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Review of Imaging Autism Spectrum Disorders with Magnetic Resonance Imaging Techniques.

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Abstract:
The pattern of autism spectrum disorder (ASD) at early stage may be identified, but difficult to conclude to some extent with specific classification. Multiple researches and reviews published in recent years to exactly define ASD patterns. Radiological imaging modalities proved significant role in imaging ASD at early stage. This configurative review aims to provide detailed importance of ASD imaging with various MRI techniques, specific to neuroanatomical regions and physiological functions; with techniques like MR spectroscopy, Diffusion tensor imaging and functional MRI imaging. The review is done by three researchers independently after selecting 32 published articles from various web sources. The present review concludes need of further research towards ASD pattern-based evolution of techniques in MR imaging; and provides various MR imaging aspects of neuroanatomy and the physiological functions of brain, specific to ASD patterns.

Keywords: Autism Spectrum Disorder, MR spectroscopy, Diffusion tensor imaging, functional MR imaging**.**

Introduction:

Autism spectrum disorders (ASD) refer to a repetitive behaviour or restricted interests-based syndrome including compromised social communication abilities with a peculiar way or pattern of activities; and has major components like autistic disorder, Asperger syndrome, and pervasive developmental disorder [1,3]. The pattern of ASD at early stage may be identified, but difficult to conclude to some extent with specific classification. Multiple researches and reviews published in recent years to exactly define ASD patterns. In multiple research evidences; grey and white matter volume abnormalities along with brain overgrowth at early stage found common in ASD individuals [2]. Radiological imaging modalities proved significant role in imaging ASD at early stage. Additional advanced techniques including surface morphometry and cortical-thickness measurements provide detailed age-related patterns of neuroanatomical and developmental conditions [5,6]. This configurative review aims to provide detailed importance of ASD imaging with various MRI techniques, specific to neuroanatomical regions and physiological functions.

Methods :

This configurative review is the amalgamation of the search strategies by three different researchers, independently done within a period of three months, with exclusive selection of 32 published articles. The study was conducted in absence of internal review board approved protocol, as it was deemed not important for the review. The entire set of data collected from various web-based sources like, Scopus, PubMed, web of science and shod Ganga; under five key aspects- autism spectrum disorder, imaging for ASD, anatomical database involved in ASD, MRI imaging of ASD, and advancement in ASD imaging. Published work on or after 2012 was preferred; but few publications having suitable information as per research requirements, were also considered even if published before 2012. The common search articles and similar concepts were strictly avoided. Inclusion of Subject based topics published only in English language were thoroughly researched and taken into consideration. A configurative approach is followed to avail most relevant information by all three reviewers. The exclusion criteria followed were- Case reports with single or minimal subjects, commentaries, expert advices, web sources without proper references, under trial studies, animal or in-vitro studies, and clinical trials involving invasive interventions.

Literature search:

With a pre- designed frame of article search strategy, total three reviewers independently searched multiple web sources like Scopus, PubMed, web of science and shod Ganga. After analysing various articles and sub articles by all reviewers, exclusively identified 32 published papers were selected to present database for the study. The key words used by reviewers were- autism, ASD, MRI imaging in autism, MR spectroscopy in ASD, functional MRI in ASD and brain structures involved in ASD. Any sort of confusion and disagreement of article search was resolved with mutual consensus.

Risk of bias assessment:

All the reviewers involved, took appropriate measures to minimize risk of bias. The search protocol was pre-defined and reviewers selected all the articles with mutual agreement, after scrutinizing them. The data was randomly obtained from multiple web data sources and at least one reviewer re-evaluated all the scrutinized articles with mutual consensus. Due to wide parameters of data diversity in various sources, quantitative assessment is not done.

Data extraction:

All the data extracted by three reviewers was accumulated together and re- evaluated. The original data information re-confirmed by going through the source data available for improving data reliability. All the inclusion and exclusion criteria were followed by reviewers at the time of data synthesis.

Discussion:

Autism Spectrum Disorder (ASD):

Autism is not just a disorder, but a spectrum of multiple changes; having its effects ranging from minimal to severe effects depending on the onset, progression and control. ASD has a vast level of control, belonging to people associated with the ASD individual; like family members, teachers, care takers, clinicians, doctors, friends and neighbours. ASD is also a prime factor for economic load to the families of ASD individual by including the treatment cost, care cost, school additional charges and other social aspects [5,6]. All the ASD individuals present different effects and are either highly communicable or are

