Copyright 2005 University of Washington

BrainInfo: A Portal to Neuroanatomy on the Web

Douglas M. Bowden, MD, Mark Dubach, PhD

Dept. of Psychiatry and Behavioral Sciences, School of Medicine, and Neuroscience Division, National Primate Research Center, University of Washington, Box 357330, 1705 NE Pacific St., Seattle, WA 98195-7330

Posted 11 January, 2005.

Abstract

The BrainInfo website is a portal to neuroanatomical information on the Web (BrainInfo 2005). It is designed particularly for neuroscientists who feel limited in their knowledge of brain anatomy and who wish to obtain a broad, rapid and accurate orientation to neuroanatomical concepts.

An unusual feature of BrainInfo is that it allows visitors to locate information by navigating intuitively according to the logic of neuroscientific inquiry rather than by navigating websites organized to simulate libraries. Users go directly from the home page to the information they seek without having to navigate a series of menus and site maps wondering whether the information is there and, if so, where. They need not learn how the website is organized, because a concept-based ontology allows the indexation and retrieval of text and image information at a high level of detail.

Once a user has found the specific information he or she seeks, the system assists in proceeding directly to the next information of interest without needing to return to a home page and regardless of whether that information is on the same server or on a server thousands of miles away.

Besides offering access to information recorded in words and numbers BrainInfo provides access to an unusually large number of illustrations, including anatomic diagrams, movies, original photomicrographs and data mapped to a standard brain atlas. Visitors to BrainInfo can display, on a single screen photos of the architectonic structure of cortical areas published by numerous neuroanatomists during a century of research, click and drag them to optimal positions for visual comparison and, if they are named differently, determine the original authors' reasons for regarding them as equivalent.

A public scientific resource BrainInfo offers rapid access to the large and growing body of neuroscientific knowledge available on the Web.

Introduction

The advent of whole brain surveys for gene expression has exposed a problem with neuranatomical nomenclature that went largely unrecognized before scientists were able to collect extensive, detailed data on brain systems unfamiliar to them. Powerful new genomic and imaging techniques have brought to neuroscience many investigators whose knowledge of neuroanatomy is minimal but who, nevertheless, have a keen interest in learning about brain structures that exhibit the phenomena they study. With estimates of the number of functionally unique cell groups in the brain ranging between 500 and 1000 and with an average of six legitimate English and Latin names for each structure (Bowden and Martin 1995; Bota, Dong et al. 2003), scientists from disciplines as diverse as molecular biology and psychiatry have every reason to be confused as they read the literature on brain areas newly of interest to them.

Fortunately the same computer and information technologies that enable scientists to acquire massive amounts of high-resolution data about the whole brain also make it possible to speed access to information about individual brain structures. The rapid adoption of the World Wide Web as a medium for sharing information about the brain, and the development of BrainInfo (BrainInfo 2005) as a portal to relevant websites, are enabling scientists to obtain in a few minutes an orientation to knowledge about specific areas that would otherwise require hours or days of poring over textbooks, atlases and review articles.

Website Description and *Modus Operandi*

Suppose a neurochemist reads a report that expression of a particular gene has been demonstrated in 'area tegmentalis' and wonders whether area tegmentalis is related to the 'prerubral area' where he himself has reported concentrations of a particular neuropeptide. If he goes to Google (Google 2005) and enters 'area tegmentalis' (Fig. 1) he obtains a long list of web addresses that may or may not contain the information he seeks (Fig. 2). Because Google knows that BrainInfo contains information about all names of brain structures that have appeared in PubMed abstracts in the past 25 years, including 'area tegmentalis', a button link to BrainInfo appears in the upper right corner of the listing. A click on 'BrainInfo Knowledge Base' takes him to BrainInfo (Fig. 3).

Figure 1: Google's search box with the entry 'area tegmentalis'.

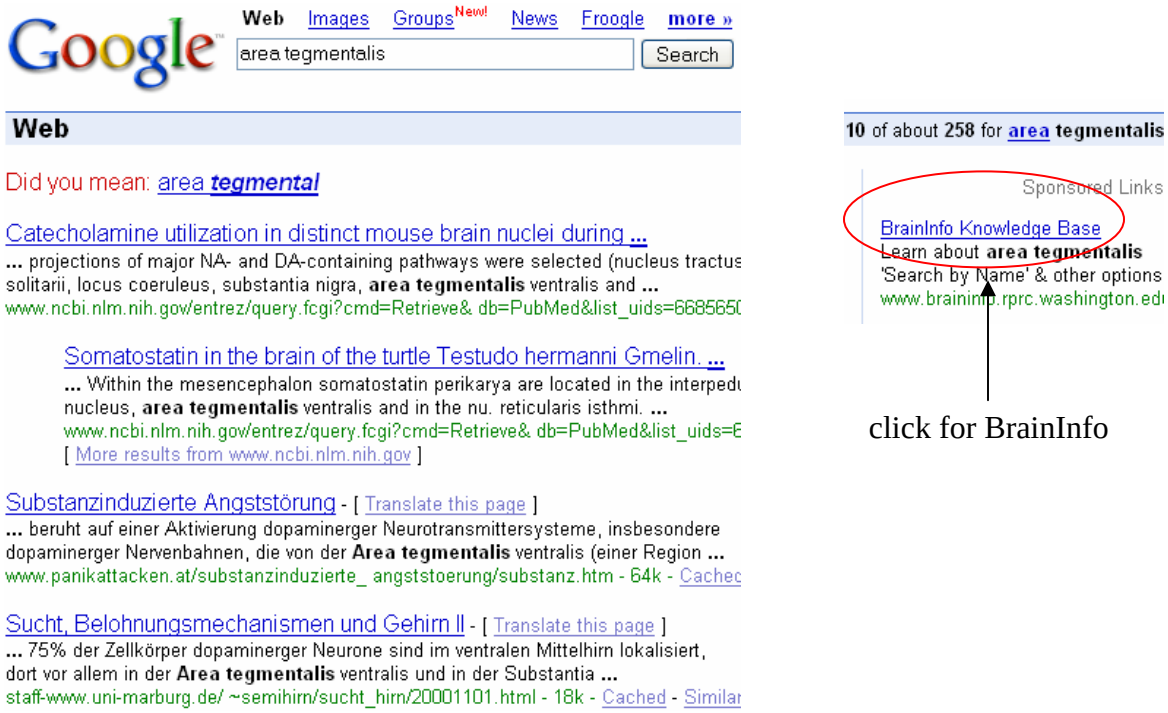


Figure 2: The first several of Google's many citations about area tegmentalis (left) and a link to the BrainInfo Knowledge Base (upper right).

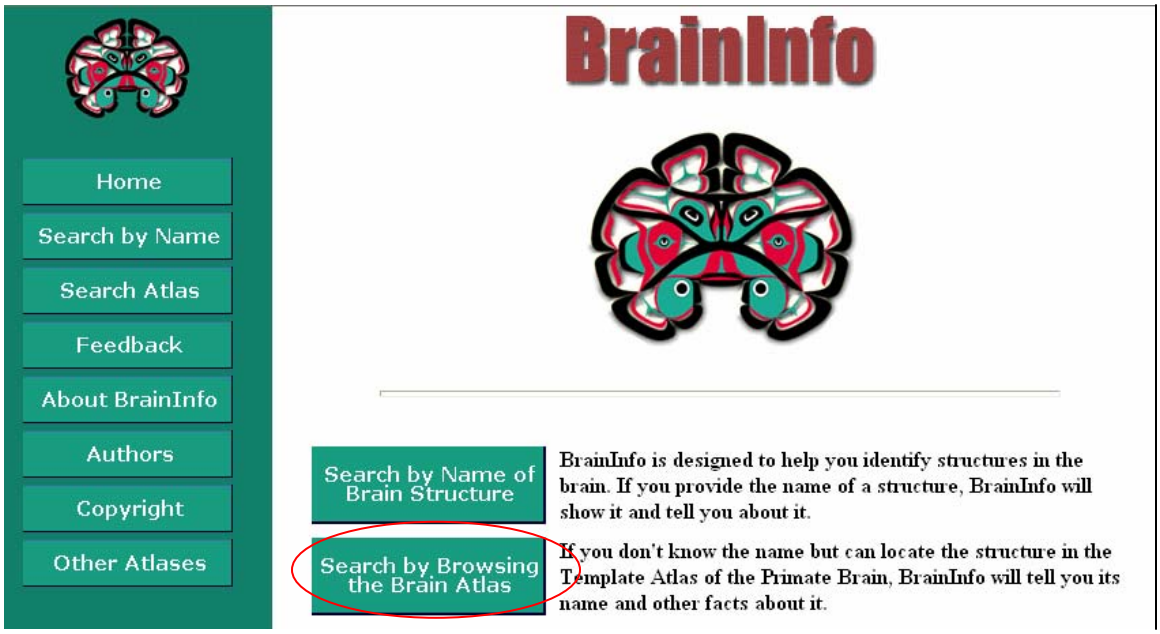


Figure 3: BrainInfo's home page.

Clicking ‘Search by Name’ on the home page (Fig. 3) enables the visitor to obtain information using any of a number of neuroanatomical names and acronyms in several languages (Fig. 4). Submission of the term ‘area tegmentalis’ produces the list of terms in Figure 5.

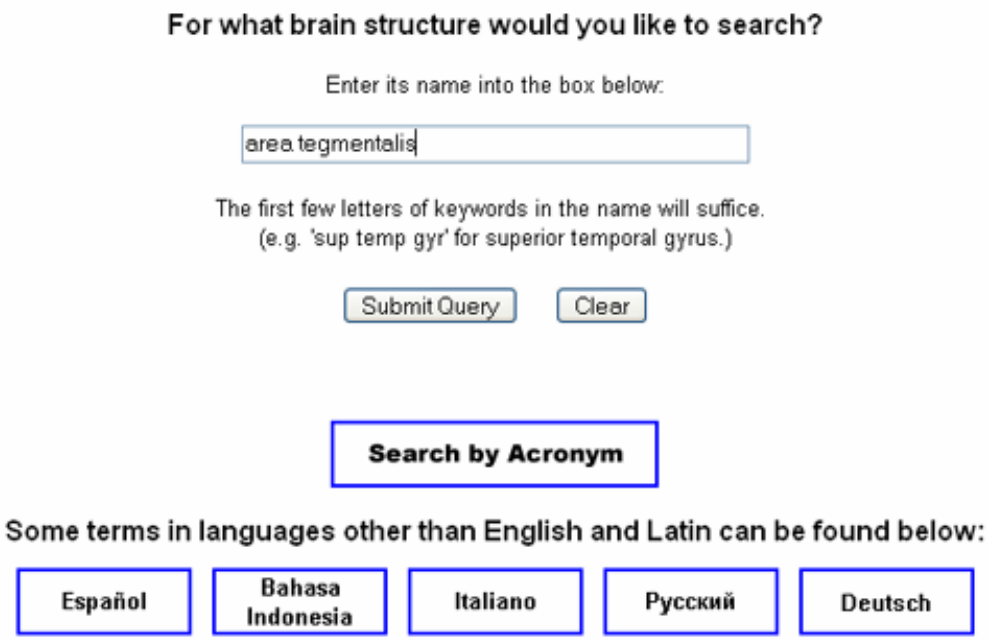


Figure 4: BrainInfo’s search page allows one to search for information using any of 15,000 neuroanatomical acronyms and terms in English, Latin and five other languages.

