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Diagnostic Error and Neuro-Ophthalmology

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Abstract

PURPOSE OF REVIEW: This review summarizes the recent literature on diagnostic error relevant to the practice of neuro-ophthalmology, and evaluates the potential of increased access to neuro-ophthalmology as a means to decrease rates of diagnostic error, thereby reducing medical harm and spending on unnecessary tests and treatments.

RECENT FINDINGS: Despite medical advances, current research continues to show alarmingly high rates of diagnostic error. Research into diagnostic error shows that many of these errors are due to cognitive errors. Recent studies on diagnostic problems relevant to neuro-ophthalmology, including studies of misdiagnosis of posterior communicating artery aneurysms, idiopathic intracranial hypertension, optic neuritis, and optic nerve sheath meningiomas, have identified major causes of diagnostic error in these conditions.

SUMMARY:

Studies on diagnostic error in neuro-ophthalmologic conditions show that prior to evaluation by a neuro-ophthalmologist, patients may undergo unnecessary tests and treatments that are costly and potentially harmful. Further research on diagnostic error will inform better utilization of neuro-ophthalmologists as a resource to decrease diagnostic error.

Keywords

Diagnostic error; medical harm; referral patterns; neuro-ophthalmology; reimbursement

INTRODUCTION

Since the publication of *To Err is Human* [1] in 1999, a report that estimated the death toll from medical errors in the United States to be as high as 98,000 per year, addressing medical errors has become a major area of research [2]. In 2005, the Committee on Diagnostic Error in Health Care expanded the definition of diagnostic error to include failure to communicate the correct diagnosis to the patient [3]. Although making the correct diagnosis is the most fundamental step in providing appropriate medical care, the rate of diagnostic error in the

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United States overall has been estimated to be as high as 15% [4,5]. Advances in medical technology have not solved the problem of diagnostic error in medicine, as seen by autopsy studies [6]. Diagnostic error continues to be a widespread problem, and may affect 5% of people in the United States [7].

The Society for Diagnostic Error in Medicine, which held its first conference in 2008 [8], was established to foster research to address these nuanced issues. However, diagnostic error remains an understudied area, in part because it is a challenging area to research [9,10].

CHALLENGES IN ADDRESSING DIAGNOSTIC ERROR

Diagnostic error is more difficult to define than other types of medical error. Similarly, it is more difficult to measure and may be less amenable to system-based prevention strategies [5,11]. In part, this is because the majority of diagnostic errors are due to cognitive errors by physicians, particularly in synthesizing the available information to identify the correct diagnosis [5, 12,13]. Educational initiatives may address knowledge gaps, but are not sufficient to address errors in analysis or synthesis. Conscientious use of analytic reasoning and “cognitive forcing strategies” has potential to reduce diagnostic error [13–16], but analytic reasoning is resource-intensive, and may be impractical in many practice settings [13]. Similarly, physician overconfidence has been shown to contribute to diagnostic error [4] and may be a barrier to widespread implementation of such strategies. Particularly in light of less-than-encouraging results from education initiatives intended to improve physicians’ thought processes and diagnostic skills, utilization of specialty training in various medical competencies has been suggested as a more effective and practical way to address diagnostic error [17–19].

DIAGNOSTIC ERROR AND NEURO-OPHTHALMOLOGY

Neuro-ophthalmology is a specialty that aims to use resource-intensive analytic reasoning in order to pinpoint diagnoses that other specialties cannot [20–21]. Patients referred to neuro-ophthalmologists have often previously seen a long list of physicians without being diagnosed, often arriving at clinic weighed down by stacks of records and the results of a myriad of diagnostic studies and imaging. Neuro-ophthalmologists spend time on extensive histories, detailed examinations, thoughtful use of ancillary tests, and methodical analysis of these data to identify an elusive, often rare, diagnosis, that usually does not have a confirmatory test [2]. Often, it falls on the neuro-ophthalmologist to identify a diagnostic error and attempt to minimize the resultant damage.

MEASURING DIAGNOSTIC ERROR

Measurement of rates of diagnostic error is difficult for a host of reasons, including reluctance to report, low autopsy rates, and limited follow up [5,11]. Studies have used various methods, from surveying physicians attending grand rounds [22], to autopsy rates (Shojania), to collecting data on return visits to the ED [23*, 24*]. Additional approaches have been proposed, such as analysis of unscheduled hospital admissions that occur shortly after primary care visits [11].

