Applying Knowledge—Challenges in Bringing Scientific Advances to Dizzy Patients

Thomas Haslwanter and James Ong

Upper Austria University of Applied Sciences, Linz, Austria

Simple diagnostic or therapeutic procedures can produce tremendous benefits for dizzy patients. To see how new ideas in the laboratory evolve into benefits for patients, an attempt to analyze how the corresponding information is distributed was made. To quantify that flow of information, a number of new scientific publications, citation numbers, and a number of new books on relevant subjects were looked at. For vertigo, this approach was facilitated by the fact that the diagnostic procedures for benign paroxysmal positioning vertigo (BPPV) and for canal paresis can be traced back to seminal publications. Results indicate that the current way of disseminating new information used here is working well, and that new ideas on diagnosis and treatment are readily available to practitioners. However, the application of new methods is limited by the availability of the required technology. It is conjectured that the technological requirements have become more complex over time, leading to a slower uptake of new technology.

Key words: **translational research; diagnosis; measurement technology; electro-oculography; video-oculography; scleral search coils; BPPV; rapid head impulse test**

Introduction

Dizzy patients can easily confound doctors, as dizziness can have many different origins. Dizziness can be due to pathology of the peripheral vestibular system or in the oculomotor system; changes in the central processing of vestibular information or in the control of eye movements; or neurological, cardiovascular or psychological problems. Therefore, it is not surprising that simple, well-understood procedures that challenge a specific aspect of the peripheral vestibular system have been a tremendous help in improving the diagnosis and treatment of dizzy patients. In this chapter, we concentrate on two pathologies where such procedures became available about twenty years ago: *benign paroxysmal positional vertigo* (BPPV), a pathology that causes transient, strong vertigo when the head is in a specific orientation; and *canal paresis*, a loss of function in one or more of the vestibular semicircular canals that transduce angular velocity.

As noted in a recent *Nature* editorial, the amount of basic research is growing rapidly and budgets are far higher than they were two decades ago. However, the impact of this research is growing much more slowly.[1] By investigating how improvements in diagnosis and treatment for these two pathologies move "from bench to bedside," we hope to obtain a better understanding of how best to bring advances to the patients. We break down the transition from research idea to real-world application into three steps: first, the idea is tested in the laboratory using available measurement technologies; second, the idea spreads through the research community; and third, this information passes on to the practitioners who are seeing the patients.

There are many ways to assess the dissemination of diagnostic tests and treatments, and the speed of their uptake by medical professionals: one can look at the frequency of peer-reviewed

Address for correspondence: PD Dr. Thomas Haslwanter, Upper Austria University of Applied Sciences, Department of Medical Technology, School of Applied Health and Social Sciences, Garnisonstr. 21, A-4020 Linz, Austria. thomas.haslwanter@fh-linz.at, http://work.thaslwanter.at/

Basic and Clinical Aspects of Vertigo and Dizziness: Ann. N.Y. Acad. Sci. 1164: 309–315 (2009).
doi: 10.1111/j.1749-6632.2008.03716.x

publications or books on these topics, ask companies selling diagnostic devices about the type and numbers of devices sold, or conduct surveys of researchers or doctors. In practice, though, not all these sources are easily available.

To assess the adaptation of new measurement technologies, we focus on the numbers of scientific publications using these technologies: this should be an indicator of their acceptance. To assess the dissemination of new diagnostic and treatment approaches, we look at the number of citations of seminal papers: this should reflect how quickly new information is picked up by the research community. Finally, to measure how quickly information can get to resident doctors who do not have the time to follow the current research, we look at the number of books appearing on these topics each year.

Methods

Publication and Citation Research

To find out how many publications have appeared on specific topics, we used the *ISI Web of Knowledge* (http://www.isiwebofknowledge.com/). This subscription-based service covers over 25,000 journals and 192,000 conference proceedings. In addition, 25 million cited references are added annually. The ISI-Web provides information about publication numbers, as well as information about citations of individual articles. Instead of using the ISI-Web, it is also possible to use other on-line publication databases like Scopus (http://www.scopus.com/) or Google Scholar (http://scholar.google.com/). Scopus boasts that it is "the largest abstract and citation database of research literature and quality web sources," but this service comes at a price. Although we found a number of academic institutions that have trialed the service, many have discontinued their subscription because of the steep cost. At the other extreme, Google Scholar is a free service available to everyone, but because it relies on free information to generate its results, many important journals cannot be included in its search. The results are also noisy, since Google's automated classification algorithms are certainly not error-free. A more detailed comparison of publication databases has been published by Jacso.[2]

