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# BrainMap: A Database of Human Functional Brain Mapping

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#### 1. Introduction

The human functional brain-mapping community has a clear need for data visualization, data management, and data sharing. The computational and structural complexity of the human brain poses an unprecedented scientific challenge. As more and more laboratories accept this challenge, keeping abreast of the field has become difficult. Unwitting duplication of experiments on human subjects is wasteful preventable only through rapid dissemination of new findings. Electronic communication can provide a solution.

Human brain mapping is performed by several techniques. These include positron-emission tomography (PET), magnetoencephalography (MEG), electroencephalography (EEG), and functional magnetic resonance imaging (MRI). For localization of function, "PET has provided the best and most complete information on human functional brain organization" (Pechura and Martin, 1991). The reasons for this are several. Modern PET cameras have a field of view spanning the entire brain, with pixel sizes of 1-2 mm, slice widths of 3-6 mm, and spatial resolution of 4-6 mm. PET data are acquired in spatially precise twoor three-dimensional arrays. Activated neural populations can be localized to within a few millimeters (Fox et al., 1986; Mintun et al., 1989). Unlike MEG and EEG dipole localization by inverse solution, PET is equally precise for any number of focal activations. Because PET can scan the entire brain in as little as 40 s, study a new behavioral condition every 10 min, and study numerous (8 to 10) behaviors in a single session, behaviorally sophisticated paradigms are widely used. PET's spatial precision, versatility, and paradigm sophistication have made PET the gold standard for functional brain mapping.

The PET brain-mapping literature is an obvious starting point for a database of human functional neuroanatomy. The field is sufficiently mature that methods for data analysis and a system for reporting of activated locations have become standardized (below). Application of these standards is almost universal (for functional activation studies), greatly facilitating database development. Although rich, the PET literature based on these standards is still of a manageable size, making this an opportune time for a database initiative. Finally, the technical evolution of other brain-mapping methods is quite rapid. The human brain-mapping literature will soon be in a phase of explosive growth. In developing a database for PET brain-mapping research, we will at least provide a model for database initiatives in other modalities. With sufficient forethought, BrainMap may even prove applicable to all modalities of human functional brain mapping, unifying these diverse communities.

# II. Methodological Standards of the PET Brain-Mapping Community

In the PET brain-mapping community, standard methods for data analysis, data reduction, and data

publication have evolved. Although methods are not identical among centers, differences are rather minor. These standards make communication among laboratories quite precise. Results from different laboratories can be compared and contrasted (i.e., meta-analyzed) quite meaningfully. These standards are the foundation upon which the BrainMap database has been erected.

#### A. The Bicommissural Coordinate Space

Bicommissural coordinates have become an international standard for reporting PET functional brain mapping. Virtually all PET brain-mapping laboratories now use bicommissural coordinates as their "least common denominator" for reporting locations of brain activation. The bicommissural coordinate space is defined by three orthogonal planes: the midsagittal plane, the plane through the anterior and posterior commissures and orthogonal to the midsagittal plane, and the plane through the anterior commissure and orthogonal to the prior two planes. Following alignment with these planes, a brain image is scaled along each axis to the dimensions of a standard brain (Fox et al., 1985, 1988; Friston et al., 1989; Talairach et al., 1967; Talairach and Tournoux, 1988). After it is "warped" into the bicommissural space, each point in a brain image is labeled by an x-y-z address referable to the atlas brain.

Using coordinates to describe brain location is counterintuitive to many outside the field. Yet, the alternatives are limited. The most precise neuroanatomical methods are histological: cytoarchitectonics, myeloarchitectonics, connectivity, and histochemistry. With few exceptions—the stria of Genari can be seen on high-resolution MRI-histology is beyond the resolution limits of noninvasive imaging. Surface features (sulci and gyri) can be visualized by 3D rendering of anatomical images (MRI or X-ray computed tomography, CT). Cortical infoldings, however, vary among individuals in number, shape, and location. Although primary sensory and motor areas are typically localized to the bank of a primary sulcus, whether any consistent relationships exist between cortical folding patterns and higher-order cortical areas remains to be proved. Bicommissural coordinates ignore surface anatomy. Locations are described within a Cartesian space-bounded by the overall shape of the brain. Intersubject variations in folding patterns and in the relation of functional areas to folding patterns introduce random noise, but do not systematically bias localization descriptions. Noise limits the ability to predict functional areas in individual subjects, but does not prevent applying parametric statisfics on groups of subjects. The effective use of bicommissural coordinates for intersubject averaging confirms that these variations are spatially random (Fox et al., 1988; Lueck et al., 1989).

