

Normal dimensions of the posterior pituitary bright spot on magnetic resonance imaging

Clinical article

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Object. The normal pituitary bright spot seen on unenhanced T1-weighted MRI is thought to result from the T1-shortening effect of the vasopressin stored in the posterior pituitary. Individual variations in its size may be difficult to differentiate from pathological conditions resulting in either absence of the pituitary bright spot or in T1-hyperintense lesions of the sella. The objective of this paper was to define a range of normal dimensions of the pituitary bright spot and to illustrate some of the most commonly encountered pathologies that result in absence or enlargement of the pituitary bright spot.

Methods. The authors selected normal pituitary MRI studies from 106 patients with no pituitary abnormality. The size of each pituitary bright spot was measured in the longest axis and in the dimension perpendicular to this axis to describe the typical dimensions. The authors also present cases of patients with pituitary abnormalities to highlight the differences and potential overlap between normal and pathological pituitary imaging.

Results. All of the studies evaluated were found to have pituitary bright spots, and the mean dimensions were 4.8 mm in the long axis and 2.4 mm in the short axis. The dimension of the pituitary bright spot in the long axis decreased with patient age. The distribution of dimensions of the pituitary bright spot was normal, indicating that 99.7% of patients should have a pituitary bright spot measuring between 1.2 and 8.5 mm in its long axis and between 0.4 and 4.4 mm in its short axis, an interval corresponding to 3 standard deviations below and above the mean. In cases where the dimension of the pituitary bright spot is outside this range, pathological conditions should be considered.

Conclusions. The pituitary bright spot should always be demonstrated on T1-weighted MRI, and its dimensions should be within the identified normal range in most patients. Outside of this range, pathological conditions affecting the pituitary bright spot should be considered.

(<http://thejns.org/doi/abs/10.3171/2013.11.JNS131320>)

KEY WORDS • pituitary • magnetic resonance imaging • hyperintensity • sella turcica

An area of T1 hyperintensity is normally observed in the posterior part of the sella turcica on MR images of the brain. This phenomenon, often referred to as the pituitary bright spot (PBS), is thought to result from the T1-shortening effect of stored vasopressin in the posterior lobe of the pituitary^{1,2} and is observed in 100% of children^{15,17} and in 52% to 100% of adults^{5,6,8,19,22} without pituitary disease. The PBS may be absent in up to 48% of normal subjects, more often in older patients.^{5,23} Individual variations in the appearance of the PBS have been observed. Physiological conditions such as very young age, pregnancy, or lactation may result in an enlarged PBS.²

An abnormal PBS can also be seen in various pathological processes. Central diabetes insipidus (DI) results from low blood levels of vasopressin and may be primary or secondary to a number of causes. In primary central DI, the PBS has been found to be absent in 25% to 100%

of cases.^{12,15,17} Secondary central DI is a feature of Langerhans cell histiocytosis, germinoma, teratoma, craniopharyngioma, idiopathic giant cell granulomatous hypophysitis, and Wolfram syndrome. When DI was a presenting symptom of one of these conditions, the PBS was always absent.^{7,9,12,15,17,18} In conditions in which the posterior pituitary is depleted of its vasopressin granules, the hyperintense T1 signal can also be lost. An absent PBS was observed in 32% of patients with uncontrolled diabetes mellitus¹¹ and in a patient with severe anorexia nervosa.²¹ Finally, when the pituitary stalk is interrupted, the vasopressin synthesized in the hypothalamus does not reach the posterior pituitary. The absence of a normal PBS in these cases is often accompanied by an ectopic bright spot due to the storage of vasopressin granules in another anatomical location. A patient with pituitary dwarfism was found to have an absent PBS with an ectopic bright spot.²⁴ Acquired section of the pituitary stalk of traumatic or surgical origin has also been found to result in an absent PBS and ectopic bright spot.¹⁰

Abbreviations used in this paper: DI = diabetes insipidus; FEG = frequency encoding gradient; PBS = pituitary bright spot.

