time PCR for amplification and analysis. Results from the real-time PCR analysis allowed for determination of OXTR genotype for each subject. Facial EMG, RMET, and DNA data were then analyzed in order to determine if there was a significant relationship between these objective measures of empathy.

3. Results

This study was designed to assess the relationship between several proposed objective measures of empathy—including facial EMG, RMET, and the presence of rs53576 in OXTR. Specifically, this study assessed whether the presence of an A allele in OXTR resulted in lower RMET scores as well as lower mean EMG activation from baseline. Facial EMG data were assessed by quantifying mean facial muscle activation [in mV] during a ten second portion of interest from each video clip, and were reported as a proportion of baseline values for each participant. The baseline values were determined by assessing mean EMG activation during the first ten seconds of the positive affective video clip, and the last ten seconds of the recovery video clip—where no emotional response should have taken place. Mean EMG activation was then assessed for each individual in each affective state. RMET scores were reported as a numerical value out of 36 possible correct answers. DNA data were reported as a nominal variable—with the presence of the SNP rs53576 indicated by a response of "A(+) genotype," and the lack of an A-allele indicated by a response of "GG genotype."

Data were analyzed using multivariate and discriminant analyses in order to determine if a significant relationship existed between the proposed objective measures of empathy, as well as if the dependent variables [RMET scores, mean CS activation, and mean ZM activation] could successfully predict group membership for the independent variable [A(+) genotype or GG genotype]. Results of the multivariate analysis showed a significant effect of genotype on EMG activation in both the positive affective state [$F(1, 59) = 6.008$, $p = .017$, $\alpha = .05$] and negative affective state [$F(1, 59) = 6.366$, $p = .014$, $\alpha = .05$] (see Figure 1).

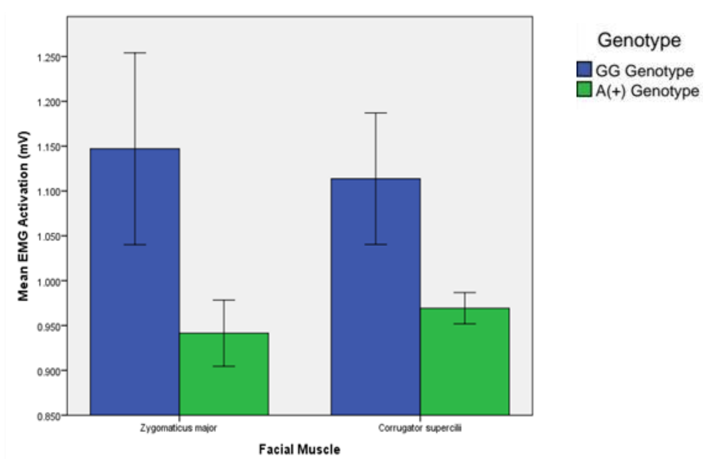


Figure 1. Comparison of mean EMG activation by genotype for each facial muscle. Error bars represent (+/-) 2 SE.

Results of this test did not show a significant relationship between genotype and RMET scores [$F(1, 59) = .153$, $p = .697$, $\alpha = .05$] (see Figure 2).

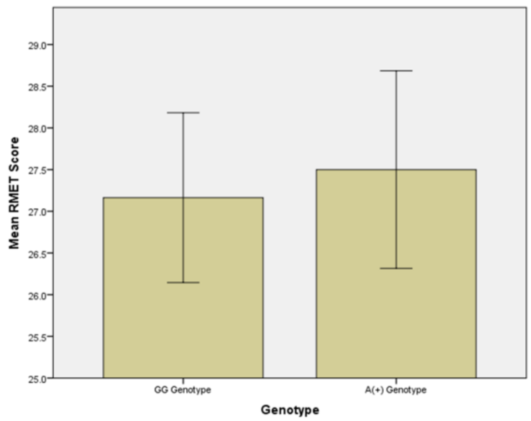


Figure 2. Mean RMET scores by genotype. Error bars represent (+/-) 2 SE.

