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The Brain-to-Brain Loop Concept for Laboratory Testing 40 Years After Its Introduction

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Key Words: Brain-to-brain loop; Laboratory test selection; Laboratory error; Error analysis; Error reduction; Decision making

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Upon completion of this activity you will be able to:

- describe how technological and social developments have changed the brain-to-brain loop in the past 40 years.
- discuss errors in the phases of the brain-to-brain loop associated with the growth of alternate site testing and direct laboratory access for patients, and with a declining number of medical technologists and laboratory directors.

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Abstract

Forty years ago, Lundberg introduced the concept of the brain-to-brain loop for laboratory testing. In this concept, in the brain of the physician caring for the patient, the first step involves the selection of laboratory tests and the final step is the transmission of the test result to the ordering physician. There are many intermediary steps, some of which are preanalytic, ie, before performance of the test; some are analytic and relate to the actual performance of the test; and others are postanalytic and involve transmission of test results into the medical record. The introduction of this concept led to a system to identify and classify errors associated with laboratory test performance. Errors have since been considered as preanalytic, analytic, and postanalytic. During the past 4 decades, changes in medical practice have significantly altered the brain-to-brain loop for laboratory testing. This review describes the changes and their implications for analysis of errors associated with laboratory testing.

According to the concept of the “brain-to-brain turn-around time loop,”¹ the generation of any laboratory test result consists of 9 steps, including ordering, collection, identification (at several stages), transportation, separation (or preparation), analysis, reporting, interpretation, and action. The current landscape of medicine has greatly impacted the brain-to-brain loop. Twenty years later, in a seminal editorial, Lundberg² emphasized that even the final step, ie, the action undertaken on the patient and based on laboratory information, is not far enough because “clinicians and laboratorians should all be concerned about the effects of that laboratory test and whether the performance of it was useful for the patient or for the public’s health,” thus stressing the need for an outcomes research agenda. In the last 2 decades, a body of evidence has been collected to demonstrate the association between laboratory tests and further diagnostic or therapeutic interventions. A recent example is the increase in the rate of first nephrology visits after the introduction of the estimated glomerular filtration rate (GFR).³ In this case, the “proximate” outcome of the estimated GFR is evident, but the ultimate effect on clinical outcomes remains to be established because many years are needed to follow up patients and collect data on the evolution of chronic diseases. In fact, the goal of reporting estimated GFR, ie, the reduction of end-stage kidney disease and related deaths and the therapeutic interventions of kidney transplantation and dialysis, must be proven in the “true” clinical setting.⁴ Indeed, the need of an outcomes agenda is common for all medical technologies because there is an urgency to “shift from a narrow biomedical perspective—which considers a technology’s safety and efficacy in terms of intermediate or short-term end points—to a wider

perspective that considers whether technology improves final outcomes of interest such as functional status, quality of life, disability, major clinical events, and death.”⁵

In the case of medical laboratories, the challenges are significant for several reasons. Traditionally, laboratory tests have been considered to have merely corroborative or exclusionary value, thus supporting the view of clinical laboratories as an ancillary service and, even more dangerously, laboratory diagnostics as a commodity.^{6,7} The availability of laboratory results derived from testing at home and point-of-care testing (POCT) and the excessive confidence in the value of laboratory results that are generated by all testing devices have led to decontextualizing laboratory diagnostics from the clinical setting and to extrapolating test results from all other clinical information. This, in turn, has led to reorganizing laboratory services into “focused factories” actively competing for the business of increasingly savvy customers.⁸

Recent technological advances and the new generation of laboratory diagnostics, namely, genetic tests, have occurred despite the relatively low importance given by most stakeholders, including clinicians and policy makers, to the ultimate impact of laboratory information.⁹ Major threats and challenges to the brain-to-brain loop mainly originate from 5 factors: the nature of errors in the total testing process, testing and delivery of test results directly to patients, alternative testing sites, increasing difficulties at the laboratory-clinical interface, and a decreased number of trainees in laboratory medicine.

