Single Photon Emission Computed Tomography (SPECT) of the Brain for Behavioral Health Disorders

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Medical Policy #: 06.01.39
Original Effective Date: February 2019
Reviewed: February 2022
Revised: February 2022

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DESCRIPTION

Single photon emission computed tomography (SPECT) is a type of nuclear imaging test that uses a radioactive dye, also called a tracer, and a special camera to create three-dimensional (3-D) image of organs in the body, including the brain. The images created by tracking the dye (tracer) can show what areas of the brain are more active or less active. SPECT has been used to study regional cerebral blood flow and to evaluate dopamine and serotonin receptor availability in the brain. SPECT brain has been proposed as a tool to assess or predict an asymptomatic individual’s risk of developing a behavioral health disorder; to diagnosis a behavioral health disorder; and in treatment planning and management of individuals with behavioral health disorders.

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In May 2009, an Action Paper was passed by the American Psychiatric Association (APA) Assembly (and approved by the Board of Trustees in July 2012) calling for the development of an APA Position Paper on the Clinical Application of Brain Imaging in Psychiatry. This paper, which was updated in 2017 (and approved by the Board of Trustees in 2018), states the following:

"In clinical medicine, considerable interest exists in developing objective, biologically-based tests for psychiatric illnesses. From a clinical perspective such advances could yield important benefits such as predicting treatment response, differentiating between related diagnostic categories, and potentially treating at-risk patients prophylactically to prevent the development of neuropathology and clinical deterioration. Nevertheless, the effect size of neuroimaging and other noninvasive biological abnormalities identified to date in psychiatric disorders has been relatively small, and the imaging measures established by replication across laboratories do not provide sufficient specificity and sensitivity to accurately classify individual cases with respect to the presence of a psychiatric illness.

Both the clinical practice of psychiatry and the development of novel therapeutics have been hindered by the lack of biomarkers that can serve as accessible, objective indices of the complex biological phenomena that underpin psychiatric illness. The inaccessibility of brain tissue, the lack of knowledge about pathophysiology, and the uncertain link between abnormal measurements on any biological test and pathogenesis all have impeded the development of biomarkers for psychiatric disorders. As a result, progress toward improving diagnostic capabilities and defining or predicting treatment outcome in psychiatry has lagged, it remains difficult to establish whether individual patients suffer from a particular disease, and how individual patients can best be treated.

For over two decades imaging has maintained a well-established but narrow place in the diagnostic evaluation of patients with psychiatric disease, largely because of the usefulness of neuromorphological magnetic resonance imaging (MRI) in detecting and characterizing structural brain abnormalities such as lesions and atrophy. Thus, the role of imaging in patients with psychopathology historically has been limited to one of exclusion of potentially etiological medical conditions: namely to rule out neoplasm, hematoma, hydrocephalus, or other neurological causes of psychiatric symptoms that are treatable with neurosurgery or medications, or to detect the presence of cerebrovascular disease or gross atrophy. Although clinically important, these conditions appear to play a role in the pathogenesis of psychiatric symptoms in only a small proportion of cases presenting for the evaluation of mood, anxiety, or psychotic disorders.

Increasingly a major quest of researchers has been to identify neuroimaging results that offer diagnostic capabilities for major psychiatric diseases as well as for their relevant differential diagnoses. Currently neuroimaging is not recommended within either the U.S. or the European practice guidelines for positively defining diagnosis of any primary psychiatric disorder. Nevertheless, advances in research applications of neuroimaging technology have provided leads that may foreshadow future clinical applications of

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imaging biomarkers for establishing diagnosis and predicting illness course or treatment outcome.

In 2009, the NIH (National Institute of Health) has defined a biomarker (i.e., biological marker) as: "A characteristic that is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention." A biomarker thus can define a physiological, pathological, or anatomical characteristic or measurement that putatively relates to some aspect of either normal or abnormal biological function or structure. Biomarkers thus may assess many different types of biological characteristics, including receptor or protein binding, hemodynamic parameters, MRI or radiographic images of structure composition, other imaging-based measures, or electrophysiological parameters.

