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# Toward a Genetic Understanding of Dental Fear: Evidence of Heritability

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## Abstract

**Objectives—**Dental fear is a prevalent problem that impacts dental treatment-seeking behavior and thus oral, systemic, and psychological health. Among other important predictors, fear of pain has been shown to be a critical component of dental fear. While learning history (*id est*, past experience) is known to shape development and maintenance of dental fear and fear of pain, minimal work has addressed genetic etiological variables for these healthcare-related anxieties. With the aim of coming to a more complete conceptualization of dental fear, this study assessed the heritability of dental fear and fear of pain, and elucidated the role of genetics in the relation between the constructs.

**Methods—**Participants ($n$ = 1370; 827 female), ages 11 – 74 years ($M$ = 29.2, SD = 12.2), in a family-based cohort study completed measures of dental fear and fear of pain. Heritability and genetic correlation were estimated using likelihood-based methods under the variance components framework.

**Results—**Dental fear was 30% heritable ($p < 0.001$) and fear of pain was 34% heritable ($p < 0.001$). Notably, there was substantial genetic correlation between dental fear and fear of pain, rhoG = 0.67, suggesting they are genetically related, but likely are distinct phenotypes.

**Conclusions—**It is clear that, in addition to environmental factors, genetic influences are important in the etiology of dental fear and anxiety, and should be considered in future studies of

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fear and anxiety associated with dental treatment and, potentially, interventions aimed at reducing distress that is a barrier to dental treatment utilization.

**Keywords**

Anxiety; Fear; Dental Anxiety; Pain; Genetics; Heredity; Behavioral Sciences

## Introduction

Fear related to dental treatment is complex and can have significant implications for an individual's health and wellness. Approximately 45% of American adults report at least moderate levels of dental fear – and between 10% and 20% of American adults report high levels of fear[1-3]. Dental phobia and dental fear are associated with avoidance of dental visits and poorer oral health[4,5], which is predictive of worsened cardiovascular disease and diabetes, dissatisfaction with one's mouth, and lower perceived quality of life, self-esteem, and morale[6-8]. As with other types of anxiety, healthcare-related fears exist on a continuum[9], with treatment avoidance presenting in people who endorse a range of fear severity, not just in those with phobic levels[3]. Thus, fear related to medical and dental care (and associated treatment avoidance) is ubiquitous. Given that problem anxiety often is chronic[10], and that the treatment avoidance associated with dental fear can detrimentally impact health, understanding the etiology of this fear is important and may inform intervention. This understanding is growing; however, little is known about the role of genetics in the etiology of dental fear.

Like other fears and anxieties, dental fear is characterized by behavioral, cognitive, and physiological manifestations of distress, including avoidance, and is thought to be the product of conditioning, social learning, cognitive factors, and temperament, whose etiology varies across individuals[3]. Learning history, personality, and environmental determinants of dental fear have been studied for decades, but a complete understanding of the etiology of dental fear may also include genetic and biological variables, which have garnered much less attention. Results from a recent meta-analysis suggest that, generally, fears and specific phobias are heritable (*id est*, traits that are attributable, to some measurable extent, to the cumulative effect or contribution of genetic variation), and moderately so[11]. Early evidence suggests that dental fear, more specifically, may be partly the product of genetic factors. For example, dental fear has been shown to be heritable[12], with some researchers suggesting that the heritability is mediated via the inheritance of the personality trait neuroticism[13], and others suggesting that the heritability is mediated by a predisposition to pain sensitivity and/or local anesthetic insensitivity[14]. In fact, variation in the melanocortin-1 receptor (*MC1R*) gene, a gene associated with redheadedness, has been specifically identified as a predictor of dental fear and dental treatment avoidance[14].

Related to dental fear is fear of pain, defined as irrational dread of nociception associated with any number of pain-inducing stimuli (e.g., small cut, injection, broken arm[15-16]). Self-reported fear of pain is associated with fears about dental treatment and, notably, has been found to be a critical component of dental fear[17-19]. Indeed, the interplay of dental pain experience and dental fear is complex[9], as heightened dental pain sensitivity impacts fears



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about dental treatment and dental fear impacts the experience of dental pain[20-22]. Though dental pain and dental fear are intricately connected, fear of pain can maintain dental fear independent (*id est*, in the absence) of actual dental pain[3]. To our knowledge, no study has focused on fear of pain from a genetic perspective.