The precision, objectivity, and wide use of bicommissural coordinates greatly simplify the task of developing a database of human brain mapping. Brain locations can be addressed without the ambiguities of conventional terminology (below). Voxel-based image analysis (below) complements the use of bicommissural coordinates. Together, these methods are highly suited to database use.

# B. Voxel-Based Analytic Methods

The purpose of voxel-based image analysis is to determine the brain areas participating in a behavior in as precise and unbiased a manner as possible (Fox, 1991). Abandoning the traditional strategy of limited sampling (defining certain areas as being "of interest"), voxel-based methods analyze every volume element (voxel) within a dataset (50,000 values, or more). Although computationally intensive, these methods optimize the precision with which activated populations can be localized.

Image subtraction is the simplest voxel-based method. Pairs of images (task and control) are subtracted to create images of task-induced change. By registering images within the bicommissural coordinate space, multiple pairs of images (e.g., from several subjects) can be simultaneously analyzed, either as images of regional change or by computing "I" statistics, "z" scores, "p" values, or other statistical parameters images (Friston et al., 1989). In images of regional change and related parameters, areas of neural activation appear as clusters of changed pixels (increased or decreased blood flow). The shape of an activated cluster approximates a 3D Gaussian, largely reflecting the spatial blurring of the image-reconstruction filter. Response locations are reported as the center of mass of these clusters.

Voxel-based analysis and center-of-mass localization are more precise than image resolution, so-called "hyperacuity" (Vernier acuity) (Fox et al., 1986; Mintun et al., 1989). For within-subject comparisons, even of averaged images, neural populations only a few millimeters apart can be separately localized with subtractive logic (Fox et al., 1986). Comparisons of different groups of subjects are based on location coordinates, adding noise and increasing the variance (above). Among subjects, functional areas typically vary in location by less than a centimeter (Fox et al.,

1986, 1987). The combined use of voxel-based analysis and bicommissural coordinates provides efficient data reduction. An entire change-image array is reduced to a few hundred centers of mass. Each center is described by an x-y-z address and a magnitude expressed as percentage change, z score, or other statistical parameter.

### C. Applicability of PET Methods to Other Human Brain-Mapping Techniques

PET brain-mapping standards promise to be surprisingly adaptable to other brain-mapping modalities. MRI brain mapping already uses voxel-based analyses, including image subtraction and imaging of statistical parameters. Using bicommissural coordinates poses no difficulty for MRI. Studies using this approach have already appeared (Belliveau et al., 1991). EEG and MEG are more problematic, as these data types are not readily placed in tomographic or volumetric spatial arrays. Even within-subject coregistration to anatomical images (e.g., MRI and X-ray CT) does not fully resolve this problem. Increasing the number of channels (e.g., to 64 or 128) and applying accurate head models will be needed to create spatially precise data. After this is accomplished, transformation into bicommissural coordinates is quite simple.

# III. Design Goals

The first step in building a database is to establish design goals. The purpose of the BrainMap database is to promote the user's ability to understand the functional anatomy of the human brain through rapid, exhaustive access to image-derived research on human functional neuroanatomy. Because "the organizing structure for information about the brain is neuroanatomy, which provides a construct for the functional expression of brain activity, ... it will be necessary to conjoin anatomy and function..." (Pechura and Martin, 1991). BrainMap's design is derived from the goal of relating function and location. Its design also reflects the standards and structure of PET brain-mapping data, as well as the needs and knowledge base of projected users.

#### A. A Searchable Atlas

"Neuroscience is an inherently visual science and, in this way, differs from other scientific fields" (Pechura and Martin, 1991). The complex spatial structure of the brain is best understood when the brain can be visualized. An efficient means of describing and depicting anatomy is the foundation of any neuroscience database. A key design goal, then, is that the user interface must include a digitized atlas of the human brain. This atlas should serve for visualizing the results of a query, and for initiating a query.

