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## Neuroendocrine Imaging

D.J. Seidenwurm

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D.J. Seidenwurm,  
for the Expert Panel on  
Neurologic Imaging

## Neuroendocrine Imaging

Imaging of the hypothalamic pituitary axis is based on specific endocrine testing suggested by clinical signs and symptoms. Endocrine disorders are generally characterized by excess or deficiency of specific hormones. Hormone excess is diagnosed under conditions that would ordinarily suppress hormone secretion. Endocrine deficiencies are diagnosed on the basis of hormone measurements under conditions of stimulation. Specific clinical syndromes of hormonal disorders are determined by the physiologic role of that particular hormone.

The hypothalamic pituitary axis consists of 2 separate neuroendocrine organs, the anterior and posterior pituitary systems. The hormones of the anterior pituitary are thyroid stimulating hormone (TSH), adrenal corticotrophic hormone (ACTH), prolactin (PRL), growth hormone (GH), and the gonadotropins (FSH and LH). These are secreted under the influence of hypothalamic trophic factors, corticotrophin releasing factor (CRF), thyrotropin releasing factor (TRF), and somatostatin- and gonadotropin- releasing hormone (GnRH). Prolactin release is under the control of a dopaminergic circuit. The hypothalamic-releasing hormones are transported to the pituitary gland by the hypophyseal portal system.

The posterior pituitary gland consists of axonal terminations of neurons whose cell bodies are located in the hypothalamus. The principal hormones secreted by these cells are oxytocin and vasopressin or antidiuretic hormone (ADH). The hypothalamus also participates in complex mediation of food intake, temperature regulation, sleep and arousal, memory, thirst, and other autonomic functions.

Structural causes of obesity, anorexia, central hypothermia and hyperthermia, insomnia, and hypersomnia are only very rarely demonstrated. Imaging in these patients absent other specific neurologic or endocrine abnormality is almost always unrewarding. An exception is children in whom the "diencephalic syndrome" of hypothalamic lesions is relatively common.

Pituitary adenomas are the most common lesions of the pituitary gland. These may secrete prolactin, TSH, GH, ACTH, or gonadotropins. Prolactinomas most commonly present as microadenomas in premenopausal females with amenorrhea and galactorrhea. Prolactin elevation by itself is nonspecific and may be due to a variety of medical, neurologic, or pharmacological causes as well as pituitary adenoma, de-

pending on serum hormone level. In males, prolactinomas may be entirely asymptomatic until visual symptoms occur, due to compression of the chiasm, or they may result in hypogonadotropic hypogonadism with loss of libido and impotence. Growth-hormone-secreting tumors generally are larger lesions manifesting clinical acromegaly. Because of the gradual onset of deformity, these tumors may be present for many years and grow to substantial size. Before puberty excessive GH may result in gigantism. TSH- and ACTH-secreting tumors may present at very small size because the impact of their hormone product is usually apparent more rapidly. Gonadotropin-secreting tumors are rare.

Precocious puberty and other neurologic symptoms can be produced by hypothalamic lesions such as hamartoma. MR imaging is generally indicated in all patients with endocrinologically confirmed precocious puberty, especially when rapid progression of development and neurologic symptoms are present.

Posterior pituitary dysfunction with loss of antidiuretic hormone results in diabetes insipidus. This may be transient after trauma or neurosurgical procedures. Imaging is performed to search for the cause of stalk transection, which can be a manifestation of numerous sellar or parasellar pathologies, trauma, or congenital. Rarely, the hormone is absent developmentally. The syndrome of inappropriate ADH is usually due to an extracranial source. Frequently, a paraneoplastic phenomenon in small-cell lung carcinoma, though a variety of pulmonary diseases and pharmacological disturbances can result in syndrome of inappropriate anti-diuretic hormone.