The aims of this study were to provide additional evidence for the heritability of dental fear and to, for the first time, determine the heritability of fear of pain. A further aim of this study was to determine the degree to which dental fear and fear of pain are genetically related, that is, to quantify the shared heritability of the two phenomena. Given existing research[12,13], it was hypothesized that self-reported dental fear/anxiety (Hypothesis 1) and fear of pain (Hypothesis 2) would be heritable. Drawing from the previously-observed correlation between the phenotypes[19], it also was hypothesized that dental fear/anxiety and fear of pain would have shared heritability (Hypothesis 3).

# Methods

## Participants

The present investigation utilized data from a large, family-based study of the Center for Oral Health Research in Appalachia, cohort 1 (COHRA1), in which participants also provided self-report ratings of dental fear/anxiety and fear of pain[23]. Written informed consent was obtained from adult participants and parents or legal guardians of child participants. Verbal assent was obtained from children who were capable of understanding and granting assent. The COHRA1 study design and all forms and protocols were approved by Institutional Review Boards of West Virginia University and the University of Pittsburgh, and study protocol was conducted in full accordance with the ethical principles outlined in the Declaration of Helsinki. Details regarding participant recruitment, inclusion/exclusion criteria, and data missingness/imputation are available in the Appendix.

There were 732 households enrolled in the COHRA1 study, which comprised 2,663 individuals (age range 0-74 years) from 740 biological families, all of whom were residing in rural Appalachia at the time of data collection, an area that is more socioeconomically disadvantaged and which suffers from poorer oral health as compared to the general USA population (see Appendix). Dental fear and fear of pain were assessed only for participants age 11 and above; thus, a total of 1,370 participants (60% female; age range 11-74 years, age $M$ = 29.2 years, SD = 12.2) were included in analyses for the current investigation (given the family-based study sampling strategy, and that recruitment specifically targeted families with young children, nearly half of the participants of the COHRA1 study were children younger than 11 years old). This sample included the following types of relative pairs: 480 parent-offspring, 146 sibling, 10 grandparent-grandchild, 31 avuncular (e.g., aunt-nephew pair), 41 half-sibling, 1 half-avuncular, and 16 first-cousin pairs (it is possible for a participant to belong to multiple types of relative pairs, and so covariance for all pairs of participants is modeled in a variance components framework, described below). The accuracy of biological relationships was confirmed using genetic marker data from a whole-genome SNP study[24] and standard relationship testing methods[25]. Due to the community-based recruitment strategy, some biological families spanned multiple households, whereas

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some households contained multiple biological families. Family size ranged from 2 to 20 individuals (*M* = 4.7 members; SD = 2.5).

### Assessment Instruments

The Dental Fear Survey (DFS) is a 20-item self-report measure of behavioral and physiological responses to dental care indicative of anxiety or fear (see Appendix for comment)[26]. The DFS contains three factor-analytically derived subscales: Behavioral Avoidance, Fear of Specific Dental Stimuli, and Physiological Arousal associated with dental treatment[26]. Responses to items are based on a 5-point Likert-type scale; the total score ranges from 20-100, with higher scores indicating greater dental fear. This widely utilized instrument has well demonstrated internal consistency, test-retest reliability, and predictive, convergent, and discriminative validity (Kleinknecht et al., 1984; McGlyn et al., 1987; Smith & Moore, 1984; Wilson & Sinisko, 1997).

The Fear of Pain Questionnaire-9 (FPQ-9) is a 9-item, self-report measure of pain-related fear[15,27]. The instrument is comprised of three subscales: Fears of Severe Pain, Minor Pain, and Medical/Dental Pain. Respondents rate, on a 5-point Likert scale, how fearful they are of experiencing the pain associated with each of a number of painful experiences (e.g., getting a paper cut, breaking your leg, having a tooth pulled). Subscale scores range from 3-15 and the total score ranges from 9-45; higher scores indicate greater degree of fear. Like the DFS, the FPQ-9 is psychometrically strong; the instrument is reliable and valid (Osman et al., 2001; Roelofs et al., 2005).

