

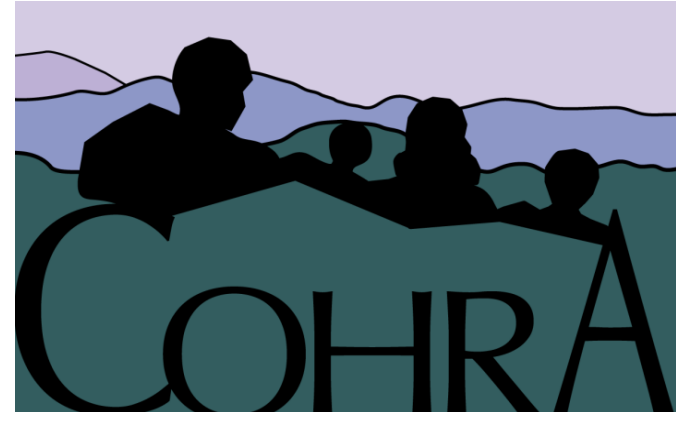


MC1R Gene Variation and Fear Related to Dental Care: Evidence of Fear of Pain as Mediator

Center for Oral Health Research in Appalachia (COHRA)

Cameron L. Randall¹, Daniel W. McNeil¹, John R. Shaffer², Richard J. Crout¹, Robert J. Weyant², and Mary L. Marazita²
West Virginia University and ²University of Pittsburgh

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Background

- Anecdotal evidence in medicine and dentistry has long suggested that individuals with red hair are hypersensitive to pain and more likely to be anxious/fearful (Conant, 2014; Melnick, 2010)
 - Variation in the melanocortin-1 receptor gene (*MC1R*; MIM 155555) is associated with general acute pain sensitivity, dental pain sensitivity, and fears related to dental care (Binkley et al., 2009; Liem et al., 2005; Mogil et al., 2005)
 - MC1R* variation is present in nearly all Caucasians with red hair, and approximately one-third of Caucasians with dark hair (e.g., Binkley et al., 2009)
- Dental fear is a prevalent and important problem
 - 45 million adults in USA report moderate fear; 10-20% report severe levels (Dionne et al., 1998; Smith & Heaton, 2003)
 - Fear is associated with avoidance of treatment and other poor oral health behaviors (e.g., Armfield et al., 2007; Meng et al., 2007)
 - Fear and avoidance are associated with poorer oral health, lower quality of life, and cardiovascular disease, diabetes, neurocognitive problems, and poor pregnancy outcomes (e.g., Armfield et al., 2009; Locker, 2003; Offenbacher et al., 1996; Williams et al., 2008)
- Fear of pain is a critical component of dental fear (McNeil & Berryman, 1989)
- Study Objective: Clarify genetic influences in the etiology of dental fear, specifically the role of *MC1R***
- The aims of this study were to:**
 - replicate the finding that *MC1R* variation and dental fear are associated
 - determine, for the first time, whether *MC1R* variation is associated with general fear of pain
 - determine whether fear of pain plays an intermediary role in the association between *MC1R* variant status and dental fear

Results

- Consistent with existing literature, 33.2% of the sample had variation in *MC1R*

Table 1. *MC1R* Genetic Variant Information

SNP	Base Pair Position (on Chromosome 16, Build 37)	Minor Allele	Minor Allele Frequency	n (%)
rs1805006	89985918	A	0.011	10 (1.2)
rs11547464	89986091	A	0.003	3 (0.4)
rs1805007	89986117	T	0.068	126 (15.4)
rs1110400	89986130	C	0.009	18 (2.2)
rs1805008	89986144	T	0.084	132 (16.2)
rs1805009	89986546	C	0.007	4 (0.5)

- As has been demonstrated before, *MC1R* variant status predicted dental fear, controlling for age and sex ($\beta = .07$, $p = .002$)
- MC1R* variant status also predicted fear of pain, controlling for age and sex ($\beta = .09$, $p = .009$)
- There was a significant indirect effect of *MC1R* variant status on dental fear through fear of pain, representing a small to moderate effect ($\kappa^2 = 0.044$, BCa CI: 0.009 to 0.082)

