VARIATION IN MC1R GENE PREDICTS DENTAL PAIN SENSITIVITY

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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)
Study: Redheads' extra pain may cause f

The New York Times

The Pain of Being a Redhead
By Tara Parker-Pope August 6, 2009 2:10 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.
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)
To further the understanding of genetic contributions to orofacial pain perception, the aim of this study was to determine whether \textit{MC1R} variation predicts dental pain sensitivity.
PROCEDURE

- Psychosocial assessment
- Genotyping
  - DNA extracted from saliva samples collected with Oragene●DISCOVER tubes (DNA Genotek)
  - Genotyped for most common $MC1R$ SNP (rs1805007)
- Dental pain sensitivity assessment
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)
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
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 ($r = .29$, $p = .005$)
**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, \(R^2 = .11, F(2,93) = 5.62, p = .005\)

<table>
<thead>
<tr>
<th>Predictor Variable</th>
<th>Unstandardized regression coefficient (B)</th>
<th>Standard Error</th>
<th>Standardized Regression Coefficient ((\beta))</th>
<th>Significance Value ((p))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of Pain Questionnaire-III Score</td>
<td>-.20</td>
<td>.09</td>
<td>-.23</td>
<td>.02</td>
</tr>
<tr>
<td>Minor Allele (T) at rs1805007</td>
<td>-8.73</td>
<td>3.91</td>
<td>-.22</td>
<td>.03</td>
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</tbody>
</table>
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.
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
SIGNIFICANCE

- This study advances the literature on genetic influences on orofacial pain perception
- It is the first known study to link \textit{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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Structural Barriers to Treatment (Access)

Psychosocial Barriers to Treatment (Utilization)

Oral Health Values

Dental Care-Related Fear/Anxiety (Aversive Behavioral, Cognitive, and Physiological Responses to Treatment)

Treatment-Seeking Patterns

Financial Limitations

Geographic Limitations

Sociodemographic, Cultural Factors

Attitudes, Beliefs about Dental Treatment

Oral Health Values

Fear of Pain

Cognitive Distortions

Direct Experience with Dentistry, Vicarious Learning, Informational Learning

Genetic/Biological Predispositions

Susceptibility to Fear Conditioning

From McNeil & Randall, 2014