Other common mass lesions that may affect the neuroendocrine system are germ-line tumors, meningioma, craniopharyngioma, and Rathke cleft cyst among others. Metastatic lesions may affect the sella. Sarcoid and other inflammatory processes occur in the sellar and suprasellar regions as well. Pituitary apoplexy is a syndrome of headache ophthalmoplegia and visual loss that results from pituitary hemorrhage. In the postpartum period, pituitary infarcts may occur, and hypophysitis is an uncommon disorder resulting in endocrine disturbance and other symptoms.

MR imaging with thin-section multiplanar imaging often before and after contrast administration is the most useful test for these indications. Supplemental techniques include CT angiography (CTA), MR angiography (MRA), direct conventional angiography, and petrosal sinus sampling.

Plain radiography and pluridirectional tomography are insensitive and nonspecific. Pituitary microadenoma and macroadenomas are frequently associated with a normal sella size. The sella turcica can be enlarged when no neoplasm or mass is present. This is due to pulsations of cerebral spinal fluid (CSF) transmitted through a developmental or acquired dehiscence

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Please address correspondence to David J. Seidenwurm, MD, Department of Quality & Safety, American College of Radiology, 1891 Preston White Dr, Reston, VA 20191-4397.

# Clinical condition: neuroendocrine imaging

	MRI Head without and with Contrast	MRI Head without Contrast	CT Head without and with Contrast	CT Head without Contrast	MRA Head	CTA Head	INV Venous Sampling
Hypopituitarism	8 <sup>a</sup>	7 <sup>a</sup>	4 <sup>b</sup>	4 <sup>b</sup>	3 <sup>c</sup>	2 <sup>d</sup>	1
Obesity/eating disorder	4 <sup>ae</sup>	4 <sup>ae</sup>	3 <sup>be</sup>	3 <sup>be</sup>	2	1	1
Hyperthyroidism (high TSH)	8 <sup>a</sup>	7 <sup>a</sup>	3 <sup>b</sup>	3 <sup>b</sup>	3	2 <sup>d</sup>	1
Cushing's syndrome (high ACTH)	8 <sup>a</sup>	7 <sup>a</sup>	4 <sup>b</sup>	4 <sup>b</sup>	3 <sup>c</sup>	2	4 <sup>f</sup>
Hyperprolactinemia	8 <sup>a</sup>	7 <sup>a</sup>	4 <sup>b</sup>	4 <sup>b</sup>	3 <sup>c</sup>	2 <sup>d</sup>	1 <sup>g</sup>
Acromegaly/gigantism	8 <sup>a</sup>	7 <sup>a</sup>	4 <sup>b</sup>	4 <sup>b</sup>	3 <sup>c</sup>	2 <sup>d</sup>	3 <sup>g</sup>
Dwarfism (proportionate)	5 <sup>a</sup>	7 <sup>a</sup>	4 <sup>b</sup>	4 <sup>b</sup>	2	2 <sup>d</sup>	1
Diabetes insipidus	6 <sup>a</sup>	7 <sup>a</sup>	4 <sup>b</sup>	4 <sup>b</sup>	4	2 <sup>d</sup>	1
Pituitary apoplexy	8 <sup>a</sup>	7 <sup>a</sup>	4 <sup>b</sup>	6	4 <sup>c</sup>	4	1
Postoperative sella	8 <sup>a</sup>	7 <sup>a</sup>	4 <sup>h</sup>	4 <sup>h</sup>	2	4	1
Precocious puberty	8 <sup>a</sup>	7 <sup>a</sup>	2	2	2	2	1

**Note:**—Rating Scale: 1, least appropriate; 9, most appropriate

<sup>a</sup> Multiplanar thin sellar imaging

<sup>b</sup> Indicated if MRI not available or contraindicated

<sup>c</sup> Indicated if better visualization of carotid arteries needed

<sup>d</sup> For surgical planning or vascular detail if MRI and MRA contraindicated

<sup>e</sup> In carefully selected patients with high clinical likelihood of structural abnormality

<sup>f</sup> Indicated if MRI is negative or equivocal

<sup>g</sup> Indicated in unusual cases in which lateralization is indeterminate

<sup>h</sup> CT may be indicated to assess bony anatomy and if MRI is not available or contraindicated.

of the diaphragm sella in the empty sella syndrome. Therefore, these imaging modalities are rarely, if ever, useful here.