One approach to creating a searchable atlas is to segment the brain into regions (Evans et al., 1988). Functional-anatomical associations are retrieved and analyzed on the basis of unique names for each region. Although it is superficially appealing, this approach has significant flaws. This strategy is best applied to medium-sized, well-demarcated structures. Very small structures are beneath the resolution of noninvasive images. Very large structures lack gross demarcations for functional boundaries. For example, the largest brain structure, the cerebral cortex, consists of an unknown but very large number of functional regions with no grossly apparent borders by which it can be subdivided. In fact, it is a goal of functional brain mapping to determine the functional parcellation of the cerebral cortex, in the absence of gross structural borders. Thus, no a priori subdivisions can be adequate. Further, the use of standard anatomical regions for database development would require that all laboratories use region-of-interest analysis for functional brain mapping. Brain-mapping laboratories, however, have largely abandoned region-of-interest analysis.

Bicommissural coordinates avoid the problems of a priori regional parcellation. Every location in the brain is assigned a unique coordinate. Activated locations are reported as the coordinate of the center of mass of the activated area, together with response magnitude and statistical significance. Any given structure, then, can be queried for reports of functional activation by identifying its center coordinate and a radius around that coordinate, rather than by a name or regional boundary. The logical appeal of the bicommissural coordinate system for data storage and retrieval, coupled with its widespread acceptance, mandates its central role in a database of human functional neuroanatomy.

## B. Relating Psychology to Structure

In a database relating function to structure, the logic for storing and retrieving behavioral information must be no less robust than that for anatomy. This poses a problem. Just as the parcellations of the cerebral cortex are as not yet known, the elementary information-processing operations of the brain are as yet

unknown. Consequently, the terminology of function is evolving, with no standards yet achieved. Nevertheless, the behavioral aspects of functional brainmapping experiments must also be entered in the database.

Functional brain-mapping studies attempt to relate information-processing stages to brain locations (Posner et al., 1988). Brain-mapping experiments are constructed as pairs of related behavioral conditions. Ideally, these pairs differ by a single cognitive component, whose location is revealed in the pixel-by-pixel comparison of the images from each condition. As the cognitive architecture of any task, however simple, is rarely known with certainty, an author's interpretation of the difference between two complex behaviors (and, therefore, of an area's function) is somewhat conjectural or hypothetical.

Brain-mapping experiments are based on behavioral conditions. A subject performs a task while the brain is imaged. Although the information-processing demands of a condition are hypothesized, the conditions themselves are a matter of observation. The instructions given to a subject, the stimuli presented, and the responses made all can be unequivocally described. However well-described, behavioral conditions do not ascribe functional properties to an area. They require interpretation.

In creating a database of human functional neuroanatomy, do we describe "functions" as bare descriptions of behavioral conditions or as informationprocessing interpretations? If we omit the author's functional interpretation, users may misinterpret the experiment. If we omit precise description of the behavioral conditions, users are prevented from entertaining alternative interpretations. Qur design goal was to include both interpretation and observation. We hope that standards for description of behavior will emerge, possibly through BrainMap and similar projects.

#### C. Meta-analysis

Mapping the functional anatomy of the brain is not as clear-cut as mapping the amino-acid sequence of a gene. Placing a functional area "on the map" is only a first approximation. Defining the functional properties and functional interactions of an area is an ongoing process. Converging experiments bring deeper understanding and more detailed models, but not final answers. A database of functional neuroanatomy, then, should reflect the current state of knowledge and its ambiguities. The database should allow an overview without oversimplification. Enabling effi-

cient meta-analysis is a design goal that influences all aspects of database design and implementation.

The design goal of meta-analysis guides the selection of the forms of data to be included. Raw image data are bulky and require extensive postprocessing to be interpreted. On the other hand, reduced data are readily transported and compared among centers, if standards exist for postprocessing (above). Reduced data, however, must retain sufficient detail to allow alternative interpretations and analysis. Meta-analysis implies the ability to critique data quality. Methodological details such as the numbers of subjects used, the imaging modality and resolution, the response magnitude and level of statistical significance (preferably in terms of strength above background noise), and all pertinent behavioral measures must be included.

#### D. Broad Audience

Human brain mapping is a field at the crossroads of diverse disciplines. Interest in this field, then, is broad. A brain-mapping database should reflect this breadth and be designed to reach as wide an audience as possible. The data types and query structures must be relevant to scientists and clinicians across a wide range of disciplines. The interface must be intuitive to users widely variant in their knowledge of human neuroanatomy, psychology, brain imaging, and computer science. Finally, the larger environment within which the database is designed must be nonrestrictive; i.e., the hardware and software environment should be widely available, inexpensive, and readily learned.

