Neuroimaging aids detection of structural, vascular, inflammatory, and metabolic causes of psychiatric symptoms in children and adolescents.

The first 15 years of the new millennium have seen a great increase in research on neuroimaging in children and adolescents who have a psychiatric disorder. In addition, imaging modalities continue to evolve, and are becoming increasingly accessible and informative. The literature is now replete with reports of neurostructural differences between patients and healthy subjects in a variety of common pediatric psychiatric conditions, including anxiety disorders, mood disorders, autism spectrum disorder (ASD), and attention-deficit/hyperactivity disorder (ADHD).

Historically, the clinical utility of neuroimaging was restricted to the identification of structural pathology. Today, accumulating data reveal novel roles for neuroimaging; these revelations are supported by studies demonstrating that treatment response for psychotherapeutic and psychopharmacotherapeutic interventions can be predicted by neurochemical and neurofunctional characteristics assessed by advanced imaging technologies, such as magnetic resonance spectroscopy (MRS) and functional MRI.

However, such advanced techniques are (at least at present) not ready for routine clinical use for this purpose. Instead, neuroimaging in the child and adolescent psychiatric clinic remains largely focused on ruling out neurostructural, neurologic, “nonpsychiatric” causes of our patients’ symptoms.
Understanding the role and limitations of major imaging modalities is key to guiding efficient and appropriate neuroimaging selection for pediatric patients. In this article, we describe and review:

- neuroimaging approaches for children and adolescents with psychiatric disorders
- the role of neuroimaging in (1) the differential diagnosis and workup of common psychiatric disorders and (2) urgent clinical situations
- how to determine what type of imaging to obtain.

**Computed tomography**

CT, which utilizes ionizing radiation, often is reserved, in the pediatric setting, for (1) emergency evaluation and (2) excluding potentially catastrophic neurologic injury resulting from:

- ischemic or hemorrhagic stroke
- herniation
- intracerebral hemorrhage
- subdural and epidural hematoma
- large intracranial mass with mass effect
- increased intracranial pressure
- acute skull fracture.

Although a CT scan is, typically, quick and has excellent sensitivity for acute bleeding and bony pathology, it exposes the patient to radiation and provides poor resolution compared with MRI.

In pediatrics, there has been practice-changing recognition of the importance of limiting lifetime radiation exposure incurred from medical procedures and imaging. As a result, most providers now agree that use of MRI in lieu of CT is appropriate in many, if not most, non-emergent situations. In an emergent situation, however, CT imaging is appropriate and should not be delayed. Moreover, in an emergent situation, you should not hesitate to use head CT in children, although timely discussion with the radiologist is recommended to review your differential diagnosis to better determine the preferred imaging modality.

**Magnetic resonance imaging**

Over the past several decades, MRI has been increasingly available in most pediatric health care facilities. The modality offers specific advantages for pediatric patients, including:

- better spatial resolution
- the ability to concurrently assess multiple pathologic processes
- lack of exposure to ionizing radiation.

A number of MRI sequences, described below, can be used to assess vascular, inflammatory, structural, and metabolic processes.

**A look inside.** Comprehensive review of the physics that underlies MRI is beyond the scope of this article; several important principles are relevant to clinicians, however. Image contrast is dependent on intrinsic properties of tissue with regard to proton density, longitudinal relaxation time (T1), and transverse relaxation time (T2). Pulse sequences, which describe the strength and timing of the radiofrequency pulse and gradient pulses, define imaging acquisition parameters (eg, repetition time between the radio frequency pulse and echo time).

In turn, the intensity of the signal that is “seen” with various pulse sequences is differentially affected by intrinsic properties of tissue. At most pediatric institutions, the standard MRI-examination protocol includes: a T1-weighted image (Figure 1A); a T2-weighted scan (Figure 1B); fluid attenuated inversion recovery (FLAIR) (Figure 1C); and diffusion-weighted imaging (DWI) (Figure 1D).