The discriminant analysis showed that scores for the three dependent variables taken collectively were able to predict correct group membership for genotype 68.9% of the time [$r = .367$, Wilks' $\lambda = .866$, $p = .04$]. Gender effects were not shown to be significant for any of the variables included in the analysis. Descriptive statistics for the sample used in the study can be seen in Table 1.

Table 1. Descriptive statistics for the sample used in the study.

Group Statistics

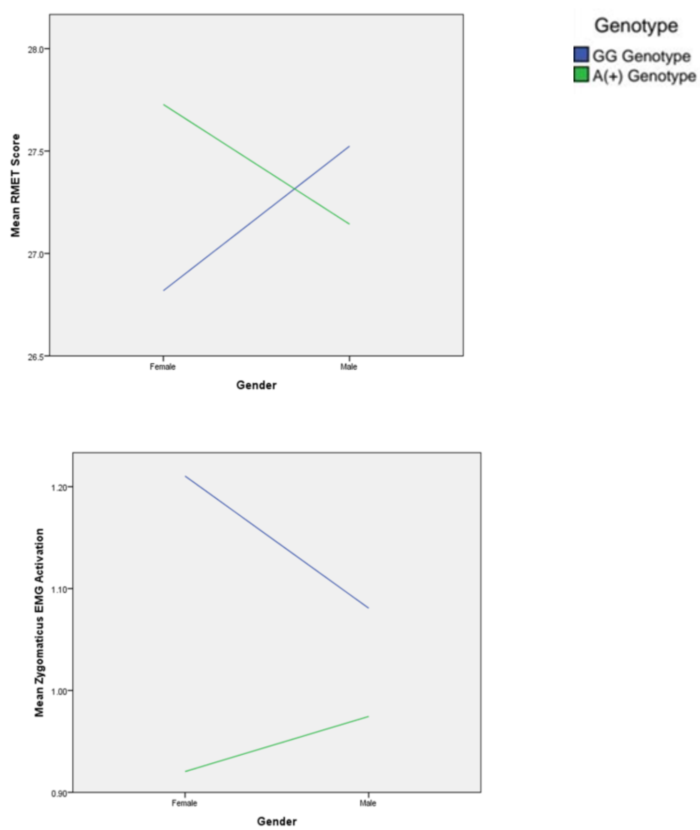
Genotype		Mean	Std. Deviation	Valid N (listwise)	
				Unweighted	Weighted
GG Genotype	RMETScore	27.1627907	3.30893619	43	43.000
	Zratio	1.1470649	.35061415	43	43.000
	Cratio	1.1136656	.24032447	43	43.000
A(+) Genotype	RMETScore	27.5000000	2.38253449	18	18.000
	Zratio	.9414681	.07831520	18	18.000
	Cratio	.9693479	.03707218	18	18.000
Total	RMETScore	27.2622951	3.04905253	61	61.000
	Zratio	1.0863970	.31101130	61	61.000
	Cratio	1.0710800	.21265705	61	61.000

4. Discussion

The results of this study would suggest that the presence of the SNP rs53576 on OXTR does seem to play a role in empathetic responding. However, the precise role of OXTR in empathetic responding remains unclear. While it was shown that genotype clearly had an effect on the magnitude of EMG responses (see Figure 1), genotype was not found to be a significant predictor of RMET scores (see Figure 2). The finding for RMET scores is in disagreement with the results of Rodrigues et al. (2009). It is possible that this finding may be due to a small sample size and large amount of variance within-groups in the current study. It is important to note that the sample size used in the study by Rodrigues et al. consisted of 192 participants, while the current study consisted of data from only 61 participants. Hong and Park (2012) have asserted that testing a single-nucleotide polymorphism marker requires a sample size of 248 or larger in order to produce the statistical power that is necessary to obtain reliable results[40]. Therefore, the results of the current study should be interpreted with caution, and future studies should include a larger sample size to determine why there is a discrepancy in these results. It is possible that errors made in allelic testing and genotyping may have also contributed to the disagreement between the findings of the current study and those of Rodrigues et al.