In considering the development of neuroimaging biomarkers as clinical diagnostics, diagnostic biomarkers are of interest to health care providers and consumers since earlier detection of disease facilitates earlier intervention, which when followed by effective, individualized treatment, can improve patient outcomes.

With respect to establishing the utility of a biomarker, it is useful to distinguish between the terms, "validation" and "qualification". Validation generally refers to the determination of the performance characteristics of a measurement, for example, the measurement's reliability, sensitivity, and specificity in measuring a discrete biological construct. The validity of a diagnostic biomarker for any medical disorder generally is established via evaluation of its sensitivity, specificity, prior probability, positive predictive value, and negative predictive value. The term qualification refers to establishing the credibility of a biomarker in its application.

A critical challenge in establishing the validity of a diagnostic biomarker in psychiatry is the clinical utility and their ability to distinguish multiple conditions from one another. In psychiatry, the need to differentiate various conditions from each other depends partly on the clinical imperative to return distinct treatment recommendations for different disorders. It might be argued, for example, that for a neuroimaging procedure to add clinical value in the evaluation of an adult patient with impaired attention, differentiation is needed between at least four categories, namely major depressive disorder, bipolar disorder, attention deficit disorder, and anxiety disorders, since the standard of care differs between these categories. Thus, the variability across raters will be relatively higher (i.e., lower inter-rater reliability) for a diagnostic imaging study that must differentiate among several psychiatric disorders that share symptomatology but require distinct treatment approaches.

A more challenging problem for the development of diagnostic biomarkers in psychiatry has been that the absence of certain knowledge about the pathophysiology of psychiatric disorders precludes the identification and validation of such biomarkers. For example, the determinations of positive and negative predictive value are limited by the absence of an established objective standard for establishing diagnosis in psychiatric disease. Also, the

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diagnostic biomarker would need to have to have a sensitivity >80% for detecting a particular psychiatric disorder and a specificity of >80% for distinguishing this disorder from other clinically relevant psychiatric or medical disorders. To be clinically useful the biomarker should show a clear improvement over the current standard-of-care in accurately establishing a diagnosis based on corroborating evidence (e.g., obtained via prospective assessment of the longitudinal disease course).

According to this standard, the psychiatric imaging literature currently does not support the application of any diagnostic biomarker to positively establish the presence of any primary psychiatric disorder. Although assessments of intra-rater reliability (assessing the extent to which readings performed under blind conditions by the same reader on the same image on different days are in agreement, as well as the extent to which the same reader returns the same results when comparing multiple images obtained from the same patient across different days) and inter-rater reliability (assessed by having multiple radiologists read the same set of images while blind to the evaluations returned by other readers) commonly are reported for quantitative neuroimaging measures, these have been limited to establishing measurement reliability (e.g., cerebral volumes or neuroreceptor binding potential), but not to the reliability of diagnostic classification. Similarly, the literature does not yet establish a predictive biomarker for therapeutic response to a specific treatment within psychiatric disorders.

In summary, although there are a number of promising results presented in this paper, the peer-reviewed scientific literature does not yet establish the clinical validity and clinical utility of an imaging biomarker or group of imaging biomarkers ("biomarker signature") for use in assessing or predicting an individual's risk of getting a particular psychiatric disorder, determining the diagnosis of a particular psychiatric disorder or predicting the therapeutic response to a particular treatment."

Summary of Evidence
Based on review of the peer reviewed medical literature to include an Action Paper by the American Psychiatric Association, the clinical validity and clinical utility has not yet been established regarding an imaging biomarker or group of imaging biomarkers (biomarker signature) for use in assessing or predicting future risk of an asymptomatic individual developing a particular behavior health disorder, determining the diagnosis of a particular behavior health disorder or predicting the therapeutic response to a particular treatment of a behavior health disorder. While there may be some promising results in some studies, further studies are warranted regarding psychiatric imaging to achieve sensitivity, specificity, and standardization of imaging protocols. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Policy Guideline and Position Statements