CT especially with intravenous contrast, to depict pathology within the unenlarged sella, occasionally facilitates diagnosis of neuroendocrine abnormality. Pituitary microadenomas and macroadenomas are often detected. There is difficulty in distinguishing tumor from the optic chiasm, diagnosis of cavernous sinus invasion is difficult, and cystic suprasellar masses may be confused with normal CSF. Additionally, artifact due to dental amalgam, difficulty in obtaining reliable contrast enhancement, and awkward positioning for direct coronal scanning limit utility. In the hands of experienced radiologists this technique can be useful, though the examinations are frequently difficult to interpret despite excellent technique.

MR imaging provides excellent noninvasive evaluation of the hypothalamus and pituitary gland. It is the only imaging technique that reliably depicts the hypothalamus usefully. It depicts the anatomy of the pituitary gland, infundibulum, optic chiasm, cavernous sinuses, and neighboring vascular structures accurately and noninvasively. The addition of gadolinium facilitates diagnosis of microadenoma and increases the confidence with which cavernous sinus invasion can be diagnosed or excluded. The specific bony landmarks are sometimes difficult to demonstrate, but sphenoid sinus mucosal signal intensity permits assessment of septa for operative planning. Visualization of vascular parasellar structures such as intrasellar carotid artery loop or aneurysm is crucial in some cases.

Angiography is reserved for those patients in whom vascular pathology is known or suspected on the basis of clinical or radiologic findings. Aneurysm is the most important vascular lesion in the parasellar region, but these lesions rarely present as endocrine disorders. Knowledge of vascular anatomy guides surgery. Occasionally, a sellar lesion may displace or encase the carotid arteries or other major intracranial vessels. Interventional neuroradiology procedures can be planned on the basis of CTA, MRA, and/or conventional angiography.

Petrosal sinus venous sampling is only performed when there is definite excess of pituitary hormone, medical management has failed, sectional imaging is negative or equivocal and surgery is planned. When significant differences in hormone level, usually ACTH, exists among the vessels studied, tumor localization is very accurate. Complications occur uncommonly in experienced hands.

A significant problem in CT and MR imaging of the pituitary, particularly when endocrine findings suggest microadenoma, is the false-positive examination. Since the endocrine studies confirm the presence of a lesion, and first-line therapy is usually medical, false-negative examinations are less problematic once chiasmatic compression has been excluded. Approximately 20% of the population may harbor incidental nonfunctioning adenomas or cysts. It is important, therefore, that the probability of disease be high in the target population if a positive MR imaging is to be relied upon for surgical planning. Additional problems are created by variations in size of the pituitary gland, which occur normally in response to physiologic hormonal changes. The gland may enlarge in puberty and pregnancy. Pituitary hyperplasia in hypothyroidism may simulate a pituitary adenoma in some patients. Similar problems arise in imaging the posterior pituitary, since up to 29% of normal subjects do not demonstrate a bright posterior pituitary.

## Review Information

This guideline was originally developed in 1999. The last review and update was completed in 2007.

## Appendix

Expert Panel on Neurologic Imaging: David J. Seidenwurm, MD, Principal Author and Panel Chair, Radiologic Associates of Sacramento, Sacramento, Calif; Patricia C. Davis, MD; James A. Brunberg, MD; Robert Louis De La Paz, MD; Pr. Didier Dormont; David B. Hackney, MD; John E. Jordan, MD; John P. Karis, MD; Suresh Kumar Mukherji, MD; Patrick A. Turski, MD; Franz J. Wippold II, MD; Robert D. Zimmerman,

MD; Michael W. McDermott, MD, American Association of Neurological Surgeons; Michael A. Sloan, MD, MS, American Academy of Neurology.<sup>1-44</sup>

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