RELATIONSHIP OF HIPPOCAMPUS AND AMYGDALA TO CORONAL MRI LANDMARKS

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Magnetic resonance imaging is playing an increasingly important role in the evaluation of the hippocampus, particularly in epilepsy, schizophrenia, and Alzheimer’s dementia. Because of the complex configuration of the hippocampus, it is difficult to compare from patient to patient. We developed a system to allow comparison of the hippocampus on coronal images. We performed 34 magnetic resonance studies on 29 normal subjects. Ten anatomic landmarks were identified. These landmarks have a consistent 5-mm periodicity regardless of usual head flexion. In the second phase of our investigation, we showed that the amygdala, hippocampal head, hippocampal body, and hippocampal tail have a consistent relationship to the coronal magnetic resonance imaging landmarks.

Keywords: Hippocampus; Magnetic resonance imaging; Epilepsy; Hippocampal sclerosis.

INTRODUCTION

The hippocampal formation and associated limbic structures play important roles in memory and pathologic processes such as epilepsy, schizophrenia, and Alzheimer’s disease.1-5 With the advent of magnetic resonance imaging (MRI), in vivo studies of these disease processes are now possible. A number of investigators have used MRI assessment of the hippocampal formation (which we will refer to simply as the “hippocampus”) and temporal lobe to study these entities.3-9 Naidich et al. has shown that the hippocampus and limbic structures can be successfully imaged with MR.10-11

While investigating hippocampal sclerosis with MRI, we discovered a need for a reproducible method of comparing identical sections of the hippocampus and amygdala in different patients. The hippocampus undergoes a radical change in size and shape as one proceeds from anterior to posterior (Fig. 1).1,10,11 The hippocampal head is bulbous, while the tail tapers markedly. The hippocampus found on a coronal MR image centered at the hippocampal head differs markedly from the hippocampus imaged 2 cm posteriorly, at its tail. The purpose of this study is to develop a standard in which one can compare and quantitate the hippocampus on a coronal MR image at a particular antero-posterior position by means of anatomic landmarks found on coronal MR slices. The first phase of this study investigates the anatomic MR landmarks. Can easily identifiable landmarks be found at 5-mm intervals on coronal MR images? The second phase studies how frequently the limbic segments (amygdala, hippocampal head, hippocampal body, and hippocampal tail) are found at particular coronal MR landmarks.

METHODS

Subjects

Twenty-nine healthy Caucasian volunteers, aged 17 to 45 years old (mean: 29 years) were studied. Twenty-five were right-handed, one left-handed, and three had mixed preferences as determined by the Edinburgh
handedness inventory.12 Sixteen were female and 13 were male.

**MRI**

Thirty-four MRI examinations were performed on the 29 subjects. Consent was obtained in accordance with institutional human investigations committee guidelines. All studies were performed on a 1.5 Tesla superconducting magnet (General Electric, Milwauk ee, WI) utilizing spin-echo sequences. A sagittal localizing series was obtained with 600/20/4 (TR/TE/excitation), 5 mm slice thickness, 2.5 mm interslice gap, 128 x 256 matrix, and a 24 cm field of view (FOV). Coronal studies were imaged with contiguous 5-mm-thick slices, 128 x 256 matrix and a 16 cm FOV. The parameters for the short TR sequence were 400/20/4. The long TR series consisted of a multiecho sequence 1700/25,50,75,100/1.

**Landmarks**

Structures chosen as anatomic landmarks are easily visible on adjacent 5-mm-thick coronal slices. Care was taken to pick structures that are at the same crano-caudal level as the adjacent amygdala or hippocampal structures. This insures that the chosen landmark always defines the same antero-posterior section of hippocampus on coronal imaging regardless of the flexion or extension of the head (Fig. 2). We divided the hippocampus and amygdala into 10 coronal sections with the following landmarks:

