AI-Driven Advancements in Autism Spectrum Disorder: Early Diagnosis, Intervention, and Genomic Insights for Enhanced Social Well-being

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Abstract
Autism Spectrum Disorder (ASD) is normally detected and diagnosed by 18 months of age, the process is lengthy and often delayed as it is not considered to be urgent. Artificial Intelligence (AI) can facilitate early diagnosis of autism which would then vastly increase the chances of reducing social impairment in patients by enabling timely intervention. AI can also play a pivotal role in intervention via robots and virtual reality (VR), which can provide a safe means of practicing their social skills before applying them to humans. Additionally, AI provides the hope of making revelations at a genomic level that could aid in the prediction of the development of autism in the antepartum period, or maybe even as a potential pre-conception test.

Keywords: AI, ASD, early diagnosis intervention, social, robots, virtual reality. genomic insights
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Introduction

The introduction of artificial intelligence (AI) into healthcare promises to gradually revolutionize the practice of medicine (1). The simulation of human cognition by AI can rapidly provide and analyze healthcare data thereby optimizing the efficiency of diagnosis and management. AI is also used in the development of drugs, medication regimes, as well as patient monitoring (2) There are numerous ways of classifying AI, but the ones most relevant to healthcare include machine learning, natural language processing, rule-based systems, administrative applications, robotic process automation, specific diagnosis, treatment applications and least commonly physical robots. In radiology, it is currently at the forefront of applications for AI in medicine (3,4). Social interactions are one of the basic principles of human life and can have a significant impact on both physical and mental health (5). A lack of social skills affects the functional aspect of a person's life and interferes with their ability to thrive in a fiercely competitive world. The impairment of social functioning is the core aspect of ASD which currently is an incurable condition but can be managed better with early interventions if diagnosed promptly (6). AI can facilitate the process of an earlier diagnosis and enable subsequent timely interventions for more favorable outcomes (7). Autism is a class of neurodevelopmental conditions also known as pervasive developmental disorders distinguished by 3 characteristic features including impairment of social communication, impaired reciprocal social interactions, as well as restricted, repetitive and stereotyped patterns of behavior, interests, and activities (8,9). ASD encompasses a range of disorders, with the 5 most diagnosed being Asperger's syndrome, Rett

syndrome, Childhood Disintegrative disorder (CDD), Kanner's syndrome, and PDD-NOS (10). Worldwide prevalence of autism is increasing, with a higher occurrence in males than females, the exact cause of this disorder is not yet known, with a range of theories having been put forward, it was historically thought to be a result of inappropriate parenting but ongoing research has indicated that autism is both familial and heritable, as well as the identification of a range of environmental factors that play a causative role in the development of autism (10).

Autism is usually a childhood diagnosis made upon referral to specialists by taking a detailed history, observations, and through the use of specially designed tools such as the Autism Diagnostic Interview-Revised (ADI-R) and the Autism Diagnostic Observational Schedule (ADOS). It is also important to rule out any secondary causes in the form of Fragile X syndrome or tuberous sclerosis via a detailed neurological examination and prevent delaying the required care (11,12). Although autism is an incurable condition, there are numerous interventions available, of which the most effective are the following, supportive educational programming, communication training, social skills support, and behavioral interventions (13). Psychologists need to be actively involved in the program-planning process and intervene in the design of curriculum and development of strategies matching the child's learning style and capabilities. Psychologists would also be closely involved in schooling, agencies, and family programs. They would also be reviewing progress and making required modifications (14). Behavior training has been shown to improve the patient's ability to adapt through the application of the concept of reinforcement. Despite having the same health requirements as children without disabilities, children with ASD are more prone to coinciding psychiatric pathologies for which newer, safer, and more specific medications are available to treat target behaviors associated with ASD (15). Most encountered forms of AI used in ASD are specific diagnostic and treatment applications.

Materials and methods

Literature searches were conducted using databases such as PubMed, UpToDate, Cochrane, Science Direct, and Google Scholar between June and July 2022 using keywords such as autism, AI, diagnostic uses of AI, interventional uses of AI, neurodevelopmental disorders, machine learning, robots, and algorithms. Inclusion criteria included all literature and systematic reviews from esteemed sources, in the English language only. Exclusion criteria ensured to avoidance of any articles that were published before 2015, sourced from a poorly reputed website or journal, or published in a language other than English.