Errors in the Laboratory Brain-to-Brain Loop in the Current Medical Landscape

According to recent evidence, most errors in the loop do not fall within the analytic phase, nor do they occur most often within the preanalytic and postanalytic steps under the control and/or jurisdiction of laboratory professionals.¹⁰⁻¹⁵ In the last decades, improvements in reliability and standardization of analytic techniques, reagents, and instrumentation, and advancements in information technology, along with quality control and assurance methods decreased by more than 10-fold the analytic error rate. More recently, the introduction of pre-analytic workstations has been proven effective in decreasing most errors involving specimen preparation, centrifugation, aliquot preparation, pipetting, and sorting.^{16,17} Likewise, significant improvements have occurred in the postanalytic phase, especially in data transcription, by interfacing analyzers and laboratory information systems. New information technologies allow for more rapid and effective validation of laboratory results, and they improve the timeliness of result notification of critical values.¹⁸ Therefore, laboratory procedures performed within the walls of the clinical laboratory and run by laboratory professionals are increasingly deemed as safer.

An exploration of the beginning and end of the loop reveals that the pre-preanalytic steps (initial procedures not performed in the clinical laboratory and not under the control of laboratory personnel) and the post-postanalytic steps (final procedures performed outside the laboratory, consisting of receiving, interpreting, and using laboratory information for patient management) are more error-prone.¹⁴ These activities are poorly evaluated and monitored, often because the process owner is unidentified and the responsibility falls in the boundaries between laboratory and clinical departments. System failures and cognitive errors coexist to allow the generation of errors in laboratory testing; they result from multiple causes and are associated with analytic and nonanalytic reasoning.¹⁹

We can assume that technological developments will reduce errors due to patient and specimen identification and delays in laboratory report transmission, while improvements in test request appropriateness and results interpretation should occur because of initiatives to improve knowledge about laboratory tests and the correct interpretation of test results. This, in turn, should be achieved by allowing easy and rapid access to knowledge sources at the point of care and/or by introducing narrative interpretation and interpretive comments in laboratory reports.^{20,21} Recent data available from different clinical settings such as primary care, internal medicine, and emergency departments clearly attest that the rates of errors in test request and result interpretation are unacceptably high and translate into missed, delayed, or erroneous diagnoses.²²⁻²⁵

Therefore, a body of evidence demonstrates that the risk of errors and patient harm in the brain-to-brain loop has been significantly decreased within the processes occurring within the laboratory, but it is relatively increased at the beginning and at the end of the loop, which lie mostly outside the traditional laboratory environment. For laboratory medicine, the relatively high rates of errors in pre-preanalytic and post-postanalytic steps require a substantial reorganization that results in improvement of the delivery of laboratory services through interdisciplinary cooperation inside and outside the laboratory because the most vulnerable steps are not, and possibly cannot be brought back, under the direct control of laboratory personnel.

Impact of Direct Access to Patients of Laboratory Testing

Direct laboratory access (DLA) refers to programs whereby individual people can approach a laboratory directly without being referred by a clinician in a traditional clinician-patient encounter.²⁶ Presumed advantages are time and cost saving by avoiding the inconvenience and expense of a physician office visit; improved privacy and confidentiality,

particularly regarding the results of tests like HIV testing or pregnancy testing; and the desire of patients to take personal control of their care.

