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INVITED REVIEW

What does artificial intelligence mean in rheumatology?

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ABSTRACT

Intelligence is the ability of humans to learn from experiences to ascribe conscious weights and unconscious biases to modulate their outputs from given inputs. Transferring this ability to computers is artificial intelligence (AI). The ability of computers to understand data in an intelligent manner is machine learning. When such learning is with images and videos, which involves deeper layers of artificial neural networks, it is described as deep learning. Large language models are the latest development in AI which incorporate self-learning into deep learning through transformers. AI in Rheumatology has immense potential to revolutionize healthcare and research. Machine learning could aid clinical diagnosis and decision-making, and deep learning could extend this to analyze images of radiology or positron emission tomography scans or histopathology images to aid a clinician's diagnosis. Analysis of routinely obtained patient data or continuously collected information from wearables could predict disease flares. Analysis of high-volume genomics, transcriptomics, proteomics, or metabolomics data from patients could help identify novel markers of disease prognosis. AI might identify newer therapeutic targets based on in-silico modelling of omics data. AI could help automate medical administrative work such as inputting information into electronic health records or transcribing clinic notes. AI could help automate patient education and counselling. Beyond the clinic, AI has the potential to aid medical education. The ever-expanding capabilities of AI models bring along with them considerable ethical challenges, particularly related to risks of misuse. Nevertheless, the widespread use of AI in Rheumatology is inevitable and a progress with great potential.

Keywords: Artificial intelligence; deep learning; image analysis machine learning; rheumatology.

INTELLIGENCE AND ARTIFICIAL INTELLIGENCE

Intelligence is probably the most human of traits. It refers to the ability to learn and process information while adapting it to the same context in which it was gathered or in other different contexts.[1] It can be broken down into an input resulting in an output that is influenced by biases and weights derived from earlier experiences of the individual (Figure 1).[1,2]

Classically, computer-based analyses have relied on fixed rules or algorithms (code) devised by human beings. Transferring the characteristics of intelligence to computers results in artificial intelligence (AI). Early types of AI included algorithms driven by logic (Boolean connectors AND, OR, NOT) or through the use of if-then rules to arrive at decisions. Subsequent developments included the use of decision trees or random forest models. Thereafter, machine learning evolved through the development of artificial neural networks which, akin to a human neuron, have inputs and outputs influenced by weights and biases. The next step in the evolution of AI was deep neural networks, which had multiple intermediate layers that were not visible in addition to the simple artificial neural network.[3,4]

The thematic analysis of images and other complex multilayer data was enabled by the development of convolutional neural networks (CNNs) which could analyze and decode non-linear relations between inputs and outputs. Auto-encoder networks had the ability to code data. Recurrent neural networks had a feedback function to enable learning from experiences. Bidirectional recurrent neural networks had a long short term memory (LSTM) function which further enabled learning.[3,4] A specific subset of deep learning is machine perception, which implies the ability of computers to perceive and sense information akin to human senses. Computer