Results

In recent times, AI has been found to be progressively worthwhile in the investigation, and diagnosis of autism, thus enabling early initiation of therapy ideally in the critical time frame to control the extent of autistic traits and intervene as soon as possible to maximize the chances of the child being able to lead a fulfilled life (12). It has therefore been found that the vast majority of AI has been developed for the purpose of diagnosing autism.

Diagnostic applications of AI in autism

One of the most common, reliable, and unbiased tools used to diagnose autism is the ADI-R which provides relevant comprehensive details about the suspected patient; however, it has the disadvantage of being extremely time-consuming as it consists of 93 questions that are to be delivered in a clinical atmosphere by a trained health care professional, and can take more than 2

hours to complete. A study used just 7 out of the total 93 questions (as shown in Table 1) from the ADI-R to formulate a decision tree that would help determine whether the individual falls into the spectrum or not with a statistical accuracy of 99.99%. The algorithm provided a score based on the answers, the answer to any question could increase or decrease the score. A negative score indicated the diagnosis of ASD, while a positive score indicated that there was no diagnosis of ASD. The exact magnitude of the score stipulated the confidence in the final qualitative outcome, with greater values indicating a greater extent of confidence. The specificity was found to range from 93.8 to 99%, with a false positive rate (FPR) of 0.013, and an accuracy of 99% (16).

ADI-R question	Abbreviation	Description
29	compsl5	Comprehension of simple language: answer most abnormal between 4 and 5
35	conver5	Reciprocal conversation (within subject's level of language): answer if ever (when verbal)
48	play5	Imaginative play: answer most abnormal between 4 and 5
49	peerpl5	Imaginative play with peers: answer most abnormal between 4 and 5
50	gaze5	Direct gaze: answer most abnormal between 4 and 5
64	grplay5	Group play with peers: answer most abnormal between 4 and 5
86	ageabn	Age when abnormality first evident

Listed are the number corresponding to the question in the full ADI-R instrument, the question code used by Autism Genetic Research Exchange (AGRE) and a brief description of the question.
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Table 1: The 7 chosen questions (out of 193) used by the decision tree to formulate a diagnosis.

Discussion

Eye tracking is a non-invasive and practical method of making the diagnosis of ASD in both adults and children. It measures eye fixation points in certain regions of interest (ROI) within an image or even video (although using videos can prove to be a challenge as it is much harder to pinpoint the frames of interest). The duration of gaze fixation in non-biological, nonsocial movements is then the parameter of choice to determine whether a patient is given the diagnosis of ASD. Despite not being a disorder-specific strategy, in the context of ASD diagnosis, it demonstrated an average precision of 90% and a specificity of 93% (17). (Table 2)Autism Barta is a smart device application that combines 23 (out of the standard 27) M-CHAT (Modified Checklist for Autism in Toddlers) screening questions with pictorial depiction for toddlers between the age of 16-30 months old, it then screens for autism based on responses provided, informs the user of their result, stores responses in a database and then recommends the nearest Autism resource center for confirmation and therapeutic measures (18).

There are specific neuroimaging findings known to be associated with ASD, including overgrown temporal and frontal lobes, excessive CSF, and structural abnormalities in the white matter at specific age groups (20). (Fig. 1,2,3)

Table 2: Important features of some studies reflecting role of AI in other psychological disorders including autism