# E. What BrainMap Is Not

No tool can perform all functions. Design exclusions are as necessary as design goals. BrainMap was not designed as an archive of raw image data; rather it manages reduced data, ready for meta-analysis. BrainMap is not a "laboratory organizer," like the BrainBrowser (Bloom, 1991); rather, it is intended for meta-analysis of an entire field. BrainMap is not a teaching tool for neuroanatomy; rather, it is a tool for the functional brain-mapping research community. BrainMap is not a tool for postprocessing or analysis of raw data, like statistical parametric mapping (Friston et al., 1989) or change-distribution analysis (Fox et al., 1988); rather, the laboratory of origin reduces the data into a format amenable to meta-analysis BrainMap is not an electronic bulletin board, like the Worm Community System (Schatz, 1991), or a citation index, like MedLine; rather, BrainMap is an environment

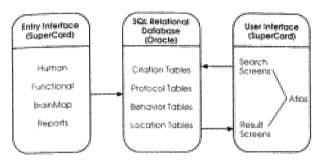


Figure 1. Database and interface interaction in BrainMap.

for in-depth exploration and interactive meta-analysis of the experimental literature of an expanding field.

## IV. Implementation

BrainMap is implemented in three parts: a graphical user interface, a graphical entry interface, and a relational database (Fig. 1). The user queries the database through the user interface by search and report

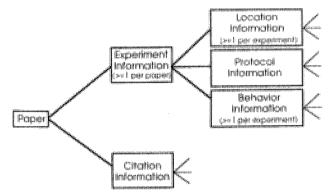


Figure 2 The database structure of BrainMap.

screens and a built-in, digitized brain atlas. The entry interface was initially designed for in-house use and will not be described here.

#### A. Database Design

BrainMap's database is constructed in a natural hierarchy (Fig. 2). The highest level is the paper. Each

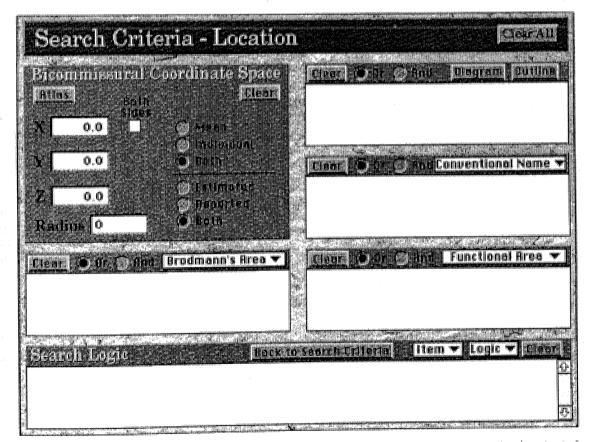


Figure 3 Location-based queries can be driven by stereotactic coordinates, lobar geometry, conventional anatomical names (e.g., putamen), Brodmann area, or functional names (e.g., area S1).

paper is divided into one or more experiments. An experiment is a grouping (typically a pairing) of behavioral conditions for which differentially activated locations are reported. Behavioral conditions are specified for each experiment. Methodological details are specified for each experiment, including imaging modality, tracer, patient population, etc. Each experiment reports one or more activated focations, the lowest level of the hierarchy. Each location (i.e., each x-y-z coordinate) carries its links up the hierarchy, allowing information at the experiment and paper levels to be rapidly retrieved.

Queries follow four paths: location, behavior, reference, and protocol. A query can specify a single parameter in a single path or specify multiple parameters along multiple paths, with relations defined by Boolian logic.

#### 1. Location Queries

Five anatomical schemes are used for data query (Fig. 3). The primary anatomical scheme is the bicommissural coordinate space (above). Brain locations are described as x-y-z addresses. Findings published in

bicommissural coordinates are flagged as "actual." When a mapping study does not publish coordinates but gives sufficent anatomical detail for an approximate coordinate to be entered, it is flagged as "estimated." "Clicking" on an atlas location automatically enters a coordinate for a search. A search can be broadened by specifying a range about that coordinate or by specifying several coordinates (Fig. 4). Search results are visualized by plotting the coordinates of activated locations into the digitized atlas. The digitized atlas is adapted from Talairach et al. (1967).

The second anatomical scheme is a geometrical parcellation of the cerebral cortex (Lobar geometry). The cortex is divided into three views: lateral, medial, and basal. Each view is divided into lobes along traditional boundaries: frontal, parietal, occipital, and temporal. Within each lobe, each axis is divided into three sections: anterior, middle, and posterior (Fig. 5).