1. **Anterior pituitary lobe (AP)**
2. **Pituitary stalk, posterior pituitary lobe, dorsum sella (PP)** (Fig. 3(A))
3. **Suprasellar cistern in which neither the pituitary nor basilar artery bifurcation are seen (SS)** (Fig. 3(B))
Fig. 3. (A)–(E), (G)–(I) are $T_1$-weighted coronal images progressing from anterior to posterior at 5-mm intervals. (A) Slice PP: Amygdala and uncus are indistinguishable from one another. (B) Slice SS: Amygdala is superior to temporal horn (small black arrows) tip. Amygdala and uncus form a gray matter complex. (C) Slice BA: The digitations (white arrow) identify the hippocampal head. (D) Slice IP: The transition from bulbous head to more uniform body occurs here. (E) RN slice: The hippocampal body (H) has an oval shape, capped superiorly by the alveus and fimbria (small white arrows). The red nucleus is difficult to discern on $T_1$-weighted images. It is easily seen on $T_2$-weighted sequences (F). CN8, identified by the cochlea, is not at the same cranio-caudal level as the hippocampus. (Figure continued on overleaf.)
4. **Basilar artery** as it bifurcates into the posterior cerebral arteries in the preopticine cistern (BA) (Fig. 3(C))
5. **Interpeduncular** cistern and cerebral peduncles (IP) (Fig. 3(D))
6. **Red nucleus** and occasionally a small portion of the interpeduncular cistern (RN) (Figs. 3(E), (F))
7. Since an anatomic landmark at this position was not found, this region was defined as a slice *posterior* to the red nucleus within the brain stem where there is no visualization of either the red nucleus nor the colliculi (PR) (Fig. 3(G))
8. **Superior colliculus** and pineal gland (SC) (Fig. 3(H))
9. **Inferior colliculus** in which there is often concomitant visualization of a portion of the superior colliculus (IC) (Fig. 3(I))

10. **Posterior** to the colliculi within the quadrigeminal cistern (PC).

**Hippocampal Angle**

In order to determine the relative degree of head extension or flexion, we measured the hippocampal angle. We defined the hippocampal angle as the angle formed by the intersection of the coronal slice with the inferior border of the left subiculum and cornu ammonis on sagittal MR (Fig. 4). Three subjects had a total of five additional coronal studies performed at various hippocampal angles by deliberate hyperflexion and hyperextention of the head. Since we failed to image through the entire length of the limbic segments in these five studies, they were not used for the second phase of this investigation.
Fig. 4. Hippocampal angle on parasagittal T1-weighted image. The hippocampal angle (θ) is defined as the angle formed by the intersection of the coronal imaging plane (line "C") with the plane (line "H") parallel to the inferior border of the hippocampal complex, the cornu ammonis and subiculum.

Limbic Structures

We defined and divided the limbic structures after Duvenoy with modifications.1 We will refer to the "hippocampal formation" as the "hippocampus". The hippocampus can be divided into three segments—the head, body, and tail (Fig. 1). The head, medial to the temporal horn, is identified by visualization of its digitations on coronal MR (Fig. 3(C)). The body is defined as that segment of the hippocampus between the head and the tail (Figs. 3(E)–(G)). The tail is defined as that portion of the hippocampus which curves behind the brain stem, ascending and tapering markedly (Figs. 3(H),(I)). The amygdala is defined as the gray matter anterior and superior to the anterior recess of the temporal horn (Figs. 3(A),(B)). The uncus cannot be separated from the amygdala by signal characteristics on coronal MR images.10,11

Landmark Periodicity

The first phase of this study evaluated our choice of anatomic landmarks by asking the question: Do these landmarks occur at consistent distances from each other? Hippocampal angles ranged from 43° to 94° with a mean of 68° in 34 studies. Landmarks were identified on T1-weighted images with the exception of the RN, which was detected primarily on T2-weighted images. Occasionally, more than one landmark was imaged on a single slice. Landmarks sometimes occurred on more than one slice. This was particularly true for IP. In order to evaluate the periodicity of our landmarks, we assessed which landmarks were found at increasing distances from a reference point (Fig. 2). A slice with IP was used as the center location (0 location). The landmark on the slice 5 mm posterior (+5 mm) to the reference IP slice was identified. This process was repeated for all slice locations posteriorly (up to +30 mm) and anteriorly (up to −30 mm).