Authors	Sample size	Objective	Form of delivery	Conclusions
Fitzpatrick et al. (31)	70 University students	The efficacy of self-help program Woebot for college students who self-identify as having symptoms of anxiety and depression	Woebot.	Woebot is accessible, engaging, and effective way to deliver CBT
Mohr et al. (32)	Layered, hierarchical model for translating raw sensor data into markers of behaviors and states related to mental health	Uncovering the potential of mobile health and its effect on mental health research and treatment	Personal sensing methods including smart phones, wearable, social media and computers	Integration into Existing Models of Care, Behavioral Intervention Technologies
Kuang and He (33)	449 Subjects	Prediction of ADHD status	fMRI	DL used for discrimination of ADHD with fMRI data
Geraci et al. (34)	366 Patients	Prediction of youth depression	DFNN	Individuals who meet the inclusion–exclusion criteria for depression research were detected
Navarro-Haro et al. (35)	44 participants	The benefits of VR Dialectical Behavioral Therapy (DBT) mindfulness	Virtual Reality (VR) and DBT	Participants reported less sadness, anger, and anxiety after VR

		skills training technique		
Gosling et al. (36)	1,600 community-dwelling adults	Internet delivery of fully automated self-help CBT-I designed to reduce insomnia and prevent depression	Online CBT-I	Program showed significant results
Spence et al. (37)	15 clinically anxious adolescents aged 12 to 18	The study examined the relative efficacy of online (NET) vs. clinic (CLIN) delivery of cognitive behavior therapy (CBT) in the treatment of anxiety disorders in adolescents	Online CBT	Minimal differences between NET and CLIN, both showed effectiveness
Ewbank et al. (38)	17,572 patients (90,934 therapy session transcripts)	Quantifying and measuring the delivery of psychotherapy using deep learning	Internet-enabled CBT for the treatment of a mental health disorder from 2012 to 2018	Deep learning model applied to the large-scale clinical data set of CBT session transcripts and generate a quantifiable measure
Castro et al. (39)	Studies that included randomized controlled trials (RCTs) examining the impact of telephone-administered	Evaluate the effectiveness of telephone-administered psychotherapy for depression in adults	A meta-analysis	Telephone-administered psychotherapy showed beneficial effects on depression severity when compared to

	psychotherapy on depressive symptoms.			control conditions

Machine learning uses specific methods to create a suitable model with these known features. This can then automatically discern patients with ASD from healthy controls. This is a software based on AI that can be used as a medical device to assist and accelerate the diagnosis of ASD, by combining 3 forms of data. This includes a caregiver questionnaire, 2 short home videos, and a questionnaire from the health care provider. It can then give 3 possible results for each patient, ASD-positive, ASD-negative, and indeterminate output, the use of this device shortens the expected 18-month wait to reach a diagnosis of ASD. The sensitivity and specificity obtained were 98.4% and 78.9% respectively (21).

Applications of AI in interventions for autism

There are a few examples of the development of AI for purposes of autism treatment, such as the QT robot, autonomous robots, and VR therapy in addition to the behavioral therapy.QT robot is a socially assistive robot that interviews the child asking them 3 questions after their name, narrates a story and asks them if they enjoyed it, and lastly plays a game involving imitation of certain gestures. Each session lasts 1.5-4.3 minutes and the results are then used to assess 3 aspects including attention span, imitation, repetitive and stereotyped behaviors. A study carried out found that children were more attentive toward the robot than toward humans, they imitated humans and robots equally, and the number of repetitive or stereotyped behaviors was found to be reduced. This provides 2 major advantages. Firstly, it provides an excellent and fully focused one-to-one learning opportunity for children with ASD. Also, the robot can be used to monitor a child's progress by providing a means to store data and analytics regarding their behavior. (22, 23). Floreo's VR is an example of the use of AI in the treatment of ASD, it provides a platform via which the user learns to engage in specific, realistic settings and situations thus developing their behavioral and social skills which are applicable in day-to-day activities. It provides the opportunity to engage in social situations from the safety of their own homes, which makes it easier for them to practice without the external pressure that can usually overwhelm them in real-life situations The user's performance is recorded and paired with an app that can then be used to supervise and monitor the learners progress as well as introduce new aspects, pride coaching, etc. (19,24). A 30-day study was conducted wherein children were given an in-home autonomous social robot with which they were interacting for a minimum of 30 minutes daily playing pre-designed interaction games that practiced joint attention, emotional and social understanding, and ordering and sequencing. The robot also shared stories and provided verbal encouragement and feedback as per a prepared script following which participants showed to have made significant social and behavioral improvements concerning eye contact, initiation of communication, and maintaining focus, these improvements were shown to persist even after termination of the experiment (19,25). Recently, AI has played a transformational role in recognizing critical causal genes and loci associated with ASD by enabling exome and genome

sequencing in neurodevelopmental disorders. It was discovered that there are 5 common causative variants present with very small risk factors, although in the setting of predominant de novo risk factors the role of these common variants is still unclear (26).
There is scope for the gene-gene interactions to be studied in greater detail as they are potentially a crucial determinant of major autistic traits and could even potentially be used in antenatal screening if a strong connection is successfully determined (26).