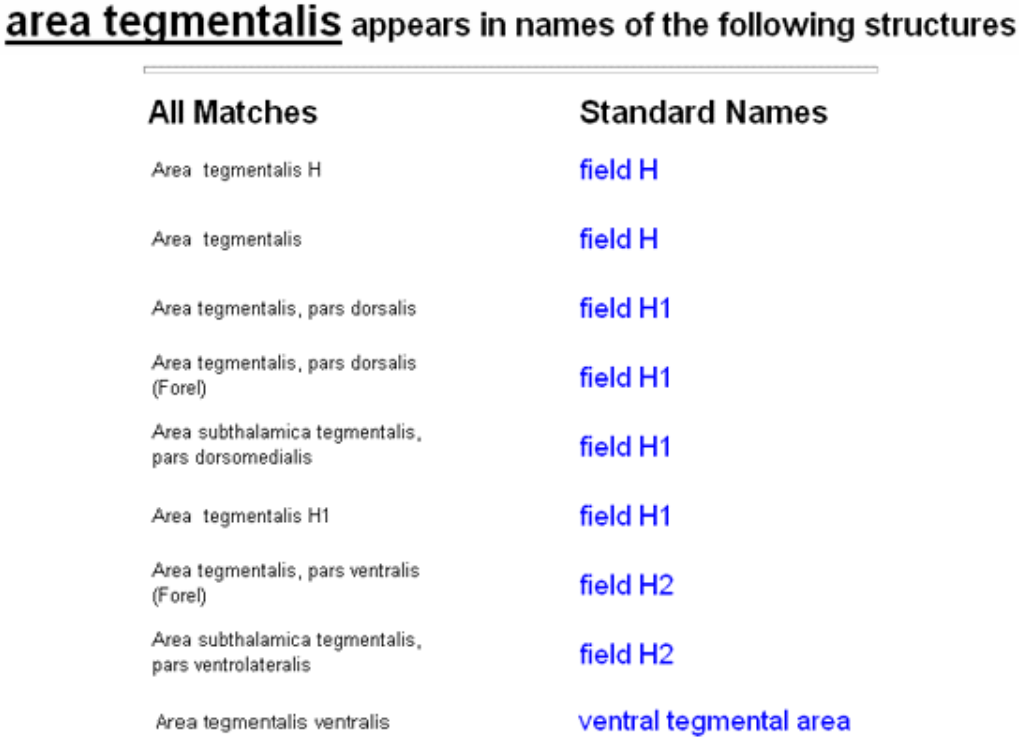


Figure 5: The string of characters ‘area tegmentalis’ occurs in names of several structures.

The string ‘area tegmentalis’ occurs in nine names for four different structures. For each name BrainInfo displays a standard name for the corresponding structure. For example, in Fig. 5 the first two terms refer to BrainInfo’s ‘field H’, the next four to BrainInfo’s ‘field H1’, and so forth. The exact match for ‘area tegmentalis’ is ‘field H’. Clicking there brings up the central directory to information about the structure (Fig. 6). To determine whether ‘field H’ is the same as the ‘prerubral area’ the visitor clicks ‘Other Names for It’.

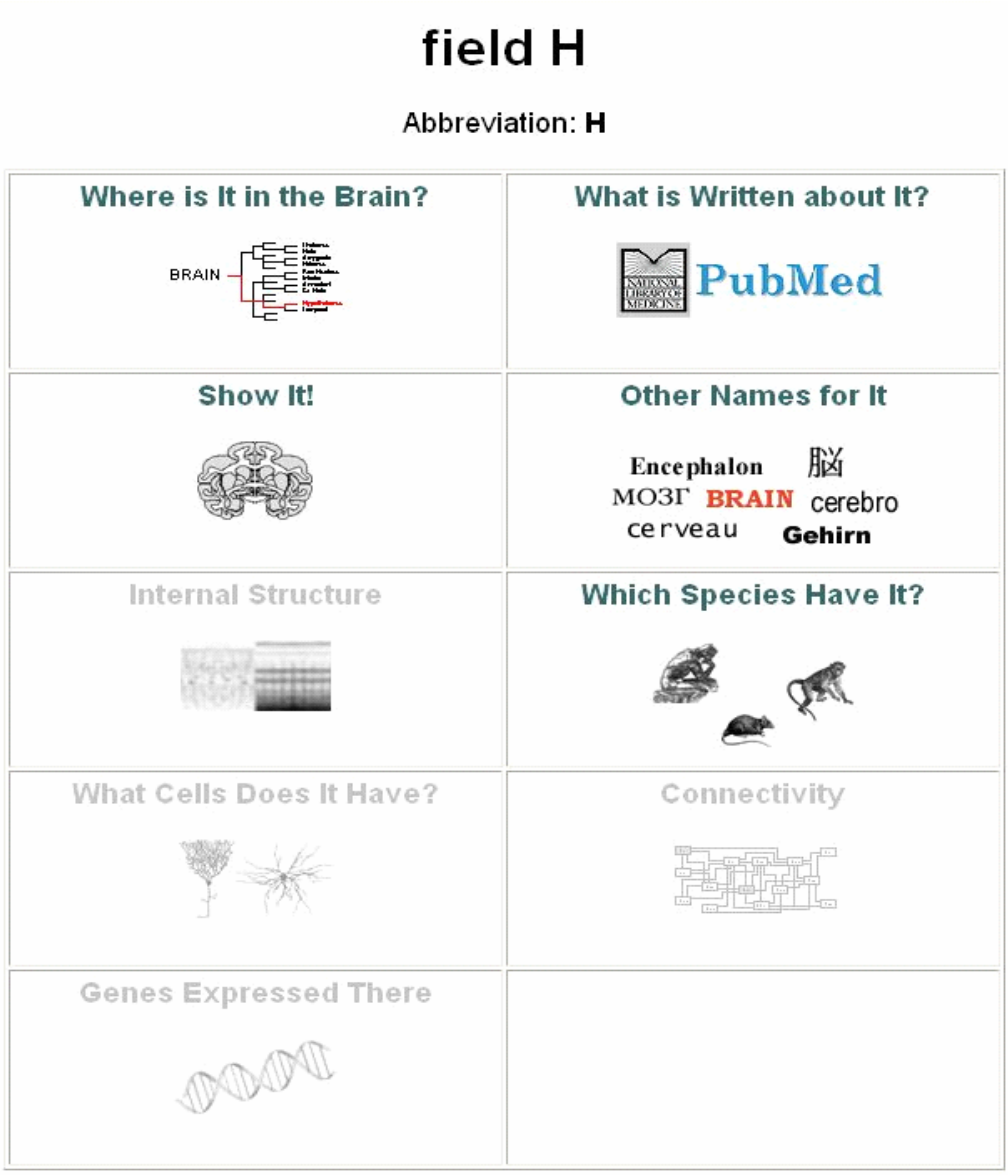
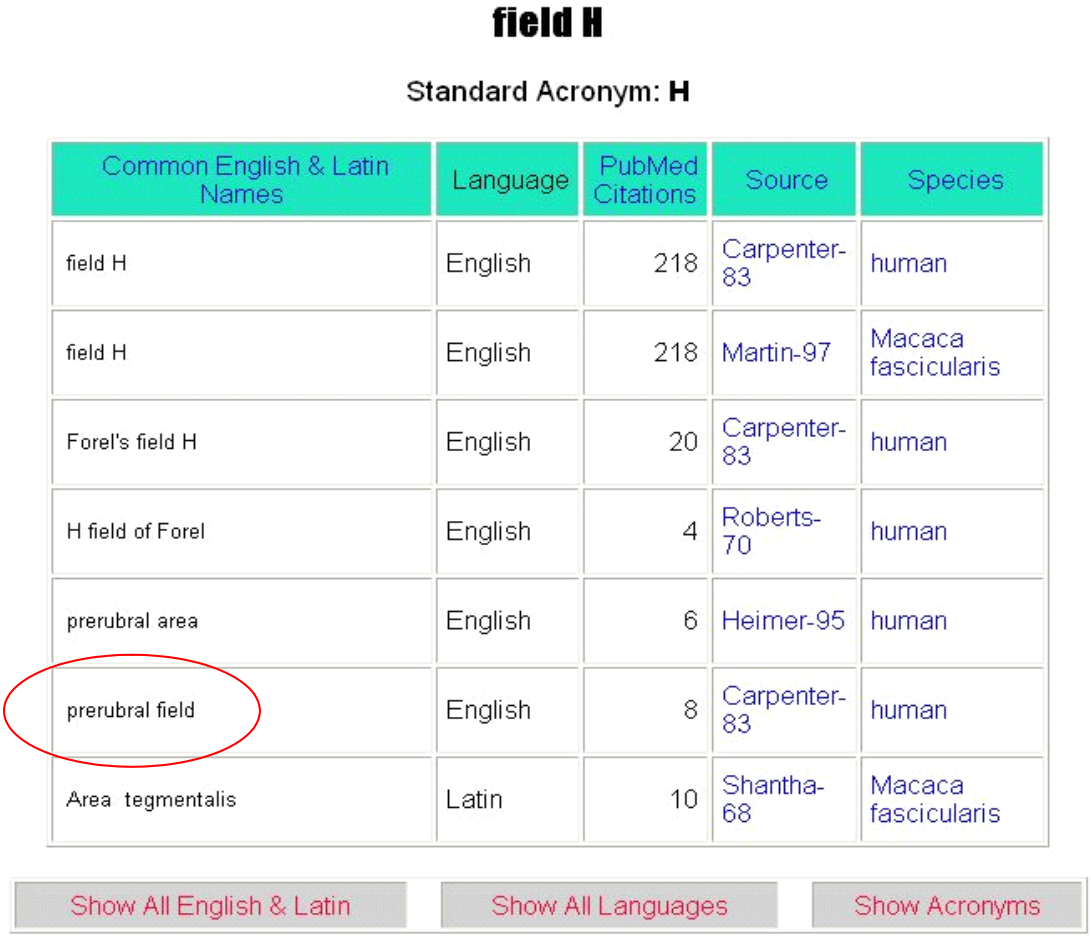


Figure 6: BrainInfo’s central directory to information about ‘field H’. Grayed cells refer to kinds of information that are not available for this particular structure.

He finds that, indeed, ‘prerubral area’ and ‘prerubral field’ are synonyms of ‘field H’ (Fig.7). He also learns that ‘field H’ is by far the most commonly used name, having appeared in 218 PubMed citations in the past 25 years (Fig. 7, Col. 3). The second most common name,

'Forel's field', appeared in only 20 publications, and 'area tegmentalis' in 10. Links in columns 4 and 5 lead to information about an atlas, textbook or article where the term in the first column is used and the species on which that source is based: human, macaque, rat or mouse.



field H

Standard Acronym: **H**

Common English & Latin Names	Language	PubMed Citations	Source	Species
field H	English	218	Carpenter-83	human
field H	English	218	Martin-97	Macaca fascicularis
Forel's field H	English	20	Carpenter-83	human
H field of Forel	English	4	Roberts-70	human
prerubral area	English	6	Heimer-95	human
prerubral field	English	8	Carpenter-83	human
Area tegmentalis	Latin	10	Shantha-68	Macaca fascicularis

Show All English & Latin | Show All Languages | Show Acronyms

Figure 7: BrainInfo lists all English and Latin synonyms for field H that have appeared in PubMed in the past 25 years. By clicking a button below the table one can view *all* English and Latin synonyms, equivalent terms in other languages and acronyms for the structure.

The visitor may wish to ask, 'Is field H located in the diencephalon or the midbrain?" In this case he returns to the central directory for field H and clicks 'Where is It in the Brain?' (Fig. 8). Because field H is a structure in the classical neuroanatomical hierarchy (IANC 1983; Bowden and Martin 1995), clicking 'Where is It?' takes him to the part of the hierarchy that shows field H to be part of the subthalamus (Fig. 9); clicking the arrow in the upper left of the screen reveals that the subthalamus is part of the diencephalon (not shown).

