

Progress Report

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Title of Project: A diagnostic profile of vestibular migraine using semicircular canal and otolith function tests

Summary

Project background

Vestibular migraine (VM) is a manifestation of migraine in which patients experience recurrent episodes of vertigo, which may coincide with a migraine headache, aura, phonophobia or photophobia (Lempert et al., 2012). Vertigo is a false sensation of movement of the self or surrounds and is a common and disabling symptom afflicting at least one million Australians each year. Vestibular migraine is the second most common cause of recurrent vertigo, but is often left undiagnosed and untreated due to the lack of clear diagnostic criteria and clinically applicable laboratory tests. Our project therefore aimed to improve the diagnosis of patients with vestibular migraine.

Unlike other episodic vestibular disorders, the duration and quality of vertigo in VM is so diverse that it can mimic many other common vestibular disorders. Very short episodes lasting seconds to minutes can be difficult to distinguish from benign positioning vertigo (BPV), intermediate episodes lasting several hours are similar to Meniere's Disease (MD) and long episodes lasting more than a day can be confused with vestibular neuritis (VN). We therefore aimed to investigate the diagnosis of VM by comparing it to the conditions it mimics, based on the duration of episodes.

Preliminary results

We planned to recruit 100 consecutive patients with definite or probable VM from the neuro-otology clinic of the Institute of Clinical Neurosciences at Royal Prince Alfred Hospital. Funding from the Brain Foundation of Australia has enabled us to recruit and collect data from 129 patients in total. Patients with clinically probable or definite migraine were recruited. Of the patients whose data has thus far been classified and analysed, 11 had probable or definite VM with *short* vertigo attacks (4 M, 7 F, aged 37-62 years) and 20 patients had *intermediate* duration attacks (6 M, 14 F, 15-68 years). We have not yet recruited patients with *long* duration attacks. In terms of patients with conditions mimicked by VM, we have recruited and test 21 patients with definite MD (7 M, 14 F, 27-85 years) and are currently recruiting patients with BPV. Clinical characteristics of patients in these groups are shown in Tables 1 and 2.

Table 1. Clinical Features (%)

| | Spontaneous vertigo | Positional vertigo | Spinning vertigo | Migraine history |
|-----------------|---------------------|--------------------|------------------|------------------|
| VM short | 55 | 64 | 55 | 100 |
| VM intermediate | 90 | 35 | 25 | 100 |
| MD | 100 | 37 | 84 | 37 |

Table 2. Symptoms during vertigo attack (%)

| | Headache | Tinnitus | Hearing loss | Fullness |
|-----------------|----------|----------|--------------|----------|
| VM short | 18 | 36 | 0 | 64 |
| VM intermediate | 65 | 15 | 20 | 40 |
| MD | 26 | 89 | 100* | 89 |

*HL was either worse during the attack or was reduced but no longer fluctuated

Intermediate-duration episodes of VM versus MD

Patients with VM with attacks lasting minutes to hours can be difficult to distinguish from those suffering from MD. While more than half of the VM group analysed so far describe having migraine at the time of vertigo (65%), a significant proportion do not, leading to a diagnosis of probable VM instead of VM. Patients with MD are less likely to describe headache as a feature of their episodes, though this does occur 26% of the time. Patients with MD report more aural symptoms, including fluctuating tinnitus and hearing loss, as expected due to the diagnostic criteria for MD. However, while the presence of tinnitus and hearing loss seem to be relatively good discriminators between the diseases, a feeling of fullness of the ear is less discriminative, as 40% of migraine sufferers also describe a sense of fullness. The other major difference is that MD patients mostly describe their vertigo as true spinning vertigo (84%), while patients with VM are more likely to complain of rocking, tilting, or other manifestations of vertigo. In contrast to previous reports, both groups of patients with VM (short and intermediate duration) are only slightly more likely to report being sensitive to self-motion (55% and 60%) or visual motion (45% and 55%) compared to patients with MD (47% and 42%).

