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Symbolic Coordinate Anatomy for Neurology (SCAN)

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Our laboratory is responsible for development and maintenance of CADUCEUS (Formerly INTERNIST-1), a computer program to provide expert advice to the clinician in the realm of medical diagnosis. In order to extend its success in internal medicine into neurology, it was necessary to provide a paradigm for neuroanatomic reasoning. In our anatomic knowledge base (SCAN), the nervous system is partitioned into a hierarchical set of nested cubes. In the computer memory, a symbol for each cube has attached to it lists of structures that are wholly or partially within the cube. The structures may be simple (e.g., right locus ceruleus*) or complex (e.g.,* midbrain*). Lists of cubes belonging to particular vascular territories as well as systems (e.g.,* visual*) are also maintained. Thus, computation of anatomic localization from a given symptom or finding is facilitated as well as characterization of consequences of vascular lesions or neighborhood effects from mass lesions.*

BACKGROUND

CADUCEUS is a computer program using the techniques of artificial intelligence to provide expert advice to the clinician in the realm of medical diagnosis. Its predecessor, INTERNIST-1, was developed over the last decade under the direction of J. D. Myers, a senior clinician, and H. E. Pople, Jr., a computer scientist.[1]

The knowledge base of INTERNIST-1 consists of a list of diseases in the field of internal medicine and a second list of manifestations of disease. These lists are arranged in a data structure that links each disease with each of the manifestations of that disease by a *frequency factor* expressed as a number from 1 to 5, where, for example, 1 indicates that the manifestation is rarely present, and 5 indicates that it is always present with that disease, with 2–4 representing intermediate frequencies.

Each of the manifestations is linked to the diseases it evokes by an *evoking factor,* numbered 0 to 5, where 5 means "pathognomonic" (everyone with the manifestation will have the linked disease) and 1 denotes a manifestation that is nonspecific for that disease.

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Additional data structures exist to characterize casual relations between diseases, and to contain information regarding ease of determining the presence or absence of a manifestation (e.g., history vs. biopsy).

Using this knowledge base, a program was constructed to provide expert advice in internal medicine diagnosis. This program is roughly capable of performing at the level of expert clinicians when tested against New England Journal CPCs.[2]

NEUROLOGIC DIAGNOSIS

INTERNIST-1 mimics the typical etiologic diagnosis paradigm used by internists. While this may be appropriate for some neurologic diseases, the neurologist often needs to use temporal (time-course) information and to make extensive use of anatomic reasoning. The INTERNIST-1 model is unable to handle such reasoning in a satisfactory manner. In addition, it was felt that states intermediate to a final etiologic diagnosis (for example, *cerebellar involvement,* or *systemic embolization*) would be a desirable addition for diagnosis in internal medicine as well as neurology.

The importance of anatomic localization to computerized neurologic diagnosis has been recognized by other workers. Meyer and Weissman[3,4] used a three-dimensional grid superimposed on the brainstem. In their paradigm, the user instantiates clinical manifestations, causing neuroanatomic pathways to be tagged. The pathways are associated with grid intersections. The user then visually inspects the matrix and localizes the lesion on the basis of the density of tagged intersections.

Catanzarite[5] used a knowledge base consisting of brainstem and spinal cord cross sections. The affected tracts on each cross section were determined and then graphically merged to determine the extent of the lesion. Both of the above algorithms assumed a single lesion.

A parallel effort in our laboratory has resulted in the development of a program, LOCALIZE,[6] to assist in anatomic localization of lesions in the peripheral nervous system. The input is manifestations (clinical or electrical) of specific muscle or muscle group involvement, and the program determines possible single or multiple sites of nerve involvement. The knowledge base of LOCALIZE is in the form of a *network* structure. Current plans include interfacing CADUCEUS to LOCALIZE as well as the geometric knowledge base for central nervous system diagnosis described below.

SCAN

Our system is currently implemented on a DEC VAX 11/780. The programs to edit and manipulate it are written in Franz LISP. In our neuroanatomic knowledge base, the human body is represented as being embedded within a large cube, 2.187 meters on a side. This cube is then divided into 27 smaller cubes, ($3 \times 3 \times 3$), each of dimension 729 mm. Each of these smaller cubes is likewise divided into 27, and so on and on, until the smallest cubes are reached, which are each 3 mm on a side. The cubes are arranged in a hierarchy so that every cube but the largest has a parent cube, and 26 sibling cubes, and every cube but the smallest ones has 27 daughter cubes. Each cube has a neighbor sibling in the dorsal, ventral, rostral, caudal, medial, and lateral directions. Each cube has a unique name, represented by a LISP *atom*.

The name is generated in such a way that the characters constituting the name itself can be used by the program to calculate the size and coordinates of the cube (sample name: BXLLM@). The largest cube is BX, and it contains the entire body. Its 27 daughter cubes are BX@, BXA, BXB, . . . BXZ. The daughter cubes of BXM are BXM@, BXMA, ...

In addition to the cubes, the knowledge base contains anatomic "objects," for example, *midbrain, l globus pallidus,* and *r central tegmental tract*. These names are also represented as LISP atoms.

The cubes and objects are associated with lists of *properties,* which describe the relationships of the cubes, objects, and vascular supply. These lists are linked in LISP to the atom names for the objects and cubes.

Associated with each cube is a list of all objects that are totally enclosed by the boundaries of the cube, a list of all objects that are partially inside the cube, and a list of all blood vessels whose territories lie inside the cube.

