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Fermented foods, neuroticism, and social anxiety: An interaction model

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ABSTRACT

Animal models and clinical trials in humans suggest that probiotics can have an anxiolytic effect. However, no studies have examined the relationship between probiotics and social anxiety. Here we employ a cross-sectional approach to determine whether consumption of fermented foods likely to contain probiotics interacts with neuroticism to predict social anxiety symptoms. A sample of young adults (N=710, 445 female) completed self-report measures of fermented food consumption, neuroticism, and social anxiety. An interaction model, controlling for demographics, general consumption of healthful foods, and exercise frequency, showed that exercise frequency, neuroticism, and fermented food consumption significantly and independently predicted social anxiety. Moreover, fermented food consumption also interacted with neuroticism in predicting social anxiety. Specifically, for those high in neuroticism, higher frequency of fermented food consumption was associated with fewer symptoms of social anxiety. Taken together with previous studies, the results suggest that fermented foods that contain probiotics may have a protective effect against social anxiety symptoms for those at higher genetic risk, as indexed by trait neuroticism. While additional research is necessary to determine the direction of causality, these results suggest that consumption of fermented foods that contain probiotics may serve as a low-risk intervention for reducing social anxiety.

1. Introduction

Social anxiety disorder (also known as social phobia) is the third most prevalent psychiatric disorder with lifetime prevalence estimates as high as 10.7% (Wittchen et al., 1999; Veale, 2003; Kessler et al., 2012). This disorder is defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as the experience of significant distress or impairment that interferes with ordinary routine in social settings, at work or school, or during other everyday activities (American Psychiatric Association, 2013). As a result, social anxiety disorder can negatively affect many areas of life including dating, school, work, and family relations, with subthreshold social anxiety showing almost the same level of impairments in daily life (Wittchen et al., 2000).

Phobias have been shown to run in families (Hettema et al., 2001). Although it is not clear exactly what is inherited, vulnerability to social phobia is associated with fundamental personality traits such as neuroticism, defined as the general tendency to experience negative emotions such as nervousness, anger, envy, guilt, and depressed mood (Matthews and Deary, 1998). In fact, according to a recent large-scale twin study, genetic factors that influence individual variation in neuroticism appear to account almost entirely for the genetic vulnerability to social anxiety disorder (Bienvenu et al., 2007).

Although treatment for social anxiety disorder typically consists of cognitive-behavioral therapy or pharmacotherapy with selective serotonin reuptake inhibitors (Veale, 2003), more recently there has been increased interest in understanding how nutritional factors, such as probiotic intake, influence psychiatric disorders (Logan and Katzman, 2005; Forsythe et al., 2010; Dinan and Quigley, 2011; Bested et al., 2013a, 2013b, 2013c; Foster and Neufeld, 2013; Wall et al., 2014). Probiotics are defined as “live micro organisms, which, when administered in adequate amounts, confer a health benefit on the host” (FAO/WHO, 2001). Preclinical studies have demonstrated potential gut-brain pathways that allow gut microbiota to exert anxiolytic effects (see Mayer et al., 2014). For example, using mouse models Bravo et al. (2011) demonstrated that ingestion of the lactic acid bacteria *Lactobacillus rhamnosus* resulted in vagus nerve dependent anxiolytic behavioral effects and modulation of GABA receptor expression. Similarly, Bercik et al. 2010, 2011 have shown that probiotic treatment can minimize anxiety induced by gut inflammation and these anxiolytic effects were associated with changes in brain derived neurotrophic factor and dependent on the vagus nerve.

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A recent study in humans has shown that consumption of a fermented milk product containing a combination of probiotics (*Bifidobacterium animalis*, *Streptococcus thermophiles*, *Lactobacillus bulgaricus*, and *Lactococcus lactis*) can modulate brain activity (Tillisch et al., 2013). After four weeks of consuming the fermented milk product, there was a reduction in brain activity in a network of areas, including sensory, prefrontal, and limbic regions, while processing negative emotional faces. Importantly, a control group that ingested a non-fermented milk product showed no such changes in brain activity, suggesting that the probiotics in the fermented milk were responsible for the modulation in brain activity. This study demonstrates that fermented foods containing probiotics can alter how the human brain processes negative social stimuli.

