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See-saw nystagmus in dogs and humans:

An international, across-discipline, serendipitous collaboration

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Before the 1991 report of achiasma in dogs,[1] there was general acceptance that all vertebrates had decussation at the optic chiasm.[2] Exactly how, within the space of a few years, the achiasmatic condition came to be recognized in two mammalian species is an interesting confluence of interpersonal scientific communication and some serendipity. "Serendipity," a word coined by Walpole in a letter written in 1754,[3] based on a fairy tale he had written several years earlier,[4] has a long history in science.[5-9]

In 1991, Robert Williams, PhD (a Memphis neuroanatomist/biologist), who had been studying the anatomy of mutant Belgian sheepdogs that had no optic chiasm, sent me videos of their eye movements, asking if they were like human congenital nystagmus (CN). I replied that although they appeared to be similar, we would have to document the waveforms of the dominant horizontal oscillation. Also visible in the video were vertical components, which are less common in human CN, and what appeared to be transient see-saw nystagmus (SSN), a disconjugate vertical nystagmus with a conjugate torsional component such that each eye intorts as it goes upward and extorts as it goes downward.[10] SSN is not part of the human CN condition, and congenital SSN is extremely rare.[11-13]

I traveled to Memphis in 1992 and (with Williams) confirmed, by both direct observation and additional videos, the presence of SSN in one dog and vertical components of the nystagmus in the others. I discussed the canine condition with Josephine Shallo-Hoffmann, PhD (working in the vestibuloocular laboratory of Michael Gresty, PhD, in London) in 1991 and 1992 and told her of my intention to present it at the 1993 Association for Research in Vision and Ophthalmology (ARVO) meeting. Shallo-Hoffmann had previously collaborated with Patricia Apkarian, PhD (working in the laboratory of Han Collewijn, MD, PhD, in Rotterdam) on several papers dealing with the visual evoked potential (VEP) diagnosis in CN and in human albinism[14,15]; they showed that the VEP asymmetry in albinism did not occur in CN without albinism. Shallo-Hoffmann discussed with Apkarian two of Apkarian's patients whose VEP data were inconsistent with albinism; indeed, the VEP asymmetry actually appeared to be the opposite of that found in albinism, where there are too many crossing fibers.[16] Shallo-Hoffmann made the connection between the achiasmatic dogs and Apkarian's two female patients and asked me whether she could tell Apkarian about the dog observations and whether she should suggest that Apkarian present the human VEP data at the same 1993 ARVO meeting. With my permission, Shallo-Hoffmann did so and prevailed on Apkarian to submit an abstract for ARVO[17] which she (Shallo-Hoffmann) edited.

Apkarian concluded from analysis of her VEP data, and verified by MRI, that her patients did indeed have achiasma. As part of the resulting VEP presentation at ARVO,[17] she showed a video of the eye movements of one of the girls. In addition to observing the horizontal CN-like oscillation, I made the diagnosis of SSN as we watched the video from the audience and pointed it out to Shallo-Hoffmann and Larry Abel, PhD, who were sitting with me. They concurred with my observation, because both the disconjugate vertical and conjugate torsional components were evident in the video to anyone with a knowledge of the characteristics of SSN. Before that moment, I had thought that my previous observation of SSN in a single achiasmatic dog might reflect a species difference. This prompted me to reexamine the other dog videos, which showed (later confirmed by recordings) that they all had SSN and some also had vertical components of their CN.[18,19]

One can only speculate whether the original observation of SSN in the dogs would ever have been made, or its importance appreciated, if it had not been for the following serendipitous occurrences: Williams invited me to study the eye movements of the achiasmatic Belgian sheepdogs; Shallo-Hoffmann knew and collaborated with both Apkar-

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ian and me; and Shallo-Hoffmann made the critical connection between the achiasmatic dogs, their nystagmus, and the possibility that Apkarian's two human subjects might also be achiasmatic.

The SSN, which was overlooked by the authors of the 1993 ARVO VEP presentation,[17] might also never have been discovered, because the expertise of the authors was not in the area of ocular motor oscillations. At the 1993 ARVO meeting, I explained the nature of SSN to Apkarian and informed her that her patient had SSN, in addition to horizontal nystagmus. I also explained that, given our earlier findings of SSN in the achiasmatic dog, this suggested a causal link between interruption of the crossing retinal fibers and the see-saw oscillation and cast some doubt on prior hypotheses about acquired SSN. I repeated these points in several discussions with Apkarian over the next 2 years. Upon returning from ARVO, I showed the Apkarian video to Robert B. Daroff, MD, R. John Leigh, MD, and two graduate students. Both Daroff and Leigh confirmed the presence of SSN.

In May 1993, after the ARVO meeting, I was invited by Apkarian and Collewijn to visit Rotterdam that September to record and study the nystagmus of one of the achiasmatic girls. I then wrote an eye-movement-recording protocol and forwarded it to Apkarian. To document the waveforms of the horizontal nystagmus (thought to be CN), the vertical see-saw, and their phase relationship, I specified that both horizontal and vertical (and torsional, if possible) eye movements needed to be recorded in both eyes simultaneously. If I had planned to study horizontal CN in isolation, recordings in the horizontal plane only would be needed. The apparatus was set up in conformance with the protocol by Hans van der Steen, PhD, and operated by Aldo Ferraresi, PhD, during our study. Before leaving Rotterdam, I wrote the abstract of our findings which we planned to submit for the 1994 ARVO meeting.[20] Several months later, Apkarian expressed some concerns about presenting the 1994 ARVO ocular motility paper to a group of experts in a field in which she described herself as an "eye movement novice." To allay her understandable concerns, I sent her my extensive preliminary analysis of the fixation data (done in Cleveland), and van der Steen wrote programs for data display and helped with the analysis of the pursuit and optokinetic data we had taken. The 32 figures resulting from my analysis contained more data than would be needed for several 10-minute ARVO talks. As a result, Apkarian presented only part of the fixation data at the 1994 ARVO meeting,[20] showing the recordings of both the horizontal CN and the primary vertical component of the SSN.

As a biomedical engineer who has spent the better part of his career working in the area of ocular motor dysfunction, I fully appreciate the benefits of seeking the help and collaboration of experts in the allied fields of neurology and ophthalmology. When such collaboration occurs, the outcome is always greater than either could have done alone. I have described an instance in science (undoubtedly not isolated) where the interdisciplinary and intercontinental collaboration among scientists, the opportunity to meet at international scientific conferences, and serendipity were responsible for bringing to light that achiasma exists in humans and is associated with SSN in both dogs and humans. Each of the abovenamed participants was in the right place at the right time to apply their particular expertise in making the critical connections and observations that resulted in a new finding with both basic and clinical implications. From the across-species observation, I hypothesized that interruption of the crossing fibers in the chiasm may be sufficient to cause the vertical-system instability known as SSN. Previously, we believed (based largely on Daroff's observations and writings[21,22]) that additional lesions in the thalamus were necessary for SSN to manifest. The clinical significance of this is, if congenital SSN is diagnosed in an infant (admittedly, a rare occurrence), one should suspect interruption of the crossing retinal fibers due to partial or total achiasma.

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