Behavior imaging

Behavior imaging is a new area of research defined as the measurement and analysis of human behavior using computational sensing and modelling strategies. It comprises the use of video, audio and wearable sensing to create an in-depth portrayal of behavior. Due to the dense sensor data available, it can detect and record features such as latency, trajectory, etc.
As it is convenient to wear, it also enables analysis in real-world situations which is more reflective of day-to-day behavior. The greatest benefit of this is the opportunity to screen, monitor changes, and review the effectiveness of interventions. It also carries additional advantages such as functional behavior analysis, the luxury to provide remote consultations, educational aids such as classroom management, and finding methods as an alternative to standardized tests to assess students with learning disabilities (27,28).

Limitations

Some of the drawbacks associated with the use of AI include lack of subjective observation, flexibility, and the contextual scrutiny based on professional experience required for making a more accurate judgement. Another important aspect to take into consideration is that AI uses simplistic classifications, and therefore limits the nature of the results, whereas professional judgment would be inclusive of multiple factors and ultimately use a larger range of classifications, and even create new classifications if necessary (29). AI relies on the input of datasets, which are formed by the contribution of multiple physicians and if they contain any biases, the algorithm would apply those biases to all samples producing biased results. Even if input bias is avoided, any input errors would incorrectly affect the results provided. Before the widespread use of AI can be condoned research is required into the accuracy of results with respect to the quality of input data. There is a need to develop a protocol for data collection to standardize the process and allow the collection of comparable results (29, 30). The extensive data required is controversial from an ethical perspective (30). The lack of research being done on adults with ASD is a notable point of interest and raises a concern about whether the advancement of AI in autism can be applied to adults too (29).

Conclusion

All initiatives thus far have proven to be successful in their intended purpose. A lot of the information currently available is still in the form of news articles and websites, a more thorough and scientifically moderated review is required. This will also help to bring these initiatives to the notice of healthcare professionals, who can then provide medically approved options to the anxious parents and carers of their patients. The discovery of certain causative genes in the evolution of autism provides a starting point for further genetic studies, which could potentially

bear the possibility of options such as gene therapy, antenatal screening, and maybe even the development of pharmacological management as a means of intervention.

Conflict of interest

The authors declare no conflict of interest

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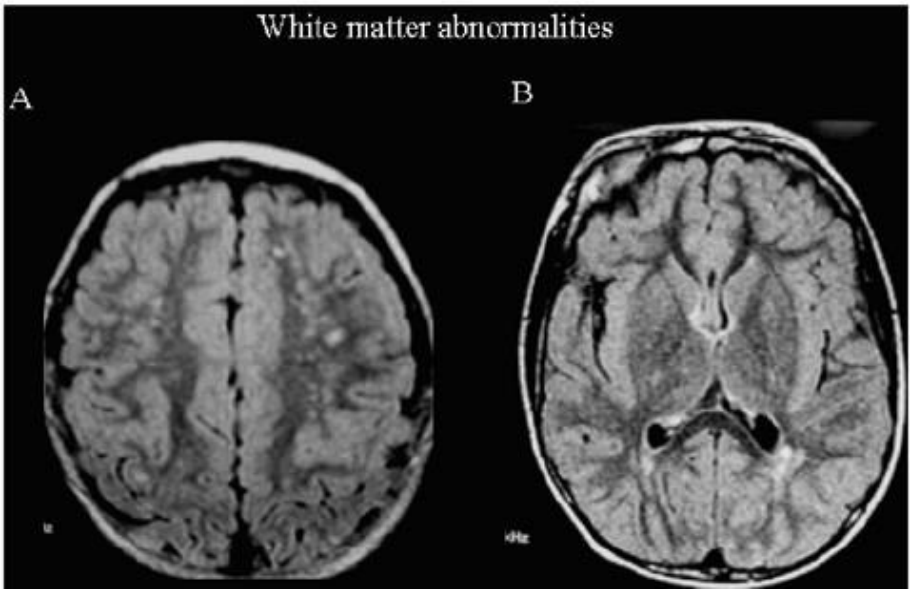

