OTOACOUSTIC EMISSION PHASE AS AN INDICATOR OF ICP CHANGE: BASIS AND OPTIMIZATION FOR FLUID SHIFTS STUDIES

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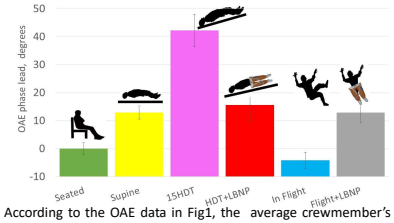
INTRODUCTION

Spaceflight-associated neuro-ocular syndrome (SANS) is a top human spaceflight risk for NASA. A leading hypothesis has been that intracranial pressure (ICP) is elevated in microgravity and that this is a root cause of many SANS signs and symptoms.

Changes in ICP can be detected non invasively through its influence on the inner ear. The otoacoustic emission (OAE) technique detects changes in the transmission of sound in and out of the ear caused by the stiffening of middle ear components under pressure from inner ear fluid. The technique has been validated in ground-based head down tilt (HDT) experiments and used successfully on crewmembers of the International Space Station (ISS) as a part of the Fluid Shifts project.

Figure 1 below shows averaged OAE phase relative to the seated position from 10 ISS crewmembers. Data from pre- and post-flight seated, supine, 15°HDT and 15°HDT with lower body negative pressure (LBNP) applied by Chibis, are compared with inflight OAE data, with and without LBNP.



According to the OAE data in Fig1, the average crewmember's ICP is not significantly raised in microgravity. And while LBNP lowers OAE's phase in HDT, it raises it in microgravity. The standard error bars show the averaged trends to be reliable, but there were anomalous values within and between sessions which sometimes made interpretation difficult for individuals. Tight FS project schedules precluded the investigation of confounding factors. We suspected these anomalies were due to a combination of poor positioning of the OAE test probe in the ear canal, transient middle ear pressure (MEP) imbalances as well as noise and real physiological changes.

AIMS AND METHODS

The aim of this study was to better understand the OAE/body tilt/ICP interaction with a view to improving the OAE method's accuracy and reliability, for example by learning how to detect and correct for individual ear probe fit variability and MEP changes.

The OAE-ICP change detection method relies on the inner ear's ability to generate a highly stable sound vibration response, called an OAE, in response to an applied stimulus (see also Fig 6). OAE stability allows the detection of very small time differences in their arrival at the ear canal. Frequency-specific measurements of signal arrival time changes are referred to as 'phase' shifts. Earlier arrival is a phase 'lead'.

The questions we wanted to answer in this study were:

- ❑ When HDT raises ICP and increases OAE phase shift, how is the phase of the stimulus sound in the ear canal affected?
- ❑ When HDT raises ICP, how is MEP affected and why?
- ❑ When MEP is changed, how are OAE (response) and stimulus phase affected?
- ❑ When the OAE probe is placed in a different position in the ear canal how are OAE phase and stimulus phase affected, and why?

To answer these questions we used all available OAE data from the main Fluid Shifts OAE project **(Expt 1)** which included measurement of changes in ear canal acoustics during HDT and spaceflight.

We also collected data from a supplementary project **(Expt 2)** on eight volunteers where we examined the effect of HDT, ear canal air pressure, ear probe fit and MEP on OAE and ear canal stimulus phase.

Finally we used OAE and MEP data from a third experiment **(Expt 3),** a study of a breathing impedance threshold device (ITD), as a possible countermeasure against raised ICP and venous congestion.

OAE phenomena are quite frequency dependent and are most affected by pressure around 1kHz. The data presented here were all derived using evoking stimuli in the frequency range 800-1400Hz. In all three experiments OAE data were collected using the *Otoport Advance* clinical OAE device (Otodynamics Ltd. Hatfield, UK).