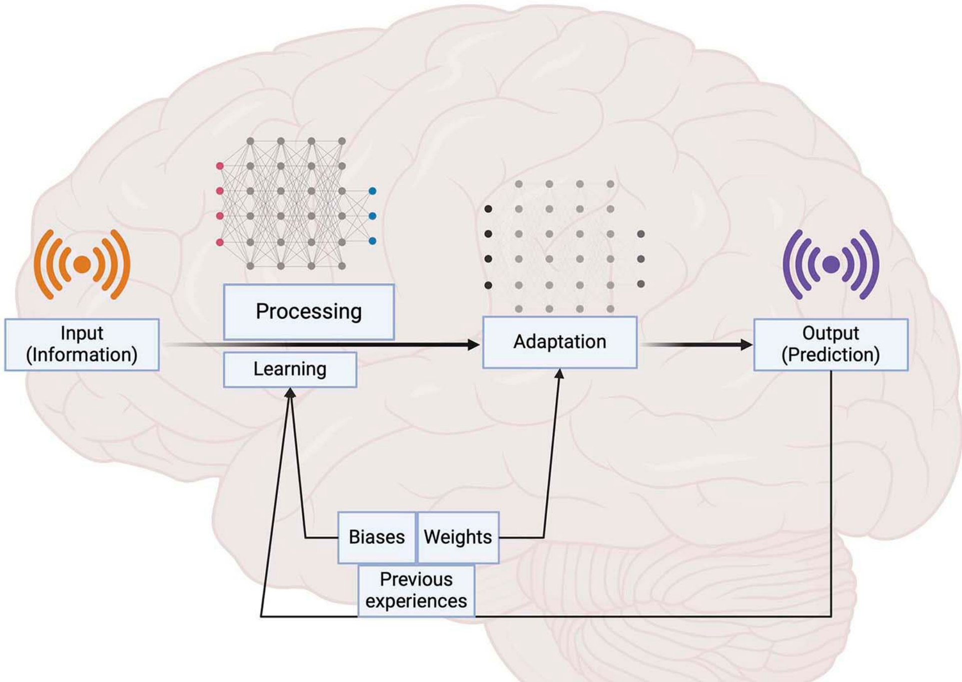

Figure 1. Schematic representation of the processes underlying (artificial) intelligence [Created with BioRender.com].

vision is the specific ability of computers to perceive and analyze information from images and videos using deep learning by breaking them down into individual components.[2]

The latest development in the field of AI was the development of transformer models. These are deep neural networks that have the property of self-attention, thereby enabling them to understand the meaning and context of relationships between data. The advent of transformers enabled the wider applicability of AI large language models (LLMs) such as the Chat Generative Pretrained Transformer (ChatGPT) which could read through voluminous literature to generate answers much like an experienced human reader.[3-5] ChatGPT4 from OpenAI,[6] Claude from Anthropic,[7] Bard from Google,[8] and Grok from X/Twitter[9] are the prominent LLMs available today. Claude is accessible from only a few countries, whereas, the other LLMs are accessible worldwide. While all these LLMs are fast with multimodal capacities, user-friendly and reasonably accurate, none have been specially generated for use in healthcare. The risk of confabulation, particularly for references, has been particularly recognized with ChatGPT4 but is likely with all the LLMs.[10] ChatGPT4 and Bard have the capacity to converse in multiple languages. Each of these LLMs is continuously being updated with improving functionality and accuracy with successive iterations. Learning through AI models could be characterized as supervised (where the outcome is given by the user and the AI is trained to predict this outcome) or unsupervised (where the AI models learn and identify patterns in the data by themselves without the help of external inputs).[3-5]

In this narrative review, we discuss the potential applications of AI to Rheumatology practice, training, and research (Figure 2). We elucidate examples from the available literature as well as hypothesize new possibilities for the use of AI in Rheumatology.

THE POTENTIAL APPLICATIONS OF ARTIFICIAL INTELLIGENCE IN RHEUMATOLOGY

Clinical diagnosis and decision-making

A question that has intrigued doctors for decades now is whether computers may eventually replace the need for a clinician to diagnose and

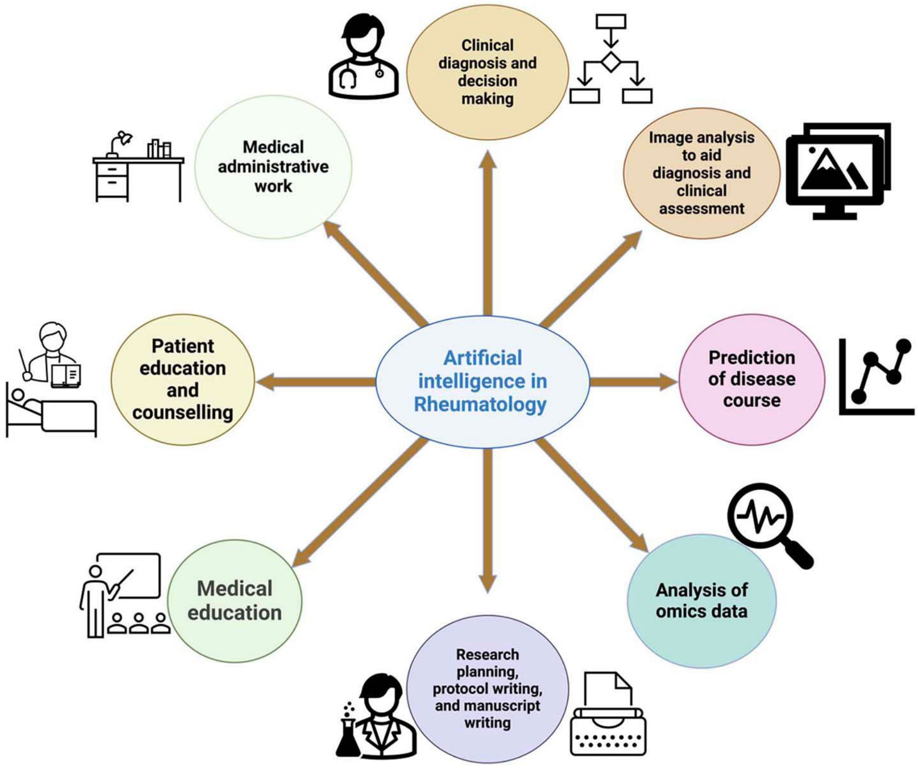

Figure 2. Potential applications of Artificial Intelligence in Rheumatology [Created with BioRender.com].

