CURRENT TOPIC

Neuroimaging in child and adolescent psychiatric disorders

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Abstract

Neuroimaging in child psychiatry is a rapidly developing field and the number of different techniques being used is increasing rapidly. This review describes the current status of neuroimaging in childhood psychopathology and discusses limitations of the various studies. As yet, no specific and consistent abnormality has been detected in childhood psychiatric disorders. Obsessive compulsive disorder has shown the most consistent findings so far, with orbitofrontal cortex and the caudate nucleus being implicated. Better understanding of the corticostriatal neural networks will shed more light on the neurodevelopmental disorders of childhood.

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In the study of the human brain, a picture is worth a thousand words. In the past 20 years, technological advances have provided and refined a variety of neuroimaging methods based on different physical phenomena. There is now considerable literature on the application of neuroimaging to children with neurodevelopmental disorders. At this stage in the field's development, replicable findings are sufficient to permit an appraisal of the progress made so far, while attempting to outline potential pitfalls and difficulties faced.

Structural imaging measures anatomic structure (radiographs, computed tomography (CT), magnetic resonance (MR) imaging) while functional imaging measures the intrinsic physical properties of tissues (for example, metabolism or blood flow) and changes that occur in disease (magnetic resonance spectroscopy (MRS), functional MR imaging (fMRI), positron emission tomography (PET), single photon emission CT (SPECT), magnetic encephalography (MEG)). The nature of the connection between the physical property measured (for example, radioactivity in some areas) and the underlying physiological phenomenon (for example, metabolism) establishes and limits the utility of different methods, and the technical constraints of each technique. Anderson and Gore¹ give a very

detailed account of the physical basis of the various neuroimaging techniques.

Brain imaging may be performed for a variety of reasons: to address needs in clinical research, patient management, or diagnosis. In clinical practice, structural neuroimaging is indicated when one suspects intracranial pathology—if the patient exhibits focal neurological signs on examination, or when there is a history of significant head trauma (that is, with extended loss of consciousness, enduring neurologic sequelae of any kind, or when there is a close temporal relation to the onset of psychopathology), refractory epilepsy, childhood onset psychoses, and when the disorder is refractory to an extensive array of conventional treatments. Apart from being indicated in complicated epilepsy, functional neuroimaging is currently only a research tool in psychiatry. Functional abnormalities are often picked up in subjects with negative structural scans.

Table 1 compares the different techniques. Although structures may show group differences, they need not show the same degree of difference in, for example, electron density (CT), phosphorylation (MRS), or oxygenation of blood (fMRI). Thus the fMRI cerebral activation may not equate to the PET activation, and both may differ from the anatomy depicted by visual inspection or tissue typing.

Neurophysiological imaging refers to the use of cerebral blood flow radiotracers (¹⁵O labelled water, ¹³³Xe) or metabolic radiotracers (¹⁸F-fluorodeoxyglucose) to spatially resolve the haemodynamic and metabolic correlates of neural circuit activity. *Neuroreceptor imaging* refers to the use of PET or SPECT radionuclides bound to ligands possessing a high and selective affinity for neurotransmitter receptors or transporters. Tracer kinetic models are used to convert local positron annihilations into estimates of receptor or transporter density, distribution, or occupancy. *Neurochemical imaging* refers to the use of PET or SPECT radionuclides bound to precursors (for example, tryptophan, dihydroxyphenylalanine (DOPA)) of enzymatic reactions that support neurotransmitter synthesis.

Normal neurodevelopmental changes that influence paediatric neuroimaging

Knowledge of the normal patterns of brain development in the clinically relevant ages

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Table 1 Comparison of different neuroimaging techniques

