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EDITORIAL

Emerging role of artificial intelligence, big data analysis and precision medicine in pediatrics

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ARTIFICIAL INTELLIGENCE AND MACHINE LEARNING IN MEDICINE

Artificial intelligence and machine learning (AI-ML) implies the ability of machines to "think" and includes the ability of computers or programs to "learn" with experience.[1] Smartphones that most of us carry epitomize the use of AI-ML in our daily lives as they continuously use this technology to improve their performance and engagement with the user. AI-ML techniques are slowly making their way into healthcare as well. Due to the increasing utilization of AI-ML in pediatrics, this annual review issue of *Pediatric Research* will highlight papers on AI-ML use and research in pediatrics and neonatal medicine from leading authors in this field from around the world. A summary of the content of this review issue follows.

NEONATAL APPLICATIONS

Baker and Kandasamy systematically reviewed AI-ML methods for predicting neurodevelopmental outcomes in premature infants, a relatively under-explored area of research. A convolutional neural network was the most common ML method used in imaging studies, mostly used to predict neurodevelopmental outcomes. Challenges remain in defining the outcomes of interest (binary vs. continuous outcomes) and exploring varied ML strategies to find the best model. A perennial limitation in health research is the absence of publicly accessible databases similar to the engineering or biomedical industry.[2] Admittedly, the challenges of data privacy and regulations in healthcare are more difficult to resolve even when anonymized data are used. Vijlbrief et al. discuss their approach for accessing and tackling big data in neonatal medicine. They highlight four angles for clinicians involved in data science to adopt: multidisciplinary teamwork, seeing data through patients and patients through data, and using education as a catalyst for progress.[3]

Sullivan et al. reviewed probably the most promising and advanced AI-ML application in neonates—for detection of neonatal sepsis, especially late-onset sepsis. While it is promising, the authors also highlighted the BARRIERS (Babies, Analytics, Reactors, Reassurance, Integration, Equipment, Re-education, and Space) to this field. These factors need to be considered and addressed as we move toward implementing AI-ML in clinical practice.[4]

Sitek et al. reviewed the use of AI in the diagnosis of necrotizing enterocolitis (NEC) in newborns. They found limited studies on the topic with none showing clinical benefits. The main limitation was the use of single-center datasets, which does not offer a large enough dataset for AI-ML to be powerful in this relatively rare disease. The authors call for multicenter collaborations to overcome these issues in an attempt to power a large database for a study on AI-ML in NEC diagnosis.[5]

Shah et al. discuss the use of AI in bronchopulmonary dysplasia and how AL-ML models may help improve neonatal care for this challenging disease. The applications include both predicting BPD and monitoring response to therapies.[6]

Grooby et al. and Sitaula et al. present two reviews in this issue—one on wearable technologies for neonatal cardiorespiratory monitoring, and the other on the AI-ML tools being used to power these wearable devices. Advances in the technology for cardiorespiratory monitoring are highlighted with some devices now standard in the NICU, but the tools used in the ML of the algorithms are constantly being updated. It is likely that the traditional ML methods will be replaced by deep learning methods in the next few years.[7,8] On similar lines, Walker et al. summarized the novel approaches (both in devices and AI-ML technologies) to capture and use continuous cardiorespiratory physiological data for monitoring, early detection, prediction and for providing care in hospitalized infants and children.[9]

PEDIATRIC APPLICATIONS

Just as AI-ML has seen many applications in neonatal medicine, its use is also advancing into all of pediatric medicine, with many areas primed for clinical innovation and future research. Healthcare generates incredible amounts of data and learning to harness "big data" in meaningful ways to improve healthcare delivery, quality, and outcomes using AI-ML that will help advance pediatric clinical care. This advancement is the focus of a review article by Macias et al.[10] Ashton et al. reviewed the key principals of machine learning necessary to understand how it can be applied to healthcare data and pediatric disease.[1] Shah et al. describe the techniques of machine learning and artificial intelligence and the current applications and limitations of this technology in pediatric critical care such as for prediction models and for clinical decision support systems.[11] Ardahan Sevgili and Senol describe the application of AI-ML to improve clinical diagnosis and decision making in chemotherapy-related complications for children with oncologic disease.[12] In the future, AI-ML technology will help better determine diagnosis, stage, treatment choices, and prognosis for a variety of cancers as large datasets become available to improve the accuracy of this emerging tool.