Clinical trials have also demonstrated anxiolytic effects of probiotics in humans, but not specifically in those with social anxiety. In a study of patients with chronic fatigue syndrome, ingestion of *Lactobacillus casei* was associated with decreased scores on the Beck Anxiety Inventory (Rao et al., 2009). Similarly, adminstration of the prebiotic trans-galactooligosaccharide, which promotes the growth of indigenous beneficial gut bacteria such as Lactobacilli, resulted in decreased scores on the anxiety subscale of the Hospital Depression and Anxiety Scale (HADS-A) in patients with irritable bowel syndrome (Silk et al., 2009). Improvement in HADS-A scores has also been shown in healthy participants from the general population following ingestion of a probiotic formulation consisting of both *Lactobacillus helveticus* and *Bifidobacterium longum* (Messaoudi et al., 2011).

The current study sought to address several open questions regarding the anxiolytic effects of fermented foods that likely contain probiotics. No previous studies have examined the specific relationship between fermented food consumption and social anxiety. Furthermore, it is unclear how natural patterns of fermented food consumption relate to anxiety in humans because all existing studies are clinical trials in which consumption of probiotics was controlled. In addition, no studies have investigated whether consumption of fermented foods that likely contain probiotics can moderate the relationship between neuroticism, a known genetic risk factor for certain anxiety disorders, and anxiety symptoms. Thus, in the current study, a cross-sectional approach was undertaken to examine whether consumption of fermented foods that likely contain probiotics was related to social anxiety in a population of young adults, and if so, to explore whether consumption of fermented foods interacts with neuroticism to predict social phobia symptoms. If this in fact the case, we hypothsize that young adults who are high in neuroticism will demonstrate lower levels of social anxiety if their fermented food intake is high when compared to those with low intake.

2. Methods

2.1. Participants

Data were collected as part of mass testing for introductory psychology classes at a medium-size public liberal arts university in Virginia which counted for partial fulfillment of a course requirement. Surveys were completed electronically using Qualtrics software by 732 students. All participants provided informed electronic consent. The study protocol was approved by the Protections of Human Subjects Committee, and the investigation was carried out in accordance with the Declaration of Helsinki.

2.2. Measures

2.2.1. Social Phobia and Anxiety Inventory (SPAI-23)

The Social Phobia and Anxiety Inventory (SPAI-23) is a 23-item abbreviated inventory to assess social anxiety and agoraphobia symptoms (Roberson-Nay et al., 2007). Participants respond using a 5-point scale ranging from 0 (never) to 4 (always) to indicate how frequently they experience symptoms related to social phobia (16 items) and agoraphobia (7 items). The social anxiety SPAI-23 Difference Score, which reflects a "pure" measure of social anxiety, is obtained by summing up the responses for each subscale separately and then subtracting the agoraphobia score (Cronbach's alpha=0.90) from the social phobia score (Cronbach's alpha=0.95).

2.2.2. Big Five Personality Inventory

The 44-item Big Five Inventory assesses the personality traits extraversion, agreeableness, conscientiousness, openness, and neuroticism (John and Srivastava, 1999). Participants respond using a 5-point scale ranging from 1 (strongly disagree) to 5 (strongly agree) to indicate how much a given characteristic applies to them. For the current study, the eight item neuroticism subscale was used (Cronbach's alpha=0.82).

2.2.3. Exercise frequency

Exercise frequency was assessed with a single item that asked: "how often do you exercise?" (see Appendix). Participants responded using a 4-point scale: 1 (never); 2 (1–3 times in the last month); 3 (1–3 times per week); and 4 (at least once per day). Scores were converted to monthly frequencies of 0, 2, 8, and 30.