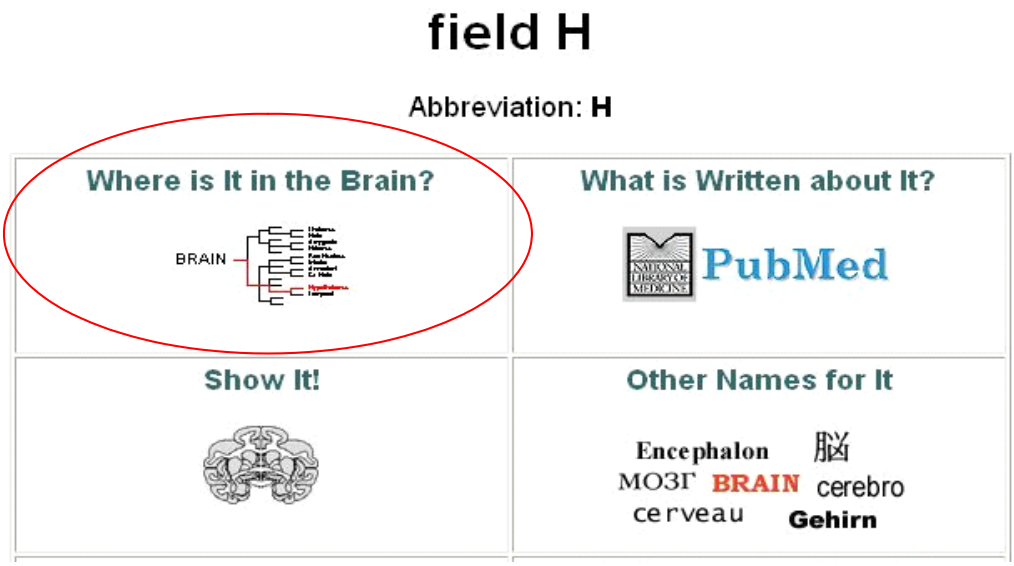


Figure 8: To determine where in the classical hierarchy of brain structures field H is located one clicks 'Where is It in the Brain'.

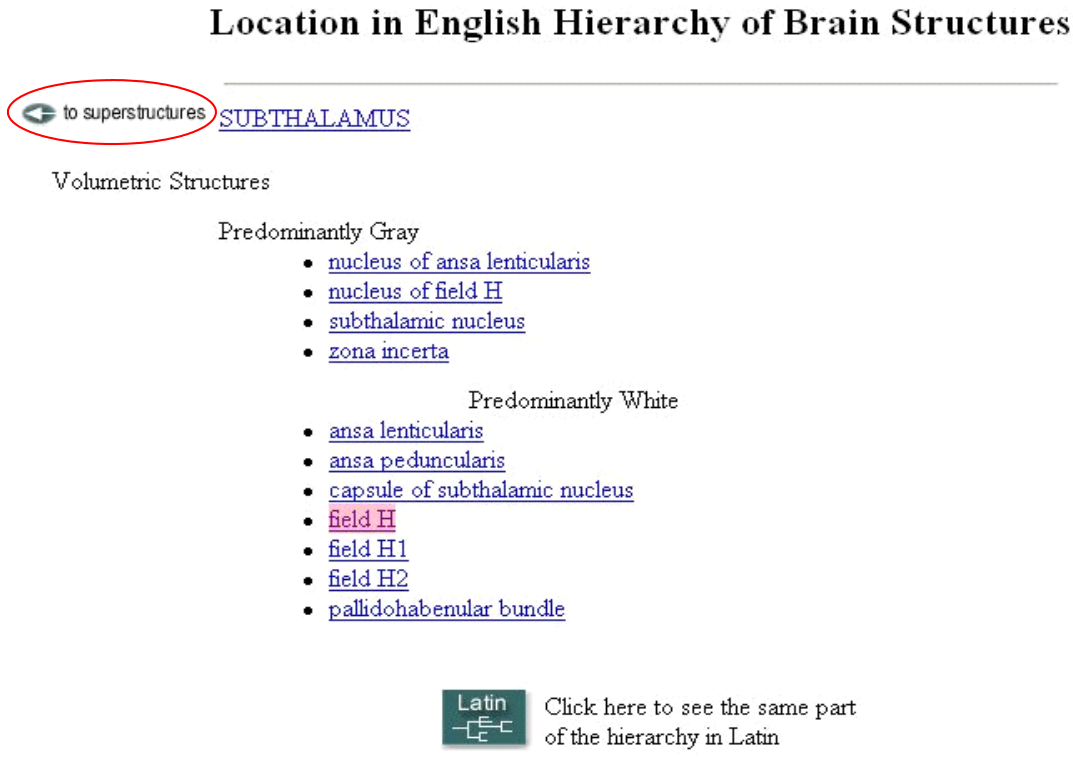


Figure 9: Field H is in the subthalamus. A click on the arrow (upper left) will show the subthalamus to be part of the diencephalon.

Perhaps the visitor has a clinical interest in whether field H (also known as area tegmentalis or the prerubral area) plays a role in brain seizures. If so, he can learn about it by returning to the central directory and clicking ‘What is Written about It?’ (Fig. 10).

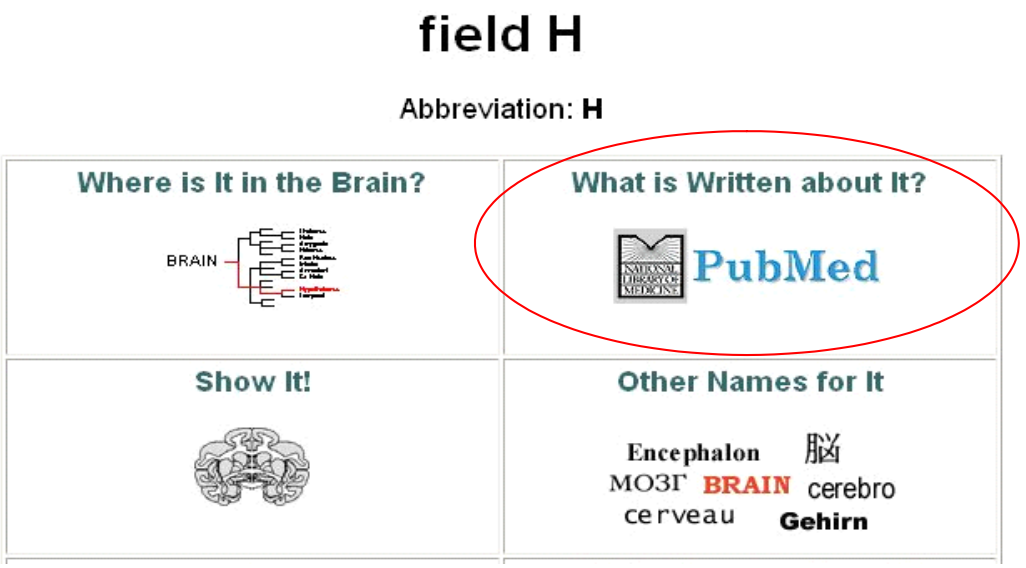


Figure 10: ‘What is Written about It?’ links the visitor to abstracts in PubMed that contain information about field H.

BrainInfo composes a query to PubMed (PubMed 2005) that includes not only the terms ‘field H’ and ‘seizures’, but all of the synonyms of ‘field H’. Thus, the visitor does not need to run separate searches for ‘seizures AND area tegmentalis’, seizures AND prerubral area’, etc.

Figure 11: PubMed displays seven citations about field H and seizures.

The examples presented so far relate to situations in which the investigator seeks information about a structure whose name he knows. BrainInfo can also provide assistance to an investigator who finds gene expression in an unfamiliar area of the brain (Fig. 12)

Figure 12: An investigator found the heaviest stain for type 1 adenyl cyclase in the circled area of the macaque brain (Kumar, Baker et al. 2001). Is it in the dentate gyrus, the hippocampus, or some other part of the hippocampal formation?

To identify such a structure she can go to BrainInfo, select ‘Search Atlas’ (Fig. 13) and select a view of the brain that corresponds to the image, in this case a coronal plane of section (Fig. 14).

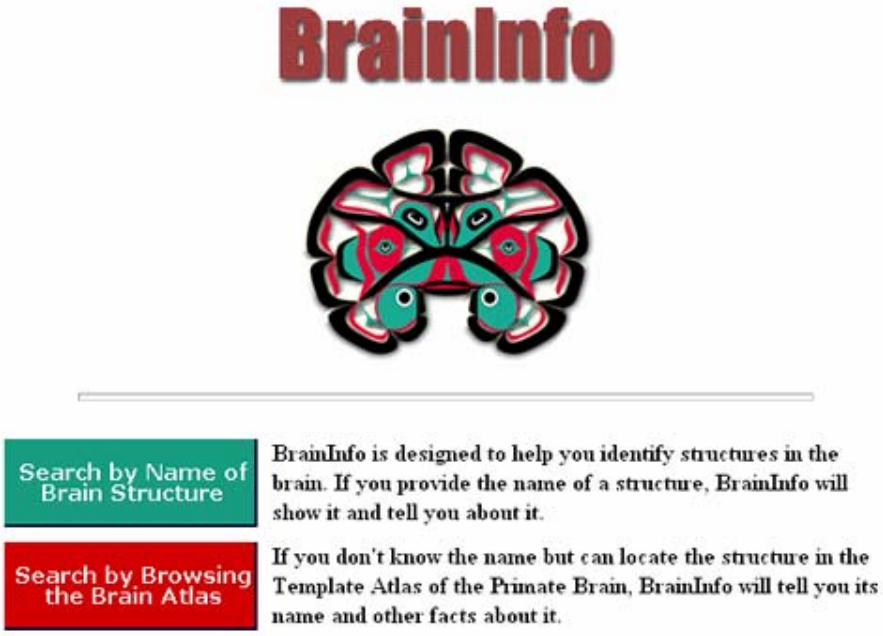


Figure 13: To identify an unfamiliar structure click 'Search by Browsing the Brain Atlas'.

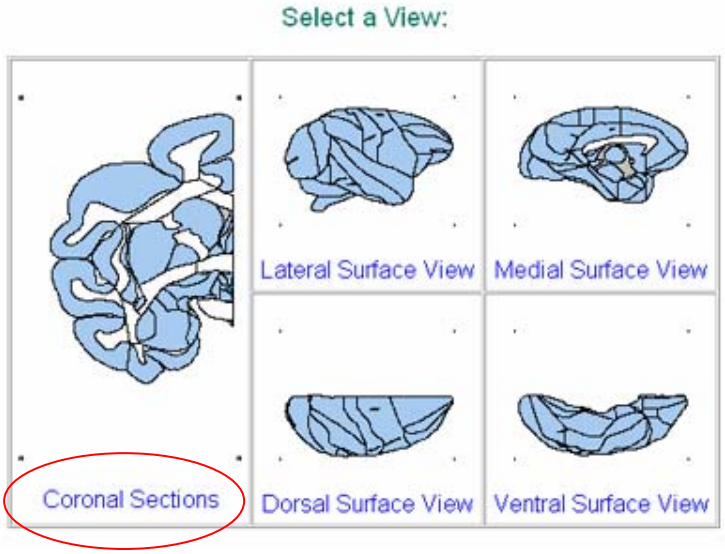


Figure 14: To select from a set of cross-sections one clicks 'Coronal Sections'.

BrainInfo displays thumbnails of cross-sections of a macaque brain from which the visitor selects a section most representative of the experimental section (Fig. 15).

