Clinical Policy Title: Brain magnetic resonance imaging for autism

Clinical Policy Number: CCP.1296

Effective Date: May 1, 2017
Initial Review Date: April 19, 2017
Most Recent Review Date: March 5, 2019
Next Review Date: March 2020

Related policies:

CCP.1124 Genetic testing for autism spectrum disorders
CCP.1024 Chromosomal microarray analysis

ABOUT THIS POLICY: Prestige Health Choice has developed clinical policies to assist with making coverage determinations. Prestige Health Choice’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Prestige Health Choice when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Prestige Health Choice’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Prestige Health Choice’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Prestige Health Choice will update its clinical policies as necessary. Prestige Health Choice’s clinical policies are not guarantees of payment.

Coverage policy

Prestige Health Choice considers the use of brain magnetic resonance imaging for routine diagnosis and/or screening for autism spectrum disorders to be investigational and, therefore, not medically necessary.

Limitations:

Coverage determinations are subject to benefit limitations and exclusions as delineated by the state Medicaid authority. The Florida Medicaid website may be accessed at http://ahca.myflorida.com/Medicaid/

Alternative covered services:
In-network visits to primary care providers, behavioral health specialists, and genetic counselors, as well as routine diagnostic and follow-up laboratory and radiographic evaluations.

**Background**

Autism spectrum disorder is a highly prevalent condition, estimated at one in 59 eight-year old U.S. children, more than double the 2002 estimate of one in 150, (Baio, 2018). Studies of autism spectrum disorder epidemiology have suggested multiple possible factors involved with the etiology of the condition, with a particular focus on hereditary transmission. People with the disorder are also more likely to have neurologic disorders, as autism is among the more common neurobehavioral comorbidities of children with active epilepsy. Children with autism are also more subject to sleep disorders and gastrointestinal symptoms.

In the U.S., the percentage of children with autism is greatest among African Americans, Asians, or Hispanics (Becerra, 2014), as well as those who have exposures to pesticides (Shelton, 2014). Others have looked at associations of post-traumatic stress disorders in mothers and autism in their offspring (Roberts, 2014).

Autism spectrum disorder is considered to be a lifelong condition impacting the affected individual’s capacity to communicate, interact socially, and manage repetitive behaviors. Typically, the manifestations of the disorder become obvious in early childhood, but may not become evident until later in childhood, adolescence, or even adulthood.

Under 2013 revisions to the Diagnostic and Statistical Manual — Fifth Edition (DSM-5; American Psychiatric Association 2013), the criteria for diagnosis of autism spectrum disorder involve both communication disorders and aberrant behaviors (Appendix A).

To date, no single standard method of diagnosing autism spectrum disorder exists. The Affordable Care Act mandates screening of young children at ages 18 to 24 months for the disorder as part of the “essential health benefits” clause of the law, but there is no specific test identified to meet this mandate. In practice, this requirement is generally met by practitioners with a “well-child examination” that employs validated and standardized screening batteries.

Among the many available screening and diagnostic tools for general development and autism spectrum disorder are:

- Ages and Stages Questionnaire.
- Communication and Symbolic Behavior Scale.
- Parents’ Evaluation of Developmental Status.
- Modified Checklist for Autism in Toddlers.
- Screening Tool for Autism in Toddlers and Young Children.
- Autism Diagnosis Interview — Revised.
• Autism Diagnostic Observation Schedule — Generic.
• Childhood Autism Rating Scale.

Magnetic resource imaging has been used to obtain functional and structural information that can help diagnose autism. This information includes social perception; social cognition; social functioning; mental inferences; interpretation of other’s mental states from biological motion; the mirror neuron system (active during imitation, action observation, and intention understanding); cognitive manifestations of restricted and repetitive behaviors; reward processing; and information about brain anatomy including gray- and white-matter volumes as well as gyrus and sulcus development (Dichter, 2012).

Searches

Prestige Health Choice searched PubMed and the databases of:
• UK National Health Services Centre for Reviews and Dissemination.
• Agency for Healthcare Research and Quality.
• The Centers for Medicare & Medicaid Services.
• Cochrane reviews.

We conducted searches on January 18, 2019. Search terms were: “autism,” “brain MRI,” and “diagnosis of autism.”

We included:
• **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
• **Guidelines based on systematic reviews.**
• **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

Findings

Several guidelines for screening for autism in young children do not address magnetic resonance imaging (Hayes, 2018; National Institute for Health and Care Excellence, 2016; U.S. Centers for Disease Control and Prevention, 2018b; U.S. Preventive Services Task Force, 2016). A guideline that combined work of the American Academy of Pediatrics and the American Academy of Neurology stated no evidence exists to support the role of routine clinical neuroimaging in the diagnostic evaluation of autism (U.S. Centers for Disease Control and Prevention, 2018a).
A guideline from the British Association for Psychopharmacology states that the pattern among autistic children of an early increase in cortical thickness may be followed by accelerated cortical thinning that results in a similar-sized brain as in normal children by age 10-15, making magnetic resonance imaging results not helpful (Howes, 2018).

An early systematic review of 208 studies produced data from magnetic resonance imaging that consistently reported abnormal function and structure problems in autistic persons, namely fronto-temporal and limbic networks with social and pragmatic language deficits, temporo-parieto-occipital networks with syntactic-semantic language deficits, fronto-striato-cerebellar networks with repetitive behaviors, and restricted interests (Pina-Camacho, 2012). Another systematic review/meta-analysis identified unusual disturbance in function of social brain regions in persons with autism, using magnetic resonance imaging (Philip, 2012).