2.2.4. Food frequency

To determine participants' consumption of foods, they were first asked to think of their food intake over the past 30 days (see Appendix). This was followed by a list of 10 items consisting of the following: 1.fruits and vegetables of all kinds, including fresh, canned, frozen, cooked, raw, and juices; 2. yogurt, 3. kefir, or food or beverages that contain yogurt; 4. soy milk, or foods or beverages that contain soy milk; 4. miso soup; 5. sauerkraut; 6. dark chocolate; 7. juices that contain microalgae; 8. pickles; 9. tempeh; and 10. kimchi. Participants were asked to indicate how often they consume each of the foods using the following 7-point scale: 1 (never); 2 (1–3 times in the past month); 3 (1–3 times per week); 4 (1–3 times per day); 5 (3–5 times per day); 6 (5–7 times per day); and 7 (more than 8 times per day). Scores were converted to monthly frequencies of 0, 2, 8, 60, 120, 180, and 240, respectively.

Given that the internal consistency of the nine fermented food items was high (Cronbach's alpha=0.89), a single score was derived as the mean per month consumption of the fermented food items.

2.3. Statistical analysis

Zero-order correlations between the SPAI-23 Difference Score and neuroticism, probiotics consumption, fruits and vegetable consumption, and exercise were calculated to examine bivariate relationships.

Before conducting the linear regression, the predictor variables were standardized (Dawson, 2014). Next, an interaction term was calculated by multiplying the standardized Neuroticism scores and the standardized IHS Fermented Food scores. A regression model was then constructed to predict the SPAI-23 Difference Score from Neuroticism, IHS Fermented Food, and their interaction (Neuroticism*IHS Fermented Food). Exercise frequency and fruit and vegetable consumption were controlled for statistically via inclusion in the model but were also examined as variables of interest. Age, sex, and race/ethnicity were also controlled for statistically via inclusion in the model.

3. Results

Of the 732 participants who completed the questionnaire, 22 were excluded due to missing data on key variables of interest, leaving a final sample size of 710 (445 female). These participants were between the ages of 18 and 38 years (M=19.1 years, S.D.=1.5). The sample was ethnically diverse (45% reported their race as Caucasian, 31% non-Caucasian, and 23% as multiracial).

Table 1
Means and distributions.

Measure	Mean	Median	S.D.	Range	Skewness	Kurtosis
SPAI difference score	19.47	18.00	10.36	−2.00–58.00	0.43	0.36
Neuroticism	23.77	24.00	6.32	8.00–40.00	0.09	−0.29
Fermented foods	9.91	2.37	24.51	0.00–240.00	6.48	51.65
IHS Fermented foods	0.86	0.69	0.57	0.00–2.68	0.65	−0.15
Fruits & vegetables	77.42	60.00	52.74	0.00–240.00	0.85	0.82
Exercise	12.70	8.00	11.12	0.00–30.00	0.79	−1.09

Note: Fermented foods, fruits & vegetables, and exercise are monthly frequencies; IHS Fermented Foods, inverse hyperbolic sine transformed fermented foods variable.

The means and distributions of the variables of interest are presented in Table 1. Skewness and kurtosis are presented to assess whether the variables used in the regression model were normally distributed. As can be seen in Table 1, the fermented foods variable is positively skewed and leptokurtic. After the fermented foods variable was inverse hyperbolic sine (IHS; Burbidge et al., 1988) transformed, all variables are normally distributed.

The zero-order correlations and *r*-squared values quantifying the bivariate relationships between the variables are shown in Table 2. Neuroticism was positively correlated with social anxiety, with those high on trait neuroticism having higher levels of social anxiety. Fermented food consumption was negatively correlated with social anxiety indicating that those who consume more fermented foods have lower levels of social anxiety. Both fruit and vegetable consumption and exercise frequency were negatively correlated with social anxiety. These correlations indicate that eating healthy and exercising more frequently is associated with reduced social anxiety.

