

VARIATION IN *MC1R* GENE PREDICTS DENTAL PAIN SENSITIVITY

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12th Annual NIH Pain Consortium Symposium

31 May 2017



THE PROBLEM OF OROFACIAL PAIN

- Orofacial pain is varied and common (Setty & David, 2014)
- Consequences include generalized distress, poor sleep, disability, lost productivity, and/or poorer quality of life (Friction & Schiffman, 1995; Vadivelu, 2014)
- Impacts essential oral health behavior and dental treatment-seeking behavior
 - Fear of pain and dental care-related fear as mechanistically important (Armfield, 2007; McNeil et al., 2014)



Background

Method

Results

Discussion

MELANOCORTIN-1 RECEPTOR GENE



Study: Redheads' extra pain may cause fear of dentists

STORY HIGHLIGHTS

- Studies: Some redheads have more sensitive pain receptors
- Redheads are twice more likely to avoid dental procedures

updated 1:33 p.m. | **The New York Times**

By Madison Park
CNN

The Pain of Being a Redhead

By Tara Parker-Pope August 6, 2009 2:20 pm

Nobody likes going to the dentist, but redheads may have good reason.

A growing body of research shows that people with red hair need larger doses of anesthesia and often are resistant to local pain blockers like Novocaine. As a result, redheads tend to be particularly nervous about dental procedures and are twice as likely to avoid going to the dentist as people with other hair colors, according to new research published in The Journal of the American Dental Association.



Why Surgeons Dread Redheads

By Meredith Melnick @meredithm | Dec. 10, 2010



As the authors of a recent study published in *BMJ* test, society's red-haired members don't always get fair shake. Hoary stereotypes, such as the idea that redheads are also hot heads, are mixed together with actual physiological differences — such as a heightened sensitivity to pain. Now science is getting better understanding of redheaded physiology than ever before.



In numerical terms, people with red hair are a small, isolated minority. They comprise just 2-6% of the population of the northern hemisphere and 1-2% worldwide. It's genetics that make them such rare birds. (More on [ime.com: How to Keep Surgeons From Leaving Things Behind](#))



...e carrot-top coloration is caused by a gene on chromosome 16 that affects the melanocortin-1 receptor (MC1R) protein, which often leads to the redheads' characteristic pale skin and light eyes, as well as a sensitivity to...
...of clinical anesthesiologists.
...Anecdotal evidence long held that redheads were



MELANOCORTIN-1 RECEPTOR GENE

- *MC1R* variation associated with pigmentation (Raimondi et al., 2008)
- Melanocortinergic pathway, including MC1R, important for pain and anxiety behavior (Chaki & Okuyama, 2005; Liu et al., 2007; Xia et al., 1995)
- *MC1R* variation associated with:
 - Acute pain perception (Beltramo et al., 2003; Delaney et al., 2010)
 - Reduced efficacy of general and local anesthesia (e.g., Liem et al., 2004)
 - Fear of pain, dental care-related fear, and dental treatment avoidance (Binkley et al., 2009; Randall et al., 2017)



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STUDY AIM

To further the understanding of genetic contributions to orofacial pain perception, the aim of this study was to determine whether *MC1R* variation predicts dental pain sensitivity



Background

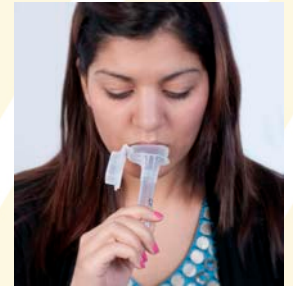
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PROCEDURE

- Psychosocial assessment
 - Fear of Pain Questionnaire-III – 30-item self-report measure of pain-related fear (McNeil & Berryman, 1989)
- Genotyping
 - DNA extracted from saliva samples collected with Oragene•DISCOVER tubes (DNA Genotek)
 - Genotyped for most common *MC1R* SNP (rs1805007)
- Dental pain sensitivity assessment



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ASSESSING DENTAL PAIN SENSITIVITY

- Pain tolerance and threshold measured for six teeth (Ramford teeth; numbers 3, 9, 12, 19, 25, 28), with subjective pain and fear reported



Kerr Vitality Scanner 2006
(SybronEndo)



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SAMPLE CHARACTERISTICS

- 96 Caucasian adults completed study protocol
 - M age = 34.8 years, SD = 11.6, range = 20-66
 - 55 (57%) female
 - M education = 16.4 years, SD = 2.8, range = 9-25
- Distribution of Fear of Pain Questionnaire-III scores was normal (M = 84.2, SD = 18.0, range = 34-133)
- 18 participants (19%) had minor allele (T) at rs1805007



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DENTAL PAIN SENSITIVITY

- The entire possible range of pain tolerance represented
 - M pain tolerance = 46.0, SD = 15.6, range = 19.2-80
- The entire possible range of subjective rating of pain intensity represented
 - M pain rating = 50.1, SD = 21.1, range = 7.2-100
- Subjective rating of pain intensity associated with:
 - Pain tolerance, $r = -.32$, $p = .002$
 - Fear of pain associated, $r = .20$, $p = .04$
- Reliable responding observed (Cronbach's alpha = .77); tolerance of electrical pain stimulation was associated with tolerance of intraoral pressure pain stimulation ($r = .29$, $p = .005$)



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MC1R + DENTAL PAIN SENSITIVITY

- Pain tolerance not associated with sex or age ($ps > .05$)
- Controlling for fear of pain, presence of minor allele at rs1805007 was predictive of lower pain tolerance, $R^2 = .11$, $F(2,93) = 5.62$, $p = .005$

Predictor Variable	Unstandardized regression coefficient (B)	Standard Error	Standardized Regression Coefficient (β)	Significance Value (p)
Fear of Pain Questionnaire-III Score	-.20	.09	-.23	.02
Minor Allele (T) at rs1805007	-8.73	3.91	-.22	.03



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CONCLUSIONS

- Variation in *MC1R* – specifically, presence of the minor allele at rs1805007 – predicts increased sensitivity to dental pain
- Dental pain perception may be a critical intermediary in the previously observed associations between *MC1R* variation and fear of pain and dental care-related fear (Randall et al., 2017)
- An electric pulp tester can be used for objective assessment of dental pain sensitivity, producing reliable and valid data



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LIMITATIONS + FUTURE DIRECTIONS

- Limitations
 - Focus on single gene (and SNP)
 - Relatively small and heterogeneous sample
- Future Directions
 - Identify mechanisms underpinning associations between *MC1R* and dental pain sensitivity
 - Identify potential implications for acute and chronic pain
 - Clarify the role of orofacial pain perception in association between *MC1R* variation and dental care-related fear



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SIGNIFICANCE

- This study advances the literature on genetic influences on orofacial pain perception
- It is the first known study to link *MC1R* variation to increased dental pain sensitivity
- It is further innovative because of its use of an experimental pain induction paradigm in the context of a study addressing associations between dental pain and dental care-related fear



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ACKNOWLEDGMENTS

- NIH Pain Consortium
- NIDCR (F31 DE023493)
- West Virginia University Foundation Grant for Distinguished Doctoral Scholars
- Center for Oral Health Research in Appalachia
- Anxiety, Psychophysiology, and Pain Research Laboratory at WVU
- Daniel W. McNeil, PhD and Mary L. Marazita, PhD
- Sarah Addicks, Linda Brown, Wendy Carricato, Stella Chapman, Deja Clement, James Hickman, Emily Kerwin, Michael Law, Jasmin Rose



THANK YOU.

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