A large area of T1 hyperintensity is seen in a number of pathologies resulting in accumulation of blood, material with high protein content, or fat—all substances with a high T1 signal. Some of the most common lesions causing high T1 signal in the sella include Rathke's cleft cysts and hemorrhagic pituitary adenomas. Other, less common causes of sellar T1 hyperintensity include abscesses, cholesterol granulomas, dermoid cysts, and lipomas.²

When evaluating T1-weighted images of the pituitary gland, there is a need to define what is a normal PBS and what is a T1 hyperintensity that is outside of the spectrum of normal anatomy. The objective of this paper is to define a range of normal dimensions for the PBS in healthy subjects and illustrate some of the most commonly encountered pathologies that result in absence or enlargement of the pituitary bright spot. By identifying the normal range, it is hoped that pathology of the pituitary gland may be more easily recognized. Examples of abnormal sellar T1 hyperintense lesions will be discussed to illustrate the application of this normal range and to demonstrate that pathology should be recognized with alterations in the normal appearance.

Methods

After receiving institutional review board approval, we reviewed all of the dedicated pituitary MRI scans done from April 2011 to September 2012. Those studies that were interpreted as normal by a neuroradiologist were selected for the study. We excluded pregnant women, as well as patients who had previous sellar or anterior skull base surgery.

The imaging protocol consisted of high-resolution MRI of the sella with sagittal and coronal T1-weighted, coronal T2-weighted, coronal dynamic contrast-enhanced T1-weighted, and postcontrast sagittal and coronal T1-weighted images with fat saturation. All studies were performed using a Siemens 1.5-T magnet with 3-mm slices or a Siemens 3-T magnet with 2.5-mm slices.

The PBS was identified on thin-slice sagittal T1-weighted images. For a given patient, the slice on which the PBS was the largest was selected for measurements, even if this slice was not perfectly midline. To ensure that the hyperintense structure to be measured was pituitary tissue and not clival bone marrow, the image was compared with the corresponding enhanced sagittal T1-weighted image with fat saturation. The craniocaudal dimension of the PBS was measured along its longest axis, and the anteroposterior dimension was measured perpendicular to this long axis (Fig. 1). The measurements were independently made by a neuroradiologist, a neurosurgery fellow, and a junior neurosurgery resident. In cases in which a measurement differed by more than 30% among the reviewers, a consensus was reached through discussion among the three. For purposes of statistical analysis, the measurements used for each individual patient were the means of the measurements made by the neuroradiologist, the fellow, and the resident.

Results

A total of 106 MRI studies were selected for the

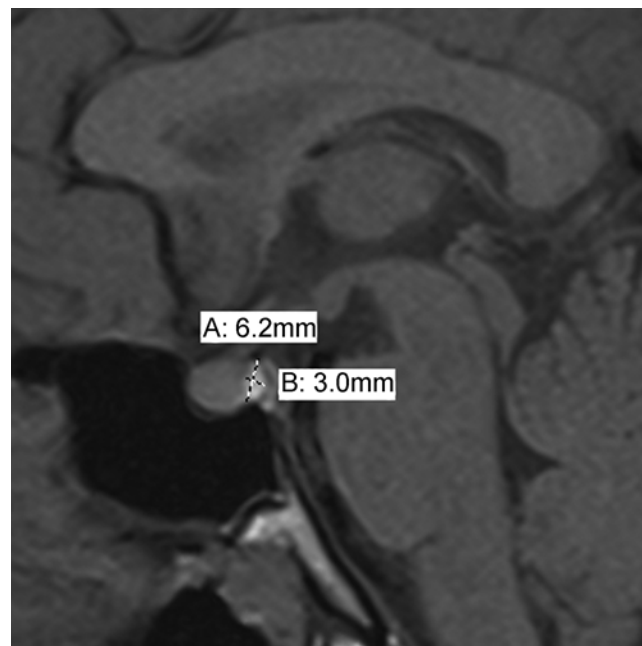


FIG. 1. Sample sagittal T1-weighted MR image showing the long and short axes of the PBS as measured on the PACS (picture archiving and communication system) workstation. The long craniocaudal axis is measurement A; measurement B is the perpendicular anteroposterior axis.

study. There were 64 female (60%) and 42 male patients, and their mean age was 40.3 years (range 13–77 years). The indications for imaging were clinical or biochemical evidence of endocrine dysfunction (56%), suspicion of a pituitary lesion on another imaging modality (24%), headaches (11%), history of malignancy (usually melanoma; 5%), or histiocytosis (1%). In 2 cases, no indication for pituitary imaging was specified.

The results of the measurements are summarized in Table 1. The mean (\pm SD) dimensions of the PBS were 4.8 ± 1.2 mm (range 1.7–7.8 mm) in the long axis and 2.4 ± 0.7 mm (range 0.9–3.9 mm) in the short axis. A PBS was identified in all patients, and in 68% of cases the PBS was in the midline.

