The Relationship Between 5-HT Transporter Gene (SLC6A4) Polymorphisms, Electrocutaneous Pain Sensitivity, and Pain Catastrophizing

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Introduction

Pain catastrophizing is a maladaptive coping strategy that has emerged as an important predictor of pain-related outcomes. Despite the importance of this construct, no known study has examined if there is a genetic risk for pain catastrophizing. The 5-HT transporter gene (SLC6A4) is a possible candidate because prior research has established linkages between SLC6A4 polymorphisms and cognitive-affective processes. For example, relative to individuals with the higher activity 44-bp promoter insertion polymorphism (LL genotype, two long alleles), individuals with the SS genotype (two short alleles) have a greater propensity for negative affectivity (depressive symptoms) and demonstrate enhanced fear responsivity. This study sought to observe the relationship between these SLC6A4 genotypes and various measures.

Objective

The aim of this study was to examine the effects of SLC6A4 genotypic polymorphisms on pain catastrophizing, depression, NFR magnitude, and pain tolerance and threshold.

Participants

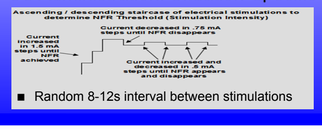
- 63 Healthy Participants
- Characteristics: 26 Men, 37 Women; White non-Hispanic (78%), single (43%), employed (59%), average yrs education = 15 yrs (*SD*=2.61), average age = 39 yrs (*SD*=14.32)
- Exclusion Criteria:
  - < 18 years of age
  - Current acute illness, cardiovascular, neurological, and/or circulatory problems
  - Recent use of analgesic, antidepressant, anxiolytic, or antihypertensive medication
  - Recent psychological trauma, specific phobia of snakes or spiders
  - Any chronic pain, Raynaud's disease

Pain Catastrophizing Scale

- 13 item self-report measure for use in clinical and non-clinical samples; used for persons with and without pain
- Items measured different facets of catastrophizing
- Internal consistency: alphas for PCS total and subscales range from .66 to .87
- **Pre-test PCS Instructions**: "Please indicate the degree to which you have these thoughts and feelings when you are experiencing pain."
- **Post-test PCS Instructions**: "Thinking back to your experience during the electric stimulations, please indicate the degree to which you had these thoughts and feelings."
- Items were summed to obtain a pain catastrophizing total score

Procedure

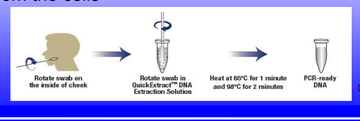
- Consent + Health Screening + Electrode application
- Pain Catastrophizing Scale (PCS) Administration: Traditional
- Center for Epidemiological Studies—Depression Scale Administration (CES-D)
- Pain/Nociceptive Sensitivity Assessment
  - **NFR Threshold Assessment**: (see figure below)
  - **Pain Threshold:** Ascending series of stimulations presented in .65 mA steps, threshold = first stimulus (in mA) rated ≥50 on rating scale
  - **Pain Tolerance:** Ascending series continued until pain rating of 100 achieved or max intensity reached
  - PCS Administration: Situation-Specific (SS)



■ Random 8-12s interval between stimulations

Procedure: DNA Collection

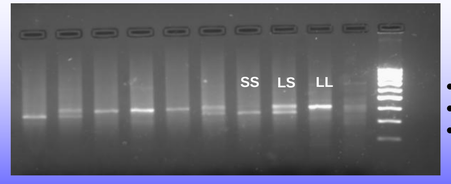
- Samples were collected from participants prior to pain testing (i.e., NFR threshold assessment)
- Buccal Swabs were used to collect cheek cells
- Epicentre BuccalAmp DNA extraction kits were used to extract DNA from the cells



Procedure: Genotyping

- The SLC6A4 locus was then amplified and characterized by Polymerase Chain Reaction (PCR) using primers and conditions as specified by Gelernter et al. (1995)
- The PCR products were then run through agarose gel electrophoresis, where the products were separated by size to allow for genotyping

