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Radiology

# NEURO IMAGING EVALUATION IN MENTAL RETARDATION

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**ABSTRACT** Mental Retardation (MR) is a developmental disorder associated with impaired cognitive functioning and difficulty in adaptive behaviors. MR impedes with quality of life and full participation in the life of the family, school and community which needs a multi modality approach. With advanced neuroimmaging modalities updated with 3D technology and software applications more accurate diagnosis is made. Many studies have addressed white matter abnormalities in patients with MR. Quantitative analysis of cortical integrity using cortical thickness measurement is providing new insights into the gray matter pathology and for clinical trials of neuro protective medications. Hence the present study of literature review was made. Definitions of abnormalities varied widely between studies and different rates of abnormalities were reported. This review study aimed to describe changes in structural pattern of white and gray matter in MR with advanced imaging.

**KEYWORDS :** Mental Retardation (MR),Corpus Callosum, Cortical Thickness, Advanced Neuro imaging, systematic review study

Mental retardation which is now renamed as intellectual disability is a type of neuro development disorder. Children who are mentally disabled usually experience delays in the physical, cognitive and social development, practical adaptive skills originating before the age of 18 years. Mental retardation can be classified as mild, moderate, severe and profound depending on I.Q score. Intellectual disability though presenting in early infancy and childhood may not be diagnosed until the child is older than 5 years of age.

The prevalence rate of mental retardation is 20 per 1000 general population while the prevalence of development delay is 30 per 1000 in the 14 year old population. About three percent of world population is estimated to be mentally retarded. In India 5 out of 1000 children are mentally retarded. This disorder is more common in boys than in girls. It is essentially a problem of school going children. It has been calculated that 33 percent of children are mentally retarded.70 percent of the mentally retarded population is based in the rural areas.80 percent of the mentally retarded is mild (or) moderate. Severe degree of mental retardation is about 5 percent. Most of the severe degrees of mental retardation come from the higher educational and income groups. On the other hand mild and moderate degrees of intellectual disability are found in the underprivileged and socially disadvantageous classes. Many of the borderline cases of mental retardation are bypassed as dull students in most of the rural and some sub urban schools,and remain unidentified as they could be involved in a semi skilled vocation and in astructured and restricted environment.[1,2]

The awareness of the problem of mental retardation is growing at all levels in India. There is an integrated approach amongst professionals for many positive development and improvement in prevention,early diagnosis and care of the mentally retarded children. Hence the present comprehensive review study is made for better understanding and application of already known patterns of abnormalities and to explore further with latest advanced imaging studies with main focus on corpus callosum and cortical thickness.

## FOETAL BRAIN INSULT IN MATERNAL STRESS:

Mental stress, harmful environment, malnutrition, familial and genetic factors during development process may have affect on cortical thickness and development of corpus callosum.. Intrauterine events may account for more than half of the causes of mental retardation along with placental insufficiency and complications of birth injury. Maternal alcohol consumption during pregnancy is another risk factor. Maternal stress during pregnancy is strongly associated with non macroscopic brain insult. Maternal stress hormones induce over production of foetal cortisol magnify foetal brain insult due to reduced oxygen and nutrition with permanent change in neuro endocrinal regulation and behavior in the offspring. The composite effect of maternal stress, malnutrition and familial factors result abnormal neuro genesis and development such a composite effect might result in gross lesions such as leukomalacia, ventricular asymmetry, neuronal losses, gliosis and thinning of corpus collosam at isthmus and reduction in cortical thickness. ). Hypoplasia occurs as a result of late destruction of the corpus callosum owing to a metabolic, infectious or ischemic origin.[3]

## DETECTABLE AREAS OF FOCAL ABNORMALITIES IN THE BRAIN OF MENTAL RETARDATION:

### 1.CORPUS CALLOSUM:

Corpus callosum is the largest white matter tract in the brain and is found only in placental mammals. It is an important route/commissure for the interhemispheric transfer of information for proper coordination of cerebral hemispheric function. The development of corpus callosum occurs between the 12$^{th}$ and 16-20$^{th}$ week of gestation. It begins with the anterior body and then continues bidirectional with the anterior portion (genu) developing earlier and more prominently than the posterior portion (splenium). Myelination of the corpus callosum occurs in the opposite direction from the splenium forwards. Though it is fully developed by 4-5 years maturation continues into the third decade of life and may be throughout life.