To confirm that the sample followed a normal distribution, a Shapiro-Wilk test was performed. The test statistic result was 0.624 for the long-axis measurements and 0.596 for the short-axis measurements, both greater than the 0.05 value chosen for the alpha level. This confirms that the data were normally distributed.

In a normal distribution, 99.7% of samples are within ± 3 standard deviations of the mean. Applied to our measurements, this rule means that the upper and lower limits are 8.5 mm and 1.2 mm for the long axis, respectively, and 4.4 mm and 0.4 mm for the short axis, respectively.

Using multivariate regression, a significant inverse linear relationship was found between the long-axis dimension and the age of the subject ($p = 0.042$), but no significant relationship was found between the long-axis dimension and sex of the subject ($p = 0.088$) or between the short-axis dimension and either age or sex of the subject ($p = 0.401$ and 0.277 , respectively).

Normal dimensions of the posterior pituitary bright spot on MRI

TABLE 1: Size of the pituitary bright spot in patients who underwent pituitary imaging

Parameter	Dimension (mm)	
	Long Axis	Short Axis
mean	4.8	2.4
range	1.7–7.8	0.9–3.9
SD	1.2	0.7
mean – 3 SDs	1.2	0.4
mean + 3 SDs	8.5	4.4

Illustrative Case 1: Rathke's Cleft Cyst

A 35-year-old woman underwent a pituitary MRI study as part of a workup for partial hypopituitarism. The images revealed a T1-hyperintense rounded area in the posterior sella measuring 9.0 × 5.0 mm (Fig. 2). Differential diagnosis included a normal PBS, a Rathke's cleft cyst, or a hemorrhagic pituitary adenoma. The large dimensions of the T1-hyperintense area argued against a normal PBS. Given this, and the fact that the patient was symptomatic from a low cortisol level and was on thyroid hormone replacement, transsphenoidal exploration of the sella was performed, and a Rathke's cleft cyst was found and drained. After surgery, the patient's symptoms improved; however, she was still receiving hydrocortisone replacement therapy 6 months after surgery.

In this case, the T1-hyperintense lesion was situated where the PBS would be expected. Since the patient's symptoms and her laboratory abnormalities could have been attributed to a number of causes, knowing the expected normal dimensions of the PBS could assist with the surgical decision making in such a situation.

Illustrative Case 2: Hemorrhagic Adenoma

A 21-year-old woman presented with galactorrhea and headaches. Her prolactin level was mildly elevated at 47 ng/ml, and her MRI study showed a T1-hyperintense lesion measuring 7.0 × 5.5 mm (Fig. 3). In the clinical context, the lesion was diagnosed as a hemorrhagic pituitary adenoma causing elevation of the prolactin level by pituitary stalk compression. The patient elected radiological and endocrinological follow-up.

The presentation of a hemorrhagic pituitary adenoma can vary from acute onset of headache and visual disturbance to a more protracted course like in this patient. In these cases, it is important to correctly identify a hemorrhagic pituitary adenoma despite mild symptoms so that adequate follow-up is ensured.

Illustrative Case 3: Langerhans Cell Histiocytosis

A 36-year-old man recently diagnosed with diabetes mellitus underwent MRI, which showed mild thickening of the pituitary stalk and failed to demonstrate a PBS (Fig. 4A). Six months later, the patient presented with increasing somnolence; a second pituitary MRI study revealed a large, enhancing suprasellar mass (Fig. 4B and C). A stereotactic biopsy of the mass revealed an inflammatory infiltrate consistent with Langerhans cell histiocytosis.