Even after a diagnostic error is identified, determining its etiology is the first step toward prevention of similar errors. However, evaluating the cause of diagnostic error involves its own set of challenges. A recent study on interrater reliability of identifying strokes versus stroke mimics calls attention to the challenges of identifying diagnostic errors [25*]. The study demonstrated 29% discrepancy among 65 physicians assessing 10 case vignettes for whether the final diagnosis was stroke versus stroke mimic [25*]. Similarly, a prospective study of the interrater reliability of classifying diagnostic errors in ophthalmology assessed the interrater reliability of 3 ocular oncologists on their analysis of errors and their root causes for 5 cases of diagnostic error in ocular oncology. The study showed that while there was 100% interrater agreement on whether there was a diagnostic error, there was less than 50% interrater agreement when assessing the root cause of the error [26*]. This implies that use of qualitative observer analysis is an imperfect method for categorizing diagnostic error.

Investigating misdiagnosis-related harm may be more objective and have more relevance to improving patient care than studies of diagnostic error in general. This approach has the potential to identify the pitfalls most relevant to preventing those harms [27]. For example, recent studies investigating the misdiagnosis of stroke, in particular studies of patients presenting to the Emergency Department with dizziness in whom the diagnosis of stroke was missed, provide a model for future studies of diagnostic error in neuro-ophthalmology [23*, 24*, 28*, 29*, 30–34]. One study of patients diagnosed with stroke after a prior Emergency Department visit during the preceding 30 days found a correlation with presenting symptoms of dizziness or headache [28*]. A study of patients diagnosed with stroke missed earlier within the same admission found a correlation with young age and decreased level of consciousness [29*]. Most significantly, Madsen et al. found that 1.1% of these missed strokes would have been eligible for acute stroke treatment with tissue plasminogen activation (tPA) if they had been identified in the ED [29*]. Two recent studies have attempted to measure misdiagnosis-related harms by capturing patients who had a stroke soon after an Emergency Department visit for dizziness that was thought to be of peripheral origin [23*, 24*].

CURRENT LITERATURE ON DIAGNOSTIC ERROR IN NEURO-OPHTHALMOLOGY

Several studies have attempted to capture the rate of diagnostic error and analyzed its root causes in real world situations relevant to neuro-ophthalmologists.

Elmaleh et al. examined 17 patients with acute, isolated painful cranial nerve 3 palsies found to be due to a posterior communicating artery aneurysm only upon evaluation in a neuro-ophthalmology clinic [35*]. Alarming, 8 of those aneurysms were initially missed on noninvasive vessel imaging—a 47% misdiagnosis rate. Failure to diagnose an acutely enlarged intracranial aneurysm may result in significant morbidity or death, reinforcing the important role of neuro-ophthalmologists in prevention of devastating outcomes. In 6 of the 7 misdiagnosed cases in which outside hospital images were available (in the 8th case outside radiology images were not obtained), the radiologist had not been provided with accurate clinical history in order to better direct review of the imaging. In 5 out of the 7

misdiagnosed cases, the radiologist did not have subspecialty training in neuroradiology. This study suggests that a complete and accurate history and a neuro-ophthalmologic examination that can accurately localize a lesion improves the accuracy of the relevant imaging and facilitates appropriate interpretation of the test obtained. Rather than imaging replacing the clinical evaluation, the usefulness of the test is *dependent* on a correct clinical diagnosis [35*, 36].

Fisayo et al. retrospectively reviewed 165 patients referred to neuro-ophthalmology out of concern for a diagnosis of idiopathic intracranial hypertension, and found a misdiagnosis rate of 39.5% [37*]. This study was the first in the neuro-ophthalmology literature to apply the Diagnostic Error Evaluation and Research (DEER) taxonomy tool [22,38] to categorize the causes of diagnostic error. The most common alternative diagnosis was pseudopapilledema (abnormal appearance of the optic nerve). The authors found that the most common source of diagnostic error, seen in 67.6% of the misdiagnoses, occurred in performance of the ophthalmoscopic examination or in interpretation of its findings [37*]. Pre-established bias, such as the idea that a young obese woman with headache must have idiopathic intracranial hypertension, was a major contributor to these misdiagnoses. Importantly, the authors also collected data on the unnecessary diagnostic tests and treatments that occurred before the time of neuro-ophthalmologic consultation as a result of the misdiagnoses, and found that almost 80% of patients underwent an unnecessary lumbar puncture, 34% had an unnecessary brain MRI, and that almost 10% had an unnecessary MRV. They also showed that 76% had received medical treatment that was not indicated, and one had undergone a lumbar drain that was not indicated. The misdiagnosis of idiopathic intracranial hypertension also delayed identification of an alternative diagnosis in almost 10% of patients.