The effect of hippocampal angle on the landmarks was investigated. We divided our results into 4 groups dependent on hippocampal angle: 43°-60° (n = 9); 62°-66° (n = 9); 68°-72° (n = 7); 75°-94° (n = 9). We then looked at the degree of dispersion of landmarks in each group by counting the number of expected landmarks/total landmarks at a particular location. For example, in an idealized model, we would expect to detect only the SC landmark in all subjects at the slice location +15 mm posterior to IP slice. Instead of finding SC as the landmark in 100% (no dispersion) at the +15 mm location, it is seen in 8 of 9 subjects in group 1, 8 of 9 in group 2, 7 of 7 in group 3, and 7 of 9 in group 4. The degree of dispersion for all locations was compared in the four groups by Chi Square Test.

Limbic Relationships

In the second phase of this investigation, we identified the limbic segments—amygdala, hippocampal head, body, and tail. The frequency of limbic segments occurring adjacent to a coronal MR landmark was then determined in the 29 subjects in 29 studies (Fig. 2). The seventh/eight cranial nerve complex (CN8) was also identified and compared to the landmarks. The effect of angulation was investigated. The hippocampal angle in the 29 subjects ranged from 53°–81° with a mean of 67°. We divided our results into 4 groups dependent on hippocampal angle: 53°–62° (n = 8); 64°–66° (n = 7); 68°–72° (n = 7); 75°–81° (n = 7). The effect of angulation was assessed by using the Chi Square test to compare the frequency of amygdala, head, body, tail, or CN8 occurring with a landmark for the four groups.

RESULTS

Phase 1: Periodicity of Coronal MR Landmarks

The chosen landmarks are found approximately 5 mm apart (Fig. 5). As one proceeds at 5 mm intervals posteriorly from −12 mm to +25 mm relative to IP, one encounters primarily PP, SS, BA, IP, RN, PR, SC, IC, and PC on successive slices. Dispersion is greatest anteriorly at −20 mm; both AP and PP are
Fig. 5. Periodicity of coronal MR landmarks. The number of observations of landmarks are plotted against slice location. Using IP as a zero reference, location is defined as distance between the landmark slice and the IP slice. Since two landmarks are occasionally seen on a single slice, there may be more than 34 observations. Each observation is plotted as a spoke on a hub. For slice locations posterior to −20 mm, the landmarks are found clustered at 5 mm intervals. There is a small amount of variation, with landmarks found ±5 mm from their expected clustered location.

frequently observed. Subject angulation (43°–94°) did not effect periodicity of landmarks (Fig. 2). Chi-Square comparison of dispersion of the 4 groups was not significant ($p = 0.57$).

Phase 2: Frequency of Limbic Segments at Landmarks

The amygdala was seen most frequently on the PP and SS slices, the hippocampal head on the BA and IP slices, the body on the RN and PR slices, and the tail on the IC slices. Transition zone was located on the BA slice for the amygdala–head, the IP slice for the head–body, and the SC slice for the body–tail (Figs. 2, 6).

The relationship of the four limbic segments to the coronal landmarks was unaffected by natural subject angulation (53°–81°). No significantly distinct hippocampal angle group was found by analyzing the frequency of amygdala ($p = 0.93$), head ($p = 0.85$), body ($p = 0.99$), nor tail ($p = 0.94$) to the landmarks.

CN8 was seen most frequently on the IP, RN, and PR slices. Less often it was detected on the BA and SC slices. Since CN8 is at a different cranio-caudal level than the limbic segments, one would expect it to be affected by angulation. Although there appears to be a trend supporting this belief, there is no significant difference among the four angulated groups, even comparing the 53°–62° group versus the 75°–81° group ($p = 0.09$) (Fig. 2). CN8 can be found on the same coronal images as the amygdala, head, body, or tail depending on angulation. It was seen most frequently with the head and body.

DISCUSSION

The hippocampal formation (Figs. 7, 8) is a complex structure composed of the cornu ammonis (hippocampus proper), subiculum, dentate gyrus, subpialgyrus, supracallosal gyrus, alveus, fimbria, and fornix.$^1,10,11$ Its superior border is the choroidal fissure. This entire complex protrudes into the medial wall of the temporal horn.