The third anatomical search scheme, the conventional name, is the name applied to the activated location by the author. The conventional name is fairly powerful for structures with unequivocal boundaries and invariant names, such as subcortical nuclei. In

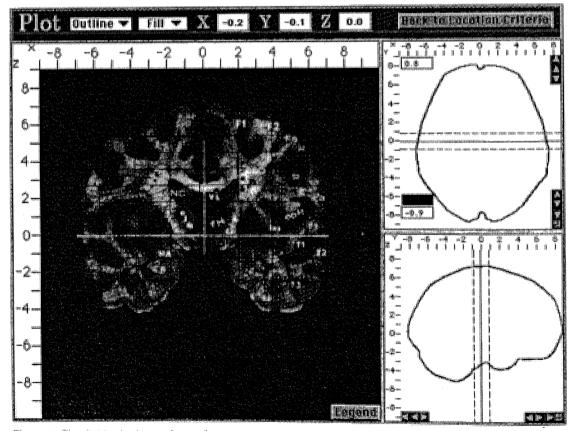


Figure 4 The digitized atlas can be used to initiate a location-based search, using stereotactic coordinates. "Clicking" on any location returns an x-y-z address in the bicommissural coordinate space. The digitized brain atlas was adapted from plates published in Talairach et al. (1967).

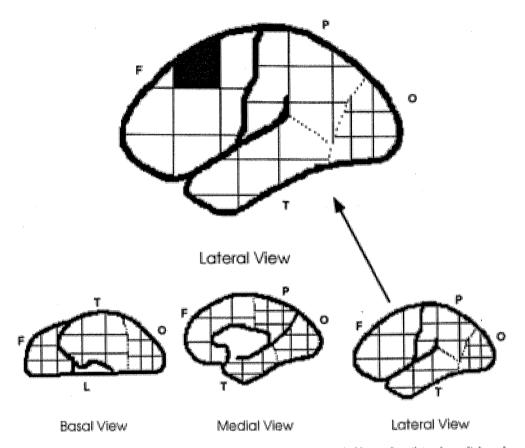


Figure 5 "Geometrical" anatomical searching. Brain locations are coded by surface (lateral, medial, and basal), by lobe (frontal, temporal, occipital, and parietal), and by sector.

the cerebral cortex, however, boundaries are vague and nomenclatures vary. Cortical locations may be named by gyral anatomy (e.g., the angular gyrus), Lobar geometry (e.g., dorsal lateral prefrontal cortex), and ill-defined quasi-anatomical names (e.g., Broca's area and supplementary motor area).

The fourth anatomical scheme is the Broadmann area. Brodmann areas apply only to the cerebral cortex. They are based solely on cytoarchitectonics, with no input from connectivity, histochemistry, or functional observations. For noninvasive imaging studies, this terminology is always presumed and never confirmed. Although Brodmann areas are by no means an ideal scheme for region naming, this nomenclature is widely used and does have some power for data storage and retrieval.

The fifth anatomical scheme, the functional area, names by the letter designations of functional areas, such as S1 for the primary somatosensory cortex or V1 for the primary visual cortex. This naming convention presumes interspecies homology, as these designations are derived from studies in other species using a variety of techniques including cytoarchitectonics,

myeloarchitectonics, histochemistry, and intracortical electrode recordings. Nevertheless, they are becoming popular in the human brain-mapping literature.

#### 2. Behavioral Queries

Three schemes are used for encoding behavioral data (Fig. 6). The behavioral domain is a hierarchical categorization applicable to an entire experiment. The initial levels are perception, motion, cognition, and emotion. Perception is further subdivided by sensory modality (i.e., vision, audition, somesthesis, gustation, and olfaction). Each sensory modality is divided into submodalities. Vision is divided into color, shape, motion, depth, luminance, etc. Submodality categories are not comprehensive and will be expanded as needed. Behavioral domain classification should be accessible to users from virtually all backgrounds.