For our investigation, articles on the ISI-Web were searched by "Topic," which includes title, abstract, and keywords. All of the databases available in ISI-Web were included. To eliminate spurious results from unrelated areas of science, subject areas that were obviously not relevant were excluded. For example, when looking for articles on "rapid head impulses," results from the subject area "Geology" were excluded. Publication dates were then sorted by year. The last complete year included in the survey was 2007. For a general overview on the numbers of new scientific articles published each year in this field of research, we counted the number of publications on the general topics "vestibular" and "oculomotor."

Diagnostic Tests

The assessment of the efficacy of information distribution for diagnostic procedures was somewhat more complicated than expected. For example, doctors were treating patients suffering from BPPV even before the mechanisms underlying that pathology were sufficiently understood. In other words, just looking at the occurrence of the term "BPPV" in the topic of articles would not provide all of the information on new diagnostic and treatment procedures that we are seeking. We tried to bypass that problem by selecting seminal publications, and by checking when and how often these seminal works were quoted by other researchers. This should provide some insight into how quickly new knowledge can spread.

BPPV is one of the most frequent causes of dizziness. It can be efficiently treated with the Epley and the Semont maneuvers and the Brandt-Daroff Exercises.[3–5] These procedures assist in the removal of otolith debris from the semicircular canals, thereby eliminating the

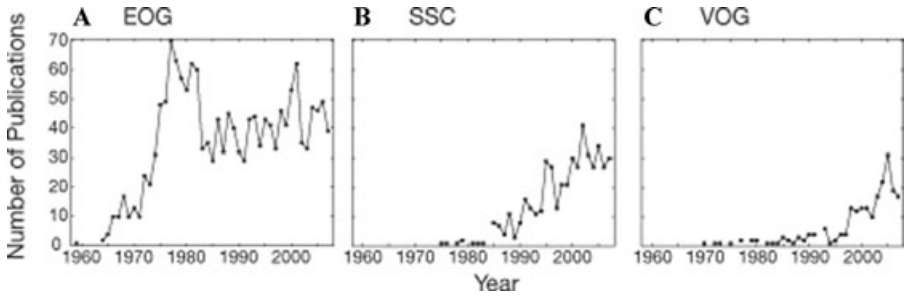

Figure 1. Number of publications from 1958 to 2007 involving (**A**) EOG (electro-oculography), (**B**) SCC (scleral search coils), and (**C**) VOG (video-oculography).

associated vertigo. BPPV can be efficiently diagnosed by observing the combined vertical-torsional eye movements caused by a repositioning maneuver. A good doctor who knows what to expect can usually correctly identify BPPV by simple observation of the eye movements of a patient during a head movement that triggers the vertigo. Unfortunately, many doctors miss those clear signs, resulting in a dismaying number of patients where BPPV is overlooked.[6]

The functional loss of an individual semicircular canal can be clearly diagnosed by the *rapid head impulse test*, a procedure suggested by Halmagyi and Curthoys to test the functional status of each semicircular canal.[7] The test exploits the fact that fast head movements silence inhibitory responses in the vestibular periphery, leaving a "clear window" on the functional status of the excited semicircular canals.

Book Searches

To check into the visibility of new methods and research ideas to resident doctors, either directly or secondhand through the prompting of patients, we looked at the rate at which they were incorporated into books. The searches were performed with the search engines at Google Books (http://books.google.com/) and Amazon.com. Neither search engine provides an interface to directly extract the number of books published as a function of time. To extract the data from Google Books, the individual search pages (with up to 100 hits per page) were saved to disk and then a simple shell script (written in *awk*) was run to extract the publication years; obvious errors in Google's automated determination of publication year were corrected manually. For the Amazon search engine, the results were sorted by publishing year in chronological order, and then the counts extracted manually. As with all Web-based search engines, the counts cannot be taken literally—instead, they should only be interpreted as rough estimates. For example, both Google Books and Amazon produce multiple hits for different editions of the same book; indeed, Google Books sometimes even produces multiple hits for one book, due to errors in Google's automated classification system.