The overall regression model testing the relationship between fermented foods, neuroticism, and other predictor variables with social anxiety symptoms was statistically significant, $F(9,700)=17.84$, $p<0.001$. Specifically, as shown in Table 3, the simple effects of exercise frequency, neuroticism, and fermented food consumption were statistically significant predictors of social anxiety. There was also a statistically significant interaction between neuroticism and fermented food consumption. To visualize the interaction between neuroticism and fermented food consumption, "low" and "high" values were calculated as one standard deviation above and below the mean (Dawson, 2014) for the neuroticism and fermented foods variables, and the predicted values of social anxiety were plotted for these combinations in Fig. 1. As can be seen in the figure, for those with low levels of neuroticism, predicted social anxiety does not differ as a function of levels of fermented food consumption. In contrast, for those with high levels of neuroticism, high fermented food consumption is associated with fewer social anxiety symptoms.

4. Discussion

Consistent with previous research on other types of anxiety (Rao et al., 2009; Silk et al., 2009; Messaoudi et al., 2011), the current results demonstrate that consumption of fermented foods likely to contain probiotics is negatively associated with symptoms of social anxiety in a sample of young adults. Moreover, the current paper is the first to demonstrate that consumption of fermented foods interacts with neuroticism to predict social anxiety symptoms. That is, those at higher genetic risk for social anxiety disorder, as indexed by high neuroticism, show fewer social anxiety symptoms when they consume more fermented foods. Because these findings are consistent with results from previous preclinical (Bercik et al. 2010, 2011; Bravo et al., 2011) and clinical trials suggesting that probiotics cause reduction in anxiety symptoms (Rao et al., 2009; Silk et al., 2009; Messaoudi et al., 2011), we hypothesize that the fermented foods assessed in the current study reduce anxiety because they contain probiotics. In combination with these studies (Rao et al., 2009; Silk et al., 2009; Messaoudi et al., 2011), the current results suggest that the probiotics likely found in the fermented foods assessed here may reduce symptoms of social anxiety directly as well as through reduction of negative affect associated with neuroticism. Importantly, we have shown evidence that the

Table 2
Zero-order correlations (r^2).

Measure	SPAI Diff	Neuroticism	IHSFermented	Fruits & veg	Exercise
SPAI Diff	–				
Neuroticism	0.38** (0.14)	–			
IHSFermented	−0.13** (0.02)	0.02 (0.00)	–		
Fruits & Veg	−0.12** (0.01)	−0.04 (0.00)	0.33** (0.11)	–	
Exercise	−0.16** (0.03)	−0.08* (0.01)	0.21** (0.04)	0.22** (0.05)	–

Note: Values of r^2 in parentheses; SPAI Diff, SPAI Difference score; IHSFermented, inverse hyperbolic sine transformed fermented foods variable; fruits & veg, fruits & vegetables.
* $p<0.05$.
** $p<0.005$.

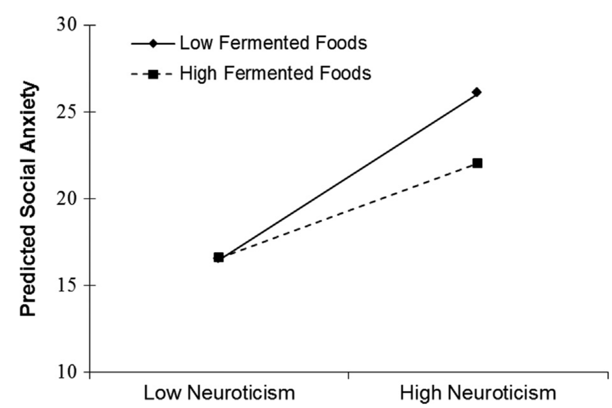

Fig. 1. Predicted social anxiety (SPAI-23 Difference Score) at low (−1 standard deviation) and high (+1 standard deviation) levels of neuroticism and probiotic consumption.

