Evaluating the Role of Calcitonin Gene-Related Peptide in Neurofibromatosis Type 1 Patients

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BACKGROUND

- Neurofibromatosis type 1 (NF1) is a multisystem genetic disorder commonly presenting with chronic pain due to a variety of features consisting of plexiform neurofibromas, migraines, orthopedic complications, and gastrointestinal issues.
- Despite pharmaceutical advances in target-specific treatment therapies, there are no current treatment options specific to chronic pain in NF1 patients.
- No human studies evaluate chronic pain in NF1, but animal models indicate calcitonin gene-related peptide (CGRP) as playing a role.
- CGRP-targeted therapies have shown promise in migraine prophylaxis, raising the question of the role of CGRP in NF1.
- Analyzing the relationship between NF1 and CGRP levels could lead to target target-based therapy to treat chronic pain in NF1 patients.

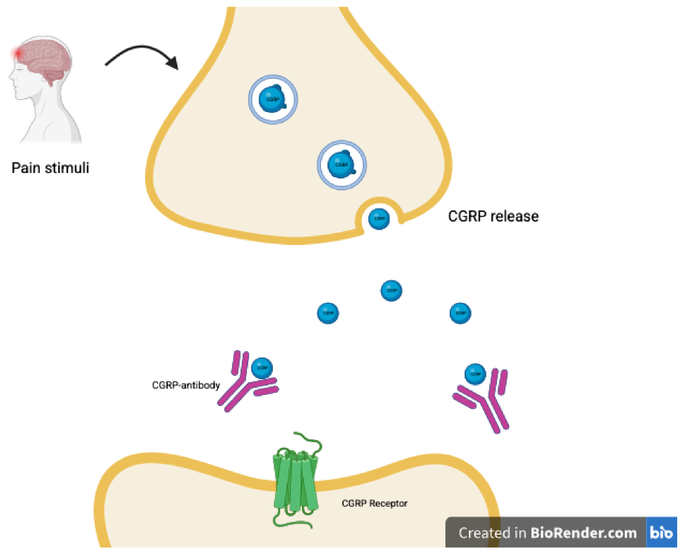

Figure 1: Role of CGRP in Migraine Treatment. Studies have shown a correlation between CGRP levels and migraine prophylaxis. In order to combat migraine, CGRP antibody therapies have been beneficial in modulating pain, therefore making this target-based therapy a potential for NF1 patients given this relationship is consistent.

OBJECTIVES

Our primary aim was to measure CGRP levels in NF1 patients to detect elevations as compared to non-NF1 patients.

METHODS

Patients from the Kentucky Neuroscience Institute (KNI) Neurofibromatosis Clinic were enrolled if :

- They met diagnostic criteria following NIH guidelines for a clinical NF1 diagnosis or had positive genetic testing
- Patient suffered from chronic pain >6 months
- Patients excluded if receiving CGRP monoclonal antibody treatment

- Participants consisted of both male and female patients over the age of 18.
- A blood sample was collected and analyzed by the Center for Clinical and Translational Science (CCTS) to evaluate CGRP peripheral blood levels with commercial ELISA kits.
- CGRP control was considered high when above 55.1 pg/mL, based on studies comparing CGRP levels for migraine and non-migraine headache patients to determine the upper limit of normal (Lassen et al. & Raffaelli et al.)

RESULTS

- NF1 individuals were found to have CGRP levels above 55.1 pg/mL, which is considered high.
- The mean (and median) value is 0.066, with a standard deviation of 0.011, and a 95% confidence interval ranging from 0.057 to 0.075.
- A one-sample t-test was completed to determine if the average CGRP value of the 8 NF1 individuals was significantly different than the value reported as being considered high.
- These comparisons were significant ($t = 2.77$, $p = 0.028$), suggesting that NF1 individual's CGRP values are significantly elevated as compared to literature-referenced controls.

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RESULTS cont.

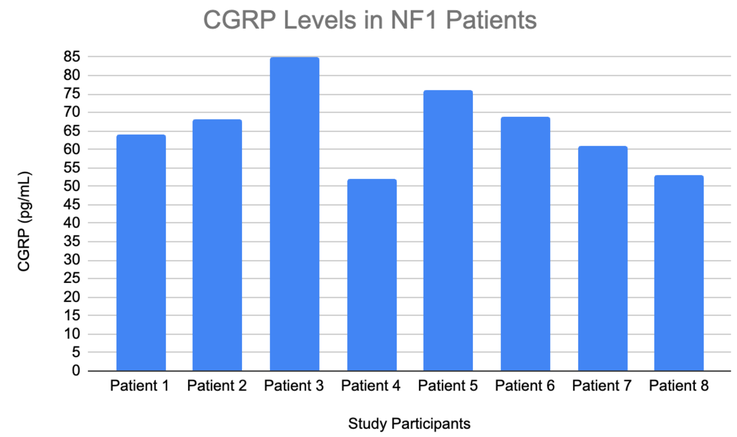

Figure 2: CGRP Levels in NF1 Patients. Study participants with a confirmed diagnosis following NIH guidelines were found to have increased CGPR levels. Six out of eight participants had CGRP levels above 55.1 pg/mL , with patients 4 and 8 falling just below this accepted control with 52 pg/mL and 53 pg/mL respectively.

CONCLUSIONS

We found CGRP levels were higher than the accepted normal in NF1 patients. In animal studies, CGRP plays a role in chronic pain in NF1, but there is a lack of human studies investigating this relationship. Based on our results, CGRP monoclonal antibody therapy is a promising potential treatment option to address chronic pain in NF1 patients. Further studies are needed to assess efficacy in this patient population.

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