treat diseases. The advent of ChatGPT and other LLMs over the past year piqued an interest in this area further. Studies demonstrated that LLMs could perform in licensing examinations such as the United States Medical Licensing Examination (USMLE) or specialist recruitment exams such as the Multi Specialty Recruitment Assessment from the United Kingdom (UK) to a similar or better level than human beings and attain a passing grade.[11,12] The LLM Med-PaLM and an advanced version of the same, Med-PaLM-2 could outperform human subjects on the diagnosis and decision-making processes tested on the USMLE.[13] The ZOE mobile application used AI to help infected individuals from the UK during the Coronavirus Disease 19 (COVID-19) pandemic self-report their symptoms. Insights from the mobile application served as a critical learning tool for medical practitioners to understand differences in the presentation of COVID-19 as it evolved from one variant to the next.[14,15] These data suggest that AI could have a role in aiding clinical diagnosis and decision-making. This was further affirmed by two studies which identified a reasonable performance accuracy of different LLMs in the diagnosis of clinical case scenarios published in The Lancet[16] and the New England Journal of Medicine.[17] A point to consider here is that case scenarios published in journals in conjunction with a clinical image or other visual cues are often classical for a particular scenario. In real life, the presentation of patients is often atypical, due to which many consider medicine an art as well as a science.[18] LLMs (which simply rely on the analysis of information) might perform sub-optimally in such instances.[19]

IMAGE ANALYSIS TO AID DIAGNOSIS AND CLINICAL ASSESSMENT

As discussed earlier, the analysis of images using AI relies on deep learning. Image or video analysis using AI has enormous potential with respect to the diagnosis and clinical assessment of rheumatic diseases. A recent paper evaluated the accuracy of the analysis of images acquired on a smartphone for the detection of active hand joints in patients with RA using CNNs. AI-based detection was reasonably accurate for the detection of active arthritis in the proximal interphalangeal joints of the index finger (accuracy 74%) or the middle finger (accuracy 83%) but less so for the wrist (accuracy 62%).[20] Another study reported an accuracy of 84% for the detection of proximal interphalangeal joint arthritis in patients with RA using a CNN to analyze hand images.[21] Gait abnormalities are important diagnostic clues to the diagnosis of rheumatic and neurological diseases. Analysis of gait-tracking data derived from infrared cameras using CNNs identified an AUC >70% for the diagnosis of abnormal gait using calculated Gait Performance Scores.[22]

Ultrasound imaging of inflamed joints is now considered as an extension of the standard clinical exam in the Rheumatology clinic. A study from Denmark evaluated the safety and feasibility of hand and wrist ultrasound performed by a robot vis-à-vis humans. Robotic ultrasound was rated similarly to humans concerning pain and discomfort during the procedure and was acceptable to a majority of patients.[23]

The analysis of radiological images of computed tomography (CT) and magnetic resonance imaging (MRI) scans using deep learning is an area of active exploration. The diagnosis of spondyloarthropathy relies on the assessment of erosions, joint space narrowing, or ankylosis of the sacroiliac joints using MRI or CT imaging. CT imaging is associated with considerable radiation exposure which has been linked to a higher risk of future hematological malignancies.[24] This is particularly concerning since spondyloarthropathy commonly affects younger individuals. A recent study utilized deep learning to generate CT images (synthetic CT) based on MRI data of sacroiliac joints. These synthetic CT images could better predict erosions, joint space narrowing, or ankylosis than the MRI images with comparable accuracy to actual CT images from this group of patients as the gold standard.[25] Studies have evaluated AI-based models to automatically identify bone marrow edema in MRI images of sacroiliitis and its significance with respect to the diagnosis of spondyloarthritis.[26] The potential for the use of deep learning to analyze radiological images is enormous, potentially helping to diagnose and evaluate healing or progression (on serial images) or synovitis, joint erosions, marrow edema, and cartilage architecture.[2] Similarly, the analysis of lung CTs using deep learning for the diagnosis and evolution of interstitial lung disease or pulmonary pathology in diseases such as systemic sclerosis, RA, anti-neutrophil cytoplasmic antibody-associated vasculitis, and sarcoidosis are areas for exploration. Ultrasound with shear wave elastography can help to quantify skin thickening in systemic sclerosis. Such images could also be analyzed using AI to facilitate the role of the radiologist.[2] Deep learning algorithms have also been used to successfully identify cardiac sarcoidosis from routine images acquired during echocardiography.[27] Deep learning has also been successfully used to analyze images of nail fold capillaroscopy in patients with juvenile dermatomyositis.[28]