**Specific MRI sequences**

**T1 images.** T1 sequences, or so-called anatomy sequences, are ideally suited for detailed neuroanatomic evaluations. They are generated in such a way that structures containing fluid are dark (hypointense), whereas other structures, with higher fat or protein content, are brighter (iso-intense, even hyper-intense). For this reason, CSF in the intracranial ventricles is dark, and white matter is brighter than the cortex because of lipid in myelin sheaths.

In addition, to view structural abnormalities that are characterized by altered vascular supply or flow, such as tumors and infections (abscesses), contrast imaging can be
particularly helpful; such images generally are obtained as T1 sequences.

**T2 images.** By contrast to the T1-weighted sequence, the T2-weighted sequences emphasize fluid signal; structures such as the ventricles, which contain CSF, therefore will be bright (hyper-intense). Pathology that produces edema or fluid, such as edema surrounding demyelinating lesions or infections, also will show bright hyper-intense signal. In T2-weighted images of the brain, white matter shows lower signal intensity than the cortex because of the relatively lower water content in white matter tracts and myelin sheaths.

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**Clinical Point**

T1-weighted MRI sequences are ideal for detailed anatomic evaluations: fluid-filled structures are dark; other structures, brighter
Fluid attenuation inversion recovery. FLAIR images are generated so that the baseline bright T2 signal seen in normal structures, such as the CSF, containing ventricles is cancelled out, or attenuated. In effect, this subtraction of typical background hyper-intense fluid signal leaves only abnormal T2 bright hyper-intense signal, such as vasogenic edema surrounding tumors, cytotoxic edema within an infarction, or extra-axial fluid collections such as a subarachnoid or subdural hemorrhage.

Diffusion-weighted imaging. DWI utilizes the random motion (ie, diffusion) of water molecules to generate contrast. In this regard, the diffusion of any molecule is influenced by its interaction with other molecules (eg, white-matter fibers and membranes, and macromolecules). Diffusion patterns therefore reflect details about tissue boundaries; as such, DWI is sensitive to a number of neurologic processes, such as ischemia, demyelinating disease, and some tumors, which restrict the free motion of water. DWI detects this so-called restricted diffusion and displays an area of bright signal.

Susceptibility-weighted imaging (SWI). In the pediatric population, SWI (Figure 2) utilizes a long-echo, 3-dimensional, velocity-compensated gradient recalled echo for image acquisition and, ultimately, leverages susceptibility differences across tissues by employing the phase image to identify these differences. SWI, which uses both magnitude and phase images and is remarkably sensitive to venous blood (and blood products), iron, and calcifications, therefore might be of increasing utility in pediatric patients with traumatic brain injury (TBI) (Figure 2B). As such, SWI has become a critical component of many pediatric MRI studies.

Magnetic resonance angiography (MRA) (Figure 3A, page 44) is helpful for assessing intracranial arteries and may be employed in the evaluation of:

- vessel pathology and injury underlying stroke, such as vessel occlusion or injury
- patterns of vessel involvement suggestive of vasculitis
- developmental or acquired structural vascular abnormalities, such as aneurysm or vascular malformations
- determination of tumor blood supply.

Clinical Point

Susceptibility-weighted MRI, sensitive to venous blood, is of increasing utility to image traumatic brain injury in a child.

B and C: Multiple foci of hypo-intense signal are seen at the gray matter–white matter interface (arrows), representing multiple small hemorrhages caused by shear forces. Hemorrhages are dark on the SWI sequence because of the paramagnetic effects of hemosiderin.
MRA can be performed without or with contrast, although MRA with contrast might provide a higher quality study and therefore be of greater utility. Of note: The spatial resolution of MRA is not as good as CT angiography; abnormalities, such as a small aneurysm, might not be apparent.

**Magnetic resonance venography (MRV)** (Figure 3B) is most commonly performed when the possibility of thrombosis of the dural venous sinuses is being considered; it also is employed to evaluate vascular malformations, tumor drainage patterns, and other pathologic states. As with MRA, MRV can be performed without or with contrast, although post-contrast MRV is generally of higher quality and might be preferred when assessing for sinus thrombosis.

