International Headache Society

FELLOWSHIP REPORT FORM

Please complete this form giving details of your IHS Fellowship.

Personal details

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Fellowship

Dates of fellowship	Mar. 2018-Mar.2019
Institution name	Institut für Systemische Neurowissenschaften, Universitätsklinikum Hamburg Eppendorf (UKE)
Mentor name	Arne May
Title of study	Exploring the cycling biomarkers in migraine

Research details

Short summary of initial plan (max 200 words)
Migraine is a periodic disorder and accompanied with phasic sensory changes. Hypothalamo-thalamo-brainstem network may be the center that drives the periodic changes. We would like to study how objective sensory measurements change before a migraine attack and how these physiological changes correlate with functional imaging changes. It would be ideal if migraine attacks could be predicted; however, clinically, it is not easy or even impossible. One feasible alternative is to study patients with menstrual-related migraine (MRM). By definition, in patients with MRM, migraine will develop during the menstruation in ≥2 of 3 of menstrual cycles, and MRM thus serves as a surrogate for predictable migraine. We aim to enroll two cohorts: an MRM cohort and an age-and sex-matched healthy control cohort without a headache history. Both cohorts will undergo -on a daily basis- a series of physiological (quantitative sensory thresholds) and high-resolution brainstem echo-planar imaging towards their upcoming menstruation (-7 to +1 day). Sequential changes of activities over regions of interest will be further compared.

Short summary of your actual research (max 200 words)

(1) We wrote a letter to the editor to raise the awareness of the phasic changes in threshold. This letter has been published in the journal of "PAIN".
(2) We did a systemic review on the issue of threshold changes in migraine. This review article has been accepted in the journal of "PAIN" with the title: Migraine understood as a phasic sensory threshold disease.
(3) We investigated on healthy participants how the threshold changes over time in different sensory modalities including thermal, mechanical, and electrical.
(4) We tested different stimulus protocol and established a suitable one applicable in the MRI.
(5) Due to the issue we encountered during the participant recruitment, we did another clinical research to investigate the effects of oral contraceptive use on migraine symptomatology. This study is completed and has been submitted in Cephalalgia Report.
(6) I took part in a parallel project on how the sensory threshold changes after the induction of secondary hyperalgesia using different stimulus methods including electrical stimulation, thermal, and topical capsaicin.

Overview of activities on a monthly basis

The first three months were getting familiar with the lab settings and equipment, participating in the parallel projects from my group, and getting used to the language. Even though all members in my group speak good English, I still have to use German to communicate with the participants most of the time. The next 3 months were exploratory. We reviewed the topic extensively and finished the first draft of the review article. During this period, we recruited approximately 20 healthy participants, and tried different stimulus modalities and protocols, to find a workable setting to be used in the MRI. The ethic application was sent after we reached the final protocol. The next 3 months, we waited for the approval from the local ethic committee, and in the meantime, we measured how thresholds changes over time outside MRI in healthy participants. Due to the issue we encountered during the patient recruitment, that a large proportion of the participants used oral contraceptive pills which change the hormonal level significantly and may serve as a main confounder, we therefore conducted another study and used the results to convince the institutional board, that this issue can be solved by matching the pill use status between migraine patients and the healthy control. The last 3 months we continued recruiting participants and conducting this study.

Has the Fellowship met all your initial aims?

Yes. Nevertheless, we have revised the original plan due to the problems we encountered.

What, if any, problems did you encounter

(1) The dealing with bureaucracy including the initial VISA application and ethic approval takes much longer time than we previously expected.
(2) The applicability of the stimulus equipment also needs to be tested. We initially intended to use a thermal stimulation in MRI. After testing several subjects, we realized the stability of a thermal stimulation with an on-the-threshold intensity is poor. Therefore, we switched to electrical stimulation in the end and changed the stimulus protocol.
(3) The recruitment of participants is also challenging, since we targeted a specific subgroup of migraine patients.

How will the fellowship affect your future career?