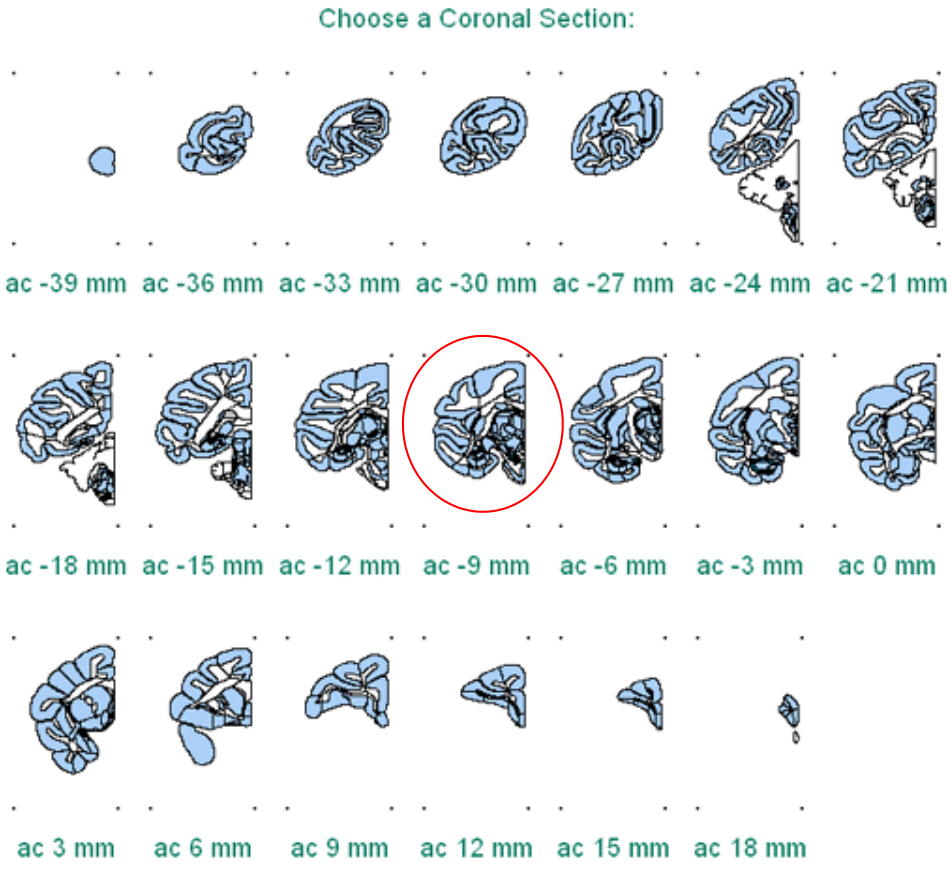


Figure 15: For the example in Figure 12, the experimental slide matches most closely section ac -9, the section 9 mm posterior to the anterior commissure.

The visitor clicks the thumbnail that most nearly matches the experimental section (Fig. 15) and BrainInfo displays an enlarged view (Fig. 16)

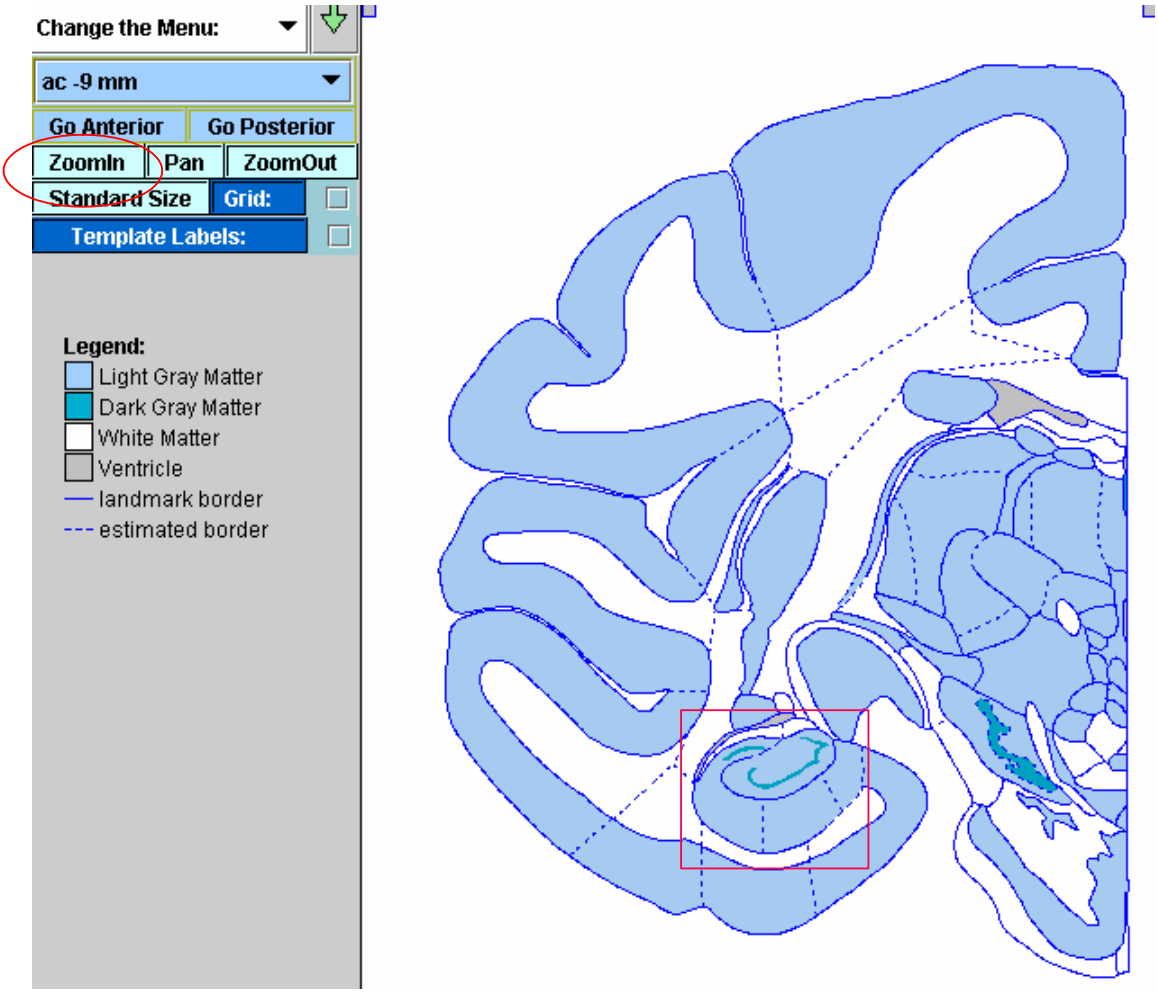


Figure 16: The visitor identifies the structure of interest, clicks 'ZoomIn' (upper left) and clicks-and-drags to produce a box around the area to be enlarged (lower center).

She identifies the area that appeared darkest in the experimental slide in the enlarged image (Fig. 17). It appears to be in the dentate gyrus or the hippocampus. To identify the structure in which it is located she clicks the check-box for Template Labels and finds that the structure where it appears is labeled 'Hi' (Fig. 18).

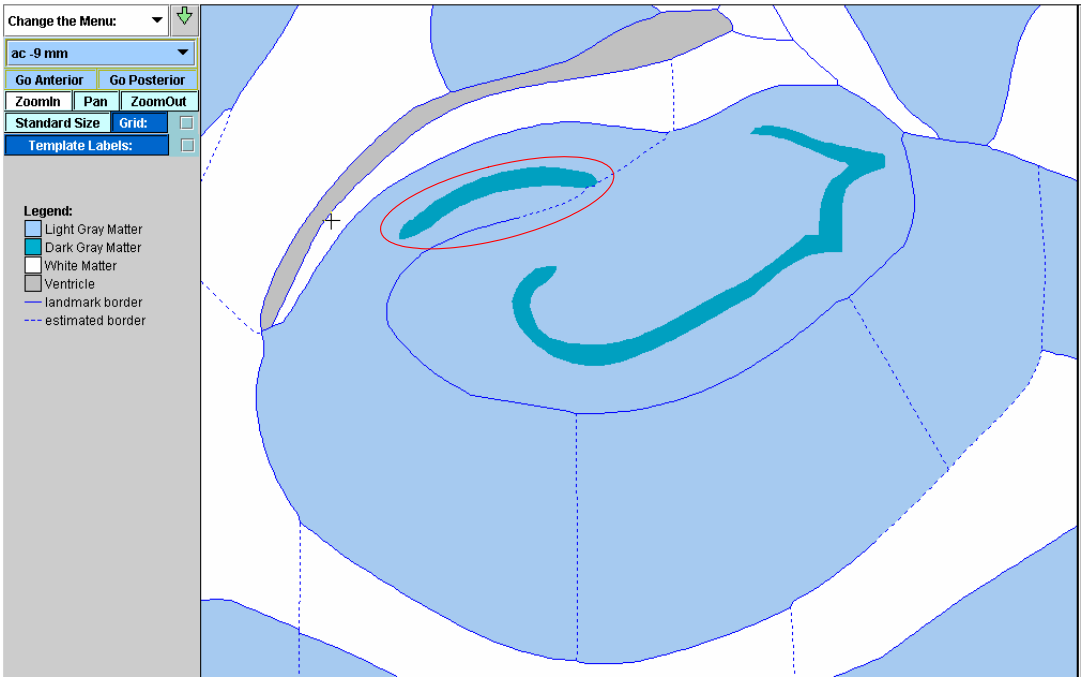


Figure 17: The location of the darkly stained area in Figure 12 corresponds to an area of 'Dark Gray Matter' in the atlas section (red oval).

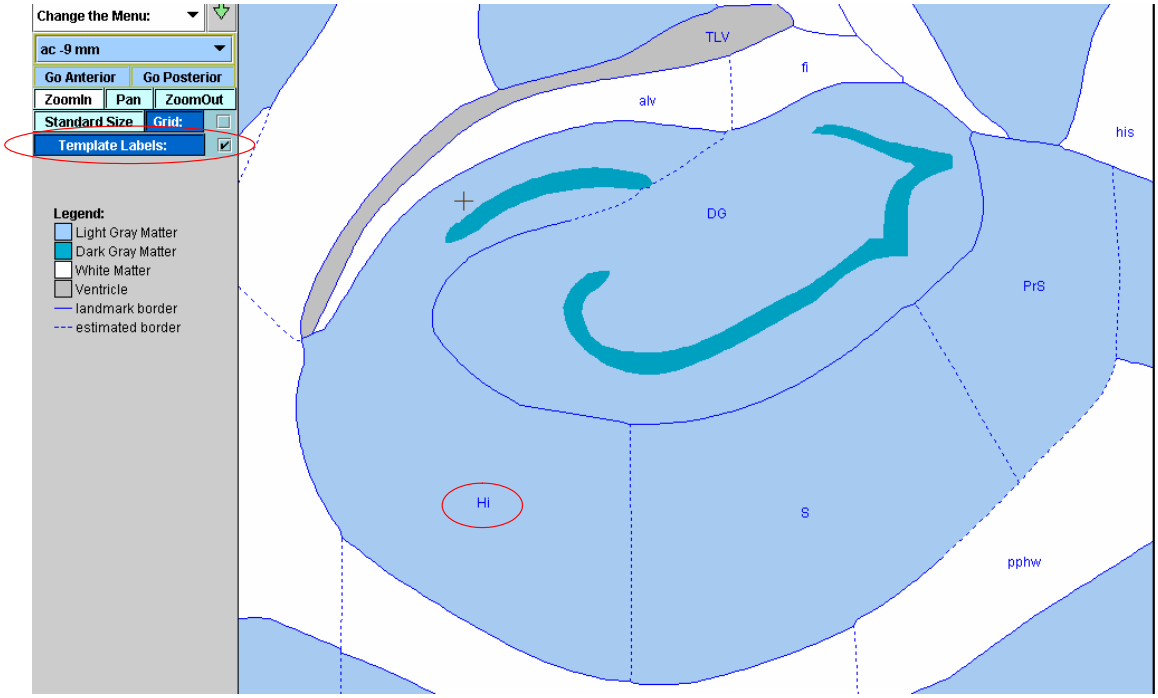


Figure 18: A click next to 'Template Labels' (upper left) shows that the structure is Hi.