The corpus callosum is approximately 10 cm in length consisits 200-300 millions of axonal projections and is C shaped, thicker Posteriorly. It has four parts rostrum genu, trunk and splenium. The callosal sulcus separates it from cingulated gyrus. The normal corpus callosum thickness was considered to be at the genu and splenium 1.1cm and at the body 0.6 cm with a variation of 0.2cm. The superior surface is covered by a thin layer of grey matter known as Indusium griseum,inferior surface is attached to a thin vertical septum pellucidum anteriorly and posterior to the fornix and its commissure. It has homatopic and heterotopic connections by means of individual fiber tracts like forceps minor and forceps major connecting to frontal,temporal and occipital lobes and to the surface of cerebral hemispheres through corona radiata. It has a rich blood supply from pericallosal arteries, relatively constant and is uncommonly involved by infarcts.The main function of corpus callosum is the communication between the two hwmispheres.The rostrum and genu connect the frontal lobes,the body and the splenium connect the temporal and occipital lobes of the corresponding hemispheres.it is hypothesized to play a primary role in cognition.the decline in cognitive function in aging adults is believed to be due to weakened integrity of corpus callosum.

## ABNORMALITIES:

The congenital anomalies of corpus callosum can be classified as agenesis (complete or partial/dysgenesis) and hypoplasia with reduced thickness. In primary agenesis the corpus callosum never forms and in secondary dysgenesis the forms normally and is subsequently destroyed. The presence of rostrum essentially excludes primary

agenesis as rostrum is the last part to be formed. Agenesis of corpus callosum occurs both in isolated form and in combination with other anomalies and is due to insult to the foetal brain during 8-12 wks of gestation. The prevalence of isolated ACC is about 50 percent of the diagnosed cases. The prognosis for neurological and mental development in isolated ACC is more favorable. Even with partial ACC the frequency of pronounced mental retardation may reach 62percent and the incidence of epilepsy is 46 percent. In cases of isolated ACC the clinical manifestation after child birth may be absent unlike ACC associated with other congenital anomalies.(Aicardi syndrome, foetal alcohol syndrome and Dandy Walker malformation).Therefore early prenatal diagnosis of anomalies of the development of corpus callosum is extremely important for prevention and rehabilitation support and care of the intellectually disabled.

**CORPUS CALLOSUM- FOCAL THINNING AT THE ISTHMUS**:

The isthmus of corpus callosum shows important growth between the ages of 6 and 15 years .The cortico cortical network supporting rapid associative relay and language function may myelinate more extensively and over long periods than rostral fiber system (ref Thompson) . Corpus callosum thickness may reflect areas where fusion was diminished and there were less fibers crossing to other cerebral hemispheres at that level. Thinning of corpus callosum occurs either focally at the isthmus or diffusely

**2. CEREBRAL CORTICAL THICKNESS:**

Brain has a significant plasticity with connections being made and retracted in response to activity. The functional connectivity is a dynamic constantly evolving process. The brain is shaped by experience. Gray and white matter is not separate compartments white matter is composed of the myelinated axons of neuronal somata that exist within the cortical layer. They need to be studied concurrently. Local cortical architecture and connectivity are linked processes and are the results of migration, organization/differentiation of development process. Cortical thickness seems to reflect dendrite arborisation and pruning within grey matter or changes in myelination at the interface of white and grey matter; whereas surface area varies with the degree of cortical folding or gyrification and is thought to depend on division of progenitor cells in the Periventricular area during embryogenesis. Cortical thickness details can provide crucial information on cortical maturation, neuro anatomical, developmental and pathological changes.

The cerebral cortex has been called the highest achievement of biological evolution and human mental abilities.the cortex has a surface area of 2.5 square feet with an average thickness of 3 mm. The cortex is a highly convoluted structure. The degree of folding is likely to be related to an evolutionary need to increase the surface area without a corresponding increase in intracranial size. The cortex is estimated to contain 14 billion neurons principally of pyramidal, stellate and fusiform varieties. The cortex mantle varies in thickness depending on the regions of cortex. There are variations between the brains of two individuals as well as between two hemispheres of the same brain. Normally cortex is thinnest 2mm in the calcarine cortex, thickest in precentral gyrus (4mm). Morphological changes in cortical thickness are associated with meaningful functional differences across the groups in mental retardation, epilepsy, dementia, schizophrenia and Alzheimer diseases. The cortex has a laminar organization into six separate layers from surface to white matter 1.Molecular layer 2.Corpuscular layer 3. Pyramidal layer 4. Granular layer 5. Ganglion layer 6. Multiform layer. The anatomic layer has distinct characteristic synaptic connections. The functional unit of cortex is the cortical column. Cortical thickness is not a property of the brain surface, but it should be definable at any point within the cortical mantle.[4]