### Procedure

The individuals and their families included in the COHRA1 study participated in a larger protocol involving interviews, questionnaires, including the DFS and FPQ-9, oral health assessment, microbiological assessment, and DNA collection. The complete study protocol has been outlined elsewhere and quality of collected self-report data for this study previously has been elucidated[28,29].

### Statistical Analyses

Analyses were performed using family-based maximum likelihood methods under the variance components framework. This heritability estimation method, implemented in Sequential Oligogenic Linkage Analysis Routines (SOLAR; Department of Genetics, Texas Biomedical Research Institute, San Antonio, Texas)[30], previously has been applied to dental traits in the COHRA1 sample[31,32] and other complex human traits[33]. Details of the variance components model and its application to the data are available in the Appendix.

The heritability of a single phenotype and/or the genetic correlation between two phenotypes was estimated by comparing phenotype assessments across all pairs of relatives and non-relatives in the sample, while accounting for the expected genetic sharing between the pairs (*id est*, that parents-offspring share 50% of their genetic material, siblings share 50%, half-siblings share 25%, and unrelated individuals share 0%). Heritability was interpreted as the proportion of variation in the phenotype attributable to the cumulative effects of all genetic factors. In other words, heritability indicated the degree of genetic contribution to a

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phenotype. Genetic correlation was interpreted as the degree to which two phenotypes were influenced by common genetic effects, and served as an indicator of whether the same or different genes were influencing a pair of phenotypes.

## Results

Demographic characteristics and summary statistics for the dental fear and fear of pain assessments are presented in Table 1. Average DFS and FPQ-9 total and subscale scores were congruent with results observed in other studies of similar populations[18]. Additionally, distributions of DFS and FPQ-9 scores were consistent with existing research such that approximately 15% of the sample demonstrated phobic levels of dental fear, with DFS and FPQ-9 scores for the remainder of the sample having a negatively skewed distribution. As has been widely observed with many fears, sex was associated with self-reports[34]. Women reported higher (DFS $M = 38.7$, SD = 18.6) and men reported lower (DFS $M = 35.2$, SD = 17.2) levels of dental fear, $t(1368) = 3.76$, $p < 0.001$. Likewise, women reported higher (SF-FPQ $M = 24.9$, SD = 8.0) and men reported lower (FPQ-9 $M = 21.6$, SD = 8.1) levels of fear of pain, $t(1368) = 8.03$, $p < 0.001$. Though very weakly, age was statistically significantly correlated with dental fear, $r = 0.15$, $p < 0.001$, and fear of pain, $r = 0.07$, $p < 0.001$. As such, sex and age were adjusted for where necessary in subsequent analyses, though final results from adjusted and unadjusted models were not different.

Statistically significant heritability estimates, which varied from 14% to 36% ($p = 0.03$ to $p < 0.001$), were observed for all dental fear and fear of pain assessment scores (Table 2). Dental fear was estimated to be 30% heritable (DFS total score $h^2 = 0.30$, $p < .001$); fear of pain was estimated to be 35% heritable (FPQ-9 total score $h^2 = 0.35$, $p < .001$). The most heritable subscale score from the DFS was the specific stimuli subscale ($h^2 = 0.36$) and the most heritable subscale score from the FPQ-9 was the medical/dental pain subscale ($h^2 = 0.35$). Sex and age accounted for only a small fraction of the variation in dental fear (2-4%), and fear of pain (2-5%). Given the data analytic strategy, other non-measured, unspecified non-genetic (*id est*, environmental, individual learning history) factors accounted for the remaining variation in these phenotypes.