To confirm the name of the structure represented by Hi she places the cursor on the label and sees the full name, hippocampus (Fig. 19).

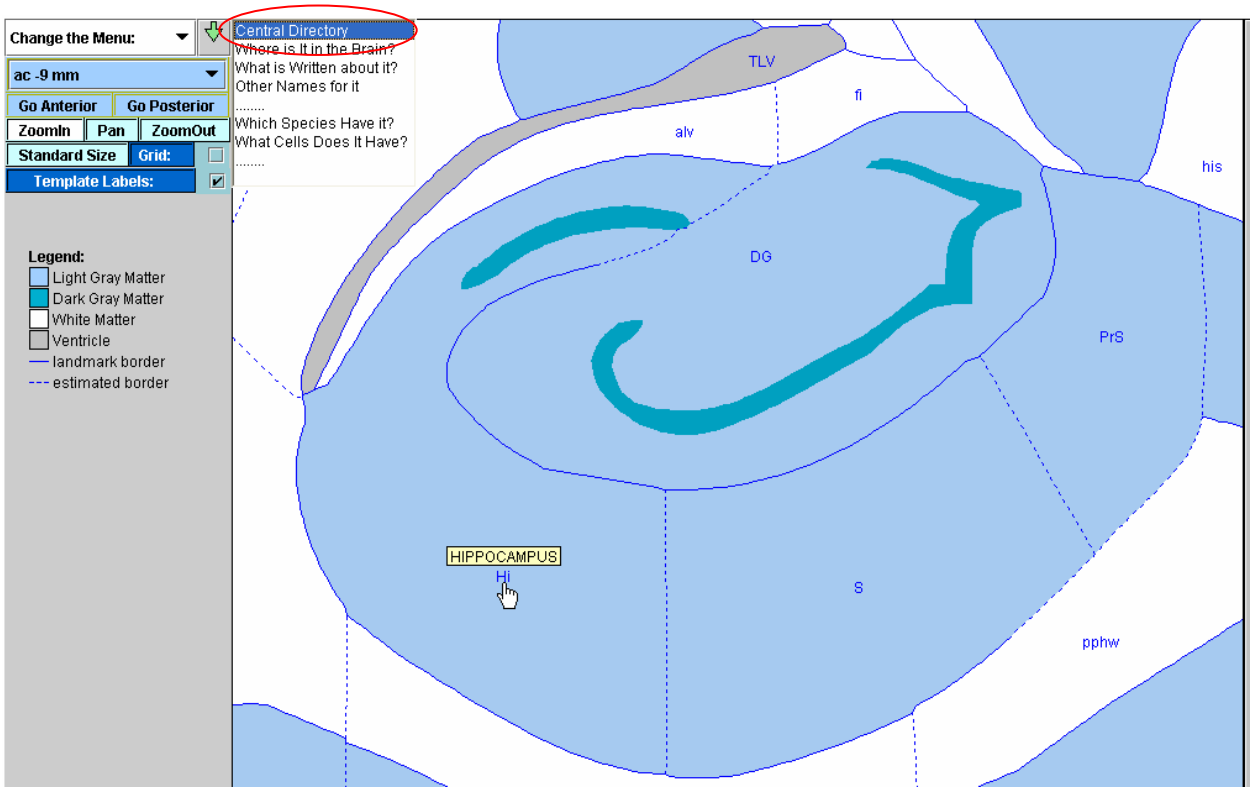


Figure 19: Placing the cursor on a label reveals the full name of a structure.

To find out more about the hippocampus, she clicks the label ‘Hi’. BrainInfo displays a message box in the upper left corner that lists the kinds of information available. Clicking ‘Central Directory’ takes the visitor to the same page she would find if she conducted a Search by Name for ‘hippocampus’ (Fig. 20).

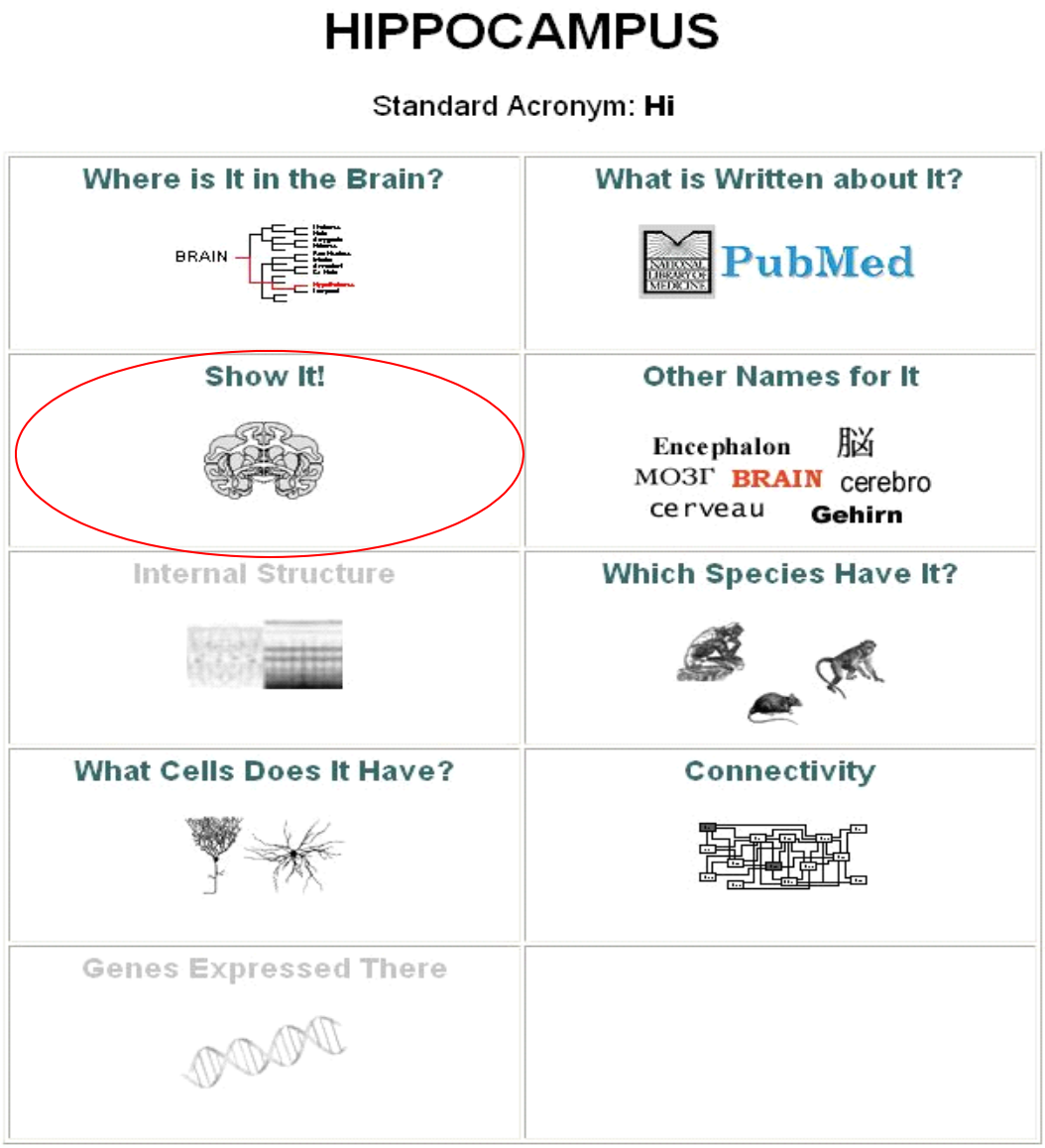


Figure 20: BrainInfo's Central Directory for the hippocampus.

If the visitor wishes to see other illustrations of the hippocampus, she clicks 'Show It!' for a page of thumbnails that shows the choices available (Fig. 21).

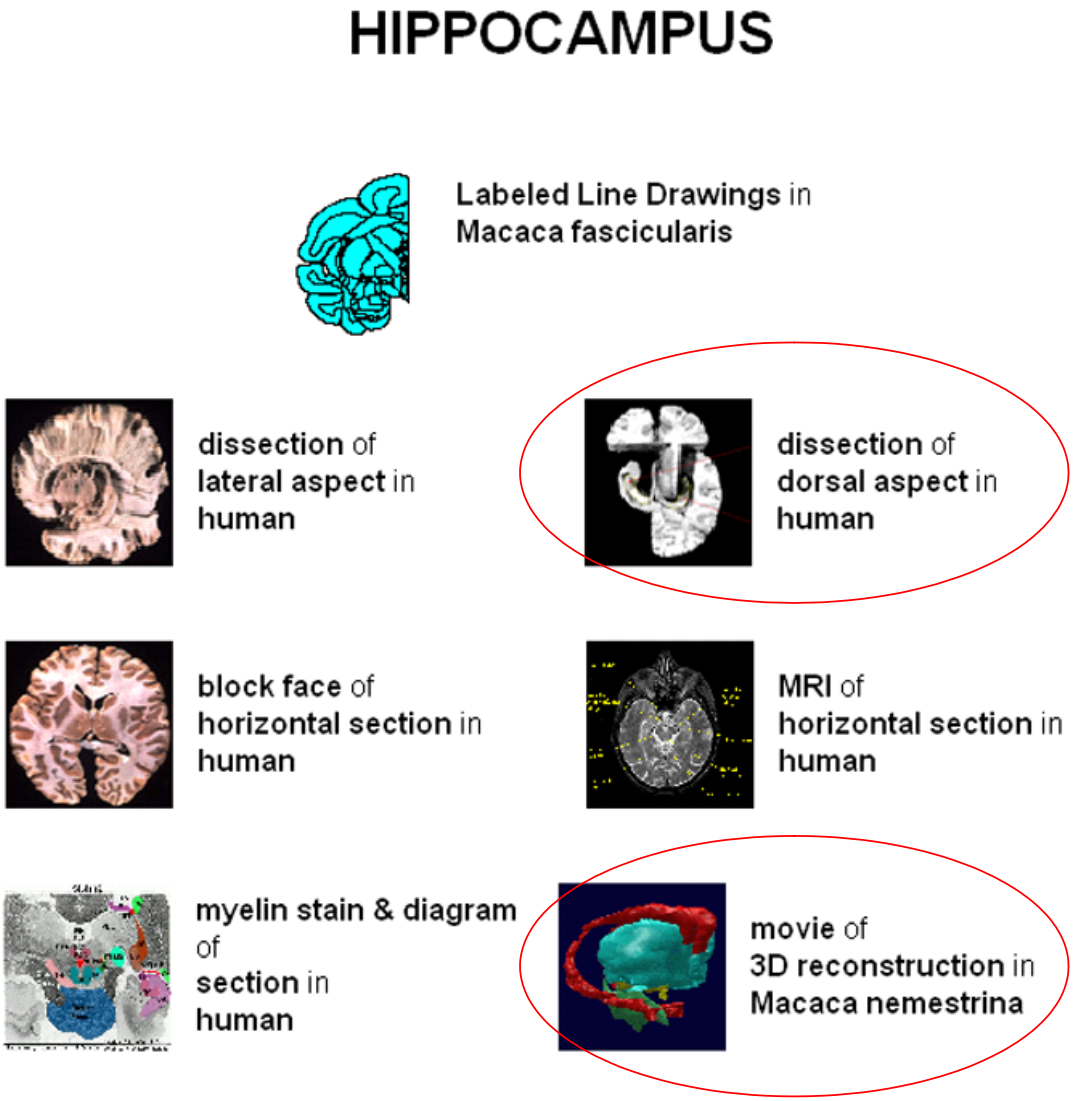


Figure 21: Thumbnail images that link to illustrations of the hippocampus at other websites.