The highly folded nature of cerebral cortex is difficult to measure manually. The cortical surface is not perpendicular to any of the cardinal axes resulting in errors in measurements. The crowns of gyri are thicker than the fundi of sulci. Sensory areas are among the thinnest in the cortex. Anterior, ventral, temporal and prefrontal cortexes are among the thickest cortical regions. The average thickness of anterior bank of central sulcus is 2.6mm and the posterior bank of central sulcus is 1.81mm.primary sensory areas are tend to have a high degree of mylination resulting in reduced contrast in these areas. The thickness of cortex is of great importance in normal development, neuro degenerative and psychiatric disorders. The morphometric properties, geometric pattern and functional properties of cerebral cortex can be analyzed with combinations of powerful technical tools and software packages.the cortical thickness can only be measured if the location and orientation of the gray and white matter and pial surface are known.The thickness of cerebral cortex across the brain can be measured by automated method with deviation of less than 0.5mm.[5]

**NEURO IMAGING EVALUATION:**

**1.ULTRASOUND**:

The diagnosis of anomalies of corpus callosum is possible in prenatal ultrasound. The corpus callosum is a thin band of white matter, which is difficult to demonstrate sonographically. It is only well visualized on mid-sagittal or mid-coronal views of the brain and requires optimal angles of insonation to demonstrate.

The evaluation of foetal brain is carried out in axial plane and does not include a direct evaluation of corpus callosum. The anomalies of corpus callosum can be suspected indirectly by evaluation of the cavity of septum pellucidum and lateral ventricles. The most common indirect finding is ventriculomegaly seen in 74% of cases at 24 weeks of pregnancy. Anterior horns of lateral ventricles show parallel course in more than 50% cases. 3rd ventricle may show dilatation or displacement in 15% cases and is not a valuable finding. Abnormal septum pellucidum will be seen in all cases of complete agenesis of corpus callosum where as in partial /dysgenesis of corpus callous septum pellucidum may be normal, abnormal and may not be seen sometimes.

Prenatal ultrasound examination can usually diagnose anomalies of corpus callosum from 22 weeks onwards.

The classic indirect signs are Absence of the cavum septi pellucidi, enlarged/widened interhemispheric spaces, upward displacement and enlargement of the third ventricle, may project superiorly as a dorsal cyst with dense echogenic choroid in the roof of the cyst.Lateral ventricles show Colpocephaly (dilatation of the trigones, occipital and temporal horns in the absence of the splenium). "Bat-wing" (racing car sign) appearance of the lateral ventricles (wide separation of the lateral ventricles with straight parallel parasagittal orientation, with absent body) Teardrop or crescentic shape to the lateral ventricles due to the longitudinal bundles of Probst, .small frontal horns widely separated. Sunray appearance or radial orientation of gyri in sagital plane due to absent or everted cingulate gyrus.

**ASYMMETRIC VENTRICLE DILATATION:**

Mild enlargement of lateral ventricle on prenatal ultra sound can be seen as a normal occurrence. Persistence of asymmetric ventricle dilatation in early childhood was associated with attention deficit hyperactivity disorder (ADHD),autism and learning disorder and schizophrenia

**PARTIAL AGENESIS (DYSPLASIA) OF THE CORPUS CALLOSUM:**

The caudal portion of the corpus callosum (splenium and body) are missing to various degrees. Partial agenesis affects only the posterior part of the corpus callosum. Indirect signs are lacking and prenatal diagnosis is therefore more difficult.

**COLOR DOPPLER**

mapping in mid sagittal plane shows non visualization of callosal artery in complete form of agenesis of corpus callosum and its abnormal course with dysgenesis. It rises upwards at the level of missing segment of corpus callosum.

**VOLUMETRIC ECHOGRAPHY:**

The application of volumetric echography allows multiplanar evaluation of fetal brain in static 3D mode. Maximum qualitative analysis can be carried out at any level and in any direction. Multiplanar reconstruction of fetal brain is used to evaluate midline structures includindg corpus callosum.Volumetric imaging and omniview technology allows building images according to a specialist assigned direction. The possibility of assessing the corpus callosum when using multiplanar regimen of volumetric echography within a period of 16-20 weeks of pregnancy reaches 84% and at the time of 21-24 weeks of pregnancy reaches 97% cases. The percentage of successful visualization of the corpus callosum in the second trimester of pregnancy varies from 88% to 100% .[6]

**MRI:**

Imaging protocols and checks lists: MR imaging is performed on 1.5T

unit and volume data is obtained with a 3D inversion-recovery. The volume images will be assessed on Multiplanar rendering software. Check list includes Lateral ventricles, third ventricle, cortex temporal lobe white matter abnormalities and other abnormalities. [7]

The most frequent MRI findings are

**1.CORPUS CALLOSUM-**
Corpus callosum thickness may reflect areas where fusion was diminished and there were less fibers crossing to other cerebral hemispheres at that level. Thinning of corpus callosum occurs either focally at the isthmus or diffusely and the associated indirect features will be seen in ventricles, white matter and and cortex as mentioned in the check list.