Positron emission tomography (PET) CT and PET MRI are increasingly being used for the assessment of large vessel vasculitis (LVV).[29-31] Deep learning and CNNs have been preliminarily explored to detect large vessel abnormalities in PET of patients with LVV and may also help to distinguish the pathologies of LVV and atherosclerosis.[32]

AI-based analysis of histopathology images is increasingly being used in the context of malignancies. This could have potential applications for the analysis of histopathologic images of joints, kidney biopsies, muscle biopsies, and other organs relevant to Rheumatology practice.[33,34]

PREDICTION OF DISEASE COURSE

Rheumatic diseases are characterized by flares of disease activity and periods of disease control. The accurate prediction of disease flares is of particular interest to Rheumatologists, as each disease flare potentially damages the joint or other organs. In this context, a recent study provided preliminary information regarding the ability of an AI prediction tool to predict flares of disease activity in rheumatoid arthritis (RA) based on the assessment of clinical features and longitudinal patterns of disease. The AI tool could predict flares with reasonable accuracy [area under the receiver operating characteristics curve (AUC) of 80% with sensitivity of 72% and specificity of 76%]. The use of this model to assist clinician decision-making improved the clinician's confidence in the decision, reduced inter-clinician variability in decisions, and actually helped to reduce the use of immunosuppressive therapies.[35] Information derived from wearable devices such as smartwatches with activity tracking can potentially help to detect flares of disease activity in rheumatic diseases. A recent study showed that decreased physical activity identified by tracking activity data from smartwatches using AI had high sensitivity and specificity (>95%) for the detection of flares in patients with RA and spondyloarthropathy.[36] AI-based prediction of future joint space narrowing in patients with osteoarthritis,[37] osteoporosis in RA,[38] and hospitalizations in patients with systemic lupus erythematosus[39] are other areas where the potential of AI to predict disease outcomes has been explored. Patients with rheumatic diseases have reported for ages an increase in joint pains with cold weather. The power of AI helped to provide scientific proof of this phenomenon by correlating self-reported pain scales with weather data from various places in the UK.[40] Wearable devices have already shown promise for the better monitoring of patients with comorbidities such as depression[41] and cardiovascular disease.[42] A recent preclinical study demonstrated the potential for the early detection of renal allograft rejection through AI-based temperature tracking of the allograft using implanted sensors around the kidney.[43] These studies just demonstrate the immense potential for AI to improve the monitoring and treatment of chronic diseases such as those often encountered in Rheumatology practice.

The prediction of the course of comorbidities is another area where AI-based modeling has enormous potential.[44,45] From a cohort of 542 patients with RA from Greece, AI-based cardiovascular event prediction based on clinical and carotid and femoral ultrasound parameters was found to be superior (AUC nearly 100%) compared to AUC between 73-80% with commonly-used cardiovascular disease (CVD) risk prediction scores.[46] Another study of 152 individuals with psoriatic arthritis revealed a slightly better CVD risk prediction accuracy with AI-based models to the Framingham Risk Score.[47] While several studies are available on the prediction of outcomes such as mortality using conventional statistical analyses,[48] the use of AI to predict short and long-term outcomes in rheumatic diseases is likely to be an area of ever-increasing knowledge in the upcoming decade. This is particularly of interest given that AI-based statistical analysis has the potential to complement the information derived from classical methods of statistical analysis.[49]

ANALYSIS OF OMICS DATA

The analysis of genomics, transcriptomics, and proteomics data involving hundreds to thousands of data elements is the norm in the current era of multi-omics research which often incorporates information from different omics. Machine learning has huge potential to explore these immense datasets. Transcriptomics analysis of whole blood from patients with Sjögren's syndrome using machine learning helped to identify putative biomarkers of the disease as well as identify potential newer therapeutic targets using molecular docking.[50] The analysis of serum metabolomics data from patients with gout using machine learning was able to identify metabolites that could predict flares of gout.[51]