If she clicks to see a dissection of the hippocampus in the human brain (Fig. 21, upper right), BrainInfo takes her to the page in the Digital Anatomist (DigitalAnatomist 2005) a different website at the University of Washington. If she elects to see a movie of the hippocampus and related structures rotating in space, she clicks the corresponding thumbnail (Fig. 21, lower right) and BrainInfo sends her to a website at the Laboratory of NeuroImaging at UCLA (LONI 2005).

A visitor interested in learning the kinds of neurons found in the hippocampus clicks 'What Cells Does It Have?' in the central directory (Fig. 20). BrainInfo sends her to the Cell Properties Database at Yale University (SenseLab 2005) where she can explore the neurophysiological and neurochemical characteristics of three cell types (Fig. 22).

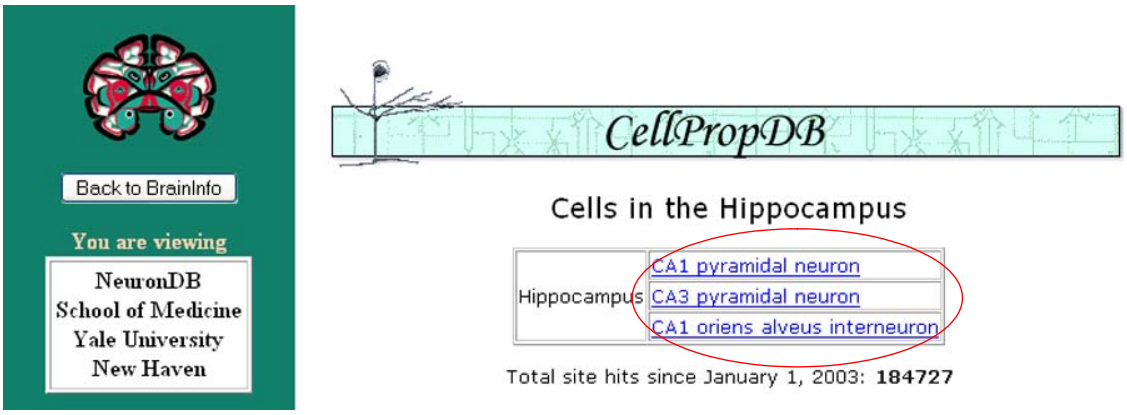


Figure 22: The cell properties part of the neuron database at Yale University provides highly detailed information about three kinds of cell found in the hippocampus.

If the visitor is interested in connections of the hippocampus with other brain structures, she clicks 'Connectivity' in the Central Directory (Fig. 20) and BrainInfo sends her to the Brain Architecture Management System at USC (BAMS 2005) (Fig. 23).

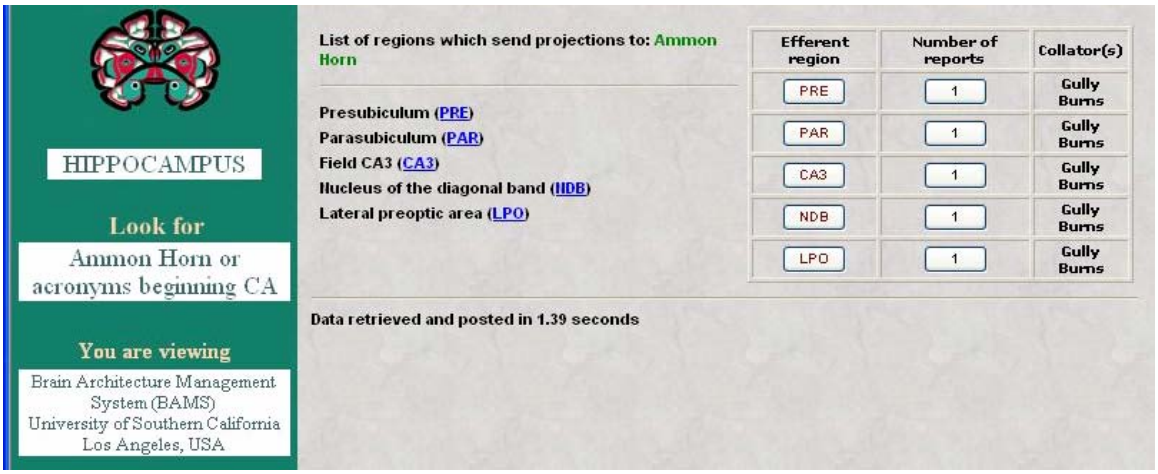


Figure 23: The Brain Architecture Management System at USC provides detailed information about afferents to the hippocampus in the rat.

One can access illustrations of the internal, architectonic structure of many cortical areas of the macaque through BrainInfo. For example, to see photomicrographs of area 4 of Brodmann, one conducts a 'Search by Name' and clicks 'Internal Structure' in the Central Directory for area 4 (Fig. 24).

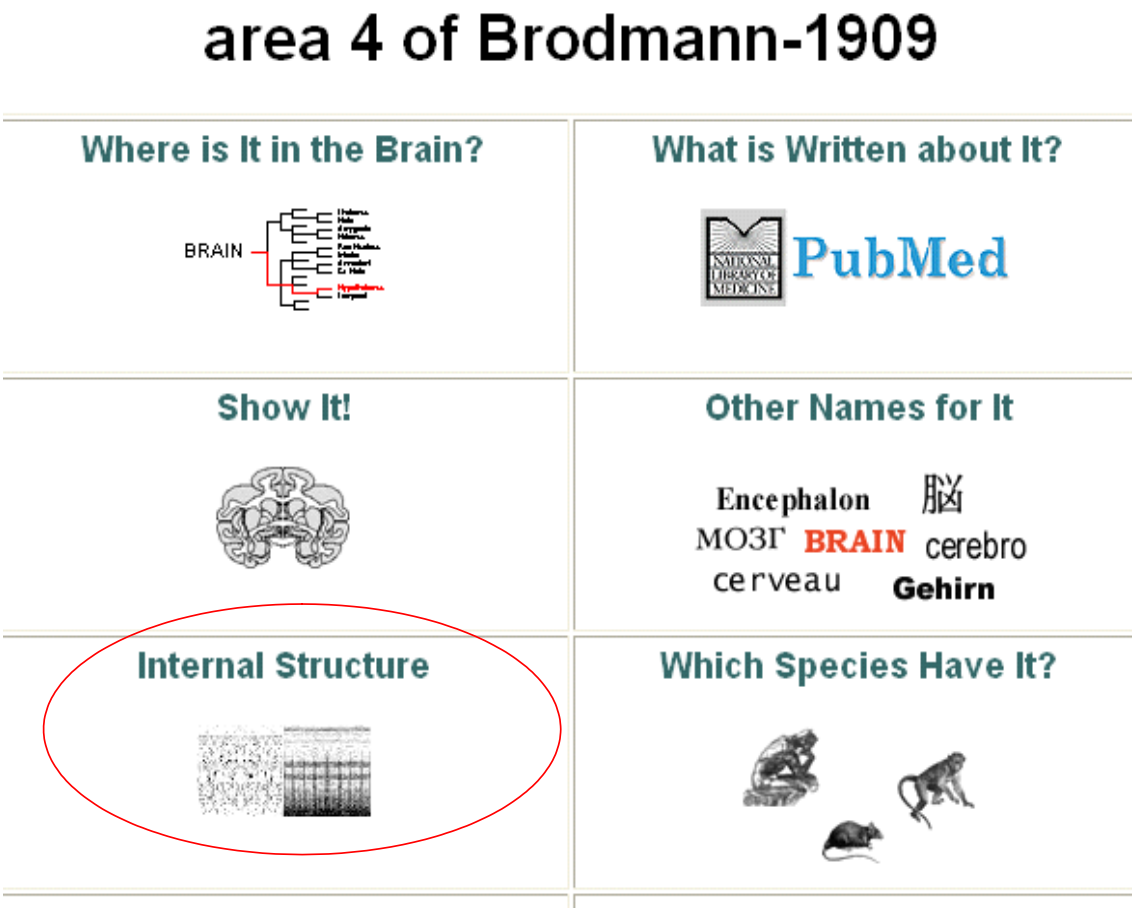


Figure 24: BrainInfo's Central Directory for Brodmann's area 4 in the macaque.

BrainInfo displays a number of thumbnails of Brodmann's area 4, some published by other authors under different acronyms (Fig. 25).

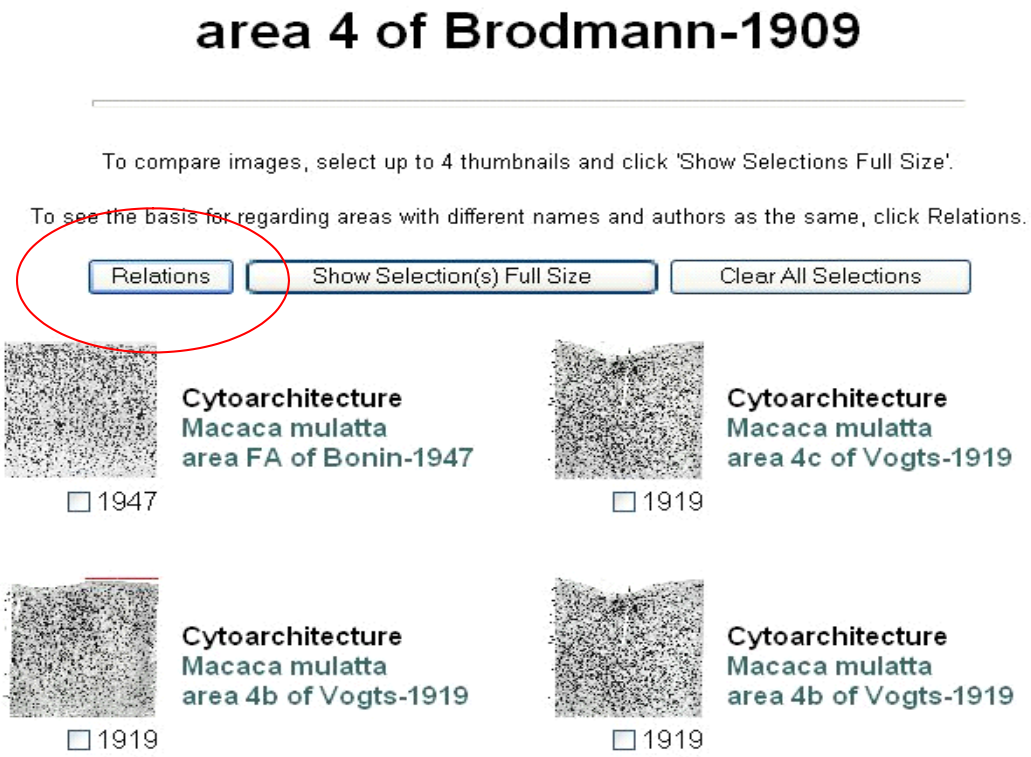


Figure 25: Thumbnail images of a few of the photomicrographs of area 4 that one can select for comparison; the images appear in reverse chronological order.

To determine how the areas illustrated by other authors relate to Brodmann's area 4, one clicks 'Relations' and a message box appears (Fig. 26).

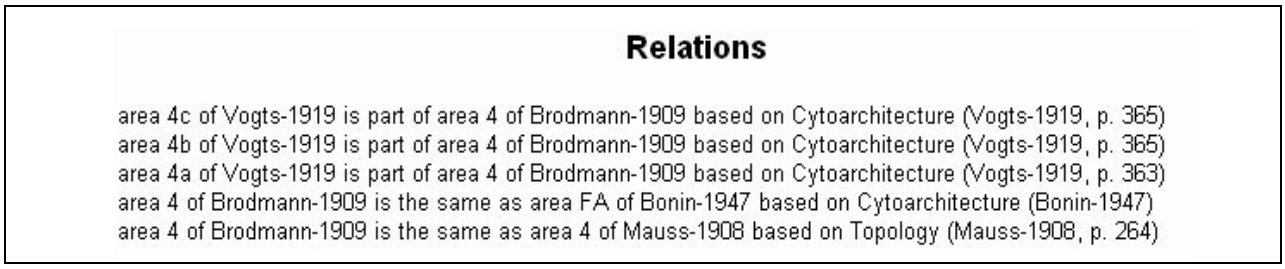


Figure 26: The 'Relations' message box gives the publications and page numbers where authors stated the relations of Brodmann's area 4 to cortical areas with other names.