Several drawbacks have, however, been identified, making DLA a controversial process. First, because current evidence has demonstrated a high rate of inappropriate interpretation of laboratory results by trained physicians, the risk of misinterpretation of laboratory data by consumers might be expected to be much higher, which may create psychological and emotional consequences. On the other hand, there is a risk that consumers will overlook the clinical significance of significant test results, missing the proper follow-up or treatment of clinical conditions. When comparing personal genomic results of tests conducted by 2 direct-to-consumer companies, Ng et al²⁷ found less than 50% agreement in disease prediction. Promotion of DLA lacking rigorous evaluation of appropriateness, analytic reliability, and clinical efficacy of laboratory testing, including genomics and pharmacogenomics, has been found to translate into real harm for consumers who make complex medical decisions without adequate clinical guidance. One of the supposed advantages of such an option is the reduction of the turnaround time between the laboratory report release and receipt of test results. Concerns about risks related to the direct delivery of test results to patients have prompted the Royal College of Pathologists²⁸ to release a specific document stating that several laboratory test results represent “professional interpretation rather than measurement and the laboratory interpretation may need to be modified by the clinician who knows the patient’s specific situation, or even at a multidisciplinary team meeting.” The document also underscores the possible negative psychological and emotional consequences related to only “apparently abnormal” laboratory results.

The Impact of Testing at Sites Outside the Clinical Laboratory

The advent of rapid alternative site testing or POCT has allowed performance of testing in intensive care units, at the patient’s bedside, and in outpatient clinics; patient self-testing can also be done at home, in an ambulance, on a helicopter or cruise ship, or in small health care clinics such as found in pharmacies. POCT devices are used by the military and have been taken on space shuttles.²⁹ POCT is the fastest growing segment of the current clinical laboratory testing market. Among the myriad of definitions by several authors, the common denominator is the “availability of the laboratory result instantly or in a very short timeframe to assist caregivers with immediate diagnosis and/or clinical intervention.”³⁰

While some benefits of POCT are evident, it has repeatedly been found that the mere transfer of testing from a central

laboratory to POCT cannot guarantee an improved clinical outcome. From a risk management perspective, it has been demonstrated that POCT might reduce errors and risks of errors in a few steps of the entire testing process, but it introduces other serious challenges.³¹ For example, in the analytic phase, major problems still exist with some commonly available POCT methods. A recent review on adverse events associated with false POCT glucose readings identified 82 adverse events: 16 (20%) were associated with death, 46 (56%) with severe hypoglycemia, and 12 (15%) with nonsevere hypoglycemia. Interfering agents most commonly associated with adverse events were icodextrin-containing peritoneal dialysate and maltose-containing intravenous immunoglobulin, explaining the significantly higher rates of adverse events with POCT glucose testing in hospitalized patients.³² This example is representative of the risks for adverse patient care outcomes associated with the measurement of analytes on easy-to-use devices. Therefore, despite their simplicity, some POCT devices can compromise patient safety.

Errors in the preanalytic POCT steps such as errors of inappropriate or excessive ordering, mistimed sample collection, and poorly performed specimen collection have all been described. Errors in the postanalytic phase are associated with manual transcription of results from POCT testing, which has resulted in missed, incomplete, and incorrect results, highlighting the importance of automated transmission of data from the POCT devices to the laboratory or hospital information system.³³

Thus, for any shortcut in the brain-to-brain loop, caveats emerge in all steps of the cycle. These latent errors present serious challenges from a risk management viewpoint. For POCT, a high level of cooperation between laboratory professionals and clinicians is necessary to decide which type of test should be used, which type of quality control and quality assurance should be adopted in the care units, and how the personnel performing POCT testing should be trained.

The Changing Laboratory-Clinical Interface

As the pace of technological advancements in laboratory medicine has accelerated, the extensive use of automation and other mass-production techniques has allowed laboratories to provide quality and timely test results despite an impressive increase in test requests and related workload.³⁴ This has, however, generated a deleterious progressive autonomy from the clinical context, leading to an increased risk of inappropriate test requests and misleading interpretation of laboratory data. The excessive emphasis by laboratory leadership on issues related to “internal” aspects of the management of laboratory services such as efficiency, productivity, and timeliness has contributed to a progressive overlooking of the mission of

laboratory medicine that is—and remains—to improve patient care through the delivery of reliable and valuable laboratory information, which is often as a direct clinical consultation.