Table 3
Regression model predicting social anxiety.

Predictor	Effects on SPAI difference score			
	B (*CI*)	*SE*	*t*	*p*
Intercept	20.31 (18.76, 21.87)	0.79	25.68	< 0.001
Age	−0.36 (−1.06, 0.34)	0.36	−1.01	0.31
Sex	−0.26 (−2.76, 0.53)	0.76	−0.34	0.73
Ethnicity (White)	−1.11 (−2.58, 1.27)	0.84	−1.33	0.19
Ethnicity (Mixed)	−0.65 (−1.75, 1.23)	0.98	−0.67	0.51
Fruits & Vegetables	−0.43 (−1.19, 0.33)	0.39	−1.11	0.27
Exercise	−0.94 (−1.67, −0.20)	0.38	−2.51	0.012
Neuroticism	3.75 (3.03, 4.46)	0.36	10.30	< 0.001
IHSFermented	−0.98 (−1.74, −0.22)	0.39	−2.52	0.012
Neuroticism*IHSFermented (interaction)	−1.03 (−1.76, −0.30)	0.37	−2.77	0.006

Note: CI, 95% confidence interval; *SE*, standard error of the regression coefficient.

protective effects found in preclinical and clinical trials correspond with similar patterns in a naturalistic follow-up, suggesting that existing variation in fermented food consumption (i.e., within the range consumed in an uncontrolled setting) may partially explain variability in anxiety among vulnerable young adults.

Preclinical studies have suggested potential mechanisms for the positive effects of probiotics on psychiatric symptoms (Foster and Neufeld, 2013). Probiotics have been demonstrated to decrease intestinal permeability, reduce gut inflammation, reduce stress response via the HPA axis, restore BDNF levels, and alter GABA receptor expression (Foster and Neufeld, 2013). Anxiety symptoms are strongly linked to gastrointestinal (GI) symptoms in the general population (Haug et al., 2002), and diagnostic criteria for many anxiety disorders include GI-related somatic symptoms (American Psychiatric Association, 2013). Notably, these somatic complaints appear to resolve following treatment for the primary psychological symptoms with anti-depressants (for meta analysis, see Jackson et al., 2000). Studies have also shown improvement in GI symptoms following probiotic administration (e.g., Koebnick et al., 2003; Diop et al., 2008). As probiotics displace harmful species, the gut microbiome becomes beneficial to the host and results in improvements in mental well-being.

Evidence from brain imaging in humans has also indicated a potential mechanism for anxiolytic effects of fermented foods. After consumption of a fermented milk product for four weeks, participants were presented with negative emotional facial expressions and demonstrated reduced brain activity in a network of brain areas involved in processing these negative social stimuli (Tillisch et al., 2013). Because social phobia is associated with hyperreactivity in response to negative facial expressions (e.g., Evans et al., 2008), reduction of the overreactive brain response to negative social stimuli may serve as a potenial mechanism for the anxiolytic effect of fermented food. Because no such changes in brain activity were observed in a control group that consumed non-fermented milk, the results demonstrate that consumption of foods containing probiotics can result in measurable changes in emotional processing in the healthy brain (see also Schmidt et al., 2014). However, as noted by Selhub et al. (2014), because fermented milk contains peptides and other chemicals that could also influence brain activity, fermented foods may have anxiolytic effects above and beyond those accounted for by probiotics alone.

In addition to fermented foods, exercise was also found to be an independent predictor of social anxiety in the current study. This relationship corresponds to the findings from a recent clinical trial that demonstrated a reduction in social anxiety symptoms following two months of aerobic exercise (Jazaieri et al., 2012). These findings are also consistent with clinical trials across other anxiety disorder diagnoses (for review, see Asmundson et al., 2013) and with population-level correlations between regular exercise and lower neuroticism and anxiety (De Moor et al., 2006). The effectiveness of exercise is likely due to the fact that exercise reduces cortisol stress hormone response which is mediated by regulation of serotonin receptors (Stathopoulou et al., 2006). Moreover, exercise releases beta-endorphins which inhibit the central nervous system (Stathopoulou et al., 2006). Together, these mechanisms may help to decrease anxiety and improve mood, although more research is needed to understand this relationship (Asmundson et al., 2013)