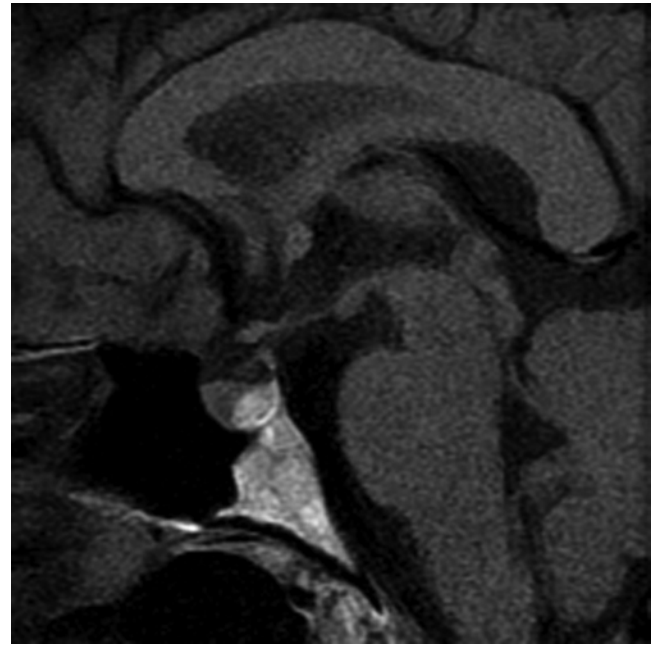


FIG. 2. Illustrative Case 1. Sagittal T1-weighted MR image obtained without contrast enhancement in a 35-year-old woman presenting with partial hypopituitarism showing a T1-hyperintense region in the pituitary sella measuring 9.0 × 5.0 mm. The lesion was found to be a Rathke's cleft cyst at resection.

After the biopsy, the patient developed DI that required prolonged treatment with desmopressin. Of note, 5 years prior to this episode, the patient had undergone a biopsy for a bony lesion of the mandible that was confirmed to

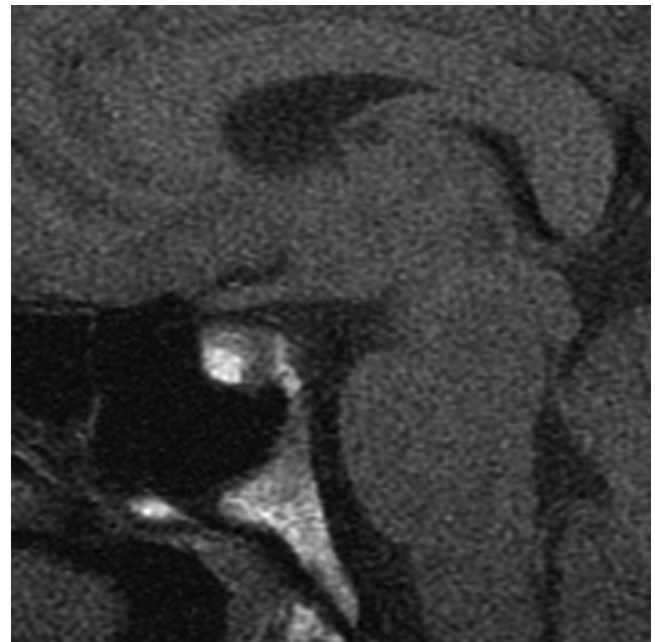


FIG. 3. Illustrative Case 2. Sagittal T1-weighted MR image obtained without contrast enhancement in a 21-year-old woman who presented with headache and mild hyperprolactinemia showing a T1-hyperintense lesion in the sella measuring 7.0 × 5.5 mm. The clinical diagnosis was hemorrhagic microadenoma.

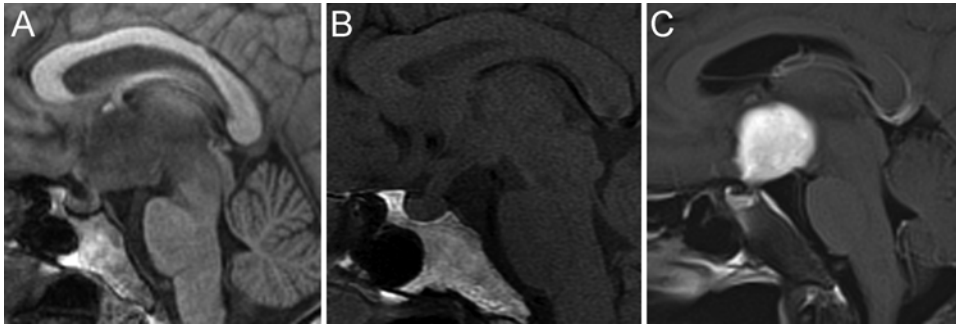


Fig. 4. Illustrative Case 3. **A:** Sagittal T1-weighted MR image obtained without contrast enhancement in a 36-year-old man 6 months before his presentation with altered mental status. This image showed no PBS. **B and C:** Sagittal T1-weighted MR images obtained without (B) and with (C) contrast enhancement at the time of the patient's presentation with altered mental status revealing a large, enhancing suprasellar mass. Biopsy demonstrated Langerhans cell histiocytosis.

be Langerhans cell histiocytosis. The patient was treated with chemotherapy after the suprasellar lesion biopsy.