The second behavioral scheme is the task descriptor. Task descriptors are key words that classify experimental paradigms. Examples of task descriptors include "Stroop task," Wisconsin card sort," "continuous performance task," "Posner paradigm," and so forth. This query path is intended primarily for users

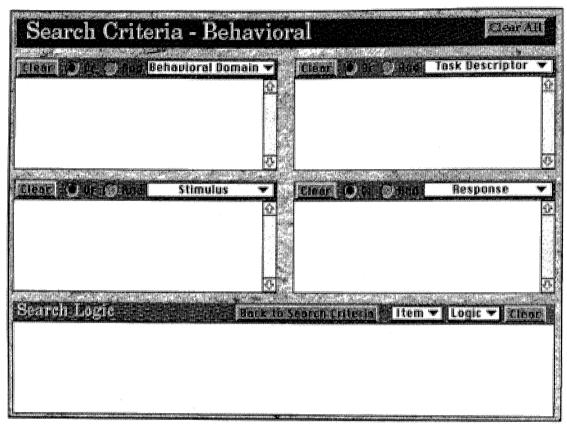


Figure 6 Behavioral queries can be developed with three distinct search axes. Behavioral domain is a general categorization of the entire experiment. Task descriptors are key words, often eponyms, that classify experimental paradigms used (e.g., Stroop task). Experimental specifications describe the behavioral conditions as stimulus, response, and instructions.

conversant in behavioral experimentation, although not necessarily in neurobehavioral imaging.

Experimental specification is the third behavioral scheme. This scheme specifies the stimulus, the response (i.e., physical movement), and the instructions given (i.e., the mental "set" established) for each behavioral condition. Entries are brief and hierarchical. Additional details about the experimental conditions are available as text fields excerpted from each manuscript, but cannot be used to initiate a query.

#### 3. Reference (Citational) Queries

Each entry has complete location information: authors, title, year, journal, volume, page numbers, and key words. Each of these fields can be used to initiate a query. All current entries in each field are provided as a pop-up list of all available entries, allowing the user to restrict a search to possible values, even before a search is initiated.

#### 4. Protocol (Methodological) Queries

This category searches the database for experiments with common methodological parameters such as modality (PET, MEG, EEG, or MRI), tracer, subject population, statistical rigor, laboratory of origin, etc.

## **B.** Graphical User Interface

The user interface is fully windowed and operates well in the multiwindowed environment of the Apple Macintosh II. The user moves through the search and display functions of the program through a series of special-purpose windows. Virtually all user actions are mouse driven. Functions are initiated by clicking soft buttons labeled with both text and icons. Search specifications are initially selected through buttons and further specified with pop-up lists of possible choices. Keyboard entries are allowed throughout, but are rarely advantageous.

The user interface includes a digitized atlas of the human brain (Fig. 7). High-resolution photographs from a bicommissural-coordinate-space atlas (Talairach, 1967) have been hand-detailed, creating outlines of cortical gray matter, white matter, ventricles, subcortical gray matter, and the cerebellum. The user has the option of viewing any plate as a gray-scale image.

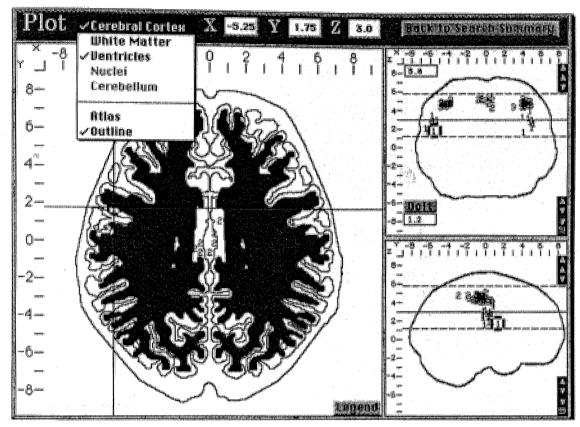


Figure 7 The user interface includes a digitized atlas of the human brain. High-resolution photographs from a bicommissural-coordinate-space atlas (Talairach et al., 1967) have been hand-detailed, creating outlines of cortical gray matter, white matter, ventricles, subcortical gray matter, and the cerebellum.

region outlines, or filled regions in any combination. The plotting routines allow the locations associated with specific behaviors to be plotted onto brain sections or silhouettes in any of the three orthogonal views (Fig. 8). Points in the plot retain their relations to behavioral and citation data. Additionally, the plotting screen itself can initiate a search on anatomical criteria by selecting a location within the atlas. The user interface is distinct from the database. Thus, the current user interface could be modified or ported to other environments with no alteration in database design or function.