Non-genetic factors that are shared among relatives (*id est*, shared environment) may be absorbed into the heritability estimates, and therefore these estimates may be inflated. To account for this issue, we expanded our variance components models to include the household effect as a proxy for unmeasured environmental factors. Household explained 0-10% of the variance in our outcomes. Many, but not all, of the DFS and FPQ-9 scores and subscales remained significantly heritable in the household models (*id est*, DFS Specific Stimuli Subscale, FPQ-9 Total Score, FPQ-9 Fear of Severe Pain and Fear of Medical/ Dental Pain Subscales; see Appendix for details).

Genetic correlations were estimated to determine the shared heritability between dental fear and fear of pain. Table 3 shows the genetic correlations ($\rho_G$) between both the DFS total score and specific stimuli subscale score, and the FPQ-9 total score and subscale scores. The DFS total score was significantly genetically correlated with the FPQ-9 total score and severe and medical pain subscale scores. Similar genetic correlations were observed for the

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DFS specific stimuli subscale score. These results, which quantify the shared heritability between dental fear and fear of pain, indicate that common genes comprised approximately 40% to 72% (*id est*, $\rho_G^2$) of the total genetic effect influencing dental fear and fear of pain.

To aid in assessing the potential role of fear of pain in dental fear, the genetic variance of the DFS total score and specific stimuli subscale score were modeled, while simultaneously adjusting for the FPQ-9 medical/dental pain subscale score. In the medical/dental pain-adjusted models, the heritability estimate of the DFS total score decreased from $h^2 = 0.30$ to $h^2 = 0.16$, and the specific stimuli subscale score decreased from $h^2 = 0.36$ to $h^2 = 0.20$, indicating that approximately 45% of the heritability of dental fear was attributable to the fear of medical/dental pain. Indeed, the FPQ-9 medical/dental pain subscale accounted for 34% of phenotypic variation in the DFS total score, and 41% of phenotypic variation in the specific stimuli subscale score.

## Discussion

Supporting Hypotheses 1 and 2 respectively, the heritability estimates of DFS and FPQ-9 total scores indicated that genetics likely plays a major role in the experience of both dental fear and fear of pain. That the most heritable subscale score of the DFS was the specific stimuli subscale and the most heritable subscale score of the FPQ-9 was the medical/dental pain subscale, which were more heritable than other subscale scores, suggests that these subscales account for much of the heritability of the total scores. Providing support for Hypothesis 3, DFS and FPQ-9 scores were genetically correlated, suggesting shared heritability. Together, study findings demonstrate, generally, that dental fear and fear of pain are partly due to genetic factors, and, specifically, that fear of pain is a major component of both the heritability and total phenotypic variance of dental fear.

These findings are the first to demonstrate the heritability of fear of pain, and confirm the heritability of dental fear. Notably, study findings provide evidence that dental fear shares its heritability with fear of pain. Dental fear, and indeed dental phobia, may develop, in part, through heightened fears about pain. This conclusion has specific implications for the treatment of dental fear and dental phobia–notably that, for some patients, it may be appropriate to address fears about pain in order to adequately treat dental phobia. These study findings also have potentially broader implications for understanding the etiology of healthcare-related fears more generally, especially where pain is experienced in conjunction with the feared health care.

Preliminary biological evidence for the association between dental fear and fear of pain is provided by study findings[19]. This evidence bolsters current conceptualizations of dental fear, refining the understanding of the mechanisms by which dental fear are developed and maintained, and highlighting the importance of both environmental and genetic factors[3]. It is clear that fear of pain, a predictor of dental fear, is genetically linked to dental phobia, and moderately if not strongly so. There is a high degree of commonality in heritable influence affecting dental fear and fear of pain. Still, given that there is not complete shared heritability between DFS and FPQ-9 scores, it can be concluded that the two phenotypes are distinct, and also influenced by other genetic contributions. It should be noted that dental

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fear, including dental phobia, are idiographic problems with etiologies rooted not only in fear of pain, but also in many other factors[3]. Thus, conclusions drawn from this study about the specific etiology of dental phobia should be made in the context of our understanding of dental fear as complex and individualized.

The strong available evidence suggesting that fear of pain is a critical component of dental fear has important consequences for the treatment of clinically significant levels of dental fear that impact oral and systemic health[5,7,35]. Given the findings of this study, psychological interventions that directly target fear of pain should be strongly considered in treatment plans for reducing dental fear.