Interestingly, RMET scores and EMG measures do not seem to be in agreement, despite both measures being shown to be valid measures of empathy in previous studies. It may be proposed that each measure is not actually quantifying the same phenomena, but rather they are measuring responses from separate brain systems that may be independent of one another. For example, the RMET may be quantifying a brain response that is purely cognitive, while EMG measures may quantify a physiological or emotional response. While both of these components may be considered valid measures of "empathy" in their own respect, it is important to consider here that what we term "empathy" may actually be broken down into separate components—including both cognitive and physiological components that may be independent of one another. This proposal is in-line with the findings of Batson et al. (2009)[41]. Batson found that the term empathy is being used to describe at least 8 separate, potentially distinct phenomena. This finding provides support to make the proposition that the phenomenon of empathy is made up of several different components, and each measure of empathy may be specific to a separate component. This would explain the disagreement in RMET scores and mean EMG activation in the current study. It is possible that the RMET is exclusive to measuring a cognitive aspect of empathy, while EMG measures quantify a physiological response to another's emotions. While these components are potentially independent of one another, each component may still be thought to contribute to what we term "empathy."

While results of this study did not show a significant effect of gender on empathy measures, this is believed to be due to a small sample size with large variance. The data would actually suggest a trend towards significance (see Figure 3).



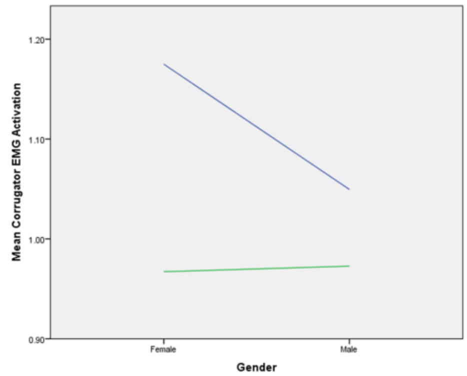


Figure 3. Mean empathy scores by gender. The data suggest a trend toward significance for an interaction between genotype and gender.

It appears that genotype differences produce greater effects in the female group when compared to the male group on RMET scores and EMG measures. This is in-line with previous research indicating gender differences in stress-reactivity and the interaction between OXTR genotype and phenotype[42,43,44,45]. It is also interesting to note that while individuals with an A allele at the location of interest on OXTR generally scored lower on all measures of empathy, this had the opposite effect in females with regard to RMET scores. This may be indicative of an interaction between genotype and gender for OXTR. It is recommended that future investigations studying the effects of gender on empathy include a larger sample size, particularly if genetic data will also be included in the analysis. This will reduce the effects of error and large variance within-groups, and produce more reliable results.

The findings of this study may be useful in the development of a more objective model for studying empathy. While these results should be interpreted with caution due to a small sample size, it appears that rs53576 does play a role in empathetic responding based on the significant relationship between genotype and EMG measures. It is encouraged that future studies attempt to further distinguish the different components of empathy so that we may have a better understanding of the systems that make up this phenomenon, as well as a better understanding of the tools that we use to measure it. Developing a widely-accepted, objective model for studying empathy could be monumental for making progress in this area of research as well as healthcare outcomes.

5. Acknowledgements

I would like to thank Dr. Jason Fritzler and Dr. Barbara Trask from the WSU Department of Microbiology and Zoology (respectively) for their assistance with methods for DNA data collection and analysis. Additionally, I would like to thank the Office of Undergraduate Research for providing the necessary funding so that this investigation could be conducted. Finally, I would like to give a special thanks to my research mentor Dr. Lauren Fowler, for her unbounded dedication to helping me be successful in my academic pursuits.

6. **References**

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