Enlargement of the infundibulum and the absence of a PBS are the most typical features of Langerhans cell histiocytosis on pituitary MRI^{13,18} and can predate the onset of DI by several months.¹⁴ As discussed, an absent PBS should alert the clinician to the possibility of a pathological condition; in this case, a history of a bony lesion diagnosed as Langerhans cell histiocytosis was an additional clue toward recognizing the central nervous system involvement by this disease.

Illustrative Case 4: Germinoma

A 14-year-old female patient was investigated for secondary amenorrhea. Her workup showed a mildly elevated prolactin level at 43 ng/ml; her other endocrine parameters were in normal ranges. This prompted us to obtain a pituitary MRI study, which demonstrated a homogeneously enhancing sellar and suprasellar mass. The PBS could not be identified on the T1-weighted image (Fig. 5). A partial resection of the lesion was performed through the transsphenoidal approach, and pathological examination confirmed the diagnosis of a germinoma. The patient was subsequently treated with chemotherapy and radiotherapy, with complete radiological response.

The differential diagnosis for this patient also included pituitary adenoma, which is the most common mass lesion in the sella; however, a PBS can be identified in 80%–81% of patients with a pituitary adenoma^{3,20} and in 93% of cases when the adenoma is < 20 mm.³ Conversely, in germinomas, the PBS is noted to be absent in 100% of cases, whether the patient presents with DI or not.⁹ Failure to demonstrate a PBS in the context of a sellar and suprasellar mass should therefore prompt the clinician to consider the possibility of a germinoma, as well as other diagnoses associated with this feature.

Discussion

The PBS is a normal radiological finding that is believed to correspond to the neurohypophysis. We found that, in 99.7% of cases, the PBS should measure between 1.2 mm and 8.5 mm in its longest axis and between 0.4 mm and 4.4 mm in the axis perpendicular to the longest axis. When the PBS is found to exceed these dimensions

in one or both axes, the physician should consider that the hyperintense signal observed may be an indication of a pathological process (although in 0.15% of individuals without pituitary disease the PBS can also exceed these measurements). Similarly, when the T1-hyperintense signal of the posterior pituitary is absent or below the lower limits, a pathological cause should be considered, as only 0.15% of studies obtained in patients without pituitary disease should fall within this range.

Ju et al.¹⁶ investigated the normal dimensions of the neurohypophysis in a series of 33 autopsy cases. The dimensions were measured in the craniocaudal and anteroposterior axes instead of along the longest and perpendicular axes. The authors found that the mean values for the vertical and horizontal dimensions were 5.8 mm and 2.9 mm, respectively. These dimensions are approximately 20% longer than our findings; this may be explained by the fact that the neurohypophysis is an anatomical structure that is larger than the region dense in vasopressin granules that is seen as a hyperintense signal on T1-weighted MRI.¹

In a study of 60 normal subjects (30 men and 30 women), the dimensions of the PBS on T1-weighted and proton density MRI were found to be 4.1 ± 1.6 mm for men and 5.3 ± 1.0 mm for women along the craniocaudal axis and 3.1 ± 0.9 mm (men) and 3.6 ± 0.8 mm (women) along the anteroposterior axis.⁸ Our finding of an average long-axis dimension of 4.8 mm seems to be in agreement with these authors' conclusions; we also observed a trend toward larger PBSs in women along the long axis, although the difference was not statistically significant. Our average dimension along the short axis is 40% smaller than that of Fujisawa et al.⁸ This discrepancy may be explained by the fact that the patients were younger in that study (mean age of 25.3 years) and that the measurements were performed on proton density images.

The dimensions of the posterior pituitary gland were also investigated with thin-section CT in a series of 320 patients. It could be identified in only 39% of patients, and when identified, appeared as a hypodense region measuring 5–6 mm × 3–4 mm in all cases.⁴ Taking into account the differences between CT and MRI, these measurements are also comparable with our own results.