EXPERIMENTAL RESULTS

❑ **Raising ICP with HDT accelerates sound transmission through the middle ear and only slightly delays stimulus phase in the ear canal.**

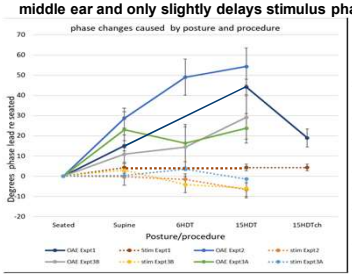


Figure 2 shows how raising ICP with HDT causes OAE phase to increase relative to seated. LBNP by Chibis (ch) reduced the effect. In contrast, the phase of the stimulating sound pressure (stim) only marginally decreased or was unchanged. Group average data are shown with standard errors. Expt 3A is with ITD treatment and 3B is without. Subject numbers were Expt1: 10, Expt2: 7, Expt3: 12.

❑ **Raising ICP exerts an outward pressure on the ear drum.**

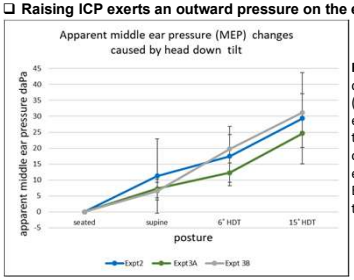


Figure 3 shows how HDT creates an apparent positive (outward) pressure on the ear drum, as recorded by tympanometry. Three parts of the two independent experiments closely agree. Expt 3A is with ITD treatment and 3B is without.

❑ **Raising or lowering air pressure on the ear drum accelerates transmission through the middle ear but retards sound in the ear canal.**

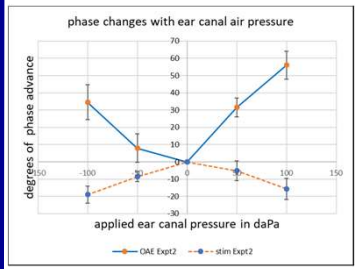


Figure 4 shows that changing the pressure in the ear canal (positive or negative) increases OAE phase similarly to HDT (Expt 2). It also decreases ear canal stimulus phase (which depends on the ear canal acoustic environment) by about 1/3 that of the increase in OAE phase. The average subjects' resting MEP was +5daPa +/- 17daPa. One of 7 subjects presented with a seated +40daPa pressure imbalance.

❑ **The depth of probe insertion & refitting has minimal effect in most cases.**

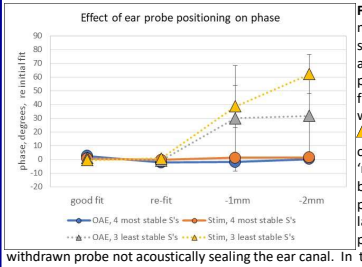


Figure 5 demonstrates that in most cases neither OAE or stimulus phase are strongly affected by the depth of probe insertion. ●● are data from 4 of 7 subjects in Expt2 with very stable phase data. ▲▲ are data from the 3 other subjects where the 'regular' fit was reproducible but the slightly withdrawn probe fittings showed much larger phase deviations. We postulate this was due to the withdrawn probe not acoustically sealing the ear canal. In these subjects the individual increases in OAE and Stim phases were similar in size and correlated (0.7).

ACKNOWLEDGEMENTS

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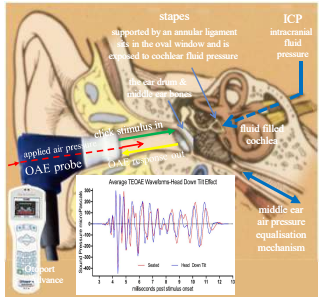
DISCUSSION AND INTERPRETATION

Ear canal acoustic measurements provide an effective noninvasive means of monitoring ICP change but the mechanism is not fully understood, and interpretation of results requires caution and attention to a number of confounding factors which have been examined in this study. **Figure 6** below shows the anatomical components involved, with the OAE probe fitted into the ear canal. The probe contains a loudspeaker, a microphone and a fine tube for air pressure control. The middle ear mechanism physically couples the ear canal to the cochlea via the stapes. Fluid in the cochlea is normally in pressure equilibrium with ICP. Raised ICP pushes on the stapes, displacing it and the middle ear bones, pushing the ear drum outwards. This increases elastic tension in the stapes annular ligament AND the tympanic membrane (drum). Tension increase in turn leads to a shortening of transmission time through the middle ear, seen as a phase change in the OAE. Inset is an example of a click evoked OAE response from Experiment 1, showing how the later, lower frequency waves arrive earlier under head down tilt (ICP is higher and annular ligament more tense).