BrainInfo also provides another useful approach to comparison of cortical areas defined by different investigators. Area 46 of Walker-1940, for example, occupies a portion of the frontal lobe segmented in different ways by different authors. If a visitor goes to the Central Directory for 'Walker's area 46' and clicks 'Show It!' BrainInfo displays a lateral cortical view of the macaque brain to which Walker's area 46 has been mapped (Fig. 27).

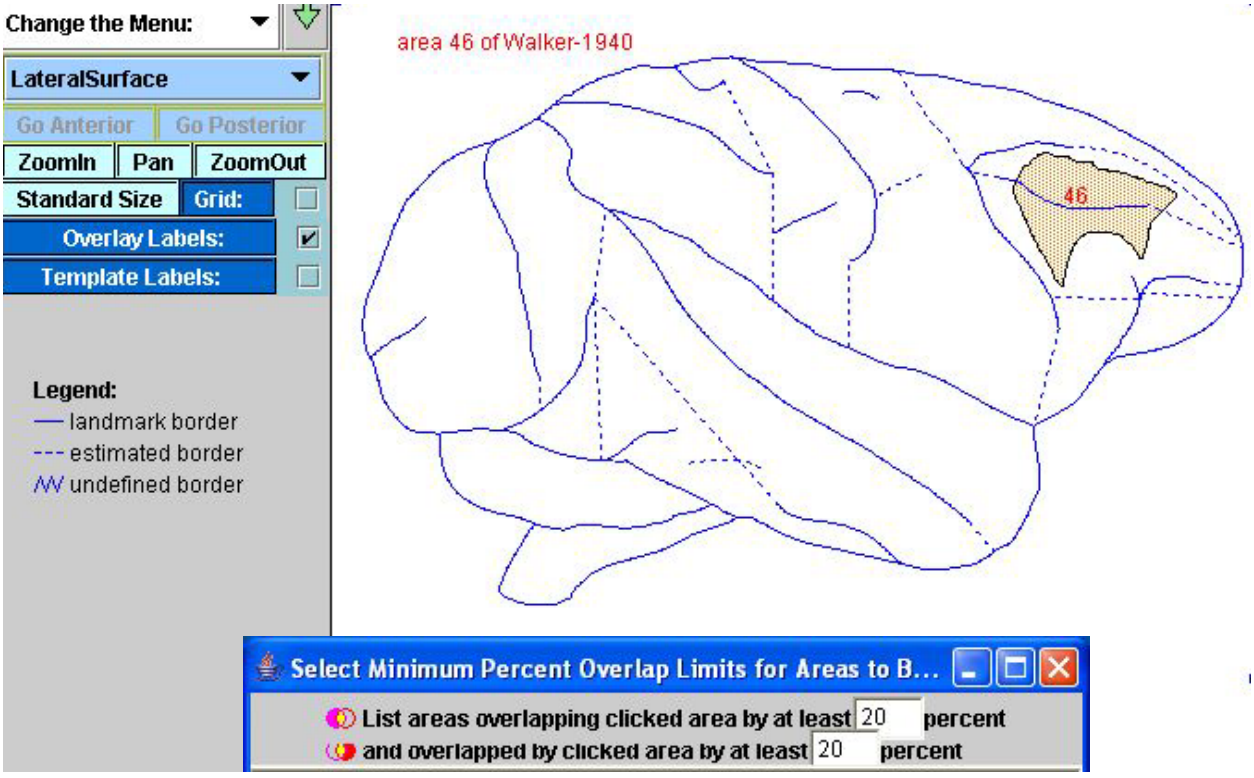


Figure 27: Walker's area 46 mapped to a lateral view of the macaque brain. The message box at the bottom of the screen allows one to specify the minimum degree of overlap that is of interest between area 46 and any other structure.

The visitor clicks in succession: 'Change the Menu' (Fig. 27; upper left), 'Overlaps Menu', and 'Overlay' to obtain a cursor that will allow him to select the area, in this case area 46, that he wishes to compare with other areas defined by different authors in the same region. The visitor specifies in a message box the minimum percent overlap between area 46 and other areas that must pertain to be of interest (here 20%). When he clicks in area 46 a box appears in the lower left corner of the screen listing all areas mapped to the same cortical view that overlap area 46, or are overlapped by area 46, by 20% or more (Fig. 28).

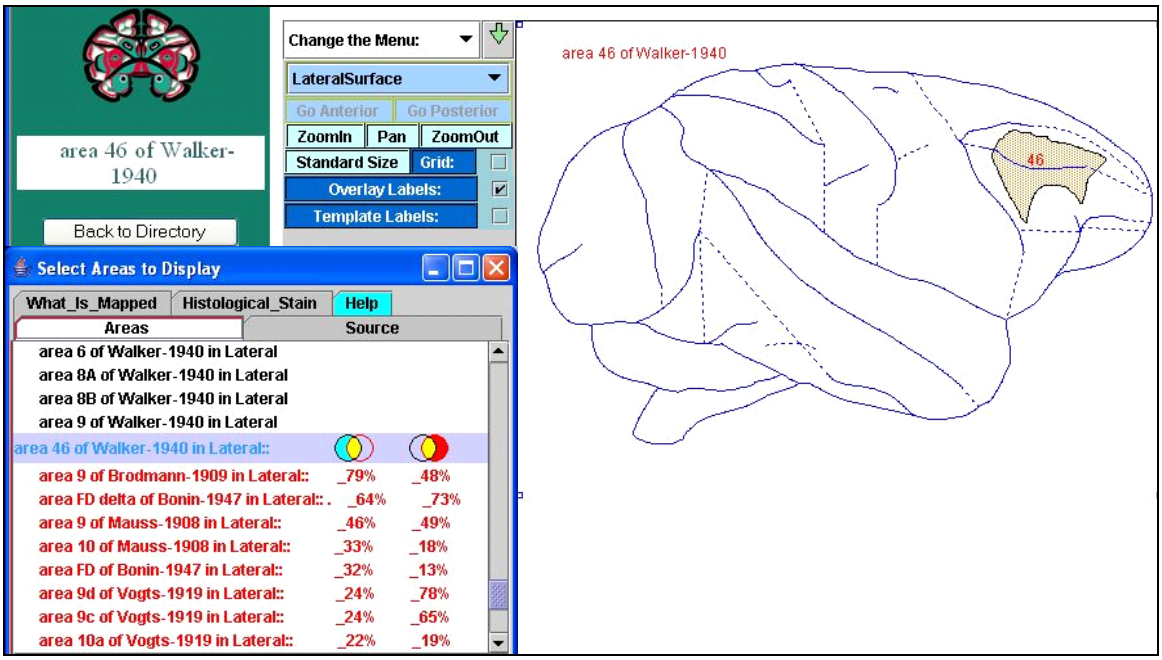


Figure 28: A box labeled 'Select Areas to Display' shows the index area in purple (here area 46 of Walker-1940) and, in red, all areas that overlap area 46 by 20% or more.

To visualize the overlap with another cortical area, such as Brodmann's area 9, he presses the Control Key and clicks the name of the second structure in the box labeled 'Select Areas to Display'. He finds that while most of area 46 (79% in the table) overlaps area 9, less than half of area 9 (48%) overlaps area 46 (Fig. 29).

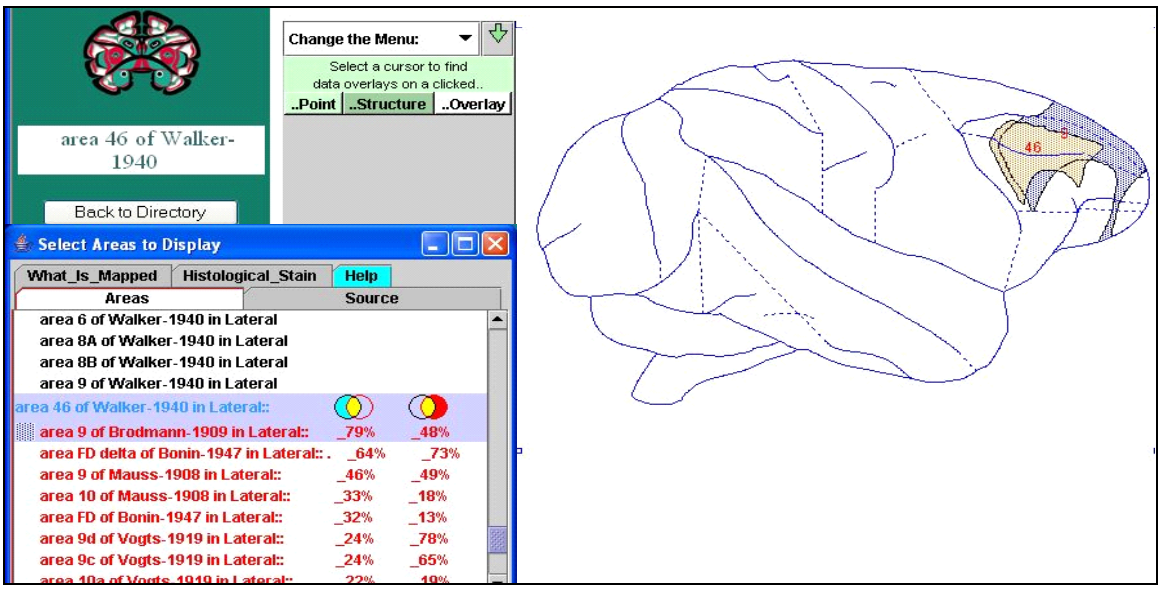


Figure 29: Area 9 of Brodmann-1909 overlaps Walker's area 46 but appears to involve a greater portion of the frontal pole.

To compare area 46 with another area, say area FD delta of Bonin-1947, the visitor presses the Control Key clicks area 9 in the 'Select Areas' box to turn it off and clicks area FD for display. He finds that the boundaries of area 46 with area FD (Fig. 30) are more nearly coincident than with area 9 (Fig. 29); this would suggest that Walker's area 46 and von Bonin and Bailey's area FD delta more likely represent the same cortical 'structure' than Walker's area 46 and Brodmann's area 9. One can test this hypothesis by examining the architecture of the three areas.