Advances in molecular biology coupled with machine learning using AlphaFold, a model based on artificial neural networks, have helped to accurately predict the three-dimensional structure of proteins from amino acid sequences alone.[52] This has the potential to aid the development of new drug targets or repurpose existing drug targets based on an understanding of pathogenesis.[53] Similarly, another machine learning model, AlphaMissense, was able to characterize whether genetic mutations were of pathogenic significance or not.[54]

RESEARCH PLANNING, PROTOCOL WRITING, AND MANUSCRIPT WRITING

Formal planning of the research work by writing a research protocol is the first step in conducting research. While it goes without saying that a research protocol should be original, the protocol might require multiple iterations such as for research ethics committee approval or funding. Application for research funding might require multiple sequential submissions to different funding agencies until funding is secured for a project. Each submission has its own format and requirements, therefore, adjusting the proposal to meet the requirements for submission involves considerable administrative efforts on the part of the research. The same goes for the submission of rejected manuscripts to other journals, each with its own formatting and referencing requirements. It is for the automation of such administrative tasks that AI (particularly LLMs) has immense potential. AI can also help to improve the usage of grammar and English language in protocols and manuscripts, particularly for researchers from regions of the world where English is not the native language.[5,55,56]

However, it cannot be overemphasized that LLMs cannot substitute for the original thinking that is required to form the basis of research projects and manuscripts.[57] In the authors' opinion, AI should only serve as a tool to help improve aspects of research protocols and manuscripts. Any help from AI regarding these aspects should be transparently declared by the authors. Some journals have explicitly forbidden the use of AI for any aspect of manuscript writing, whereas, others have allowed this with transparent declaration and others even have encouraged this.[5,58] It is important to refer to journal instructions to understand and respect the requirements of specific journals.

PATIENT EDUCATION AND COUNSELLING

Since AI chatbots like ChatGPT can read and analyze volumes of data to generate responses, a potential utility of such software could be to help answer patients' questions regarding diseases and counsel them. These aspects are of particular importance in Rheumatology where chronic diseases requiring long-term patient-caregiver interaction are the norm. A recent study revealed that LLMs could actually generate reasonably accurate and empathetic responses to patients' queries regarding their disease which were comparable to those from a physician.[59]

MEDICAL ADMINISTRATIVE WORK

Electronic health records (EHR) are being increasingly used across the world across specialties in medicine. Transcribing notes into EHR can be a cumbersome task which takes away precious time from actually interacting with patients. AI could have a role to play here, in recording and transcribing physician-patient interactions into the her.[60] Software for this purpose is already available.[61] Data from EHR and other sources of data from the clinic, so-called real-world evidence, is increasingly being recognized as an important source of information regarding the phenotype and course of diseases in the clinic.[62,63] AI algorithms could potentially help to analyze and interpret such data for both clinical audit and research purposes. One such attempt was to develop a tool to diagnose RA from a review of medical charts. While this attempt was not successful, progress in AI models shall likely result in better diagnostic accuracy based on routine medical records in the future.[64] Another study successfully devised a natural language processing (NLP) algorithm to automatically calculate disease assessment scores in patients with RA from clinic notes with a sensitivity of 95% in the development cohort and 92% in the validation cohort.[65]

MEDICAL EDUCATION

The potential role of AI, particularly LLMs, in medical education is enormous. These could serve as a ready reckoner for students to answer their queries. However, this must be balanced with the need to inculcate the reading of textbooks and medical literature among medical students. LLMs could help students prepare notes for later review or exam preparation.[66,67] A potential hurdle posed by LLMs in medical education is the ability to generate written assignments based on prompts from the medical student, which could then be passed on as the student's own work (i.e., plagiarism). To partly circumvent this pitfall, some universities started asking students to submit hand-written assignments after the advent of ChatGPT.[5] The promises and pitfalls of LLMs for medical education need wider deliberation and greater research.

CONCLUSION AND FUTURE PERSPECTIVES

The year 2023 has been a landmark in the evolution of AI, marked by significant strides in LLMs. The ever-expanding capabilities of these AI models bring along with them considerable ethical challenges, particularly related to the risks associated with their misuse. Vulnerabilities with security, the lack of transparency in AI algorithms, the potential for confabulation or hallucinations in AI-generated content, and overall safety and accuracy are paramount, especially in critical applications like medical diagnostics where decisions might mean the difference between life and death.

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