American College of Radiology (ACR)
(2021) The American College of Radiology (ACR), the American Collene of Nuclear Medicine (ACNM) the Society of Pediatric Radiology (SPR) and the Society of Nuclear

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Medicine and Molecular Imaging (SNMMI) issued a revised practice parameter for the performance of single-photon emission brain perfusion imaging (including SPECT and SPECT/CT) states the following: Clinical indications for brain perfusion imaging examinations include, but are not limited to:

1. Evaluating patients with suspected dementia
2. Localizing seizure foci
3. Mapping of brain perfusion during interventions
4. Detecting and evaluating cerebrovascular disease
5. Corroborating the clinical diagnosis of brain death (note that these examinations can be performed with SPECT or planar imaging)

According to the above indications this practice parameter does not indicate SPECT of the brain for neuropsychiatric disorders.

National Institute of Mental Health (NIMH)

The National Institute of Mental Health (NIMH) made the following statement in their brochure titled Neuroimaging and Mental Illness: A Window into the Brain:

- Brain imaging scans, also called neuroimaging scans, are being used more and more to help detect and diagnose a number of medical disorders and illnesses. Currently, the main use of brain scans for mental disorders is in research studies to learn more about the disorders. Brain scans alone cannot be used to diagnose a mental disorder, such as autism, anxiety, depression, schizophrenia, or bipolar disorder.

  "No scientific studies to date have shown that a brain scan by itself be used for diagnosing a mental illness or to learn about a person's risk for disease.

(*Accessed and updated February 2022*)

PRIOR APPROVAL

Not applicable.

POLICY

Single photon emission computed tomography (SPECT) of the brain is considered **investigational** for all behavioral health disorders and indications, including but not limited to the following:

- Assessing or predicting an asymptomatic individual's future risk of a behavioral health disorder
- Confirmation of a diagnosis of a neurobehavioral disorder
- A development of treatment planning and management

Based on review of the peer reviewed medical literature to include an Action Paper by the American Psychiatric Association, the clinical validity and clinical utility has not yet been established regarding an imaging biomarker or group of imaging biomarkers (biomarker signature) for use in assessing or predicting an individual's future risk of a

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particular behavior health disorder, determining the diagnosis of a particular behavior health disorder or predicting the therapeutic response to a particular treatment of a behavior health disorder. While there may be some promising results in some studies, further studies are warranted regarding psychiatric imaging to achieve sensitivity, specificity and standardization of imaging protocols. The evidence is insufficient to determine the effects of the technology on net health outcomes.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 78803 Radiopharmaceutical localization of tumor, inflammatory process or distribution of radiopharmaceutical agent(s) (includes vascular flow and blood pool imaging, when performed); tomographic (SPECT), single area (e.g., head, neck, chest, pelvis), single day imaging

SELECTED REFERENCES

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- National Institute for Mental Health (NIMH). Neuroimaging and Mental Illness: A Window into the Brain.
- American Psychiatric Association (APA) Resource Document on Neuroimaging.
- American Psychiatric Association (APA) Practice Guideline for the Psychiatric Evaluation of Adults: Third Edition.
- American Psychiatric Association (APA) Practice Guidelines for Treating patients with acute stress disorder and post-traumatic stress disorder.
- American Psychiatric Association (APA) Practice Guidelines for Treating bipolar disorder.
- American Psychiatric Association (APA) Practice Guidelines for Treating obsessive-compulsive disorder.
- American Psychiatric Association (APA) Practice Guidelines for Treating schizophrenia.
- American Psychiatric Association (APA) Practice Guidelines for Assessing and treating suicidal behaviors.
- American Psychiatric Association (APA) Practice Guidelines for Treating borderline personality disorder.
- American Psychiatric Association (APA) Practice Guidelines for Treating eating disorders.

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- American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with autism spectrum disorder.
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POLICY HISTORY

Date	Reason	Action
February 2022	Annual Review	Policy Revision
February 2021	Annual Review	Policy Revised
February 2020	Annual Review	Policy Revised
February 2019		New Policy

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

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