having restricted social interaction. Few have repetitive activities, while others may have bound activities. ASD presents a group of people having their own world of activities, irrespective of culture, society or socioeconomic group. ASD is considered a consequence of developmental changes prior to birth and has high prevalence [1,6,7]. ASD can be diagnosed by paediatricians, psychiatrists, radiologists and psychologists; and is assisted by other department sources. Standard medical diagnostic methods are- (1) the Screening Tool for Autism in Toddlers and Young Children (2) Autism Diagnostic Observation Schedule. All such medical diagnostic tools assist clinicians to work ahead for the management and treatment of ASD. Sometimes caregivers are subjected to present ASD conditions with interviews to provide with diagnostic, communication and multidimensional activity-based aspects of the ASD individuals. Computer assistance and 3-dimensional presentation of ASD diagnosis is emerging at present [8,9]. As per Global Burden of Disease study 2010 report, males are more prone for autism than females with a ratio of 4:1. All such evidences are time to time justified by epidemiological and community-based studies as well [10]. Certain studies are performed by directly getting population-based data; while other studies are conducted with the administrative data retrieved from survey offices and administrative offices; which provides irrelevant data details sometimes [11]. Multiple theories including social, cognitive, developmental and motivation deficit theories have been suggested to explain the behavioural and developmental aspects of autism [12]

MRI assistance in autism detection:

MRI proves itself an advanced tool for diagnosing various conditions with accurate pathophysiological conditions. Autism is one of the conditions, diagnosed by various MRI techniques with par accuracy by means of anatomical and physiological aspects diagnosing ASD.

The MRI studies of paediatric ASD cases suggests no specific difference in total brain volume, cortex, cerebellum and lateral ventricles [13,14,15,16]. While there are significant changes with respect to increased white matter volume in frontal and parietal lobes along with increased volume of amygdala, cerebellum and hippocampus [17,19].

MR spectroscopy (MRS) in ASD:

Magnetic resonance spectroscopy proves its existence in diagnosing ASD with various biomarkers presenting changes in ASD individuals. Major studies show decreased level of creatinine and phosphocreatine in thalamus, grey matter, white matter and cerebellum [20, 21,22,23] in ASD. Decreased N- acetyl aspartate noticed in grey matter and white matter of frontal, parietal and bilateral areas of brain, is another biomarker representing ASD [24,25,26,27]. Choline has quite different appearance, presenting itself more pronounced in hippocampus and amygdala areas [23] while has decreased appearance in temporal lobe, cortex and thalamus; for ASD individuals [21,22]. Glutamine, glutamate metabolites reduce in ASD, specially in grey matter and cerebellum [20]; while notified studies found its enhancement for ASD individuals in thalamus region, for the individuals having ASD affected motor system [22]. Due to its region specific and pathophysiological diagnosis abilities, ASD diagnosis proved its major dependence on MR spectroscopy imaging.

Diffusion tensor imaging (DTI) in ASD:

The changes within ASD individuals are well notified even with diffusion tensor imaging, which is trending MRI based advanced techniques. While studying ASD individuals with Diffusion tensor imaging, multiple studies found increased mean diffusibility in short range and long-range fibres of frontal lobe,

cortex- thalamus connecting areas, and white matter of left hemisphere areas [28,29,30]. An increased fractional anisotropy notified in main tracts of corpus callosum of infants and in white matter tracts of corpus callosum of toddlers [31,32]; while noticeable reduction in fractional anisotropy of white matter tracts in frontal, parietal lobe as well as in corpus callosum found in ASD individuals between the age group of 6-14 years [33,34]. DTI presents age related changes in ASD individuals and also reflects the progress of the spectrum.

Functional MRI imaging (fMRI) in ASD:

Functional MRI presents the activity based physiological functions of ASD individuals. Most of the studies are done at resting state, which present significant role of fMRI in diagnosing the spectrum and its progress. ASD in fMRI imaging presents increased connectivity of putamen and caudate region with the pons and brain stem region; and increased connectivity of posterior cingulate cortex and retro-splenial cortex with temporal cortex region, lingual gyrus, and posterior para-hippocampal gyrus [35,36]. fMRI also reflects decreased connectivity of right superior frontal gyrus with posterior superior frontal gyrus, and minimal connectivity of posterior cingulate cortex with medial prefrontal cortex [37,38]. These observations are just a glimpse of the actual physiological functions detailed by fMRI imaging for ASD individuals.

Conclusion:

The present review details various important features of MRI techniques like MRS, DTI and fMRI; for early diagnosis and spectrum progress of ASD. Clinical and rehabilitation strategies must be accompanied with the diagnostic tools of the spectrum. The metabolite details, white matter fibre tracts diffusibility and fractional anisotropy along with the functional connectivity details of brain seed areas; presents vast importance of MRI techniques in ASD imaging. Though modifications in the present techniques of MRI imaging provides relatively high diagnostic details of neuroanatomy and pathophysiology of ASD, but lack of availability of conclusive research to find absolute diagnostic tool for ASD imaging is yet to be strived. Repetitive contradictory approach towards various spectrum details (age and anatomical region associated) are other challenges requires further detailing. Functional MRI imaging studies are mostly associated with resting state, which further requires detailed activity-based associations with the spectrum.

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