TITLE: Clinical Characterization and Imaging of Triggered Attacks in Chronic Migraine and Posttraumatic Headache

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Chronic posttraumatic headache (PTH) is a disabling disorder that affects millions of individuals worldwide. The Principal Investigators (PIs) of this application proposed to develop human models of PTH by characterizing clinical features and correlated changes in brain activity before and during triggered attacks. The PIs hypothesized that the different headache triggers nitroglycerin (NTG) and prostaglandin E2 (PGE2) would produce different types of headache and would be associated with different patterns of brain metabolism that would reveal fundamental mechanisms of PTH. The studies were submitted for and achieved IRB approval at UCLA, and plans were in place to begin subject recruitment for the studies. However, because of administrative issues at UCSF (Dr. Goadsby’s move leading to a part-time appointment there), and because of an unexpected inability to obtain pharmaceutical grade PGE2, the actual research studies were not initiated, and the study has now been terminated. We are in the process of establishing a collaboration between UCLA and King’s College London (the location of Dr. Goadsby’s new position) and plan to move ahead with a similar but revised study once this formal collaboration is established. We will therefore continue to pursue the goals of this study in the future, but at this time the study is terminated.
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1. INTRODUCTION:
The subject of the proposed research was the characterization of triggered attacks in patients with persistent post-traumatic headache (PTH). The purpose of the proposed research was to investigate basic mechanisms of PTH. The scope of the proposed research was to characterize clinical features and changes in brain metabolism associated with attacks of headache triggered by either nitroglycerin (NTG) or prostaglandin E2 (PGE2) using PET and fMRI approaches. The study was terminated early because of unforeseen administrative reasons.

2. KEYWORDS:
Chronic migraine, post-traumatic headache, nitroglycerin, prostaglandin, positron emission tomography, functional magnetic resonance imaging.

OVERALL PROJECT SUMMARY:
Task 1. Recruitment and clinical characterization of patients with persistent post-traumatic headache for study (Months 1-30)
   a. Obtain IRB approval for recruitment of patients and data collection (Month 1-2)
      This task was completed, including development of an approved protocol and infrastructure for performance of the study.
   b. Recruitment of patients for study and screening for inclusion and exclusion criteria (Months 3-30).
      No patients were formally recruited for the study
   c. Enrollment of subjects with informed consent (Months 3-32).
      No patients were enrolled in the study

Task 2. Characterization of the clinical responses to nitroglycerin (NTG) in patients with persistent posttraumatic headache (Months 3-36)
   a. Perform detailed recording of premonitory symptoms, headache, and postdromal symptoms in subjects following intravenous administration of nitroglycerin (Months 3-36)
      Dr. Goadsby carried out related studies in patients with chronic migraine (in a separate project), but did not perform any of the specific studies proposed here.
   b. Characterize response of triggered symptoms to therapy with subcutaneous sumatriptan (Months 3-36)
      These studies were not performed
Task 3. Characterization of the clinical responses to prostaglandin E2 in patients with persistent posttraumatic headache (Months 3-36)

a. Perform detailed recording of premonitory symptoms, headache, and postdromal symptoms in subjects following intravenous administration of prostaglandin E2 (Months 3-36)

b. Characterize response of triggered symptoms to therapy with subcutaneous sumatriptan

These studies were not performed, in part because pharmaceutical grade PGE2 became unavailable after the study was approved.

Task 4. Functional brain imaging of NTG-triggered attacks in patients with persistent posttraumatic headache (Months 6-36)

a. Perform 18-fluorodeoxyglucose (FDG) PET scans during a NTG-triggered attack and on a separate occasion at baseline at least 1 week prior to or after triggering session in patients with persistent posttraumatic headache. (Months 6-36)

b. Perform a baseline anatomical and resting-state functional MRI in the same subjects at the same time as the baseline PET scan. (Months 6-36)

c. Compare patterns of brain metabolism at baseline and during triggered attacks. (Months 6-36)

These studies were not performed.

Task 5. Functional imaging of PACAP-triggered attacks in patients with persistent posttraumatic headache (Months 6-36)

a. Perform 18-FDG PET during a PACAP-triggered attack and on a separate occasion at baseline at least 1 week prior to or after triggering session in patients with persistent posttraumatic headache. (Months 6-36)

b. Perform a baseline anatomical and resting-state functional MRI in the same subjects at the same time as the baseline PET scan. (Months 6-36)

c. Compare patterns of brain metabolism at baseline and during triggered attacks (Months 6-36)

These studies were not performed.

Task 6. Comparison of baseline brain connectivity and metabolism between patients with persistent posttraumatic headache and normal controls (Months 12-36).
None of these studies were performed.

4. KEY RESEARCH ACCOMPLISHMENTS
IRB approval for triggered attack studies in patients with persistent post-traumatic headache was achieved at UCLA. Development of an infrastructure for future collaborative studies with Dr. Goadsby on clinical characterization and imaging of patients with PTH.

5. CONCLUSION:
The study was terminated early due to unforeseen administrative issues

6. PUBLICATIONS, ABSTRACTS, AND PRESENTATIONS:
Publications None
Abstracts None
Invited Presentations None

7. Inventions, patents and Licenses None

8. Reportable Outcomes None

9. Other Achievements
Establishment of a collaboration with Amgen for future studies of pathophysiology and therapy of chronic post-traumatic headache.

10. REFERENCES None

11. APPENDICES: None