The pilot data has shown higher rates of otolith abnormality in the patients with MD than VM (i.e. cVEMP and oVEMP asymmetry ratios). cVEMPs were abnormal in 40% of MD patients compared to 20% of VM patients, and oVEMPs were abnormal in 20% of MD patients and only 5% of VM patients. This is consistent with preliminary data collected by the Dr Welgampola, suggesting that VEMPs are robust in patients with VM (Taylor et al., 2012). oVEMPs were significantly smaller in affected vs unaffected MD ears ($P < 0.05$), even after exclusion of frankly abnormal responses, suggesting the presence of subclinical damage to the otoliths.

Semicircular canal function (i.e. the gain of the vHIT in each canal plane) fell in the normal range for all patients with VM, while 17/20 patients with MD had normal results. Two patients had canal paresis of all three canals in the affected ear, while another had reduced function of the right posterior canal on the affected side. Group analysis (excluding the 3 patients with frank abnormalities) additionally showed that the gain for the affected posterior canal was significantly lower ($P = 0.002$) in the MD patients (0.83) than the VM patients (0.94), suggesting that MD produced subclinical abnormalities that might become significant over time.

Short- versus intermediate-duration episodes of VM

There are already interesting differences emerging between the migraine patients who report having short (<5 mins) compared to intermediate length (mins-hours) vertigo attacks. Patients with very short episodes are less likely to describe their vertigo as occurring spontaneously and more likely to complain of positional vertigo (64% vs 35%). The positional component of vertigo, along with the short duration of attacks, is the feature that most resembles BPV and causes difficulty in diagnosis. In the short episode group, the temporal link between migraine and vertigo is relatively weak (18%), while the patients report surprisingly high rates of tinnitus (36%) and fullness of the ear (64%) during attacks, features more usually associated with MD.

Hypothesis vs Findings

The proportions of patients with short (up to 5 min) and intermediate (5 min to 24 hours) vertiginous episodes in our sample are likely to ultimately match the rates expected based on previous reports (40% and 30%, respectively), but we have not yet recruited any patients with long duration (greater than 24 hours) episodes (Dieterich and Brandt, 1999; Lempert et al., 2012). This might be due to the fact that patients with long episodes are often initially diagnosed with vestibular neuritis, and only present for follow-up once a new episode occurs, which may be some time after the first attack.

We have encountered higher rates of vestibular abnormality in the patients with MD than VM, as expected based on previous research on otolith reflexes (e.g. Taylor et al., 2012). However, the findings concerning semicircular canal function, as assessed by head impulse testing in all three canal planes for each ear, are novel.

As expected, there are already differences emerging in the clinical characteristics and test results of patients with different durations of VM and between VM and one of its mimics, MD. However, as the number patients with definitive diagnosis and classification in our study is currently small, it is premature to conduct full regression analysis to determine the clinical and test factors that most discriminate between patients.

Unanswered Questions

We hope that our full data analysis, to be conducted after the final diagnosis and classification of tested patients, will provide a means of separating VM patients from patients with conditions mimicked by VM. It is possible that inclusion of larger numbers of subjects may alter the proportions of abnormalities reported in the preliminary analysis.

What these research outcomes mean

The above data has now been used as the basis of an NHMRC Project Grant application for a larger project on vestibular migraine in the 2015 round of applications.

The preliminary data analysis has raised interesting questions about the differences within different groups of vestibular migraine patients. Patients who have short episodes of vertigo may have different combinations of symptoms than those with intermediate duration episodes. Although patients with both types of attack would be similarly classified as having VM, there may be differences in the underlying mechanisms producing the symptoms.

The rate of vestibular abnormalities was lower in patients with intermediate duration VM than with MD, and in fact patients with VM had largely normal vestibular reflexes. This means that a problem with the vestibular organs is not likely to be a contributing factor to vestibular migraine. In contrast, patients with Meniere's Disease were more likely to show vestibular loss and had smaller reflexes overall.

When all test results and clinical characteristics are considered together, it is hoped that these small differences found on individual tests will combine to provide a disease profile that allows MD to be more readily distinguished from VM, one of the main aims of this study. Diagnosis is often based on complex pattern recognition and we believe that our expanded study will provide new information about the clinical and test patterns in vestibular migraine in turn which will guide diagnosis.

References

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