**2.ASSYMETRIC VENTRICLE DILATATION :**
**3.PERIVENTRICULAR LEUKOMALACIA**:
The white matter distal and lateral to the external angle of lateral ventricle is considered to be vascular border zones. In premature infants the Periventricular tissue at the level of optic radiation adjacent to the trigone of the lateral ventricle and in frontal white matter adjacent to the foramen Monro shows focal necrosis due to hypoxic insult to the brain seen as hyper intense lesions inT2 in peri trigone regions with or without enlargement of lateral ventricles.

**4.GLIOSIS AS A FOCI OF HYPERINTENSE SIGNALS**
of small round or oval lesions localized at Periventricular or sub cortical white matter on T2 weighted and FLAIR images ,iso intense on T1.They are common incidental findings in adults due to chronic low grade vascular insufficiency with sub clinical manifestations.

**5. CORTICAL THICKNESS**:
is the more direct and biologically meaningful measurement to reflect the size, density and arrangements of cells. In mental retardation significantly reduced cortical thickness is found in the bilateral lingual gyrus, the bilateral fusiform gyrus ,the bilateral parahippocampal gyrus, the bilateral temporal pole, the left inferior orbito frontal gyrus and right precentral gyrus.[8]

**MRI DATA ACQUISITION**:
Quantitative maps analysis of cortical thickness and integrity with advanced imaging process may provide new insights into the pathology of gray matter and for clinical trials of neuro psychiatric medication by conventional MRI. Traditionally by manual outlining of region of interest which is subjective and laborious, the voxel based morphometry and surface based generalized linear model (GLM) tool to map the cortical thickness.

Segmentation and surface reconstruction of cortex by voxel based morphometry with surface based coordinate system with advanced computer isation may contribute for further understanding of the cortex and white matter disorders in psycho neurological disorders and monitor therapeutic out comes.

Voxel based cortical thickness measurement in MRI imaging: cerebral cortex has a complex three dimensional structure and is measured by current MRI imaging techniques of automated generating voxel based cortical thickness (VBCT) maps which do not require the construction of three dimensional surface model. The thickness calculation requires an accurate map of grey and white matter, the boundaries can be determined by tissue segmentation methods; with voxel based cortical thickness maps it is possible to detect a smaller difference of less than 1mm.with sub sampled data. Cortical thickness will be a volumetric measure of voxel in the cortical mantle. Neither the neurons nor the cortical layers are differentiated even with the 0.5mm slice thickness. Cortical layering is visible with high resolution MRI with cryosection data. For the application of cortical thickness various data sets are available for the evaluation of epilepsy, mental retardation, development disorders and dementia. Diffusion Tensor Imaging gives insight into the structure of white matter by measuring water diffusion within a tissue. The tightly organized white matter tracts restrict the diffusion of water producing anisotropic diffusion where as water diffusion in grey matter tend to be less restricted.[9]

A further detailed review is beyond the scope of this article due to technical limitations in MRI, systems and soft ware packages. But still the study can be useful and valuable for an integrated and multidisciplinary approach in the field of neuroscience and neuroimaging.

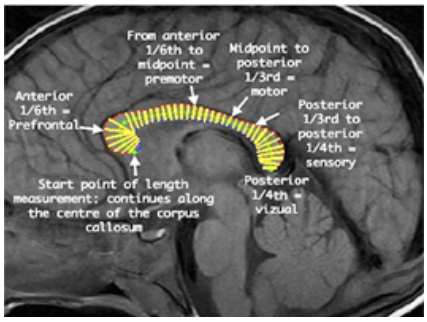


**Fig.1: segments of corpus callosum**

**Fig.2: lateral ventricles dilatation**

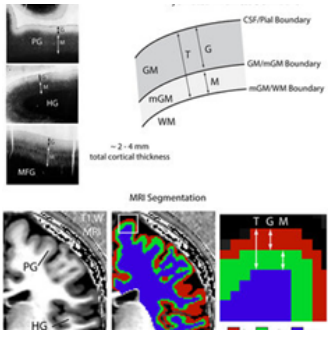


**Fig 3 : | Myelinated cortical thickness measurements.**

The depth of the human cerebral cortex can be roughly subdivided into lightly myelinated and heavily myelinated portions, as seen in representative 40 µm thick histological sections stained for myelin (adapted from Braitenberg, 1962). This leads to intracortical contrast on heavily T1-weighted MRI, which can be used to segment the cerebrum into lightly myelinated gray matter (GM), heavily myelinated gray matter (mGM), and white matter (WM) tissue classes. Measuring the thickness of the GM and mGM tissue classes yields the thickness of the lightly myelinated (G) and heavily myelinated cortical layers (M). Overall cortical thickness (T) is also measured. The mGM class is thicker in regions known to be highly myelinated, such as the primary motor cortex in the precentral gyrus (PG) and the primary auditory cortex in Heschl's gyri (HG), MFG, middle frontal gyru Ref [10]

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