Neuroimaging technique	Mechanism	Advantages	Disadvantages
Computed tomography	Collimated beams of x rays are rotated around the head and pass through the brain, losing energy in proportion to the density of the various tissues (grey matter, white matter, and CSF).	Excellent images of skull, sulci, and ventricles. Volumetric and dynamic images can be obtained if spiral CT is used.	Artefacts often arise in regions containing very dense structures, especially in posterior fossa and areas close to bony interfaces. Patient is exposed to ionising radiation. Only transverse slices obtained.
Magnetic resonance imaging	Brief radiofrequency pulses activate the inherent distribution of hydrogen atoms in the brain, following which the hydrogen atoms align themselves in the strong magnetic field generated by the superconducting magnet around the head. The different realignment times after the burst of radiofrequency perturbation, are used to delineate the different tissues of the brain.	Primary method of choice for brain imaging. Superior images with high spatial resolution. Safe, no exposure to radiation. Repeated scans possible even in very young children. Arbitrary planes, transverse/coronal/ sagittal images can be generated.	Pacemakers, shell injury, plates, screws, or metallic implants are contraindications. Subjects have to remain relatively still. Scanner noise is quite loud. Constrained environment within receiver coil.
Functional magnetic resonance imaging	Changes in blood flow (characterised by altered levels of oxygen or oxygenated blood) establish a new equilibrium of the oxygen dependent magnetic properties of haemoglobin, detected through high field magnets.	Can map brain's functional responses to specific stimuli. Non-invasive and safe. Will help us learn more about neurophysiology in both disease and health. Reference anatomic images are simultaneously acquired with the functional data.	Image analysis techniques need to improve in children. Artefacts near skull base limit its use. Constrained environment within receiver coil.
Positron emission tomography	Based on the detection of annihilation photons arising from the decay of injected radiotracer. Arrays of scintillation detectors are used as an electronic collimation system, which transforms the photons into visible light; this is ultimately filtered and reconstructed to form the image showing either the blood flow or glucose metabolism, receptor occupancy or neurochemical binding in the brain (depending on the tracer).	Exact quantification of cerebral blood flow and metabolism. Whole head imaging is more reliable. Neuroreceptor concentration and affinity can be measured.	Radionuclide scanning technique. Cannot be used repeatedly, or in pregnancy. Cyclotron is necessary to provide the radiotracers with very short half life. Constrained by need to inject isotope for each new task. Anatomic data need to be obtained separately.
Single photon emission tomography	Similar to PET. Measures changes in blood flow, receptor activity using appropriate radiotracers. Detectors specialised for localising photons (γ rays) emitted by positron annihilation are used. The data are processed to create images of slices of brain in the transaxial, coronal, and sagittal planes.	Available in most departments of nuclear medicine. Large numbers of radiotracers available. Cost effective.	Radionuclide scanning technique. Cannot be used repeatedly, or in pregnancy. Absolute quantification is not possible, and bilateral symmetrical reduction is difficult to recognise.
Magnetic resonance spectroscopy	This exploits the slight differences in resonant frequency of protons (usually ^1H and ^{31}P) bound to different cell associated structures. It characterises the molecular state of both bound and free tissue water and the chemical microenvironment of cells and provides a profile of the status of intermediary metabolism within a selected tissue volume.	Provides a direct investigation of phosphorylated intermediate metabolites and neurotransmitters such as GABA and glutamate.	Long procedure if one is interested in quantification at molecular level. Only limited substrates are measurable.
Magnetic encephalography	Uses specialised superconducting detectors and sensory coils to measure magnetic fields that surround the currents which give rise to EEGs and ERPs. The magnetic fields reflect currents induced within the dendrites of neurones oriented parallel to the sulci.	Can help to locate and measure the strength of electrical impulses from the brain. Safe procedure, no exposure to radioactive compounds.	Bias favours only some neurones and not all in a particular field and hence may not be accurate. Structural scans necessary separately, to transpose findings onto a brain map.

from 4 to 18 years is necessary to interpret the subtle brain imaging findings reported in the literature. Giedd and colleagues report the best data to date, from the ongoing NIMH paediatric neuroimaging project.²⁻⁴ Cortical grey matter decreases with age, while white matter and CSF volumes (to a lesser extent), gradually increase with age. Lateral ventricles, corpus callosum, basal ganglia, amygdala, and the hippocampus also increase in size with age. Although total brain volume appears to approach adult size by school age, this belies an active and sex specific dynamic balance achieved between growth and regression of certain brain structures throughout childhood and adolescence. Similarly, brain metabolism (as shown by PET studies) rapidly increases during the first years of life, peaks during childhood, and then declines to adult levels during adolescence.

Speculatively, the observed gender differences in incidence, age of onset, and symptom

profiles of developmental neuropsychiatric disorders could arise from complex interactions between the gender specific differences in brain development and the child's environment. For example, the lower incidence of attention deficit-hyperactivity disorder (ADHD) in girls might be related to having a relatively larger caudate nucleus than boys. Also, the male only adolescent increase in lateral ventricular volume^{3,4} is intriguing in light of consistent findings of enlarged ventricular volume in adolescent onset schizophrenia, which is more predominant in boys.