Given the wealth of "big data" in pediatrics, there are common challenges to the use of AI-ML technology across a range of pediatric applications. Ramgopal et al. describe using AI integration into clinical decision support and the challenges, potential benefits, and risks of this technology in pediatric healthcare.[13] In their article, Vesoulis et al. review the features of big data and how they can be applied to the complexity of pediatric healthcare data.[14] Several pediatric big data networks have been established and include a variety of types of data including genomic, physiologic, health record data, and neuroimaging data that are contributing to our

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understanding of a vast range of diseases and outcomes. Misra and Mukhopadhyay review pediatric data that have been harnessed so far for predictive analysis, for disease diagnosis, for medical safety, improved health system performance, and for precision medicine approaches.[15] Bowe et al. explored how big data and AI-ML can be used to identify children in the community setting at risk for impaired neurodevelopmental and cognitive outcomes and call for needed future research in this area.[16]

Biological system data from micro-RNA and "omics" analysis can also be applied to AI-ML models of disease. In an article by Hicks et al., they review pediatric diseases encompassing different organ systems in which micro-RNA has been identified as a useful biomarker of disease. MiRNA is also making its way into therapeutics for infectious diseases and for cancers, among other conditions. This precision medicine work and miRNA biomarker discovery are enabled by AI-ML technology.[17] In a review by Ozen et al., the ability of omics technologies with AI and ML to identify high-risk pregnancies with risk for adverse neonatal and child outcomes is continuing to expand. Pammi et al. reviewed the exciting prospect of combining multi-omics and clinical datasets to improve earlier detection and precision treatment of perinatal conditions. Applications for both pregnancy-related and neonatal complications are ongoing, and the authors concluded further evaluation of the clinical and ethical aspects of this technology is required.[18] Clinical testing with omics approaches in the future may diagnose adverse conditions prior to clinical symptoms that may lead to reduced perinatal, neonatal, and child morbidity.[19]

PARTNERING WITH CONSUMERS

Both healthcare providers, patients, and their families are consumers of healthcare big data and AI-ML technology. A major goal of AI-ML is to better understand complex human diseases and improve individualized care through personalized medicine. The future of healthcare will see the integration of technology into diagnosis, treatment decisions, and prognosis for patients from the prenatal period through childhood and beyond. This is already starting to be seen with tracking apps on smartphones and watches, and clinical decision tools becoming a part of daily practice. In this issue, Dr Knake provides a thoughtful insight into the rapidly changing world we and our patients live in regarding the access to technology, changes in medical training, the big data all around us, Apps at our fingertips, and how pediatrics must be ready for AI technology.[20]

Visram et al. discuss the importance of engaging with consumers including children and young people who will be utilizing AI-ML advances.[21] They conducted a workshop of these key stakeholders to understand their perceptions of AI in healthcare and themes for future research. They found that children and young people are eager to share their insights about the role of AI in healthcare. Adding to this, McCradden comments on the practical and ethical side of including children and youth in AI for healthcare advancement.[22] Workgroups including patient and public involvement should include representatives of different racial and ethnic groups, ages, sexes, and community backgrounds.[22]

FUTURE

This review highlights the great advances occurring in the field of AI-ML, big data and precision medicine, but there is still a long way to go. As compared to engineering and non-health-related use of AI-ML technology, the human body is a complex entity offering almost infinite permutations and combinations for health and disease. This means for any AI-ML or precision medicine tool to succeed, we first need to build huge databases for health conditions and diseases of clinical and research interests. This can happen only with large-scale collaborations between clinicians, scientists, hospitals, research institutions, universities, and consumer groups. Ethical issues pertaining to data privacy are paramount in this era of data breaches and compromised digital security.

Steps needed to maximize and optimize the progress of AI-ML, big data, and precision medicine in the pediatric and neonatal space will include:

1. Building large databases of physiological data and encompassing different health conditions across the age spectrum with large international collaborative networks.
2. Strong ethical and clinical oversight through all steps of technology development.
3. Testing AI-ML models to ensure clinical benefits.
4. Real-world evaluation of technology after optimization.
5. Human oversight to enable a safety net exists even when technology is well evaluated and robust.

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COMPETING INTERESTS
The authors declare no competing interests.

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