The hippocampal formation may be divided into three parts—the bulbous anterior head, the body, and the posterior tail (Fig. 1). Notching of the head is termed “digitationes hippocampi” or hippocampal digitations.$^1$ Although usually called the pes hippocampus, this is a confusing term since it refers to the “foot”–like appearance in the “head”. As the head tapers posteriorly it becomes the body, the true horizontal portion of the hippocampus and the most reliable region to quantitatively assess the hippocampus histopathologically and by MR.$^7$ The tail is seen posterior to the brain stem, as the hippocampus markedly narrows and sweeps vertically (Figs. 1, 2, 3(l)).

On coronal sections, the hippocampal formation predominantly consists of two U-shaped interlocking gray matter structures, the cornu ammonis and dentate gyrus (Fig. 8).$^1$ The cornu ammonis (or hippocampus proper) can be divided into four zones—the
Fig. 6. Relationship of limbic segment to coronal MR landmark. At each coronal landmark, we plotted the frequency (number of patients) with which a particular limbic segment was found. The amygdala is found predominantly at the PP and SS slices, the head at the BA and IP slices, the body at the RN and PR slices and the tail at the IC and PC slices. Transition zones are at the BA level for amygdala–head, IP level for the head–body, and SC level for the body–tail.

cornu ammonis fields, CA1 to CA4. The subiculum is transitional cortex that connects the cornu ammonis to the neocortex of the parahippocampal gyrus (Fig. 8).

The fornix, alveus and fimbria are the major white matter tracts of the hippocampal formation and form the main efferent pathway from this region. The alveus is a thin white matter layer covering the cornu ammonis, immediately subjacent to the ependyma of the medial surface of the temporal horn. As the alveus converges along the superomedial aspect of the hippocampus, it becomes the fimbria, which in turn continues posterosuperiorly to form the fornix (Figs. 1, 7, 8).

The amygdala (amygdaloid body or nucleus) is found anterosuperior to the temporal horn tip. It is immediately lateral to the uncus of the parahippocampal gyrus. The gray matter of the amygdala and uncus are inseparable on MRI (Figs. 1, 3(A), 3(B)).

In an attempt to standardize the MR evaluation of the amygdala and hippocampus, we have shown that selected anatomic landmarks, PP to IC, are approximately 5 mm apart regardless of usual head angulation (Fig. 2). They are never found more than ±5 mm from their expected location relative to the interpeduncular fossa (IP) slice. In the second phase of this study, we showed a relationship between limbic segment and coronal anatomic landmark. Naturally occurring subject head angulation is relatively unimportant because the landmarks were chosen to occur at the same cranio-
caudal level as the limbic segments. This is particularly true of landmarks within 15 mm of IP. CN8, however, occurs at a different cranio-caudal level. With head extension, there is a trend for CN8 to occur with more anterior landmarks whereas with flexion CN8 occurs with more posterior landmarks (Fig. 2).

The goal of this study was to establish an easy method for evaluating regional hippocampal abnormalities. This facilitates the description of hippocampal disease in terms of relatively defined regions rather than vague or poorly defined terms such as the "anterior hippocampus." Our rationale for partitioning the amygdala and hippocampus into 5-mm slices intervals rather than thinner sections was due to the following consideration. Although easily recognizable landmarks are found at approximately 5-mm intervals, inherent variations increase this range to 10 mm (as demonstrated in the previous paragraph). Thus, use of thinner slices would not have changed our results.

MR evaluation of the hippocampus has been hampered by the complex hippocampal configuration. Quantitative studies have been performed volumetrically,13,14 but have not allowed evaluation of hippocampus without including the uncal-amygdaloid complex (without arbitrary separation). Awad et al. developed a method to quantify temporal lobectomy by MRI, but their landmarks did not account for head angulation.15 We have developed a system to evaluate discrete sections of the hippocampus, rather than the entire uncal-amygdaloid-hippocampal complex. The inherent difficulties associated with appraising the amygdala as part of the hippocampal complex can be avoided. This system has facilitated investigation of the normal hippocampus16 and hippocampal sclerosis.7,17 We have been able to compare the hippocampus at the red nucleus level, with the knowledge that the hippocampal body will always be present.7 This system can also be helpful for evaluation postinsertion of depth electrodes in the hippocampus when susceptibility artifacts obscure the adjacent amygdala and hippocampus. The reproducibility of this system provides a means for further studies of the relationship of the hippocampus to pathologic processes such as epilepsy, Alzheimer's dementia, and schizophrenia.

REFERENCES