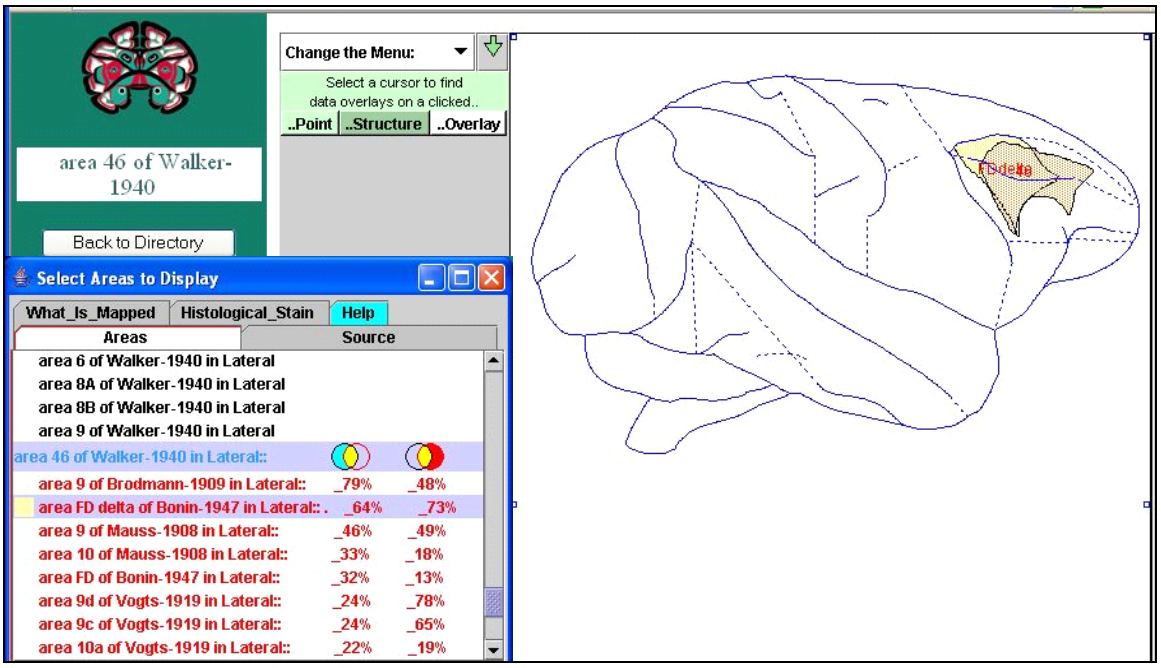


Figure 30: The boundaries of area 46 are more nearly coincident with those of area FD delta shown here than with those of area 9 shown in Figure 29.

To view the architectonic structure of area 46 and related areas without losing the screen display of overlaps, the visitor opens BrainInfo again in a new window, navigates to the Central Directory for area 46 of Walker and clicks 'Internal Structure' (see Fig. 24). He clicks to select thumbnail images of the photomicrographs he wants to compare and clicks 'Show Selection(s) Full Size' (see Fig. 25).

The source of each photomicrograph is identified by placing the cursor over it (Fig. 31). For detailed visual comparison he can click-and-drag individual images into proximity.

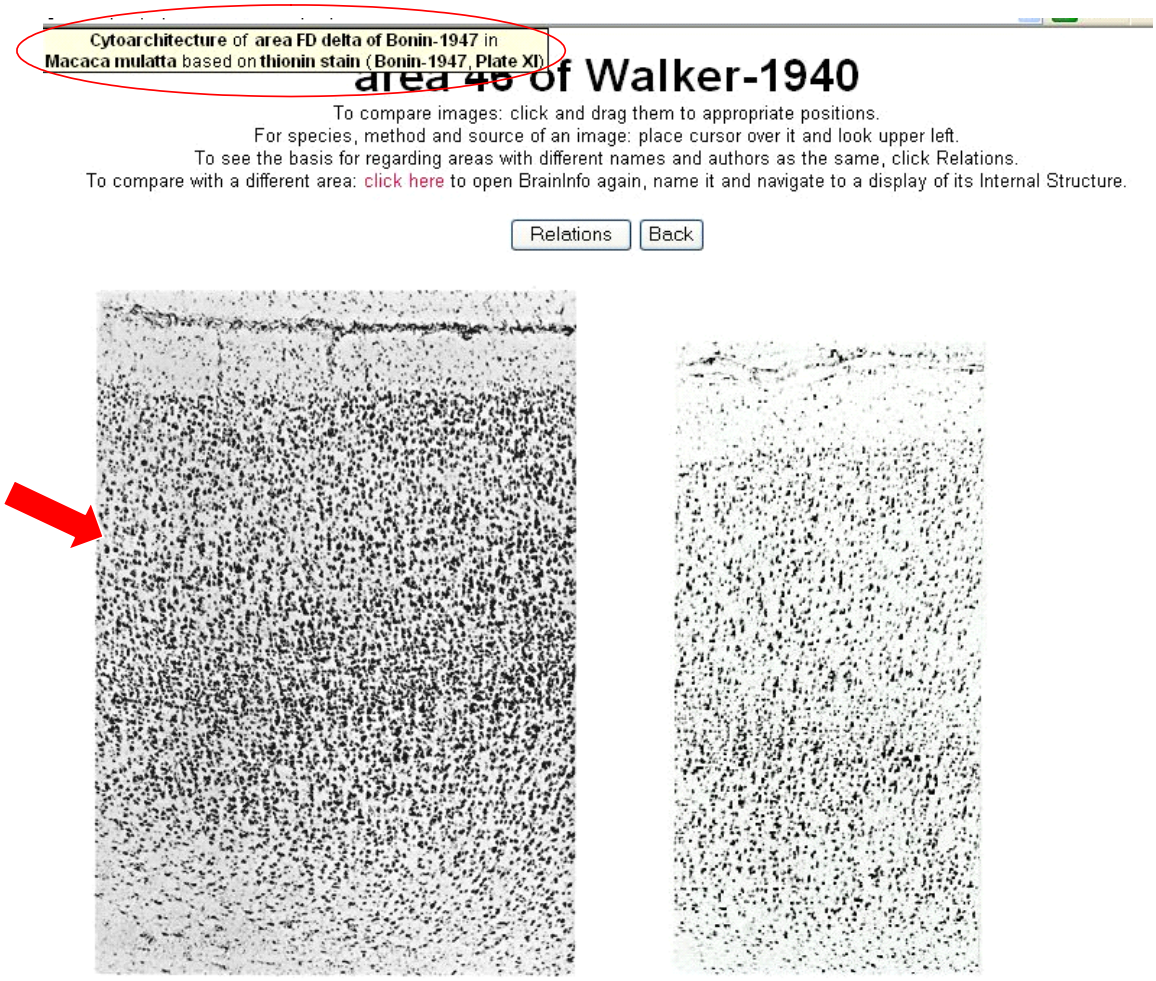


Figure 31: For the name of the cortical area, species, stain, author, and source of a photo one moves the cursor (red arrow) over it and reads the message box (upper left).

Discussion

BrainInfo (2005) is a public repository and portal to neuroanatomical information on the Web. Its power as a rapid purveyor of detailed information about the brain is based on a unique combination of a text/numeric object-oriented database (SQL), a geographic information systems (GIS) image database and a webserver (IIS powered by asp.net on an MS Windows 2000 server). In contrast to many neuroscientific web resources, it allows visitors to locate information by navigating intuitively according to the logic of neuroscientific inquiry as opposed to navigating the websites organized as virtual libraries. In BrainInfo users go directly from the home page to the information they seek without having to pick their way through a series of menus and site maps wondering whether the information exists at the site and guessing where therein it may be

located. They need not learn how the site is organized, because a structured ontology based on NeuroNames (Bowden and Martin 1995; Bowden and Dubach 2003) and a Template Atlas of the primate brain (Bowden and Martin 1992; Martin and Bowden 2000) allow the indexing of text and image information at an unmatched level of detail. Once users have found the specific information they seek, the system assists them in going directly to the next information they are likely to want, seamlessly and transparently, regardless of whether the next information is on the same server or on a server thousands of miles away.

BrainInfo is also unique in that a query to Google (2005) about any one of some 2000 neuroanatomical names that have appeared in one or more PubMed (2005) citations in the past 25 years produces a listing with a link to BrainInfo on the first page (Fig. 2). BrainInfo extends the indexing power of search engines like PubMed and Google by applying semantic search strategies based on a systematic ontology of more than 14,000 names and 1500 acronyms for more than 2,400 neuroanatomic concepts defined in terms of some 500 primary structures of the human and nonhuman primate brain.

The system addresses directly the challenge that, in neuroscience above all, images are as important for communication as words and numbers. The neuroanatomical coordinates of data in a standard, stereotaxic space is as important an indexing attribute as its name in a standard, controlled vocabulary. BrainInfo is designed to provide direct access to every kind of textual and image data that is usefully indexed to primary structures of the mammalian brain, from MRI activation to cell types to histological evidence of gene expression.

BrainInfo enables web access to images of original data, such as photomicrographs of the internal structure of cortical areas published by multiple authors over many decades. A visitor to BrainInfo can display multiple images on a screen, click and drag them to optimal positions for visual comparison and, if they are named differently, identify the original authors' reasons for regarding them as equivalent (Fig. 26). In addition, BrainInfo enables one to view hundreds of surface views of cortical areas extracted from the literature and mapped to standard views of the brain, to compare their locations and shapes visually and to obtain a quantitative measure of their overlap.

Table I: Websites to which BrainInfo serves as a portal.

- Currently
  - Brain Architecture Management System (BAMS, USC)
  - Brain Atlases (UC Davis)
  - Digital Anatomist (U Washington)
  - Human Neuroanatomy (Loyola U)
  - Laboratory of Neuroimaging (LONI, UC Los Angeles)
  - Neuron Database (Yale U)
  - Van Essen Lab (Washington U, St Louis)
  - Virtual Hospital (U Iowa)
  - Whole Brain Atlas (Harvard U)
- In Progress
  - Allen Brain Atlas (Allen Brain Institute, Seattle)
  - Cell Centered Database (BIRN, UC San Diego)
  - CoCoMac (H Heine U, Duesseldorf)
  - Functional MRI Database (fMRIDC, Dartmouth U)
  - GenSAT (Rockefeller, NIH)

In 2004, BrainInfo, in addition to providing access to its own macaque brain database, served as a portal to information at nine different websites and was preparing to link into five others (Table 1). An average of 240 visitors per day downloaded more than 10,000 pages per day.

Acknowledgments

The authors express great appreciation to Hwa Jun (Evan) Song for his dedicated and creative approach to development of the BrainInfo website, and to Erik MacArthur and Andra Erickson for mapping data from the literature into the image database. Development of the system is supported by grants from the National Library of Medicine (LM06243), the Human Brain Project/NIMH (MH069259; and the National Center for Research Resources (RR-00166) to the University of Washington.

References

BAMS (2005). Brain Architecture Management System. Neuroscience Program, University of Southern California, Los Angeles: http://brancusi.usc.edu/bkms.

Bota, M., H. Dong, et al. (2003). "From gene networks to brain networks." Nature Neuroscience **6**(8): 795-9.

Bowden, D. and M. Dubach (2003). "NeuroNames 2002." Neuroinformatics **1**: 43-59.

Bowden, D. M. and R. F. Martin (1992). A comprehensive computerized hierarchical nomenclature for structures found in the human and nonhuman primate brain. WA/Regional Primate Research Center, Seattle, WA.

Bowden, D. M. and R. F. Martin (1995). "NeuroNames brain hierarchy." Neuroimage **2**: 63-83.

BrainInfo (2005). BrainInfo: A Portal to Neuroscience on the Web. Neuroscience Division, NPRC, University of Washington, Seattle: http://braininfo.rprc.washington.edu.

DigitalAnatomist (2005). The Digital Anatomist Information System. Structural Informatics Group, Dept. of Biological Structure, University of Washington, Seattle: http://sig.biostr.washington.edu/projects/da.

Google (2005). Google Search. http://www.google.com.

IANC (1983). Nomina Anatomica. Baltimore, MD, Williams and Wilkins.

Kumar, P., L. Baker, et al. (2001). "Expression of type 1 adenylyl cyclase in intrinsic pathways of the hippocampal formation of the macaque (Macaca nemestrina)." Neuroscience Letters **299**: 181-184.

LONI (2005). Laboratory of Neuro Imaging. Dept. of Neurology, UCLA, Los Angeles: http://www.loni.ucla.edu.

Martin, R. and D. Bowden (2000). Primate Brain Maps: Structure of the Macaque Brain. Amsterdam, Elsevier.

PubMed (2005). Entrez PubMed. National Library of Medicine, Bethesda: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi.

SenseLab (2005). SenseLab: Cell Properties Database. Dept. of Neurobiology, Yale University, New Haven: http://senselab.med.yale.edu/senselab.