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 fear of dentists

The New York Times

updated 1:33 p.m. 1
By Madison Park
CNN

(CNN) – Despite having red hair, a trait that's often associated with a lack of pain sensitivity, redheads actually experience more pain than people with other hair colors, according to a study published in the journal Pain.

A growing body of research shows that people with red hair need larger doses of anesthesia and are more likely to experience pain after dental procedures, a finding that is likely due to the fact that redheads have a genetic predisposition to experience pain more intensely.

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 are more likely to experience pain after dental procedures, a finding that is likely due to the fact that redheads have a genetic predisposition to experience pain more intensely.
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>
</tr>
</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 *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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