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Magnetization Transfer Imaging of the Pituitary: Further Insights into the Nature of the Posterior "Bright Spot"

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Abstract

Purpose: After more than a decade of investigation, the chemical nature of the posterior pituitary "bright spot" remains elusive. Speculations into the source of this high signal have included relaxation of water by phospholipid vesicles, vasopressin, paramagnetic substances, and membrane-associated proteins. We hypothesized that if the T1 shortening observed in this structure were caused by water/macromolecular interactions, this interaction could be modulated by the use of magnetization transfer (MT) saturation.

Method: Twenty-five normal subjects were recruited over a 2 month period who were identified on routine T1 sagittal head images to have pituitary bright spots with cross-sectional area of >2 mm^2. Thin section (4 mm), T1-weighted (SE 450/20) sagittal MR images were obtained both with and without the use of an MT suppression pulse (1,000 Hz offset, 200 Hz bandwidth, peak amplitude 7.3 μT). Region-of-interest measurements were made of the posterior pituitary lobe, anterior pituitary lobe, genu of corpus callosum, and pons, with MT ratios (MTRs) calculated for each structure.

Results: Relatively low (and similar) MTRs were observed in both parts of the pituitary gland: anterior lobe, 12.3%; posterior lobe 10.8%. Paired *t* test analysis demonstrated no statistically significant difference between the MTRs of the anterior and posterior pituitary lobes ($p = 0.23$). Considerable suppression of signal was noted in the genu (MTR = 25.0%) and pons (MTR = 21.9%). The MTRs of both portions of the pituitary differed significantly from those of the genu and pons ($p < 0.00001$).

Conclusion: The high signal of the posterior pituitary gland suppresses only slightly on MT images, having a behavior similar to that in the anterior lobe but significantly different

from the rest of the brain. These findings suggest that direct water/macromolecule, water/membrane, or water/phospholipid interactions are not likely to be responsible for the appearance of the bright spot. The experimental results are more consistent with water interacting with a paramagnetic substance or low molecular weight molecule (e.g., vasopressin, neurophysins).

Few issues have excited as much interest or controversy in the recent neuroradiology literature as those surrounding the nature of the pituitary "bright spot" [(1)]. This high signal region in the posterior portion of the sella was easily seen even on early-generation MR scanners and was originally thought to arise from an intrasellar fat pad [(2)]. A number of subsequent investigations showed that the signal did not arise from extrapituitary fat, but rather from water protons within the neurohypophysis [(3-7)]. Furthermore, the presence and size of the bright spot are related to the gland's functional state [(6-9)]. Specifically, the bright spot disappears in diabetes insipidus, and its size can be modulated pharmacologically or by manipulation of serum osmolality. Although the anatomic locus of the bright spot is now firmly established, the substance(s) responsible for T1 shortening is not. Candidates have included antidiuretic hormone (ADH), phospholipid vesicles, and neurophysins [(7,9)].

To further elucidate the chemical nature of the pituitary bright spot, we set out to study this structure in a group of normal subjects using magnetization transfer (MT) saturation pulses. MT techniques employing high power, off-resonance saturation probe water/macromolecular interactions and help differentiate molecular mechanisms responsible for MR image contrast [(10-14)].

SUBJECTS AND METHODS

Twenty-five normal patients and volunteers were recruited over a 2 month period who were identified on routine T1 sagittal head images to have pituitary bright spots with cross-sectional area of >2 mm^2. The subjects were 11 females and 14 males, ranging in age from 5 months to 54 years (mean age 21.6 years). Thin section (4 mm), T1-weighted (SE 450/20) sagittal MR images were obtained both with and without the use of an MT suppression pulse. Other imaging parameters included field of view 20 cm, interslice gap 1 mm, image acquisition matrix 192 × 256, receiver bandwidth 16 kHz, and one excitation.

The MT sequence employed was implemented in research mode on a clinical 1.5 T Signa unit (GE Medical Systems, Milwaukee, WI, U.S.A.) operating in research mode. The MT pulse was produced by modifying in software the standard chemical shift selective saturation pulse available on this system [(15)]. Our resultant MT saturation pulse had a bandwidth of 250 Hz and an envelope composed of a 16 ms, apodized sinc function with two side lobes. The frequency offset of this pulse was set at 1,000 Hz downfield from the water resonance. The pulse amplitude was maximized to produce a peak radiofrequency field flux density (B_1) of 7.3 μT. After each MT pulse, gradient homospoiling was performed by turning on the y-axis (phase-encoding) gradient to maximum amplitude for ≈5 ms. Allowing for gradient ramp times, the interval between the end of the MT pulse and the beginning of the 90° pulse was ≈6 ms.