Current status of neuroimaging in childhood psychopathology

Despite accumulating neuroimaging research in children, findings are often inconsistent and not replicable across centres. Many problems exist in the application of neuroimaging to children and these are detailed later in this article. The important findings in childhood disorders are summarised below.

Language impairment and reading disability—Children with specific language impairment have been reported to have a significantly smaller left pars triangularis, with rightward asymmetry of language structures.⁵ Similarly, in those with specific reading disability, the degree of left cerebral asymmetry has been found to correlate with both reading skills and skills in phonemic analysis of spoken language.⁶

ADHD—Although methodological problems remain, there is increasing agreement on the role of the prefrontal-striatal-thalamo-cortical circuit in ADHD, with a preponderance of the evidence suggesting that the right sided circuit is primary, at least at the level of the basal ganglia. Recent reviews in this field include those by Castellanos,⁷ Filipek,⁸ and Overmeyer and Taylor.⁹ Neuroimaging in ADHD has advanced greatly to unpick the neural subsystems involved in its pathophysiology. Hyperactive adolescents have recently been shown to have different functional brain abnormalities when tested on two tasks, a motor inhibition task, and a motor timing task.¹⁰ Adolescents with ADHD in comparison to matched controls, show lower power of response in the right mesial prefrontal cortex during both tasks, and in the right inferior prefrontal cortex and left caudate during the stop task. Figure 1 depicts the findings for the response inhibition task (stop task) from this study.¹⁰

Autism—Despite the presence of numerous brain imaging studies attempting to isolate brain regions or pathways specifically implicated, the literature remains inconclusive.

Figure 1 fMRI differences between children with ADHD and controls, during a response inhibition task (stop task). The first two rows show generic brain activation maps ($p < 0.003$) for nine controls and seven adolescents with ADHD during performance of the stop task. The right side of the image corresponds to the left side of the brain. The last row shows the areas of significant difference (ANCOVA) in power of activation between ADHD and non-ADHD adolescents during task performance ($p < 0.05$). Controls show increased blood oxygenation level dependent (BOLD) response in right mesial frontal cortex, right inferior and middle frontal cortex, and left caudate (courtesy of Dr Katja Rubia PhD, London UK).

Autism has been associated with increased regional brain volume, with the occipital, parietal, and temporal lobes (in decreasing frequency) being enlarged.^{11,12} Reports that cerebellar vermis lobules VI and VII are specifically affected in autism (either being hypoplastic or hyperplastic),¹³ remains controversial because few others have been able to replicate it. Recently, the ability to attribute independent mental states to self and others (theory of mind), has been associated with the activation of the left medial frontal gyrus (Brodmann's area 8) and the posterior cingulate cortex,¹⁴ areas which are not activated in Asperger's syndrome during similar tasks.¹⁵ Using the recently developed voxel based whole brain analysis of structural MRI, Abell *et al*¹⁶ report structural abnormalities in a distributed system centred on the amygdala, in autism. They report decreases of grey matter in anterior parts of this system (right paracingulate sulcus, left inferior frontal gyrus) and increases in posterior parts (amygdala/peri-amygdaloid cortex, middle temporal gyrus, inferior temporal gyrus) and in the regions of the cerebellum. These findings are appealing because the structures involved have been previously implicated in social cognition by animal and histopathological studies. Using neurochemical imaging, an increased serotonin synthesis capacity in autistic children (using α -¹¹C-methyl-L-tryptophan PET) has been reported, and is hypothesised to be related to the disruption of the normal developmental pattern of brain serotonin synthesis.¹⁷

Tourette's syndrome—Increased dopamine transporter availability in the caudate in ¹²³I-BZM SPECT studies,^{18,19} and fMRI based activation of the orbitofrontal cortex, bilateral premotor regions, and the head of right caudate, and decreased activation of the bilateral globus pallidus and thalamus during tic suppression tasks²⁰ have been reported.

Obsessive compulsive disorder (OCD) has been extensively studied and subjects show orbitofrontal and anterior cingulate hypermetabolism at rest. Successful attenuation of OCD symptoms results in the attenuation of the hypermetabolism of the orbitofrontal cortex, caudate nucleus, and anterior cingulate cortex, irrespective of whether the treatment used is behaviour therapy or medication. Subjects with OCD show increased activation in bilateral orbitofrontal cortex, right caudate nucleus, and anterior cingulate cortex, during symptom induction procedures, with the degree of induced obsessionality being positively correlated with the magnitude of activation within an anterior orbitofrontal locus. Furthermore, individuals with OCD fail to recruit normally the corticostriatal system during cognitive-behavioural activation paradigms, and instead activate the medial temporal lobe system (involved in conscious information processing). Rauch *et al*²¹ have provided an in depth review on the subject.