Results

To assess the role and effect of new technological requirements, we looked at the prevalence of the three most common methods to measure eye movements: electro-oculography (EOG), scleral search coils (SSC), and video-oculography (VOG).

Technologies for Eye-Movement Recordings

Figure 1 shows the number of new publications on EOG, SSC, and VOG. Historical and technical details about EOG and VOG can be found in a recent review article by Haslwanter and Clarke,[8] as well as in a review by Borah.[9]

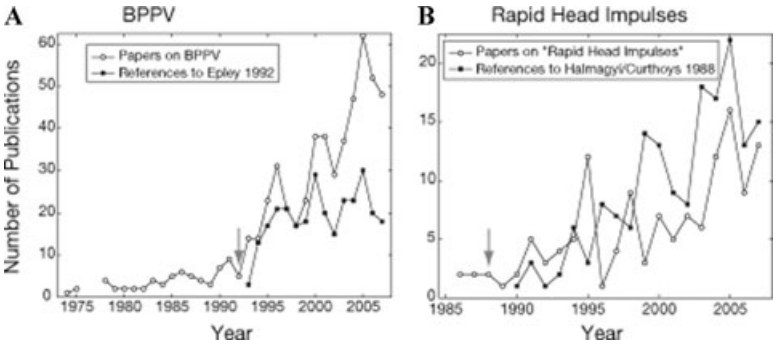

Figure 2. (**A**) *Clear circles:* 582 references to benign paroxysmal positioning vertigo (BPPV) (1972–2007); *black squares:* 293 citations of the 1992 article by Epley. (**B**) *Clear circles:* 151 references to rapid head impulses (1985–2007); *black squares:* 178 citations of the 1988 article by Halmagyi and Curthoys.

EOG: A comparison of the graphs in Figure 1 shows that EOG has remained one of the most common ways of recording eye movements in a research setting, despite the advent of other tracking methodologies. It started to become popular when electronic amplifiers became easily available. Taking different terminologies for EOG into account (Query: "Topic = (EOG OR electro oculography OR electro nystagmography) AND Topic = (human*)"), the ISI-Web came up with 1630 publications (Fig. 1A).

SSC: In 1975, Collewijn and colleagues made a practical version of the SSC available by embedding the search coils into a soft silicon annulus,[10] a principle that is still currently used. However, it took approximately 10 years (ca. 1975–1985) before the technique became widely used for recordings in human subjects. Figure 1B shows the 466 articles involving the use of SSCs with human subjects, arising from the query: "search coil*" and "eye*" and "human.*"

VOG: A similar development can be observed with video-based systems for eye-movement recordings. While researchers had been investigating and improving VOG systems since 1933,[11] they remained expensive and were for decades only available in a small number of laboratories. All in all, it took more than 20 years (ca. 1970–1997) for availability and usability to reach the point where VOG systems could be commonly used. Figure 1C shows the 231 results for the search on the query: "VOG OR video oculography OR video nystagmography."

Application to Vestibular Problems

To understand the factors contributing to the dissemination of medical knowledge, we investigated publications on BPPV and on the rapid head impulse test.

BPPV: The problem of vertigo that is precipitated by certain head orientations has been known for a long time. The first systematic way to treat patients afflicted with BPPV was described in 1992.[3] (The corresponding paper by Epley is also by far the most frequently cited work in this field, with almost 300 citations.) This coincided with a better understanding of the underlying mechanisms of BPPV.[12] Figure 2A shows how quickly Epley's paper was taken up by the scientific community (query "benign paroxysmal positional vertigo OR BPPV").

Rapid Head Impulses: The seminal publication that triggered the use of rapid head impulses for the clinical diagnosis of the functional status of the semicircular canals was apublication article by Halmagyi and Curthoys in 1988.[7] Figure 2B shows that this procedure also became well known in the medical and scientific community within a few years. Here, it should be noted that it was almost impossible to

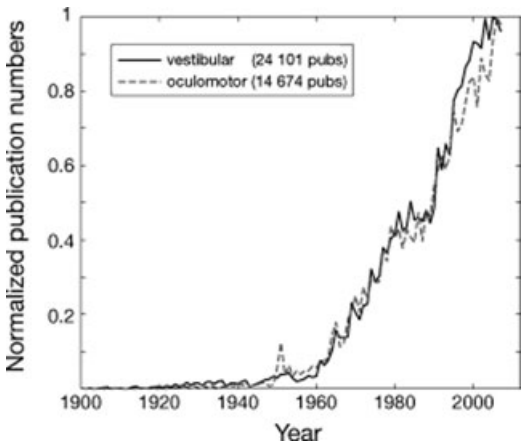

Figure 3. New publications on the topics "vestibular" and "oculomotor," 1900–2007.