Associated with each object is a list of all cubes that totally enclose the object, a list of all cubes that contain part of the object, and a list of all blood vessels that supply the object.

Objects may be simple or complex. A simple object has no subunit objects, for example, the *r locus ceruleus*. A complex object, such as the *l thalamus,* may have many subunit objects, such as *l pulvinar*. A list of subunits is associated with each objects.

More complex data structures can easily be built from these fundamental components—a system consisting of objects that have functional relationships in the nervous system, for example: *r superior temporal visual field: ((r-inferior-nasal-retina l-inferior-temporal-retina) (r-optic-nerve l-optic-nerve) chiasm l-anterior-knee-of-von-Willebrand l-optic-tract l-lateral-geniculate l-inferior-geniculocalcarine-tract l-inferior-calcarine-cortex).*

The anatomic data base was created by using a specially constructed editor program, written in LISP, to make the associations listed above. The source of the anatomic knowledge was largely taken from Schaltenbrand and Wahren's sterotaxic atlas,[7] supplemented by several other sources.[8–13]

APPLICATIONS

With this anatomic knowledge, CADUCEUS will be able to add anatomic reasoning to its repertoire of diagnostic tools. The instantiation of a given manifestation of disease allows generation of a list of structures hypothetically involved. If there are multiple manifestations, they may generate lists that (1) have common members (or intersections), (2) have members in close spatial proximity (in the same cube), or (3) have members lying within a specific vascular territory.

In neurology, the site of involvement forms the essential link between the disease (which often has a predilection for certain sites) and the manifestation. The addition of anatomic reasoning may also allow parsimonious explanation of multiple manifestations arising from a single lesion, or allow the program to query the user regarding the presence of manifestations of involvement of areas that might be expected to be affected by whatever clinical state the program has under current consideration, whether it be a vascular, regional, or systemic involvement.

There are currently 987 objects and 8,896 cubes in the data base. The hierarchical arrangement of the nested cubes ensures rapid convergence during searches, because if the sought object is *not* found in a parent cube, there is no need to search for it in any of the parent's children cubes.

EXAMPLES

Using our example in the visual system, mentioned above, let us see how the clinical entity *junctional scotoma* might be dealt with. Suppose the user alleges a defect in the right superior temporal visual field. With this information, CADUCEUS could hypothesize involvement of any of the structures listed. If no further information was given, CADUCEUS would have to query the user regarding manifestations of involvement of the other structures; for instance, involvement of one of the optic nerves may lead to pallor of the corresponding optic nerve head, known as *optic atrophy*. But suppose the user had additionally entered *left central scotoma*. Such a finding implicates involvement of the left optic nerve. When this is combined with the absence of a *right central scotoma* (implying the right optic nerve is intact), and the right superior temporal defect (fibers from only that area of the right retina cross into the left optic nerve at its junction with the chiasm in a structure known as the anterior knee of von Willebrand), a single lesion can be postulated in the smallest cube that contains both the *left anterior knee of von Willebrand* and the *left optic nerve*, or BXLLMIM. (The knowledge necessary to explain this combination of deficits is often not present in those uninvolved with the subspecialty of neuroophthalmology.) Involvement of the chiasm would cause bilateral temporal field defects, while involvement of any of the other structures posterior to the chiasm would produce homonymous hemianopias. In the absence of any of these, the probable extent of the lesion has been determined.

Of course, it could be argued that the same result could be obtained by INTERNIST-1 style programming of a pathologic entity called *left junctional scotoma* containing the manifestations *left central scotoma* and *right superior temporal scotoma*, and in some instances this sort of thing will be done, giving a redundant method of hypothesis generation. But anatomic knowledge is advantageous in that it allows CADUCEUS to explain its reasoning to the user, and in addition, it can flag other structures near the site of the lesion (the pituitary, for instance) for further investigation as likely sites of disease leading to compression of the visual tracts. Exhaustively programming the presence of nearby structures into every node like *junctional scotoma* and the multitude of other intermediate pathologic states soon becomes computationally prohibitive.

Now, instead of a left central scotoma, suppose that along with the right superior temporal field defect, the user alleges an indentical (congruous) left field defect, as well as a *paralysis of upgaze* and *irregular right pupil*. One commonality of these three manifestations is that they lie within the basilar artery territory, and using the anatomy knowledge base, CADUCEUS will be able to discover that fact and hypothesize a vascular origin of the manifestations.

OTHER APPLICATIONS

Although this knowledge base was developed for use by CADUCEUS, it may have other applications. With a graphics display, sections of the brain may be displayed with a resolution equal to the size of the smallest cubes. While one may not think 3 mm is fine enough resolution, when it is coupled with the additional knowledge regarding the functionality of the anatomic structures, a powerful tool may be constructed. For instance, making an interface between the graphic display and the knowledge base, using a light pen or a graphics tablet (bit pad), users may trace out lesions as seen on CT or brain slices for correlation with involved structures automatically by the computer program. A series of strokes could be entered with clinical findings, and the program could correlate the involved structures, as shown by CT or autopsy with the clinical findings, perhaps allowing discovery of some previously unrecognized relationships.

Combining the knowledge base with imaging data may permit development of a program that is capable of automating CT interpretation, since high or low-density structures could be correlated with normal anatomy and hypotheses generated for densities outside the normal range.

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