Childhood onset schizophrenia (COS), defined as schizophrenia with onset by 12 years of age, provides a unique research opportunity to test the neurodevelopmental hypothesis of schizo-

Table 2 Brain regions involved (from neuroimaging data) in childhood psychiatric disorders

Disorder	Frontal	Parieto-occipital	Temporal	Caudate	Putamen	Limbic	Corpus callosum	Cerebellum	Altered laterality
ADHD	Probable	Possible	Possible	Probable	Likely		Likely	Possible	Possible
Autism	Possible	Possible	Probable	Possible		Probable		Likely	
Tourette's	Probable			Possible	Probable	Possible			Likely
OCD	Probable			Probable				Likely	Likely
Schizophrenia	Possible		Probable			Possible	Likely	Likely	Possible
Mania	Possible								
Depression	Possible					Possible			
Dyslexia	Possible	Probable	Probable			Possible			Possible

phrenia. Children meeting strict criteria for COS show smaller cerebral volume and thalamic area, and increased basal ganglia and lateral ventricular volumes,²² the size of the effect being similar to that observed for adult populations. In adolescents with COS, the caudate enlargement appears to be secondary to exposure to typical neuroleptics.²³ Smaller volumes of cerebellar vermis (inferior posterior lobe) have also been reported, which is consistent with observations in adult schizophrenia.²⁴ Patients with COS are reported to have a four-fold greater decrease in cortical grey matter volume during adolescence, with a disease specific reduction in the frontal and temporal regions.²⁵

Affective and depressive disorders—Reviews on affective disorders implicate the prefrontal cortex (especially orbital), basal ganglia, thalamus, and amygdala, with possible dopamine and serotonin underpinnings.^{26–27} Decreased frontal lobe volume and increased ventricular volume have been reported in children with depressive disorders, with a significant inverse relation between age and frontal lobe volume.²⁸ Temporal horn enlargement and deep white matter hyperintensities, with the absence of normal frontal asymmetry have been reported in children and adolescents with bipolar illness. These findings in childhood affective disorders have largely been replicated in adults with similar disorders.

Post-traumatic stress disorder (PTSD)—MRI based hippocampal atrophy, and PET based failure of hippocampal activation during the performance of memory tasks have been reported in women with childhood sexual abuse related PTSD.²⁹ Children and adolescents with PTSD resulting from child maltreatment, have recently been shown to have smaller intracranial and cerebral volumes than matched controls.³⁰ Brain volume positively correlated with age of onset of PTSD trauma and negatively correlated with duration of abuse.³⁰ This suggests that intense stress in childhood can lead to long term structural and functional changes in the brain. On the other hand, in *anorexia nervosa*, the observed morphological and functional cerebral alterations (enlarged CSF spaces especially of cortical sulci), are interpreted to be consequences of the anorexic state, which is at least partially reversible with weight gain.³¹

After reviewing the neuroimaging findings in the various disorders (summarised in table 2), it seems possible that some symptoms (irrespective of diagnosis) have common underlying pathophysiology (for example, inattention in mania has been shown to be associated with

prefrontal dysfunction, which is similar to that reported in ADHD). This is in keeping with the recently proposed model for the management of psychopathology in neurodevelopmental disorders.³² Tourette's syndrome, OCD, depression, and ADHD frequently co-occur clinically, which may be related in part to common elements in their pathophysiologies, which at the level of the brain organisation may involve particular cortical-subcortical circuits. It is possible that putamen dysfunction leads to sensorimotor symptoms of Tourette's syndrome, ventral caudate nuclear dysfunction leads to obsessions and compulsions, dorsolateral caudate nuclear involvement leads to hyperactivity and inattention, and predominant involvement of the nucleus accumbens results in affective or anxiety disorders.²¹

Limitations of neuroimaging studies in childhood

It cannot be emphasised enough that it is very difficult to obtain consistency in neuroimaging findings in children and adolescents. One must be cautious in generalising findings because the existing published literature reflects a publication bias towards studies with positive findings. With an increasing number of centres becoming involved in neuroimaging research, findings being reported are not uniform. The probable reasons for this are detailed below.