Fig. 1 White matter abnormalities in autism. Two children illustrating the principal categories of white matter signal abnormalities. Figure 1A. Punctate T2 Hyperintensity: Abnormal findings were placed in this category when small (, 2 mm) rounded abnormalities were found scattered bilaterally in the white matter (white arrow). They were asymmetric and homogeneous, and no findings suggest that necrosis was present. They were very intense compared with adjacent white matter on T2 and FLAIR sequences, and did not involve the basal ganglia, the periventricular white matter fibers or the sub-cortical U fibers. These abnormalities were generally found in association with other supratentorial abnormalities. Figure 1B. Posterior T2 Hyperintensity. Abnormalities placed in this category were ‘‘plaque-like areas’’ of mild white matter hyperintensity relatively symmetrical bilaterally at the posterior horns of the lateral ventricles (black arrow). There was no deformation of the lateral ventricular contour adjacent to these lesions. No abnormality of the sub-cortical U fibers was observed.
https://www.researchgate.net/figure/White-matter-abnormalities-in-autism-Two-children-illustrating-the-principal-categories_fig1_23995216

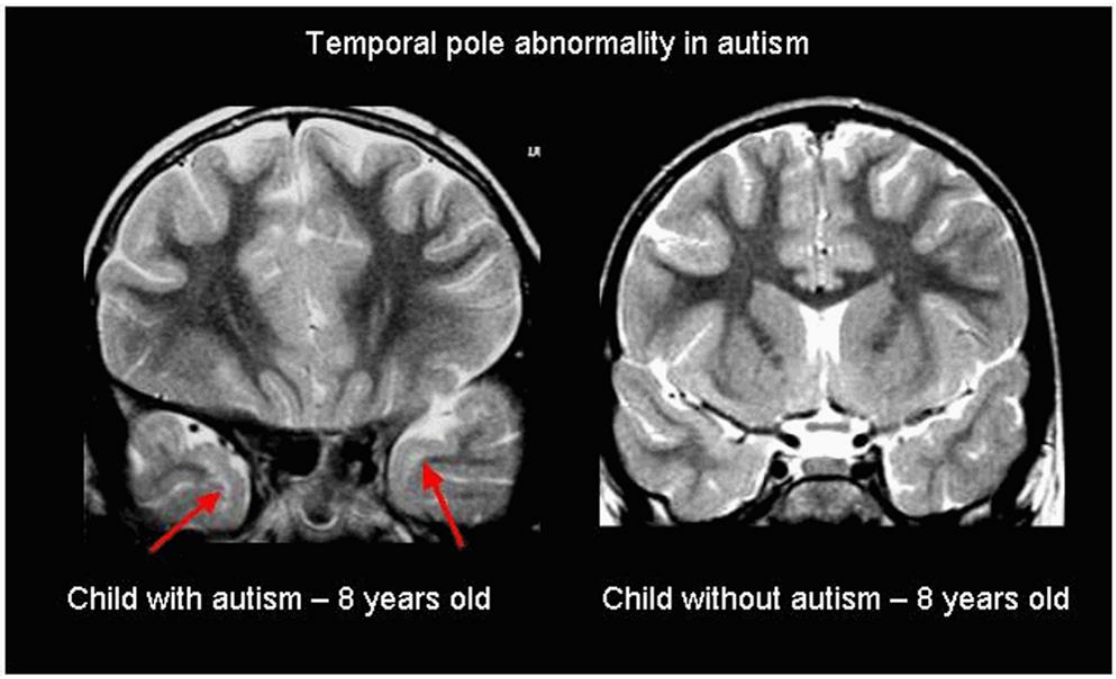

Fig 2 – Structural abnormalities have been demonstrated in those with autism, but it is unclear how this produces the features of the disorder. This is an example of typical sub-cortical hyperintensities on T2-weighted coronal images localized in the temporal poles observed in children with autism (red arrows) and a normal image of a control child without autism.https://teachmepaediatrics.com/community/neurodevelopmental-disorders/autism-spectrum-disorder/