**Magnetic resonance spectroscopy (MRS)** resides at the border between research and clinical practice. In children and adolescents, MRS provides data on neuronal and axonal viability as well as energetics and cell membranes. Pediatric neurologists often use MRS to evaluate for congenital neuro-metabolic disease; this modality also can help distinguish between an active intracranial tumor from an abscess or gliosis.

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**Clinical Point**

Magnetic resonance spectroscopy is often used to distinguish pediatric intracranial tumor from abscess or gliosis.

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**Neuroimaging in pediatric neuropsychiatric conditions: Evidence, guidance**

**Delirium (altered mental status).** The acute neuropsychiatric syndrome characterized by impaired attention and sensorium might have a broad underlying etiology, but it is always associated with alteration of CNS neurophysiology. Children with neurostructural abnormalities might have increased vulnerability to CNS insult and therefore be at increased risk of delirium. Additionally, delirium can present subtly in children, with the precise signs dependent on the individual patient’s developmental stage.

Neuroimaging may be helpful when an infectious, inflammatory, toxic, or a metabolic basis for delirium is suspected, or when a patient has new focal neurologic findings. In this regard, focal neurologic findings suggest an underlying localizable lesion and warrant dedicated neuroimaging to localize the lesion.

In general, the differential diagnosis should guide consideration of neuroimaging. When considering the possibility of an unwitnessed seizure in a child who presents with altered mental status, neuroimaging certainly is an important component of the workup.

As another example, when underlying trauma, intracranial hemorrhage, or mass is
a possibility in acute delirium, urgent head CT is appropriate. In non-emergent cases, MRI is the modality of choice. In immunocompromised patients presenting with delirium, maintain a low threshold for neuroimaging with contrast to rule out opportunistic intracranial infection.

Last, in children who have hydrocephalus with a shunt, delirium could be a harbinger of underlying shunt malfunction, warranting a “shunt series.”

**ADHD.** The diagnosis of ADHD remains a clinical one; for the typical pediatric patient with ADHD but who does not have focal neurologic deficits, neuroimaging is unnecessary. Some structural MRI studies of youth with ADHD suggest diminished volume of the globus pallidus, putamen, and caudate; other studies reveal changes in gyrification and cortical thickness in regions subserving attentional processes. However, intranidividual and developmental-related variability preclude routine use of neuroimaging in the standard diagnostic work-up of ADHD.

Nevertheless, neuroimaging should be strongly considered in a child with progressive worsening of inattention, especially if combined with other psychiatric or neurologic findings. In such a case, MRI should be obtained to evaluate for a progressive neurodegenerative leukoencephalopathy (eg, adrenoleukodystrophy).

**Depressive and anxiety disorders.** In pediatric patients who exhibit depressive or anxiety symptoms, abnormalities have been observed in cortical thickness and gray matter volume, and functional signatures have been identified in the circuitry of the prefrontal amygdala. No data suggest that, in an individual patient, neuroimaging can be of diagnostic utility—particularly in the absence of focal neurologic findings.

That being said, headache and other somatic symptoms are common in pediatric patients with a mood or anxiety disorder. Evidence for neuroimaging in the context of pediatric headache suggests that MRI should be considered when headache is associated with neurologic signs or symptoms, such as aura, or accompanied by focal neurologic deficit.

**Pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS).** Neuroimaging studies of patients with
confirmed PANDAS or PANS are rare, but group analyses suggest a decreased average volume of the caudate, putamen, and globus pallidus in patients with PANDAS compared with healthy comparison subjects, although total cerebral volume does not appear to differ.15 Moreover, thalamic findings in patients with PANDAS have been noted to be similar to what is seen in patients with Sydenham’s chorea.