We have not included the volume of the PBS in our study. Other authors who have investigated the appearance and size of the PBS on MRI have also reported only linear

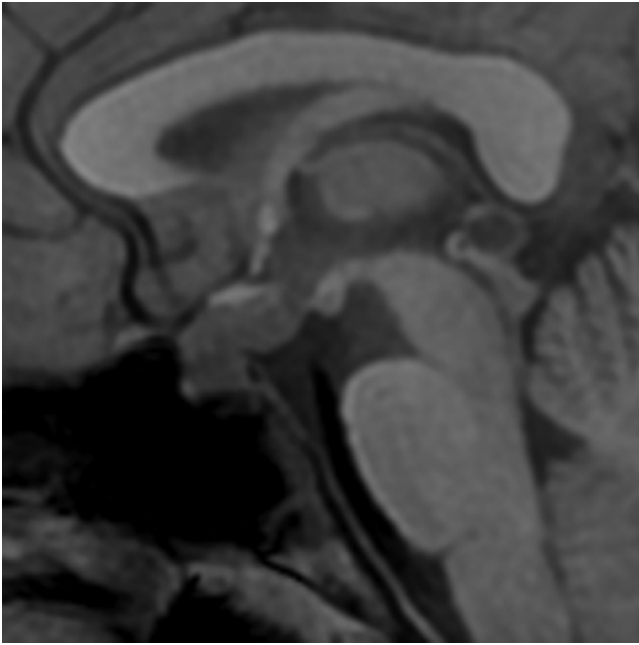


Fig. 5. Illustrative Case 4. Sagittal T1-weighted MR image obtained without contrast enhancement from a 14-year-old girl presenting with mild hyperprolactinemia showing no PBS. Biopsy demonstrated germinoma.

dimensions because the small size of the PBS results in inaccurate volume measurements.⁸ Moreover, linear measurements are more commonly used in clinical practice when the question of differentiating a large PBS from an abnormal T1-hyperintense lesion of the sella occurs.

We identified a PBS in 100% of the patients whose studies we evaluated. The rate of detection of a PBS in normal adult subjects varies from 52% to 100%,^{5,6,8,23} but the direction of the frequency encoding gradient (FEG) was found to have an impact on the rate of detection. When the FEG direction was anteroposterior, the PBS was detected in 100% of cases in one study, whereas it was detected in only 54% of cases when it was directed caudocephalad.²² In our study, the sagittal T1-weighted images were obtained with an anteroposterior phase-encoding direction and a caudocephalad FEG direction; we are therefore unable to confirm whether the direction of the FEG has an impact on the rate of detection of the PBS. The fact that the PBS was detected in all of our cases, however, combined with the results of our analysis showing that 99.85% of all pituitary MRIs should show a PBS with dimensions of at least 1.2 mm in the long axis and 0.4 mm in the short axis, suggests that the true absence of a PBS on a good-quality pituitary MRI should prompt the investigation for a pathological cause.

We have also found that the size of the PBS decreases with age. In other studies, the rate of detection of the PBS decreased with patient age;^{5,23} it was hypothesized that the higher plasma osmolality in older subjects leads to increased release of vasopressin, resulting in the disappearance of the PBS. We believe that, instead of disappearing, the PBS becomes smaller as less vasopressin is stored in the posterior pituitary, which leads to the decrease of the PBS size with patient age that was observed in our study.

We assumed that the population included in this study was representative of the general population. This may be a limitation, as all of our patients had an indication to undergo pituitary imaging—most often endocrine abnormalities or suspicion of a pituitary lesion on another imaging modality. Nevertheless, we believe that our population is representative of the population of patients who undergo pituitary imaging, to whom the results of this study are meant to be applied.

Conclusions

We determined that, in 99.7% of cases, a PBS should be identifiable and should measure between 1.2 and 8.5 mm in the long axis and between 0.4 and 4.4 mm in the short axis in patients who do not have any pituitary abnormality. The dimension of the PBS in the long axis should be expected to decrease with patient age. When the size of the region of T1 signal hyperintensity in the sella is outside this range, or when the PBS is absent altogether, the clinician should consider a pathological cause such as those discussed above.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Couldwell, Côté. Acquisition of data: Côté, Salzman, Sorour. Analysis and interpretation of data: Côté, Salzman. Drafting the article: Côté, Salzman. Critically revising the article: Salzman. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Couldwell. Study supervision: Couldwell.

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Manuscript submitted June 21, 2013.

Accepted November 14, 2013.

Please include this information when citing this paper: published online December 13, 2013; DOI: 10.3171/2013.11.JNS131320.

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