#### C. Environment

BrainMap has been developed in the Macintosh environment and operates on the Macintosh II series and Quadra series of computers. This environment choice reflected the low cost and wide availability of Macintosh computers, the sophistication of the Macintosh user interface and its fully windowed environment, the high quality of Macintosh graphics, and the sophistication of available prototype-development tools (i.e., SuperCard).

BrainMap's user interface was created in the SuperCard prototyping environment. Supercard is a set of tools for developing custom software on Macintosh computers. SuperCard combines two powerful metaphors for building software familiar to Macintosh users: windows and pulldown menus for navigating through a program, and cards and stacks of cards for storing information. Supercard is divided into an editing mode in which windows and related objects are defined, and an execute mode in which program scripts are attached to each object and the program is run. Supercard supports multiple windows, variable window sizes, 256 colors, and easy inclusion of external commands and functions. Finally, software developers can distribute standalone applications without licensing fees.

BrainMap's database is built in Oracle, a transact-SQL database management system. SQL is the industry standard for large-scale projects and has been called "the database of the 90's" (Gruber, 1990). In the Macintosh operating system, Oracle supports input and output using SuperCard or X-windows. Oracle-SQL code is embedded into BrainMap's user interface and entry interface. Through SuperCard, the

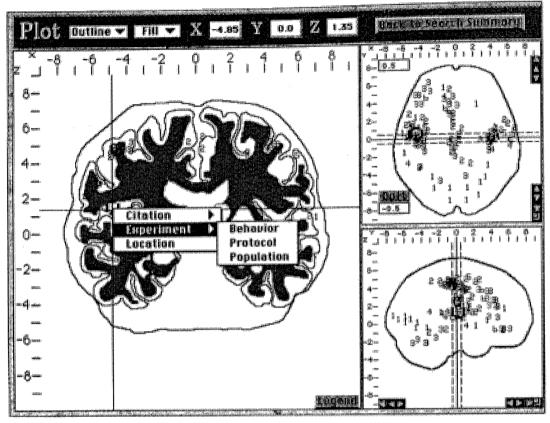


Figure 8 The digital atlas is used for displaying retrieved data. Locations reported as being significantly activated are plotted on the atlas.

BrainMap user interface issues SQL statements to drive query and entry. BrainMap operates both in a standalone mode and in a client/server mode. In standalone mode, a single Macintosh runs both the user interface and the database (in Oracle). In client/server mode, the user interface is run locally, but queries the database through a network link to the server. Because Oracle is highly portable, this software architecture will allow BrainMap's database to be served by a high-speed processor over Internet to multiple clients at remote sites.

# V. Distribution and Further Development

#### A. Beta Testing

A beta version of BrainMap is complete. Refinement will incorporate input from brain-mapping laboratories. To this end, a BrainMap Advisory Group has been established. The Advisory Group includes representatives of the fields of PET, EEG, MEG, and MRI brain mapping, neuroscience database development, cognitive science, computational neurobiology, and human and primate behavioral neuroscience. The Advisory Group began its interaction with the Brain-Map development team through a workshop (November 29 through December 1, 1992). The workshop provided a detailed critique of the BrainMap concept and sought consensus on its viability, prioritized future developments, and planned the means and scope of future distribution. Beta testing began at the end of Workshop I and will continue through Workshop III.

Data updates will be managed by the development site—the Research Imaging Center at the University of Texas Health Science Center at San Antonio. All brain-mapping laboratories using bicommissural coordinates are encouraged to submit preprints and high-quality copies of figures upon manuscript acceptance.

#### B. New Tools: New Environments

In the short term, development will be aimed at adding functions given highest priority at the initial workshop and in the early phases of beta testing. Tools for report generation will need to be designed. Tools for constructing and testing neural-systems models would be highly desirable (Friston et al., 1991). Following beta testing, distribution will be expanded. The present strategy for expanded distribution is to port BrainMap's database (in Oracle) to a high-speed UNIX server; to serve the BrainMap database from a central location to clients running the user interface in client/server mode at remote sites through Internet, and to port the user interface to additional popular environments, such as Microsoft Windows for DOS and UNIX/X-windows/Motif.

Long-range goals of the Human BrainMap Database Project include incorporating datasets more inclusive than those in the published literature, developing the logic for inclusion of non-PET brainmapping data (e.g., MRI, MEG, and EEG), building tools for local (in-house) comparisons of unpublished data (e.g., pilot data) with published data, and gaining community acceptance of BrainMap as an international, electronic registry for human brain-mapping data.

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