Evidence confirms the dangers of progressive autonomy of medical laboratories from the clinical context.³⁵ Current trends are leading the clinical laboratory to increasingly act as an insular department, focusing almost exclusively on its own silo and progressively overlooking any proactive and interactive relationship with the clinical setting. As such, clinical laboratories are increasingly organized as focused factories with the goal of maximizing productivity and improving internal efficiency by consolidating structures in mega-laboratories and outsourcing testing to independent facilities.⁸ The dichotomization between the clinical world and the isolated production of laboratory test results represents a fracture of the brain-to-brain loop and also results in ineffective care associated with an uncoordinated patient journey through the health care process.

The Effect of Fewer Trainees in All Areas of Laboratory Medicine

Declining student interest in the field of laboratory medicine, as medical technicians/technologists and as doctoral level laboratory directors, has been highlighted, particularly in the United States. A recent report shows an impressive decline in clinical laboratory science programs producing medical technologists between 1975 and 2005, resulting in fewer and fewer graduates each year. This decline has translated into high vacancy rates for medical technologists and medical laboratory technicians in the United States.³⁶ It has been reported that approximately 40% of the laboratory workforce will be eligible to retire in the next 10 years.³⁷ The increasing gap between number of available positions projected in 2016 and the expected number of medical technologists and laboratory technicians has received attention by the US lay press, which is concerned because of the eventual risk for patients.³⁸ Similar concerns have been raised in the United Kingdom.³⁹

The personnel shortage affects not only medical technologists but also medical graduates entering pathology specialties.⁴⁰ Several reasons for declining student interest are offered, including lower salaries than in other health care professions, state licensing requirements that make relocation difficult, less visibility to patients than other health care professions, and, for physicians, limited direct contact with patients. It is important to note that formal teaching of laboratory medicine is a relatively neglected component of the medical school curriculum,⁴¹ thus discouraging students from entering the field because they are never exposed to it. This has led to some dramatic consequences in the clinical

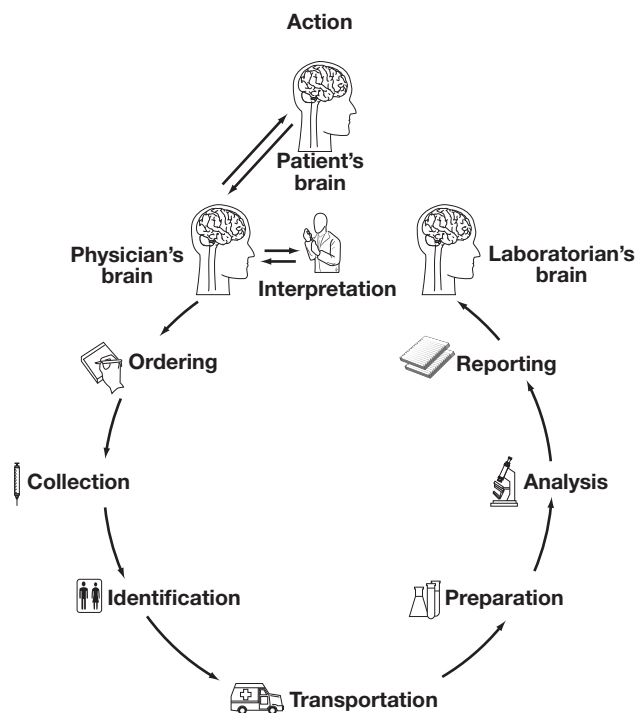


Figure 1 The brain-to-brain loop for laboratory testing 40 years later.

setting. In a British survey, 18% to 20% of medical graduates described themselves as “less than competent” in using laboratory testing, and more than 20% thought they were less than competent in all diagnostic areas.⁴² Thus, the lack of knowledge in laboratory medicine by medical graduates, the laboratory staff shortage, and the impressive decline of clinical laboratory science programs represent significant challenges for the brain-to-brain loop.

Conclusions

The brain-to-brain loop in laboratory testing represents a working paradigm to better establish the physician-laboratory and the physician-patient relationship **Figure 1**. It is essential to maintain laboratory information within the right clinical context, avoiding the risk of inappropriate test requests and result interpretation.⁴³

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