SUBJECT VARIABLES

Gender

Cerebral volume is about 9% larger in males, and lateral ventricular volume increases at about twice the rate per year in males, occurring mostly after 11 years of age (important when ventricular to brain ratios are calculated). While boys have larger globus pallidi, girls have larger caudate nuclei than boys. Similarly, while amygdala volumes increase sharply in boys (about six to seven times that of girls), hippocampal volume increases more rapidly in girls (at about three times that of boys).

Handedness

As symmetry differences are often key features in discriminating controls from patients with disorders such as ADHD,³³ dyslexia,³⁴ or Tourette's syndrome,³⁵ it is necessary to control for handedness in paediatric neuroimaging studies.

Body size

This is a very poor indicator of brain size in humans.³⁶ Children have a larger head to height

ratio than adults, with large interindividual variations.

Intelligence

Intelligence has been reported to have a statistically significant relation to brain size.^{37–39} Socioeconomic status and education have also been reported to relate to brain size, although the interdependence with factors such as prenatal care, nutrition, and IQ is not clear.

Inherent variability in children

A striking feature of brain morphometric data on normal children and adolescents, is the high degree of variability of brain structure size, even in well screened healthy cohorts, leading to the need for larger sample sizes to detect significant differences. Most of the studies to date do not meet the projected numbers necessary to rule out type II errors.

Developmental age

Cortical and subcortical grey and white matter, and CSF volumes change rapidly during childhood and adolescence, resulting in problems when children of a wide age range are studied.

Cognitive style

Cognitive strategies being used to solve tasks during functional imaging may be different at different ages, leading to different activation patterns in subjects.

Ethical issues

Ethical issues that need to be addressed include the possibility of overprotection by policy makers and institutional review boards—arising from the recognition of children's special vulnerability, without equal recognition of their need for research; assessment of the risk–benefit ratio; the difficulty of justifying risk for normal controls; development and use of age graded consent; development of child friendly imaging procedures; and disposition of unwanted or unexpected knowledge about individuals, including the subject's right not to know and parent's right not to tell, among other things.⁴⁰

STUDY VARIABLES

Subject selection

As subtle neuroimaging findings have been reported in many childhood disorders, it is important to have good normative data from a control group. Ideally, normative data should be acquired from scans of community recruited subjects who have been assessed prior to the scan.

Sample size/study design

The high variability of brain sizes and the non-linear pattern of most developmental curves call for large samples and longitudinal study designs in order to adequately characterise neuroanatomic patterns of development in children.

Lack of hypothesis driven neuroimaging research

It needs to be recognised that investigations using new techniques in the absence of guiding

hypotheses can lead to confusion. Chance associations are bound to occur from exhaustive analysis of small numbers of subjects, receiving a disproportionate emphasis in the literature.

IMAGING VARIABLES

Image acquisition and anxiety

Many children become anxious during scanning and become uncooperative, leading to inflated drop out rates and difficulty in unpicking the anxiety related findings (artefacts) during functional neuroimaging. Familiarity and comfort with the people acquiring the scan, undergoing scanning in the evening when natural sleep is more likely, reading a bedtime story or bringing in a favourite blanket or stuffed toy, and being allowed to stop the procedure at any time for any reason can all increase the chances of acquiring adequate scans and make the experience more pleasant for the child.

Movement artefacts

Movement during scanning produces significant artefacts and needs to be monitored and adjusted for. The advent of new collars to prevent movement will help improve the quality of the scans.

Scanning parameters

Thicker slices result in less spatial resolution and greater partial volume effects, a critical consideration for quantifying small but clinically pertinent structures such as the caudate nucleus, putamen, or globus pallidus.

Image analysis

Analysis of MR images has benefited enormously from advances in computer technology. However, the absence of a “gold standard” hampers the validation of these techniques and comparison with results obtained from manual tracing by expert human raters remains the best standard. Developmentally correct child brain maps are not yet freely available, resulting in the use of adult brain maps—Talarach space, for analysis. This could result in computerised programs picking up wrongly identified areas during analysis. Statistical threshold adjustments for multiple comparisons, and uncertainty regarding the heterogeneity of the condition under study also affect the reliability of results. Nonetheless, imaging offers distinct advantages over non-imaging methods in assessing function and structure.