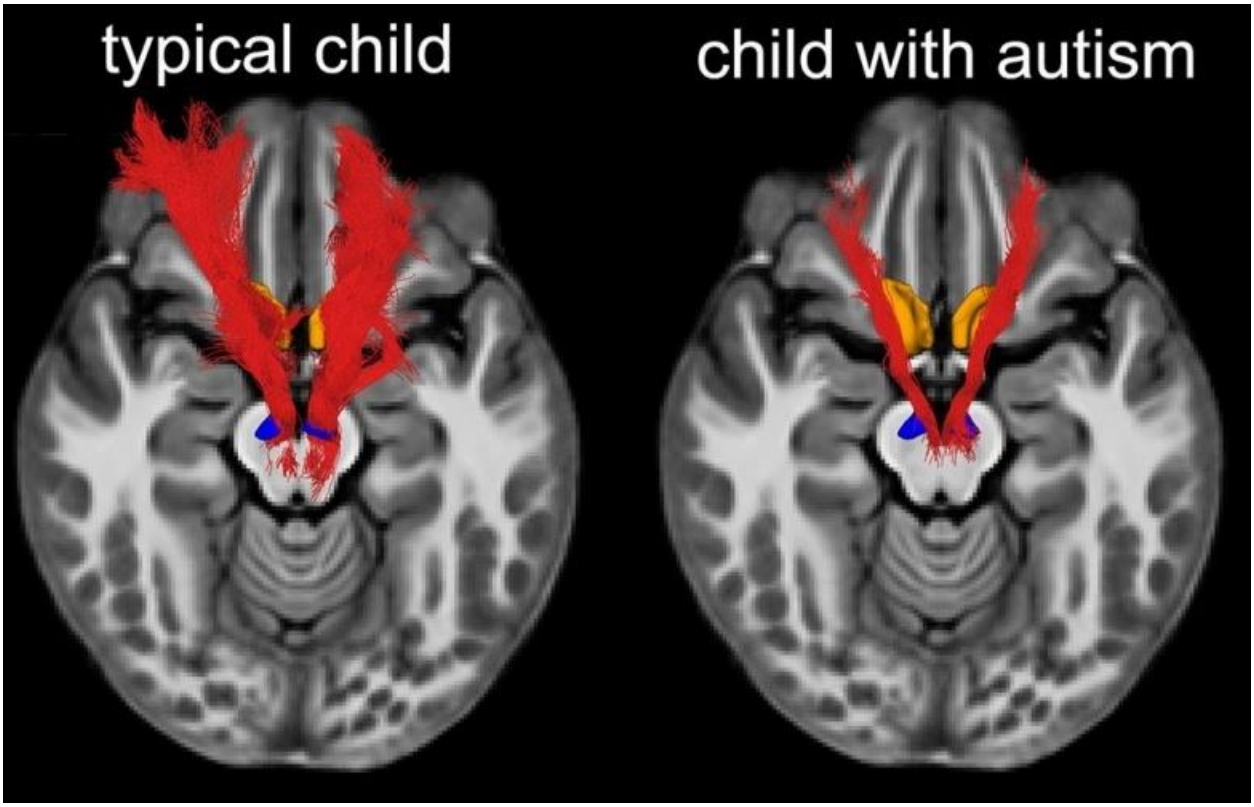

Fig. 3. MRI Scans revealed that kids with autism have deficits in a brain pathway that normally makes social interaction feel rewarding. Nerve-fiber tracts along the pathway, in red, are less dense in children with autism than in typically developing children. https://med.stanford.edu/news/all-news/2018/07/key-social-reward-circuit-in-the-brain-impaired-in-kids-with-autism.html