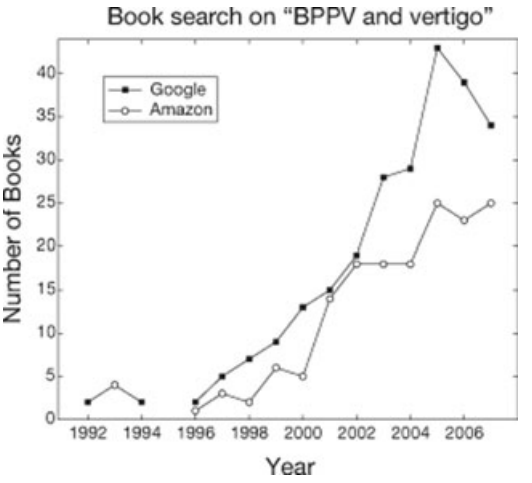

Figure 4. Book searches on "BPPV and Vertigo" with Google Books (*black squares*) and with Amazon (*clear circles*).

restrict the query results to the clinical rapid head impulse test, as many publications on whiplash and similar biomechanical questions use similar keywords and expressions. Indeed, the 1988 article by Halmagyi and Curthoys was not found either with queries for "head impulse test" or for "high acceleration AND head rotation." [Figure 2B: results of query "(rapid AND head rotation) OR (head impulse test) OR (high acceleration AND head rotation) AND (diagnos*)"].

Publication Numbers—Context

In order to put the publication numbers just mentioned into context, we checked the number of "vestibular" and "oculomotor" articles that have been published in general. Searching the topic "vestibular" delivered over 24,000 hits, and the topic "oculomotor" close to 15,000 hits. Figure 3 shows the publications per year, normalized to a maximum number of 1. In 2007, the last full year available, 616 new oculomotor papers and 945 new vestibular papers were published. Note that the total number of articles in each field goes up steeply.

Book Searches

In spite of the inaccurate nature of Web search results, general trends are still clearly present in our searches with Google Books and Amazon (Fig. 4). The search on "BPPV and vertigo" returned a small number of hits between 1992 and 1998, and then a steadily rising number of hits thereafter. Note that the first hits, occurring in 1992, came out in the same year that the seminal paper of Epley was published. Altogether, 271 books were found with Google Books, and 162 with Amazon.

Discussion

Somewhat to our surprise, the literature research indicates that the current ways to disseminate knowledge work remarkably well. In our analysis, we observed that for some newer diagnostic procedures, seminal "starting" publications can be identified. For BPPV, the 1992 publication by Epley changed the diagnosis and treatment of this pathology.[3] Similarly, the basis for the rapid head impulse test was the 1988 publication by Halmagyi and Curthoys.[7] In both cases, no technical infrastructure was required to apply these tests in practice, and the information became well known in less than five years. In other words, the time required to get information to researchers is not a limiting factor in the dissemination of new

medical procedures. Considering that the writing and publication of a new book normally takes one to two years (compared to the six to nine months that usually pass between submission and publication of a scientific manuscript in a peer-reviewed journal), the delay of book-based coverage of BPPV was also very short. Thus, the information is readily available for doctors who try to keep up with current diagnostic and treatment innovations.

In contrast, the development of technical foundations typically takes substantially longer. We speculate that this could be caused by the increasing technical complexity of modern measurement systems, as well as by the growing bureaucratic requirements for the certification of medical technologies. The corneoretinal potential, which forms the physiological basis for EOG, was well known before 1960. However, only the invention of the transistor[13] and the subsequent availability of operational amplifiers made EOG practical for routine medical applications. For SSC, the limiting factor was the availability of an appropriate sensor. The principle behind SSCs was first employed in 1963 by Robinson.[14] To attach the coil to the eye, Robinson used a vacuum pump that produced suction between the eye and the coils. While this was acceptable (at the time) for his research laboratory, it was too invasive for general use. Acceptable sensors only became available through the work of Collewijn.[10] Similarly, VOG had already been employed by 1963, with Melville-Jones using standard 16-mm film cameras.[15] But it was the introduction of digital image processing that has brought the price of VOG systems down and has made them more widely available.