Interpretation of data

The interpretation of data using “subtraction paradigms” has major limitations. It assumes that successive cognitive tasks lead to linear cerebral activation, and discounts the current understanding that the process is clearly more complex. Problems of averaging results across groups of subjects and unreliable identification of boundaries, structures, sites of activation, and their changes over time further lower reliability.

Measured parameter versus inference

The measured changes of physical parameters in the various methods (for example, nuclear MR signal decay time triggered by changes in the electron structure of iron, in MRI), is often quite distant from the biological event that induced the change. This introduces doubt into the assumption that neuroimaging accurately measures brain structure or function. It is possible that there is no clear quantitative relation between the biological change and the magnitude of the signal acquired for imaging.

Implication of abnormality

The demonstration of abnormality does not necessarily indicate that it is of current aetiological significance. Abnormalities in brain structure can result from various early experiences encountered by the subject, shaping its development including unstimulating environments, physical insults, and genetic alterations. Neuroimaging studies often neglect to appreciate the brain based adaptive capacity and compensatory responses that accompany chronic childhood psychiatric disorders, when attributing findings to disease process, even though this may only be compensatory.

Future trends and implications of neuroimaging in child psychiatry

The future will possibly see the increasing use of functional neuroimaging in treatment planning and monitoring response in psychiatry. The functional methods will continue to evolve and the primary challenge will be to develop better computerised image analysis techniques capable of handling the wealth of anatomic and functional neuroimaging data in children. Some of the important developments in the field are detailed below.

Research into new radiopharmaceuticals has opened up the possibility of using SPECT and PET, to study a wider range of clinically relevant neurotransmitters and receptors (for example, D_1 antagonists in prefrontal cortex, hippocampus, and amygdala; a D_2 receptor agonist which localises mainly in the striatum; 5HT_{1A}, 5HT_{2A}, 5HT_{2C} receptor ligands). Ligands which help quantify receptors such as N-methyl-D-aspartate (NMDA), α -amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA), ion channels, γ -aminobutyric acid B (GABA-B) etc, will help the understanding of the neurodevelopmental disorders.

The ability to study in vivo pharmacokinetics of agonists and antagonists of dopaminergic, serotonergic, noradrenergic, GABA, opioid, and muscarinic receptors has opened up new research avenues. PET activation studies using radioligand tagged drugs (for example, ¹¹C-methylphenidate) will increasingly be used to predict drug response. Probes investigating the clinically relevant neuroreceptor subsystems will help in aetiological understanding of disorders such as ADHD, leading to more targeted treatments. Appropriate pre- and post-drug treatment receptor occupancy data using neuroreceptor scanning techniques, will help predict side effect propensity (for example, tardive dyskinesia) and clinical response. Dy-

namic PET studies using receptor ligands (for example, opioid or dopamine receptor ligands) will help in understanding the site, and the neurochemical basis of neuronal activity, leading to designing innovative pharmacological strategies.

Judicious combination of complementary methodologies (multimodal imaging) is necessary to understand the relation between structure and function, and will at the very least be necessary to explore whether altered regional metabolism or receptor densities arise due to an underlying change in the volume of that structure.

Studies on normal children will shed new light on the neurological underpinnings of normal cognitive and emotional processes, helping us to understand the deficits in children with specific problems (for example, the localisation of brain regions involved in phonologic processing, providing compelling evidence that disturbances in phonologic processing is a core deficit in reading disability).

The recent findings in PTSD have aroused interest in the interrelation of psychosocial stressors, brain function, and structure. It would be possible to harness functional neuroimaging techniques to test hypotheses based on the biopsychosocial models of childhood psychopathology. Understanding the mechanism of trauma related alteration of brain function (and probably structure), is important to plan appropriate preventive strategies, and to improve long term outcome in traumatised children.

Genetic information will increasingly be used to leverage the probability of locating brain abnormalities, as the effects of genetic lesions can be mapped with reasonable certainty to specific brain regions. This powerful methodology remains largely untapped to date. Knowing where in the brain these genes will express themselves will in the future permit studies of the secondary effects of these genes on maturation, development, and adaptation of brain structure and function. The approach of studying specific genetic/chromosomal disorders (for example, fragile X syndrome, William syndrome, Rett syndrome) will also help elucidate the manner in which gene-brain-behaviour associations develop and vary across developmental disability.