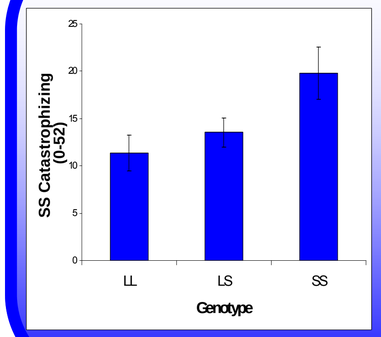
Results: Genotypes



- LL, *N* = 21
- LS, *N* = 32
- SS, *N* = 10

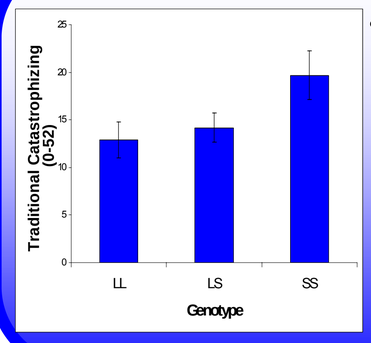
- Agarose gel electrophoresis was used to determine genotypes
- SLC6A4 polymorphisms are visible in the 300-400 base pair (bp) region

Situation-Specific Catastrophizing



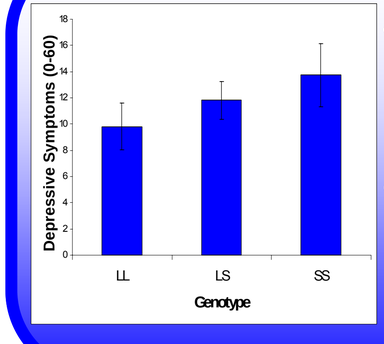
- The main effect of genotype was significant for SS catastrophizing (F[2, 60] = 3.20, p = .048, η^2 = .096).
- This indicates that individuals with the SS genotype displayed higher levels of situation-specific catastrophizing, relative to those with the LL genotype.

Traditional Catastrophizing



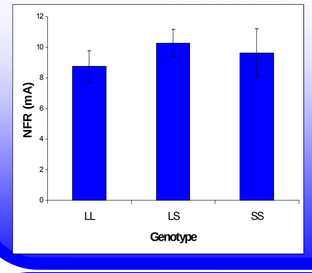
- The main effect of genotype was not significant for traditional catastrophizing (F [2, 65] = 2.42, p = .097, η^2 = .069), indicating there was no significant relationship between SLC6A4 genotypes and traditional catastrophizing.

Depressive Symptoms



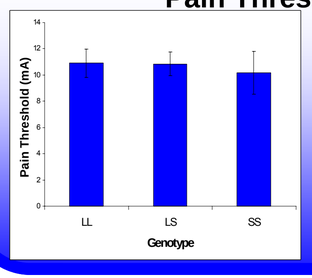
- The main effect of genotype was not significant for depressive symptoms (F [2, 64] = .906, p = .409, η^2 = .028).
- This indicates that there was no significant association between SLC6A4 genotypes and depressive symptoms.

NFR Threshold



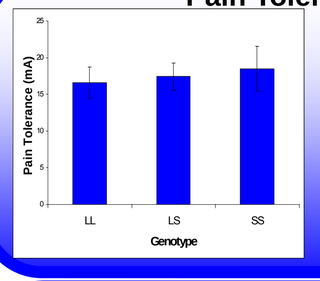
- The main effect of genotype was not significant for NFR (F [2, 59] = .625, p = .539, η^2 = .021), indicating there was no significant association between SLC6A4 genotypes and NFR.

Pain Threshold



- The main effect of genotype was not significant for Pain Threshold (F [2, 56] = .082, p = .922, η^2 = .003), This indicates that there was no significant relationship between SLC6A4 genotypes and Pain Threshold.

Pain Tolerance



- The main effect of genotype was not significant for Pain Tolerance (F [2, 55] = .132, p= .876 η^2 = .005), indicating there was no significant association between SLC6A4 genotypes and Pain Tolerance.

Conclusions

- Results indicated pain sensitivity was not associated with SLC6A4 polymorphisms; however, individuals with the SS genotype reported significantly higher situation-specific pain catastrophizing than persons with the LL (p=0.015) or LS (p=0.053) polymorphisms, an effect that explained 9.6% of the variance.
- Interestingly, there was no significant association found between traditionally-measured catastrophizing and genetic polymorphisms; however, it is possible that with a larger sample size, such an association may be obtained.
- SLC6A4 polymorphisms were not significantly associated with self-reported depressive symptoms in this study, suggesting the gene-catastrophizing association was not mediated by depression.