Consistent with previous work, fear of pain could be conceptualized in this study as a causal and maintaining factor driving the development of dental phobia[17,19]. Heritability analyses indicated that that fear of pain shares genetic variance with dental fear or, at its extreme, dental phobia. In such a case, fear of pain might be thought of as an endophenotype of dental fear. Several criteria, some of which cannot be met given the available data in this study, have been outlined as critical for labeling endophenotypes[36,37]. As such, additional work is necessary to confirm that fear of pain is an endophenotype of a dental fear; however, the early evidence presented here (*id est*, shared heritability and familial co-aggregation) is compelling. In considering the search for mechanisms important in the etiology of dental fear and dental phobia, other potential endophenotypes also may be worth consideration. For instance, general cognitive style (*id est*, cognitive vulnerability)[38,39], neuroticism[40,41], anxiety sensitivity, differential dental pain tolerance and threshold, amygdala activity, or certain facets of amygdala function theoretically are of interest. Nevertheless, it is widely held that non-shared and individual-specific environmental effects generally have a stronger influence than shared environmental effects (and genetic effects) on behavioral/psychological phenotypes. A complete conceptualization of dental fear etiology includes the undeniable and strong role of such non-shared and individual-specific effects (e.g., past experiences, temperament/personality); however, budding science, including findings from the current study, suggest a meaningful genetic component, and likely interactions between genotype, endophenotype, and environment.

Conclusions drawn from the findings presented here should be understood within the context of a number of limitations. First, the dental fear and fear of pain phenotypes were measured using only self-report instruments. Reliance on single and unimodal measures can be problematic, as more complex or multimethod assessments of psychopathology generally are understood to be more reliable and valid. The psychometric properties of the self-report instruments used for this study are excellent; however, use of *additional* assessment tools such as interviews, and/or behavioral or psychophysiological recording, would have further strengthened study design by providing converging validity, and would have potentially allowed for more nuanced conclusions about the specific role of genetic factors in the manifestation(s) of dental fear. Second, the majority of study relatives lived together, which may have introduced environmental confounds (e.g., children of fearful parents may be conditioned to be fearful themselves through social learning). In order to help account for non-genetic components of variance that may be shared among relatives (and therefore inflate our estimates of heritability), we included a household component in our model (see

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Appendix). However, our sample was not ideally-suited to differentiating household and genetic components of variance due to their similar covariance structures in our sample of mostly first-degree relatives residing together. Although, it should be noted that some relatives included in these analyses actually lived in different households (*id est*, approximately one-third of the households included individuals who were biologically related to individuals in other households to form extended families), which benefits our analysis and may have mitigated the problem of inflated heritability estimates due to non-genetic familial sources of variance. Third, DFS and FPQ-9 total scores are comprised of subscale scores, which means that the comparison of the heritability of total score and subscale score phenotypes must be done with the understanding that, as a result of measurement technique, one phenotype naturally is embedded in the other. Additionally, given that most of the phenotypic and genetic overlap between dental fear and fear of pain is borne out of fear of medical/dental pain, there may be some tautology. Further, fear of pain may share genetic variance with healthcare-related phobias more generally, not only dental fear more specifically. Lastly, it is important to note that this study relied on data from participants living in North Central Appalachia, which may limit generalizability (see Appendix for additional comment on this point).

The analytic approach used in this study represents one method for understanding in greater detail the heritability of complex behavioral phenotypes such as clinically significant fears. While very strong, this approach has some limitations, and it is important to recognize that even in light of our varied biological and household relationships, it may not be possible to fully disentangle genetic and non-genetic familial effects using our modeling framework (see Appendix for comments on guarding against limitations of the statistical model used and on unmeasured environmental effects). Future work in this arena could utilize genome-wide association studies to identify specific genes that are important in the etiology of dental phobia and to clarify which underlying biological processes are involved (e.g., heightened pain sensitivity, overactivation of anxiety pathways, underactivation of parasympathetic processes). Though heritability is evident, it is unclear what role genes play in the development and maintenance of dental phobia. Thus, future work also may identify and target other important related phenotypes and potential endophenotypes such as dental pain sensitivity, and even personality factors such as neurotocism[41]. Additional studies may elucidate the role of sex in the heritability of dental phobia.