Transcranial magnetic stimulation (TMS), is a new, non-invasive technique for directly stimulating cortical neurones, with the hope of a therapeutic effect.⁴¹ This technique is closely related to the MRI technique. Preliminary investigations using rapid rate TMS, to improve motor speed in Parkinson's disease and mood in depression, have been encouraging. This could soon prove to be an important neuropsychiatric tool in the assessment and management of neurodevelopmental disorders.

As in utero brain development is abnormal in many neurodevelopmental disorders, methods of assessing brain development in utero will become a priority, to understand the relation between observed in utero brain development, postnatal brain neurocognitive development, and the subsequent development of

neuropsychiatric disorders. Ultrasound based mild ventriculomegaly in utero (in the absence of other abnormalities) is associated with mild developmental delay in about 20% of children.⁴²

DEVELOPMENTS IN IMAGING TECHNOLOGY

This will be ongoing and the areas of focus will be: acquisition of ever faster images, improvement of activation paradigms, such as event related task designs which offer more flexibility than block design paradigms, examining data beyond averaging. Co-registration of scan data across time will help define the differences in subjects over time, leading to longitudinal changes being picked up. The future of brain imaging in child neuropsychiatry will probably be different for each technique.

In structural MR imaging, faster image acquisition techniques may help improve the cooperation of distressed children, and better head restraint systems combined with software and hardware development that corrects each acquisition for motion artefacts will help greatly and allow the study of developmentally delayed children and those with movement disorders. Higher field strength magnets used in MR imaging could improve image quality, but may need to go through ethical committees and may need the demonstration that higher fields are a minimal risk for younger subjects. Voxel based whole brain analysis and connectivity analysis will increasingly be used to understand neural circuitry.

Functional MR imaging will increasingly be used, with improvements in technology tackling the problem of movement artefacts, imaging data reduction, and postimaging data processing.⁴³ The sound of the scanner will also possibly decrease significantly, helping to reduce the effect of noise on functional MR imaging. Rapid MR scanning (including gradient echo, fast spin echo, and planar sequences), the recently developed event related fMRI, contrast based fMRI techniques, diffusion MR imaging, arterial spine labelling (ASL) techniques, and dynamic susceptibility MR perfusion imaging of the brain offer clinically relevant physiological data not obtainable by conventional MR imaging, and may be used in child psychiatric disorders in the near future. They are likely to be at least as sensitive and specific as radionuclide based techniques, and offer the added advantage of higher intrinsic resolution, convenient co-registration with conventional MR imaging, as well as time and cost effective imaging in patients who require routine MR imaging.

MR spectroscopy involving ³¹P for the evaluation of membrane lipids, and ¹³C for the evaluation of glutamate neurotransmission and excitotoxicity will be increasingly used. MRS technology has already improved to include approaches voxel tailored to the needs of each individual and disorder.

In PET, the progress will probably involve improved scanning resolution with newer tracers, requiring lower radiation dose. An important step in understanding cerebral function will be the increasing use of "autoradiogra-

phy", helping to understand the time course of minute differences between subjects, to differentiate acquired from developmental abnormalities, and to understand cerebral reorganisation. Fluid attenuated inversion recovery (FLAIR), diffusion anisotropy imaging, and event related PET scanning (for example, EEG spike related PET changes) are all strategies that will have a role in the near future in understanding complex neural mechanisms in neuropsychiatry (especially the epilepsies).

In SPECT, there will be an improvement in image resolution; more novel radiotracers will become available, and will become used widely as a cost effective technique to which most departments will have access.

Conclusion

Neuroimaging in child psychiatry is a rapidly developing field and the different techniques being used are increasing so quickly that no single individual will be able to be conversant in all of the methodologies. As yet, no specific and consistent abnormality has been detected in childhood psychiatric disorders. Findings have frequently been inconsistent owing to various factors that affect neuroimaging in children. Obsessive compulsive disorder has shown the most consistent findings so far, with orbitofrontal cortex and the caudate nucleus being implicated. Better understanding of the corticostriatal neural networks will shed more light on the neurodevelopmental disorders of childhood.

The design of developmentally correct paediatric brain maps, for computerised analysis of paediatric neuroimaging data should become a priority. Identification of homogeneous subgroups in paediatric research using genetics, molecular biology, or immunology could improve the specificity of neuroimaging findings. Despite all the pitfalls of paediatric neuroimaging, refinements of the techniques and improvements in the field could help improve diagnosis, triage, and in predicting and monitoring medication response and side effects.

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