The most recent consensus statement regarding the treatment and assessment of PANDAS and PANS recommends ordering brain MRI when other conditions are suspected (eg, CNS, small vessel vasculitis, limbic encephalitis) or when the patient has severe headache, gait disturbance, cognitive deterioration, or psychosis.16 Furthermore, the consensus statement notes the potential utility of T2-weighted imaging with contrast to evaluate inflammatory changes in the basal ganglia.16

**Autism spectrum disorder.** Significant progress has been made during the past decade on the neuroanatomic characterization of ASD. Accumulating data indicate that, in pediatric patients with ASD,
Several studies have examined the presence of patient-level findings in samples of pediatric patients with ASD. Approximately 8% of pediatric patients with ASD were found to have some abnormality on routine brain MRI, the most common being white-matter signal abnormalities, dilated Virchow-Robin space, and temporal lobe abnormalities. Although abnormalities might be present in a large percentage of individual scans, routine screening MRI is unlikely to be of clinical utility in youth with ASD. In fact, no recommendation for routine MRI screening in patients with ASD has been made by the American Academy of Child & Adolescent Psychiatry, the Child Neurology Society of the American Academy of Neurology, or the American Academy of Pediatrics.

However, in patients with an underlying neurostructural disease that is phenotypically associated with ASD-like symptoms, imaging might be of use. In tuberous sclero-
sis, for example, MRI is especially important to classify intracranial lesions; determine burden and location; or identify treatment options (Figure 4, page 45). For patients with tuberous sclerosis—of whom more than one-third meet diagnostic criteria for ASD—MRI study should include FLAIR, spin-echo, and gradient-echo sequences.

**Movement disorders.** Hyperkinetic movement disorders, including tic disorders and drug-induced movement disorders (eg, tremor) are common in pediatric patients. In pediatric patients with a tic disorder or Tourette’s disorder (TD), neuroimaging typically is unnecessary, despite the suggestion that the caudate nucleus volume is reduced in groups of patients with TD.

Many CNS-acting medications can exacerbate physiologic tremor; in pediatric patients with symptoms of a movement disorder, home medications should be carefully reviewed for potentially offending agents. When the patient is clinically and biochemically euthyroid and medication-induced movement disorder has been ruled out, or when the patient meets clinical diagnostic criteria for TD or a tic disorder, routine neuroimaging generally is unnecessary.

When tremor accompanies other cerebellar signs, such as ataxia or dysmetria, strongly consider MRI of the brain to evaluate pathology in the posterior fossa. In addition, neuroimaging should be considered for children with a new-onset abnormality on neurologic exam, including rapid onset of abnormal movements (other than common tics), continuous progressive worsening of symptoms, or any loss of developmental milestones.

Last, although tics and stereotypies often are transient and wane with age, other abnormal movements, such as dystonia, chorea, and parkinsonism (aside from those potentially associated with antipsychotic use), are never expected during typical development and warrant MRI.

**Traumatic brain injury.** Prompt evaluation and intervention for TBI can significantly affect overall outcome. Moreover, there has been increased enthusiasm around the pre-hospital assessment of TBI severity using (1) any of several proprietary testing systems (eg, Immediate Post-Concussion Assessment and Cognitive Testing [ImPACT]) plus (2) standard clinical staging, which is based on duration of loss of consciousness, persistence of memory loss, and the Glasgow Coma Scale score.

The goal for any TBI patient during the acute post-injury phase is to minimize continued neuronal injury from secondary effects of TBI, such as cerebral edema and herniation, and to optimize protection of surviving brain tissue; neuroimaging is a critical component of assessment during both acute and chronic recovery periods of TBI.21

The optimal imaging modality varies with the amount of time that has passed since initial injury.22 Urgent neuroimaging (the first 24 hours after brain injury) is typically obtained using head CT to assist decision-making in acute neurosurgical management. In this setting, head CT is fast and efficient; minimizes the amount of time that the patient is in the scanner; and provides valuable information on the acuity and extent of injury, degree of cerebral edema, and evidence or risk of pending herniation.