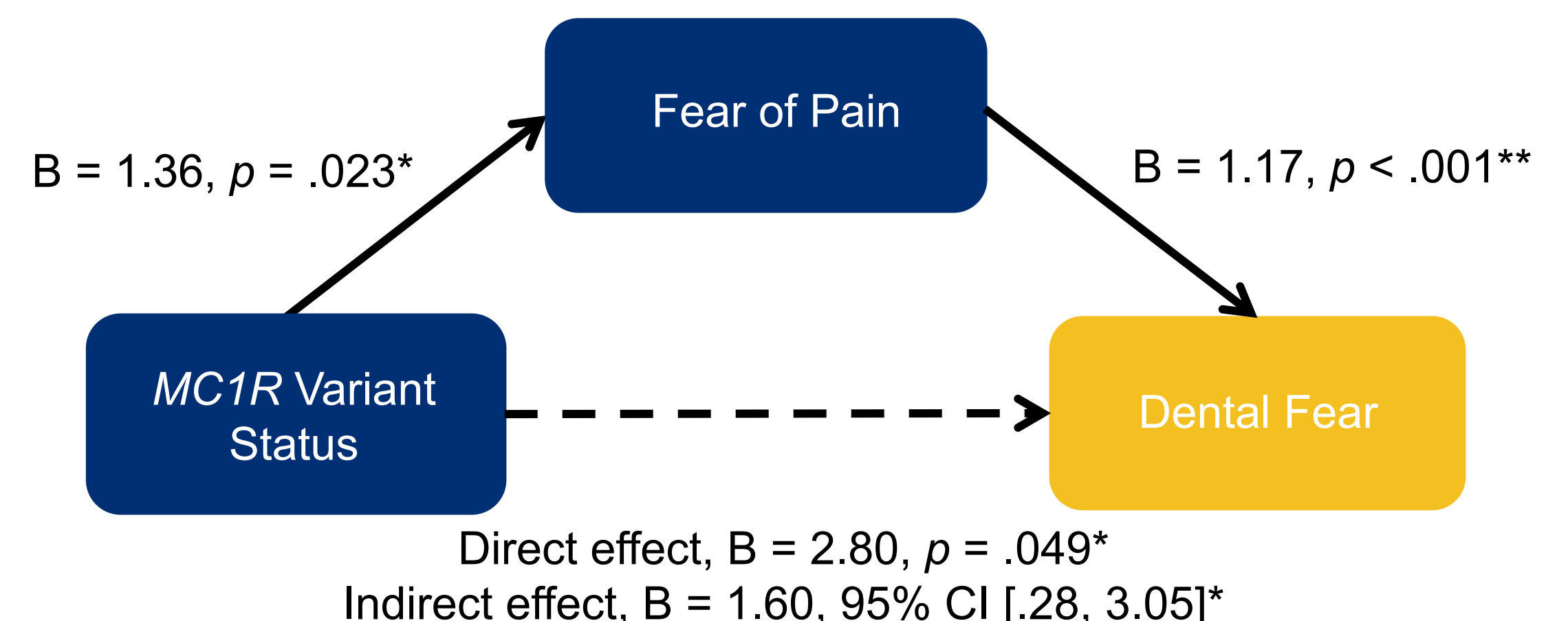


Figure 1. Fear of Pain Mediates Relation between *MC1R* Variant Status and Dental Fear

Method

Utilized existing data from a large, family-based cross-sectional study on determinants of oral diseases at the community-, family-, and individual levels (COHRA Cohort 1) (Marazita et al., 2005; Polk et al., 2008; Randall, McNeil, Crout et al., 2013)

Participants

- 732 households (containing at least one biological parent-child pair) enrolled; For data analyzed, sample included Caucasian adults who were not biologically related (N = 817, 62.5% female)
- Mean age = 34.7 years (SD = 8.7, range = 18-67)

Self-Report Assessment Instruments

- Demographic questionnaire (see Polk et al., 2008)
- Fear of Pain Questionnaire-9 – FPQ-9 (McNeil et al., 2015)
- Dental Fear Survey – DFS (Kleinknecht et al., 1973)

DNA Collection, Genotyping, and Risk Score Calculation

- DNA collected for all participants from blood, saliva, or cheek swab samples; Genotyped on Illumina platform
- Assessed variation at the following *MC1R* SNPs: rs1805006, rs11547464, rs1805007, rs1110400, rs1805008, rs1805009 (as in Binkley et al., 2009)
- Genetic data combined across variants to calculate risk score (positive variant status – one or more *MC1R* variants; negative variant status – zero *MC1R* variants)

Data subjected to simple regression and mediation analyses (single-mediator model) with PROCESS macro, SPSS (Hayes, 2013)

Conclusions

- MC1R* variation is associated with fear of pain and dental fear, and fear of pain fully mediates the relation between *MC1R* genotype and dental fear
- MC1R* variation may influence orofacial/dental pain and, in turn, predispose individuals to develop fears about pain; this may contribute to the genesis of dental fear
- Future experimental work will determine more definitively the mechanisms by which the *MC1R* gene is associated with fear of pain and dental fear, with particular attention paid to its role in dental pain sensitivity
- Future work will seek to identify other biomarkers of dental pain sensitivity, fear of pain, and dental fear

Contact, Support, & Acknowledgements

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Cameron L. Randall
53 Campus Drive, Box 6040
Morgantown, WV 26506-6040
CRANDAL1@mix.wvu.edu
www.cameronrandall.com

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