Region-of-interest measurements were made of the posterior pituitary lobe, anterior pituitary

lobe, genu of corpus callosum, and pons, with MT ratios (MTRs) calculated for each structure. The MTR is a convenient index to quantify the degree of signal suppression experienced by a given tissue during an MT experiment. This ratio is calculated by the formula where SI_0 is the signal intensity of the tissue before the MT pulse and SI_m is the signal intensity after the MT pulse has been applied. The MTR indicates the percentage of signal loss occurring during the irradiation of the immobile pool of protons and consequently is proportional to Forsén and Hoffman's pseudo-first-order rate constant for saturation transfer between two chemical species [16].

$$MTR = (SI_0 - SI_m)/SI_0 \times 100\%$$

Equation 1A

RESULTS

Relatively low (and similar) MTRs were observed in both parts of the pituitary gland: anterior lobe, 12.3%; posterior lobe, 10.8%. Paired *t* test analysis demonstrated no statistically significant difference between the MTRs of the anterior and posterior pituitary lobes ($p = 0.23$). Considerable suppression of signal was noted in the genu (MTR = 25.0%) and pons (MTR = 21.9%.) The MTRs of both portions of the pituitary differed significantly from those of the genu and pons ($p < 0.00001$). This visually apparent result is shown in Fig. 1.

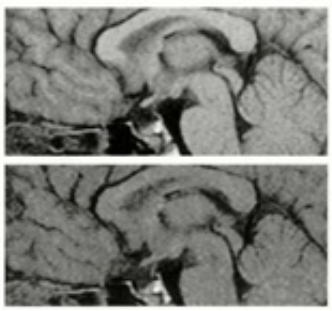

Fig. 1

DISCUSSION

Few subjects have elicited as much interest or controversy in the recent radiologic literature as the pituitary “bright spot.” This high signal region in the posterior sella was originally misidentified as a sellar “fat pad” [2]. Shortly thereafter, Fujisawa et al. provided evidence from T2-weighted images and chemical shift experiments that the signal from the bright spot did not arise in fat, but from water protons in the neural lobe [3,4,6,8]. These conclusions were initially met with great skepticism, however, since no direct MR/anatomic correlations were provided and the results directly contradicted the prevailing sellar fat pad theory [17]. By 1987, however, the evidence had become inescapable that the bright spot did indeed correspond to the neural lobe [3-7] and was also related to its functional state [6-9]. Specifically, the bright spot was noted to disappear in patients with diabetes insipidus [8,9], and its size could be modulated pharmacologically [5] and by manipulation of serum osmolality [6].

Although the anatomic locus of the bright spot is now firmly established, the substance(s)

responsible for T1 shortening is not. The signal does not originate from lipid protons [17], although facilitated relaxation of water protons by aliphatic substances remains a possible mechanism. An appealing hypothesis is that granules of ADH are responsible for the short T1 values, but simple solutions of ADH apparently do not possess the appropriate relaxation characteristics [7]. Kucharczyk et al. [7] demonstrated that suspensions of phospholipid vesicles similar to those found in the neurohypophysis do have short enough T1 relaxation times; some question remains, however, concerning whether their T2 values are too long [18]. The ADH carrier proteins known as neurophysins have also been postulated to be potential enhancers of T1 relaxation, but their role in making the bright spot "bright" remains entirely speculative at present [19].

MT imaging is a relatively new MR technique in which image contrast is modulated by selectively saturating a pool of tightly coupled protons in macromolecules and their associated "bound" water [10-15]. Although many variations of this method exist [20], the usual MT technique consists of applying a presaturation pulse with center frequency shifted from the water resonance by several hundred to several thousand Hertz. This off-resonance pulse has sufficient power to saturate protons in the macromolecular pool without directly affecting those in free water. After the MT saturation pulse has been applied, a routine MRI sequence (e.g., SE, GRE) can then be performed. MT saturation of the pool of macromolecular protons is transferred to nearby water molecules, presumably by means of dipolar crosscoupling and chemical exchange interactions [21]. Through these complex interactions, tissue relaxation parameters are altered and new image contrasts may be revealed [11]. At frequency offsets below 2,000 Hz, Ulmer et al. [14] and Moran and Hamilton [22] have recently shown that spin lock relaxation phenomena sensitive to tissue T1/T2 ratios also contribute to MR signal characteristics during MT saturation.

Although the precise mechanisms underlying the MT phenomenon are incompletely understood, there is general agreement that the central effect of MT pulses is to reduce signal from tissues rich in macromolecules, particularly those containing relatively large numbers of hydrogen nuclei incorporated into cell membranes, phospholipids, enzymes, and proteins. We therefore reasoned that if the T1 shortening in the pituitary bright spot resulted from water interactions with membrane proteins or phospholipid vesicles, its MR signal should be easily suppressed by MT pulses.

The results of our MT experiment do not support a mechanism of T1 shortening based on water/phospholipid vesicle interactions. The MTR of the posterior lobe was only 10.8%, slightly lower than that of the anterior lobe (12.3%) and significantly lower than that of the brainstem (21.9%) or corpus callosal white matter (25.0%). If significant direct water/macromolecule, water/membrane, or water/phospholipid interactions were present in the neurohypophysis, we would expect appreciable suppression of its signal on the MT images. The fact that we observe so little MT suppression in the neurohypophysis suggests that an alternative relaxation mechanism should be considered. Possible candidates for T1 shortening consistent with our MT experiments include water interactions with paramagnetic substances or a low molecular weight molecule (e.g., vasopressin, neurophysins).

In summary, the high signal of the posterior pituitary gland suppresses only slightly on MT images, having a behavior similar to the anterior lobe but significantly different from the rest

of the brain. These findings suggest that direct water/macromolecule, water/membrane, or water/phospholipid interactions are not likely to be responsible for the appearance of the bright spot and that alternative mechanisms should be considered.

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