Figures 1 and 2 illustrate the results of the primary application of this technique, namely to register ICP changes. It is unclear why the average magnitude of the effect is different in each experiment (Figure 2), as the equipment and data processing were identical. The stimulus is virtually unchanged by HDT.

Figure 3 demonstrates that HDT results in outward pressure on the ear drum. This is probably the effect of mechanical displacement of the middle ear bones driven by stapes displacement increasing drum tension. It appears as a positive middle ear pressure under tympanometry likely due to ICP, not air pressure. The acoustic pressure gain from drum to stapes is about 22, mainly due to the smaller area of the stapes receiving all the force on the drum. Taking stapes-to-drum transfer as the inverse, 1/22, we convert the 30daPa drum pressure at 15° HDT to the ICP change at the stapes, and get 660daPa, or 50mmHg. Invasive ICP measurements with posture (e.g. Petersen et al. 2016) predict a 205daPa or 15.4mmHg rise in ICP from seated to 15° HDT. Our prediction is just over 3 times too large. The simplest explanation is that the transmission of static pressure from stapes to drum is greater than the 'acoustic' value of 1/22; more like 1/7. Subject to this transfer ratio being validated, and no source of air displacement being identified during HDT, ICP change detection should be feasible from MEP.

Figure 4 shows how increasing middle ear tension by applied ear canal air pressure also changes OAE phase. This potentially provides a means to 'calibrate' ICP-induced OAE phase changes as physical pressure change. For example Figure 4 predicts that the 45° OAE phase change caused by 15°HDT in Expt 1 (Figure 2) would be counteracted by ~100daPa of air pressure on the drum. If we apply the 1:7 middle ear inward static pressure transfer ratio indicated by the MEP data to the 100daPa air pressure, for 15° HDT we obtain an estimate of 700daPa or 53mmHg of ICP change at the stapes. This is over 3 times the invasive ICP value, indicating that the transmission of static pressure from drum to stapes may be nearer 1:2 than the 1:22 with acoustic pressure. The drum is exposed to the applied air pressure and the tension affects ear canal acoustics. This is demonstrated by the concurrent negative stimulus phase changes (Figure 2). Stimulus phase change was only 3 times smaller than the OAE change and may indicate that ear canal air pressure does not fully reproduce the effects of ICP at the stapes.

CONCLUSIONS

- ❑ ICP change is reliably indicated by OAE phase change but similar changes can be caused by air pressure imbalances across the ear drum. This is potentially a large source of experimental error, but it can be easily measured and corrected for.
- ❑ ICP change appears to be detectable by simply tympanometry, as a middle ear pressure change. ICP values comparable with invasive measures can be obtained if an appropriate middle ear static pressure transfer factor is used.
- ❑ Our experiments have demonstrated how it is possible to calibrate OAE phase changes to yield quantitative mmHg values for ICP change. Individual ear pressure calibrations may reduce inter-subject variability. However pressure conversion factors needed still need to be refined and verified.
- ❑ OAE probe placement is not an intrinsically large variable in OAE phase measurements, but incomplete sealing of the probe does introduce large phase errors

Reference: Postural influence on intracranial and cerebral perfusion pressure in ambulatory neurosurgical patients. L. G. Petersen, J. C. G. Petersen, M. Andresen, N. H. Secher, M. Juhler. *Am J Physiol Regul Integr Comp Physiol* 310: R100–R104, 2016.