We were surprised by the persistence of well-established measurement technologies: while the introduction of SSC and VOG has led to the frequent prediction of the demise of EOG, our results indicate it is still the most commonly used method of recording eye movements.

Theoretically, the prevalence of medical systems could also be estimated by the number of sales by companies selling such systems. However, fewer than 10% of all manufacturers of video-oculography systems that we contacted were willing to provide information about their sales numbers. As a result, this information was not included in our study.

Despite the overwhelming success of the procedures on BPPV and canal paresis described here, only a few laboratories worldwide have the technology to perform these methods in a quantitatively controlled way. As a result, BPPV is still often overlooked.[6] In addition, no commonly agreed upon standard has been developed for the assessment of the functional status of the semicircular canals, based on the rapid head impulse test. To address these problems, our group is trying to develop simple, affordable, and reliable diagnostic procedures for the two chosen pathologies using VOG: We are trying to contribute to a standardized, quantitative evaluation of eye movements elicited by rapid head impulses through the elimination of camera slippage artifacts in VOG systems; and we are trying to develop a simple, VOG-based quantitative BPPV test to reduce the number of misdiagnosed BPPV patients. We hope that our results will remove the remaining technical hurdles for a quantitative evaluation of BPPV treatment and the rapid head impulse test.

Acknowledgment

This study was supported by the Austrian Science Fund (FWF), Grant No. L425-N15.

Conflicts of Interest

The authors declare no conflicts of interest.

References

1. COPY EDITOR. 2008. Translational research: Getting the message across. *Nature* 453[7197].
2. Jacso, P. 2005. As we may search—Comparison of major features of the Web of Science, Scopus, and Google scholar citation-based and citation-enhanced databases. *Curr. Sci.* **89:** 1537–1547.

3. Epley, J.M. 1992. The canalith repositioning procedure: for treatment of benign paroxysmal positional vertigo. *Otolaryngol. Head Neck Surg.* **107:** 399–404.
4. Brandt, T. & R.B. Daroff. 1980. Physical therapy for benign paroxysmal positional vertigo. *Arch. Otolaryngol.* **106:** 484–485.
5. Semont, A., G. Freyss & E. Vitte. 1988. Curing the BPPV with a liberatory maneuver. *Adv. Oto-Rhino-Laryngol.* **42:** 290–293.
6. Oghalai, J.S., S. Manolidis, J.L. Barth, *et al*. 2000. Unrecognized benign paroxysmal positional vertigo in elderly patients. *Otolaryngol. Head Neck Surg.* **122:** 630–634.
7. Halmagyi, G.M. & I.S. Curthoys. 1988. A clinical sign of canal paresis. *Arch. Neurol.* **45:** 737–739.
8. Haslwanter, T. & A.H. Clarke. 2008. Eye movement measurement: electro-oculography and video-oculography. In *Vestibular and Balance Disorders*. D.S. Zee & S.D. Eggers, Eds. Elsevier, New York.
9. Borah, J. 2006. Measurement techniques for eye movement. In *Encyclopedia of Medical Devices and Instrumentation*. J.G. Webster, Ed.: 1–23. John Wiley & Sons, New York.
10. Collewijn, H., F. van der Mark & T.C. Jansen. 1975. Precise recording of human eye movements. *Vision Res.* **15:** 447–450.
11. Machemer, H. 1933. Eine kinematographische Methode zur Pupillenmessung und Registrierung der Irisbewegung. *Klin. Monatsbl. Augenheilkd.* 302–316.
12. Brandt, T. & S. Steddin. 1993. Current view of the mechanism of benign paroxysmal positioning vertigo: cupulolithiasis or canalolithiasis? *J. Vestib. Res.* **3:** 373–382.
13. Shockley, W. 1956. *Electrons and Holes in Semiconductors, with Applications to Transistor Electronics*. Krieger, Melbourne, FL.
14. Robinson, D.A. 1963. A method of measuring eye movement using a scleral search coil in a magnetic field. *IEEE Trans. Biomed. Eng.* **10:** 137–145.
15. Melvill-Jones, G. 1963. Ocular nystagmus recorded simultaneously in three orthogonal planes. *Acta Otolaryngol.* 619–631.