A review of 25 papers shows little support for the belief that mirror neuron system dysfunction in persons with autism causes difficulties in social interaction and communication, including when magnetic resonance imaging was used (Hamilton, 2013).

A meta-analysis of 16 studies of voxel-based morphometry (using magnetic resonance imaging) of 277 persons with autism and 303 controls showed six significant brain structure changes between groups, in the lateral occipital lobe, pericentral region, medial temporal lobe, basal ganglia, and proximate to the right parietal operculum (Nickl-Jockschat, 2012). Another meta-analysis of 21 studies of voxel-based morphometry for 506 persons with autism and 549 controls showed differences in cortical matter thickness, concentration, and volume metrics, suggesting age-related decreases in grey/white matter in parietal/inferior temporal brain areas, and age-related rises in gray matter in frontal and anterior-temporal regions in autism (DeRamus, 2014).

A systematic review of 16 studies showed little consistency across studies and across types of imaging techniques in quantifying neurobiological differences of persons with or without autism (Tang, 2015).

In a systematic review/meta-analysis of 13 studies functional magnetic resonance imaging in 226 individuals with autism and 251 healthy people identified autism-related hyperactivation in subcortical structures, including bilateral thalamus, bilateral caudate, and right precuneus, and autism-related hypoactivation in the hypothalamus, especially in peractivation of the left caudate (Aoki, 2015).

A meta-analysis of 22 studies compared 328 persons with autism and 324 healthy controls who were given magnetic resonance imaging or positron emission tomography. The autism group had increased right hemisphere activity in core language areas; bilateral middle temporal gyrus hypo-activation across many different paradigms; and increased activation of the left lingual gyrus in tasks where they had intact performance, but no differences in other measures of language problems (Herringshaw, 2016).
A meta-analysis of 13 studies using magnetic resonance imaging documented individuals with autism had stronger effects in the anterior inferior parietal lobule, along with altered effects in the occipital cortex, dorsolateral prefrontal cortex, cingulate cortex, and insula, compared with controls (Yang, 2016).

A systematic review of 123 articles used magnetic resonance imaging to try and establish biomarkers in autism. Results were mixed; consistent changes in autistic patients were increased brain size, especially under age six, and increased 1) volume in frontal/temporal lobes, 2) cortical thickness in the frontal lobe, 3) surface area and cortical gyriﬁcation, and 4) cerebrospinal fluid volume. Inconsistent results in autistic patients included trajectory of brain volume and cortical thinning with age, and volume differences in white matter, hippocampus, amygdala, thalamus, and basal ganglia (Pagnozzi, 2018).

A systematic review of 44 studies (n = 5225) of young children used brain imaging studies to confirm significantly larger head circumference in autism compared to controls; 15.7 percent of autistic children had macrocephaly, highest in the lowest-functioning (Sacco, 2018). However, the guideline published several years later and cited in this section asserts this excess disappears by age 10 to 15 (Howes, 2018).

A systematic review acknowledges that while individuals with autism spectrum disorder should find social stimuli less rewarding than do normal persons, functional magnetic resonance imaging studies of reward processing have not produced such a consistent finding (Clements, 2018).

A large review of 42 studies (26 of which were randomized controlled trials) on screening children age 12 to 36 months, made no mention of imaging techniques being used for screening (McPheeters, 2016).

Policy updates:

A total of five guidelines/other and nine peer-reviewed references were added to, and two guidelines/other and eight peer-reviewed references removed from this policy in January, 2019.

The clinical policy number was changed from CP#09.01.15 to CCP.1296 in January, 2019.

References

Professional society guidelines/other:


**Peer-reviewed references:**


Centers for Medicare & Medicaid National Coverage Determinations:

No National Coverage Determinations identified as of the writing of this policy.

Local Coverage Determinations:

No Local Coverage Determinations identified as of the writing of this policy.

Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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Appendix A

Diagnostic and Statistical Manual-5 criteria for the diagnosis of Autism Spectrum Disorder
A. Deficits in use or understanding of social communication and social interaction in multiple contexts, not accounted for by general developmental delays, and manifest by all three of the following:

1. Deficits in nonverbal communicative behaviors used for social interaction, ranging from poorly integrated verbal and nonverbal communication, through abnormalities in eye contact and body language or deficits in understanding and use of nonverbal communication, to total lack of facial expression or gestures.

2. Deficits in social-emotional reciprocity, ranging from abnormal social approach and failure of normal back and forth conversation through reduced sharing of interests, emotions and affect and response to total lack of initiation of social interaction.

3. Deficits in developing and maintaining relationships appropriate to developmental level (beyond those with caregivers), ranging from difficulties adjusting behavior to suit different social contexts through difficulties in sharing imaginative play and in making friends to an apparent absence of interest in people.

B. Restricted, repetitive patterns of behavior, interests, or activities as manifested by two of the following:

1. Stereotyped or repetitive speech, motor movements or use of objects (e.g., simple motor stereotypies, echolalia, repetitive use of objects or idiosyncratic phrases).

2. Excessive adherence to routines, ritualized patterns of verbal or nonverbal behavior, or excessive resistance to change (e.g., motoric rituals, insistence on same route or food, repetitive questioning, or extreme distress at small changes).

3. Highly restricted, fixated interests abnormal in intensity or focus (e.g., strong attachment to or preoccupation with unusual objects, excessively circumscribed or perseverative interests).

4. Hyper-or hypo-reactivity to sensory input or unusual interest in sensory aspects of environment (e.g., apparent indifference to pain/heat/cold, adverse response to specific sounds or textures, excessive smelling or touching of objects, fascination with lights or spinning objects).