Stunkel et al. retrospectively reviewed 122 patients referred to neuro-ophthalmology out of concern for a diagnosis of optic neuritis, and found a misdiagnosis rate of 59.8%. The most common alternative diagnosis in this study was migraine, which was the ultimate diagnosis in 22% of misdiagnosed patients. This study also used the DEER taxonomy tool to categorize the causes of diagnostic error, and found the most common diagnostic error, seen in 33% of cases, to be eliciting or interpreting the history, followed by failure to generate an appropriate differential diagnosis with alternative diagnoses, seen in 32% of cases. [39*]. These results support prior evidence that diagnostic errors are often due to cognitive error in the diagnostic process [4,12–13]. The optic neuritis study [39*] also attempted to capture the unnecessary diagnostic tests and treatments that resulted from these misdiagnoses, and found that 16% of patients had undergone unnecessary MRI imaging, 16% had undergone lumbar puncture, and 11% had undergone treatment with intravenous steroids before the time of neuro-ophthalmic consultation [39*].

Kahraman-Koytak et al. retrospectively-reviewed 35 patients with unilateral optic nerve sheath meningioma, and found that 71% had a delayed diagnosis, on average of 62 months. Many of these diagnostic errors were due to cognitive factors, including failure to consider ONSM as a possible diagnosis. Twenty percent of the misdiagnosed patients had already undergone unnecessary lumbar puncture, 48% had undergone unnecessary laboratory tests, and 24% had received unnecessary steroid treatment before the time of neuro-

ophthalmologic consultation. Neuroimaging contributed to rather than prevented misdiagnosis—69% had prior MRIs that were read as normal. In more than half of these cases, the MRI was not sufficient to identify an ONSM due to lack of orbital sequences or contrast, and in the rest, the ONSM was visible on the MRI but was missed by a radiologist who did not have specialized neuroradiology training. Critically, 64% of the misdiagnosed patients had a poor visual outcome. [40*].

Identifying compressive optic neuropathies versus glaucomatous or other optic neuropathies is a long-standing diagnostic issue in neuro-ophthalmology. A retrospective review of 91 patients with unexplained optic atrophy found that 20% had compressive lesions identified on imaging [41*]. Choudhari et al. presented a case series of 6 patients who were misdiagnosed with glaucoma when they actually had a compressive optic neuropathy. This case series cannot be used to project a misdiagnosis rate, but the authors attribute these misdiagnoses to nonadherence to the routine comprehensive eye examination, and use the cases to identify characteristics that should prompt neuro-imaging in cases thought to be glaucomatous optic neuropathy, including young age, unilateral or highly asymmetric neuropathy, rapidly progressive or early visual loss, visual loss out of proportion to the degree of cupping, color vision impairment, pallorous rim, visual field defects other than nasal step or arcuate defect, headache, and diplopia [42*]. One retrospective review of 68 patients diagnosed with “normal tension glaucoma” found no missed compressive optic neuropathies [43*], but a prospective study of 132 glaucoma patients found that 6.5% of those diagnosed with “normal tension glaucoma” had a compressive lesion [44*]. Dias et al. identified 16 patients with optic neuropathies that most resembled glaucoma, and then asked a glaucoma specialist to select, based on fundus photographs and VF results alone, the nonglaucomatous optic neuropathies out of a group including glaucoma cases. Nonarteritic ischemic optic neuropathies and congenital optic disc anomalies were the most common diagnoses to be wrongly identified as glaucoma. However, this study was limited in its generalizability as it used a single observer, and used only visual fields and fundus photographs for diagnosis [45*].

Although there is no doubt that modern neuroimaging greatly facilitates the diagnosis of numerous neurologic disorders, diagnostic errors have not disappeared with the advent of modern imaging techniques. Indeed, improvements in imaging do not replace the need for rigorous diagnostic reasoning. Interpretation of brain imaging is difficult and relies both on detailed clinical information and communication with the radiologist, who must have an idea of how to best direct their assessment [35*,36].

Briggs et al. performed a retrospective review of 506 brain scans that were originally read by a general radiologist and then sent for second opinion by a neuroradiologist, and found a 13% rate of discrepancies that significantly affected patient management [46*]. Although strictly speaking this study evaluated the importance of neuroradiologists rather than neuro-ophthalmologists, like the Elmaleh et al. study [35*], it supports the notion that utilization of physicians with subspecialty training has the potential to decrease the rate of diagnostic error [46*].