On the other hand, MRI is superior to CT during 48 to 72 hours after injury, given its higher resolution; superior imaging of the brainstem and deep gray nuclei; and ability to detect axonal injury, small contusions, and subtle neuronal damage. Specifically, SWI sequences can be particularly helpful in TBI for detecting diffuse axonal injury and micro-hemorrhages; several recent studies also suggest that SWI may be of particular value in pediatric patients with TBI.23

Additionally, given the increased sensitivity of MRI to detect subtle injuries, this modality can assist in identifying chronic sequelae of brain injury—thus contributing to determining of chronic therapy options and assisting with long-term prognosis. Gross structural changes resulting from TBI often are evident even in the acute post-injury phase; synaptic remodeling continues, however, for an indefinite period after injury, and this remodeling capacity is even more pronounced in the highly plastic brain of a young child.
Microstructural changes might not be detectable using traditional, readily available imaging sequences (CT, MRI). When those traditional modalities are used in concert with functional imaging techniques (eg, PET to evaluate cerebral metabolism and SPECT imaging which can detect abnormalities in cerebral blood flow), the combination of older and newer might provide a more complete picture of recovery after TBI.24

The important role of neuroimaging in severe TBI is intuitive. However, it is important to consider the role of neuroimaging in mild TBI in children, especially in the setting of repetitive mild injury.25 A growing body of evidence supports close, serial monitoring of children after even mild closed head injury for neurologic and psychiatric sequelae. Although it is rare that a child who is awake, interactive, and lacking focal neurologic deficits would need emergent (ie, CT) imaging after mild closed head injury, there might be a role for MRI later in the course of that child’s recovery—especially if recovery is complicated by clinical sequelae of mild TBI, such as cognitive impairment, headaches, or altered behavior.

When is additional neuroimaging needed?
It’s worthwhile briefly reviewing 4 scenarios that you might encounter, when you work with children and adolescents, in which urgent or emergent neuroimaging (often with consultation) should be obtained. The Table (page 46) describes these situations and appropriate first- and second-line interventions.

1. When the presentation of your patient is consistent with an acute neurologic deficit, acute TBI, progressive neuropsychiatric decline, CNS infection, mass, demyelinating process, or toxic exposure, neuroimaging is likely critical.

2. In patients with progressive neurologic decline, including loss of developmental milestones, MRI, MRS, and referral to neurology should be part of the comprehensive evaluation.

3. In young children who exhibit a decrease in head circumference on growth curves, MRI is important to evaluate for underlying structural causes.

4. Pediatric patients with symptoms consistent with either stroke (ie, a new, persistent neurologic deficit) or a demyelinating process (eg, multiple episodes of variable transient focal neurologic symptoms), MRI should be obtained without compunction.

Consultation with pediatric neuroradiology
In deciding whether to obtain neuroimaging for a particular case, you should discuss your concerns with the pediatric radiologist or pediatric neuroradiologist, who will likely provide important guidance on key aspects of the study (eg, modifying slice thickness in a particular scan; recommending the use of contrast; including MRS in the order for imaging; performing appropriate vessel imaging). Consider asking 1 or more important questions when you discuss a patient’s presentation with the pediatric radiologist or pediatric neuroradiologist:
- “What neuroimaging studies are appropriate, based on my differential diagnosis?”
- “Are there specific imaging sequences that we should consider?”
- “Are there contraindications to the imaging modality for my patient?”
- “Is my patient likely to have difficulty tolerating the imaging procedure?”
- “Does my patient need sedation to tolerate this procedure?”
- “Should additional regions be included in the scan?” (Examples: In a child with stroke it might be important to include neck and chest vasculature and the heart. Other conditions might warrant imaging of the spinal cord.)

References
4. Cecil KM. Proton magnetic resonance spectroscopy:
Related Resources

- Radiopaedia. www.radiopaedia.org (a radiology educational resource archiving representative images of many of the pathologic states described in this article).

Clinical Point

Seek guidance from the pediatric radiologist or neuroradiologist on the optimal scanning modality for your patient.

Bottom Line

Making appropriate decisions about neuroimaging in children who have a psychiatric disorder depends on an excellent medical history and physical exam (including a neurologic exam). In the absence of abnormal neurologic findings, neuroimaging is often unnecessary. In the event that there is concern for an acute change in neurologic status, head CT can be obtained quickly and efficiently; otherwise, the preferred pediatric neuroimaging modality is typically MRI, given its superior resolution. It is important to consider expanded imaging options such as dedicated vessel imaging and magnetic resonance spectroscopy when appropriate.