I had been previously trained as a clinician and most of my previous research experience was purely clinical. Even though my mentor is a professor in Neurology, he is more of a clinician-scientist. I have been exposed in an environment, in which the pathophysiology of migraine is investigated from a different angle. I have learned to

approach a clinical phenomenon from a pathophysiological point of view, to design a study to explore the unanswered questions, to actually conduct a physiological / imaging study, and to overcome the challenges encountered during the process. Of course, I have also become familiar with several techniques and learned the niches pertinent to the quantitative sensory test. Last, the IHS fellowship will definitely be a highlight in my resume when I try to apply for grants in the future and continue headache researches.
What would you recommend to future IHS Fellowship applicants?
One-year in a foreign country is relatively short, especially when you need to deal with the bureaucracy and settling down in the first few weeks to months. I would recommend, specifically for a one-year project, to find a topic with the techniques and resources that are readily available in the lab. That saves lots of time. The mentor is of vital importance. Fortunately, my mentor and the working group have been very supportive throughout the time. Last, I would recommend the application of a 2-year fellowship when one wishes to complete a larger project.
Please include five photos/images of your stay


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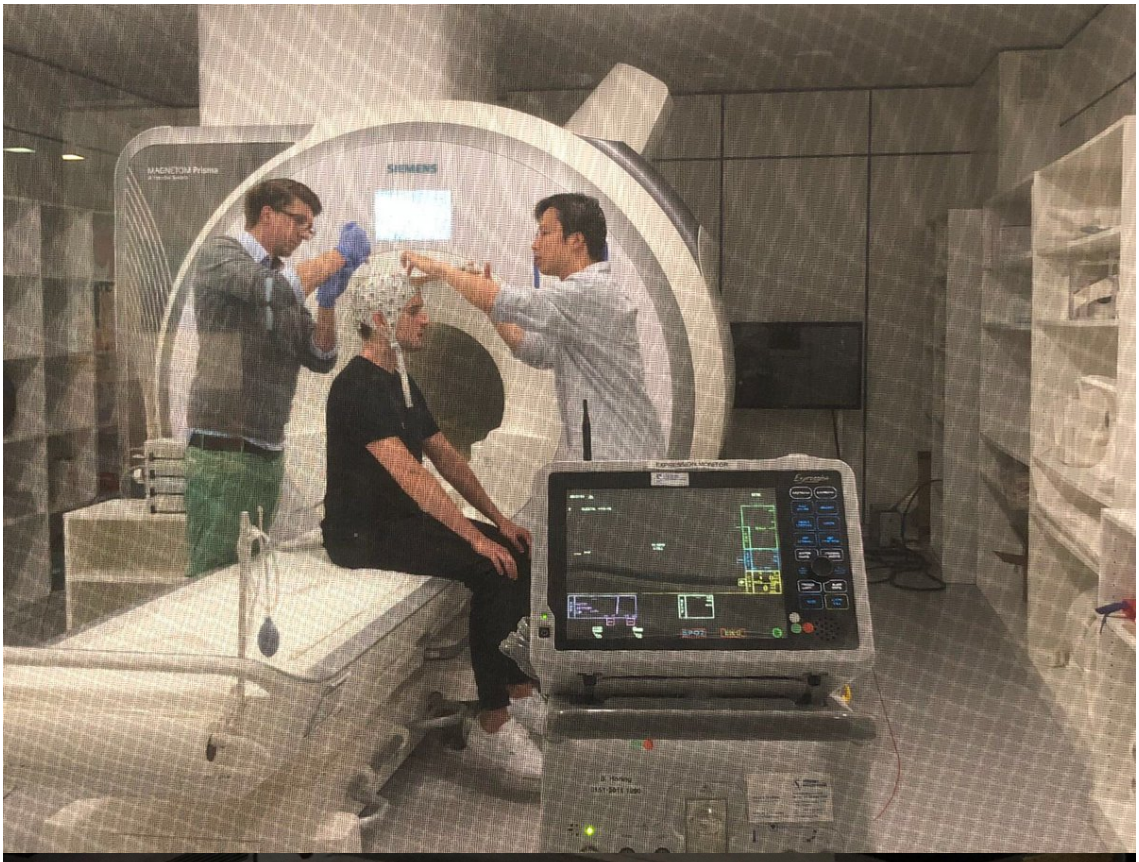
BEWARE
Mooring line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Signature: _____ Date: 22.03.19

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