A prospective cohort study by McClelland et al. showed that studies ordered before neuro-ophthalmologic evaluation may not be appropriate to answer the correct clinical questions. In their study of 84 patients who underwent neuro-imaging before neuro-ophthalmologic evaluation, 38.1% had suboptimal imaging due to failure to image all locations of interest, incorrect study type, or poor image quality, and 28.6% required additional neuro-imaging, thereby increasing overall cost. Generally, the evaluating neuro-ophthalmologist agreed with the radiologist's interpretation, but discrepancies were higher in smaller anatomic regions where pathology is more difficult to visualize, such as the optic nerve and the brainstem [47*]. The authors suggested, similar to the Elmaleh et al. study [35*], that correct localization by a neuro-ophthalmologist can improve the diagnostic accuracy of the radiology interpretation [47*]. Similarly, although without quantitative data, Wolintz et al. summarized frequent errors that may lead to diagnostic error in radiology relevant to neuro-ophthalmologic diagnosis, including failure to order the most appropriate study to answer the clinical question and failure to provide the radiologist with clinical information that would appropriately direct their interpretation [48].

Of note, the majority of the studies above defined misdiagnosis as an ultimate diagnosis that was not consistent with the referral diagnosis. In some cases, referring to evaluate for these conditions was appropriate—neuro-ophthalmologic consultation was needed to rule out the diagnosis. However, as the data above show, in many cases these misdiagnoses led to unnecessary invasive studies or treatments BEFORE neuro-ophthalmologic evaluation occurred. It is likely that earlier neuro-ophthalmologic consultation would have prevented unnecessary tests and treatments, accelerated the appropriate management, and resulted in better outcomes. A low threshold for referral to neuro-ophthalmology may be important for preventing diagnostic error.

THE ECONOMIC IMPACT OF DIAGNOSTIC ERROR

Diagnostic error may lead to direct costs due to unnecessary diagnostic tests and treatments [37*, 39*]. Additionally, diagnostic errors constitute a large portion of paid malpractice claims. From 1986 to 2010, diagnostic errors accounted for almost 30% of malpractice claims, and constituted more than 35% of payments, resulting in 38.8 billion dollars in payments [49]. A 2017 study found that between 1992 and 2014, more than 30% of paid malpractice claims overall and 54% of those within the field of neurology were related to allegations of diagnostic error [50].

These studies demonstrate the potential impact of research evaluating the rate and causes of misdiagnosis relevant to neuro-ophthalmologists, and hint at the impact that easier access to neuro-ophthalmology may have on the overall rate of misdiagnoses, as well as the potential to avert harm and save costs that result from unnecessary diagnostic tests and treatments that follow from those misdiagnoses. However, there are relatively few neuro-ophthalmologists. Accordingly, neuro-ophthalmologic evaluation is a finite resource [51–53].

CONCLUSION

Diagnostic error of neuro-ophthalmologic conditions leads to unnecessary treatments and diagnostic tests, which are costly and may be harmful. Wider access to neuro-ophthalmologic evaluation has the potential to decrease inappropriate utilization of treatments and diagnostic tests, improve the usefulness of diagnostic tests by directing appropriate utilization of tests, and improve patient outcomes.

Limitations of the current literature on diagnostic error in neuro-ophthalmologic conditions include the small number of studies, the retrospective study design of most of them, the varied definitions of misdiagnosis used, and the wide range of methodologies, making comparison difficult. In the future, it will be useful to further measure the extent to which patient outcomes are affected by delayed access to neuro-ophthalmology, with more precise evaluation of diagnostic errors and delays, and emergency department visits and hospitalizations that could have been prevented by quicker access to neuro-ophthalmology. It will also be informative to better measure the financial costs of those harms.

Our current reimbursement structure rewards volume (and consequently speed) over the time-intensive, complex neuro-ophthalmologic evaluation. This makes neuro-ophthalmology as a subspecialty less viable economically, resulting in fewer neuro-ophthalmologists, and therefore limited access to neuro-ophthalmologic evaluation [51–53]. Despite research demonstrating that diagnostic error occurs in medicine at nontrivial rates, there is a proposal to change the structure of medical reimbursements in a way that will additionally undervalue complex diagnostic processes [54]. This has the potential to further decrease the number of neuro-ophthalmologists, thereby limiting access to neuro-ophthalmologic evaluation, leading to increased diagnostic error rates and increased spending on unnecessary testing and treatments. Research into diagnostic error in neuro-ophthalmology is needed to demonstrate that fair reimbursement for the diagnostic expertise of neuro-ophthalmologists is cost-effective in the prevention of diagnostic error.

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KEY POINTS

- Despite medical advances, current research continues to show high rates of diagnostic error.
- Many diagnostic errors are due to cognitive errors.
- Neuro-ophthalmology as a specialty is uniquely positioned to improve diagnostic error because of the methodical, analytic diagnostic process.
- Improving diagnostic error will likely decrease medical harm and spending on unnecessary tests and treatments.