In conclusion, this study presents support for the assertion that genetic variation is important in the etiology of dental fear, and demonstrates shared heritability for dental fear and fear of pain. This conclusion provides promising possibilities for improving interventions for dental phobia and fear, which may improve utilization of dental treatment and reduce rates of this public health concern.

## Supplementary Material

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**Table 1**

**Demographic Characteristics and Dental fear and Fear of Pain Assessments**

| **Sample Characteristics** | **Mean (SD, Range) or *n* (Percentage)** |
|---|---|
| Demographics | |
| Sex (men / women) | 543 (39.6%) / 827 (60.4%) |
| Age (years) | 29.2 (SD = 12.2, 11-74) |
| Ethnicity/Race (white / African American /Hispanic / Native American / Asian / Other) | 1201 (87.7%) / 138 (10.1%) / 11 (0.8%) / 1 (0.1%) / 6 (0.4%) / 13 (1.0%) |
| Dental Fear Survey | |
| Total Score | 37.9 (SD = 18.2, 20-100) |
| Avoidance Subscale | 12.7 (SD = 7.1, 8-40) |
| Specific Stimuli Subscale | 14.4 (SD = 7.4, 6-30) |
| Physiological Arousal Subscale | 8.7 (SD = 4.4, 5-25) |
| Fear of Pain Questionnaire-9 | |
| Total Score | 23.6 (SD = 8.2, 9-45) |
| Minor Pain Subscale | 6.0 (SD = 2.6, 3-15) |
| Severe Pain Subscale | 9.7 (SD = 3.7, 3-15) |
| Medical/Dental Pain Subscale | 7.8 (SD = 3.4, 3-15) |

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## Table 2
## Heritability of Dental fear and Fear of Pain Assessment Scores

| **Phenotype** | **$h^2$ (±SE)** | **$R^2$** | ***p*** |
|---|---|---|---|
| Dental Fear Survey | | | |
| Total Score | 0.30 (±0.08) | 0.03 | < 0.001 |
| Avoidance Subscale | 0.22 (±0.08) | 0.02 | < 0.01 |
| Specific Stimuli Subscale | 0.36 (±0.08) | 0.02 | < 0.001 |
| Physiological Arousal Subscale | 0.14 (±0.08) | 0.04 | < 0.01 |
| Fear of Pain Questionnaire-9 | | | |
| Total Score | 0.35 (±0.08) | 0.05 | < 0.001 |
| Fear of Minor Pain Subscale | 0.16 (±0.08) | 0.02 | < 0.05 |
| Fear of Severe Pain Subscale | 0.30 (±0.08) | 0.05 | < 0.001 |
| Fear of Medical/Dental Pain Subscale | 0.35 (±0.08) | 0.04 | < 0.001 |

*Note*. $h^2$ = Residual Heritability estimate, % of the phenotype that is accounted for by genetics; $R^2$= Proportion of variance of outcome that is due to those factors that have been controlled (*id est*, sex and age).

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## Table 3

**Genetic Correlations ($\rho_G$) between Dental Fear Survey and Fear of Pain Questionnaire-9 Scores**

| | Dental Fear Survey | | | |
|---|---|---|---|---|
| | Total Score | | Specific Stimuli Subscale | |
| **Fear of Pain Questionnaire-9** | $\rho_G$ (±SE) | *p* | $\rho_G$ (±SE) | *p* |
| Total Score | 0.66 (±0.12) | < 0.001 | 0.68 (±0.11) | < 0.001 |
| Fear of Minor Pain Subscale | 0.19 (±0.25) | 0.5 | 0.27 (±0.22) | 0.3 |
| Fear of Severe Pain Subscale | 0.64 (±0.16) | < 0.001 | 0.63 (±0.14) | < 0.001 |
| Fear of Medical/Dental Pain Subscale | 0.82 (±0.09) | < 0.001 | 0.85 (±0.08) | < 0.001 |