The most common evidence-based approach for treating social anxiety is cognitive behavioral therapy (CBT) (Veale, 2003), but a selective serotonin reuptake inhibitor (SSRI) may also be prescribed (Ballenger et al., 1998). However, these established treatments may provide only a partial decrease in symptoms for many patients and may not reach enough patients in need. In a review of clinical trials of probiotics, no adverse effects were reported (Naidu et al., 1999). This suggests that probiotics can likely be safely used in conjunction with traditional therapeutic approaches for psychiatric disorders (Logan and Katzman, 2005). Because the use of alternative strategies such as exercise and probiotics have excellent safety profiles, and as a result are relatively low risk interventions, they may be recommended by any clinician as a complement to current strategies. Future research should investigate the use of fermented foods and probiotics in the treatment of social anxiety symptoms, both alone and as a supplement to cognitive behavioral therapy and/or pharmacotherapy.

4.1. Limitations

Although the findings from the present study are consistent with those from preclinical and clinical trial studies, there are limitations to this study. We assessed consumption of fermented foods likely to contain probiotics, but some of the foods consumed may not have actually contained active cultures. Thus, it is possible that something other than the probiotic content of the foods influenced social anxiety. In addition, because the current results were from a cross-sectional study, the direction of causality cannot be definitively determined from our results. It is possible that low levels of social anxiety causes increased consumption of fermented foods, or that an unmeasured variable causes both increased consumption of fermented foods and reduced social anxiety. Moreover, the use of a college student sample may limit the generalizability of the findings to the general population. Additionally, use of antidepressant or anxiolytic medication, or the use of probiotic pills and supplements was not assessed in the current sample. Future research should recruit a more diverse sample of participants in a prospective cohort study. In such a study, participants' probiotic intake could be manipulated over a period of time while assessing other healthful behaviors, such as consumption of healthful foods and exercise, as well as use of prescription medications. This approach would provide insight into how additional factors contribute to the relationship between fermented foods and social anxiety. However, because participants were not individually interviewed or tested, these questions were beyond the scope of the current study.

4.2. Conclusions

This study provides the first connection between natural fermented food consumption patterns and anxiety. Increased consumption of fermented foods likely to contain probiotics was associated with fewer social anxiety symptoms. This effect was qualified by an interaction with neuroticism; those who were highly neurotic showed fewer symptoms of social anxiety with greater consumption of fermented foods. Also of note, increased frequency of exercise was associated with decreased social anxiety. Taken together with the results of previous preclinical and clinical studies (Rao et al., 2009; Silk et al., 2009; Messaoudi et al., 2011; Tillisch et al., 2013), the current results suggest that fermented foods likely to contain probiotics may have a protective effect against social anxiety symptoms for those at higher genetic risk, as indexed by trait neuroticism. While a follow-up prospective cohort study or clinical trial is necessary to determine the direction of causality, these results suggest a possible clinical benefit of fermented foods, a low-risk intervention, on social anxiety.

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Appendix

For the following questions, think of your food intake over the past 30 days.

On average, how often have you consumed:

	More than 8 times per day	5–7 times per day	3–5 times per day	1–3 times per day	1–3 times per week	1–3 times in the last month	Never
fruits and vegetables of all kinds; fresh, canned, frozen, cooked, raw, and juices?							
yogurt, kefir, or food or beverages that contain yogurt?							
soy milk, or foods or beverages that contain soy milk?							
miso soup?							
sauerkraut?							
dark chocolate?							
juices that contain microalgae?							
pickles?							
tempeh?							
kimchi?							

How often do you exercise?

_At least once per day.

_1–3 times per week.

_1–3 times in the last month.

_Never.

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