Standardized Digital Mapping Of The Central Nervous System Connections In Humans

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Abstract

This paper attempts to unite different aspects of knowledge of both, human neuroanatomists and neuroinformatics engineers, related to the same problem of presentation of human brain connections. During the history, until to the end of twentieth century, presentations of the central nervous system connections or pathways in humans were related to technical and printing limitations, as well as to insufficient knowledge and data. Explosion of both, information technologies and neurosciences, caused fundamental changes of this almost traditional situation. Different presentations and different approaches in collecting neuroanatomical data resulted in very incoherent systems of data presentation about central nervous system connections, which situation itself became now additional limiting factor. In this paper we propose a standardized system of presentation, or better to say, of mapping of nervous pathways in geographical terms. In order to contain the maximum of information and to remain practical for use, here described system of presentations of connectivity data should be based on following principles: 1. presentation of one functional system by one basic colour; 2. exactly defined colour in RGB (red, green, blue) system for each of “neurons” in neuronal chain forming a pathway; 3. simplicity in visual presentation with several levels (magnifications) of details presentation; 4. design for use primary in computer systems, including the possibility of addition of new data (extensibility and adaptability).

In creation of such readable representations that are capable to be updated effectively, aesthetics also should be considered. Several examples in mapping of motor, sensory and limbic pathways are presented. Also, problems present in creation of such one system are discussed, especially those related to neuroanatomical terminology, as well as possible solutions which offer new technologies.

Introduction

During the last two centuries large amount of data about the connections within the central nervous system (CNS) of vertebrates has been accumulated. In addition to directions of fiber pathways, also the sizes of these fibers, transmitters, actions (e.g. excitation- inhibition) and other relevant data were reported, identified or described. Throughout the neuroscience community, there is a general frustration with the volume of data that are generated, and their relative inaccessibility in forms other than narrative text [1]. The development of graphical visualization tools that enable and enhance scientific interaction with large-scale databases is the next step in neuroimaging informatics and there is a need for a next generation visual interaction framework [2]. There is no established common practice in the computational neuroscience literature for how to visualize what, or which notation to use [3]. Because of the lack of a generalizable, computable representation of anatomy, developers of computable terminologies and ontologies in clinical medicine and biomedical research represented anatomy from their own, more or less divergent, viewpoints resulting in heterogeneity [4]. Unification in theoretical medicine is necessary for international communication and proper exchange of results [5], and data sharing can indirectly benefit and affect computational neuroscientific tool development [2].

However, both in anatomy and in neuroscience, the accurate and uniform way of visual presentation of all of these data combined, has not yet been established or even proposed. In different texts, including textbooks and monographs, different ways of these presentations were applied and used. Here we present, only as examples (Fig. 1), the illustrations published in high quality textbooks from three different periods of twentieth century [6, 7, 8], and it is obvious the diversity in graphic forms of presentations of human brain connections.

Fig. 1

It is easy to understand that the minimal knowledge about human CNS connections (macro- and microconnectivity) and pathways, as well as the absence of corresponding printing and processing technologies, justified such situation in the past. Current situation with a huge amount of dispersed details about human CNS, different level of their significance and importance, and different potential usage, cannot be synthesized into more coherent
system of knowledge without adequate system of presentation, mainly of mapping. The basic language of neuroscience is neuroanatomy [1], and in neurosciences the term "mapping" was almost exclusively related to different procedures of estimation of functions and connections of cortical areas [9], or to a tracer studies in different parts or systems of brain [10].

During our work in science and in education appeared that different brain systems were presented differently. Most known example is that motor projection pathways are marked usually in red and somatic sensory systems in blue color. This originates from early circulation illustrations with arterial flow (as efferent- from the heart) in red and venous flow (as afferent- to the heart) in blue color. But increasing knowledge about brain revealed that this, almost symbolic, way of presentations is far than sufficient enough. As illustration of successful but isolated (particular) presentation of only basal ganglia connections is Figure 2 (reproduced with permission) from a relatively recent book of Nolte [11]. In this figure excitatory connections are shown in the green color and inhibitory ones in red color, as in traffic regulation. This way is suggestive and reasonable for motor systems (go/stop), but cannot be included in some wider presentations of neural systems. In nearly opposite example, the excitatory connections are shown in red, and those considered inhibitory were shown in blue [12].

In this paper we consider a new, standardized and potentially universal system of presentation of CNS connections, convenient for integration of different databases. This paper is aimed only as an indication of the problems which require international organized collaboration of experts and high technology. Here proposed presentations of connections are only the illustration of what the potential solution may be and what are the currently noted problems. The American physicist R. Feynman once argued that the history of mathematics is the history of improved notation. The less cumbersome notation becomes, the more the mathematician’s mind is freed to leap into new logical spaces. Replace ‘notation’ with ‘visualization’, and it is also true that scientific progress often follows from new ways of visualizing problems [13]. Complex ideas are best conveyed through well-designed illustrations which play an important part in science, and are technical illustrations rather than technical drawings, differing in their purposes and thus their appearance [12]. However, currently most neurodatabases are accessible solely by textual queries [2].

Necessary are the efforts directed to the creation of increasingly dynamic, interactive maps of human CNS pathways that can be manipulated digitally. Also, this proposal could be practical as it was the introduction of unique anatomical terminology (Nomina Anatomica and Terminologia Anatomica), more than century ago [see 14, 15]. Great and excellent work in the study of only one, and relatively small part of rat brain (bed nucleus of stria terminalis) [16] illustrates the proportions proposed enterprise.

Below, we first review principles of visualization, before giving several examples of what is necessary to be illustrated in a neuronal network, followed by discussion about some aspects of such mapping, and potential highlights and problems.

**Methods**

In this paper we consider the standardized use of colours, combined with often used traditional markings of directions of neural connections (circles and lines with terminal bifurcation) within the central nervous system. Connections belonging to one functional system should be precisely numerically defined always by one standardized colour (hue), including its different, but also precisely defined tonal range. Definition of colours in this presentation is within the RGB (red, green, blue) colour model, which is an additive colour model widely used in creating computer graphics. Proposed RGB system corresponds to the existence of 3 types of cone cells in human retina, red, green and blue (primary colours), according to their maximal spectral sensitivity [17]. Proposed use of RGB system can be even more valuable in the future, when only the information about wave length of colours would be sufficient for their definition, what is different from recently used even defined, monitor colours. Disadvantages are in degree of discrimination of colours by human eye. Our approach is directly opposite to the approach in image analysis of biological specimens, and therefore avoids the problems and limitations of tresholding, image and analysis of biological specimens, and therefore avoids the problems and limitations of tresholding, image and colour quality, resolution, signal to noise ratio and of input-output devices [18]. The efforts in imaging techniques, image processing and image analysis are made to identify and separate all possible hues and intensities of colours obtained on staining [18], while we determine in advance (standardize) exact definition of colour which computer should produce.

This proposal includes the exact definition of colour (colour profile), for the first, second, third, fourth, etc. neuron (synapse). The starting point (first neuron) in any chain of connections could be marked as the
darkest one, and that each following, i.e. consecutive neuron, should be in lighter tone of same defined colour. Attached pop-up information box should contain exact definition of colour, and/or some basic neuroanatomical data or links. In order to contain the maximum of information and to remain practical for use, the system of presentation of connectivity data should meet following requirements: 1. accuracy; 2. clarity and simplicity (allowing no confusion), 3. possibility of comparison and interchange of data, 4. possibility of addition of new data (extensibility and adaptability). Aesthetics is also recommended in creation of such readable representation that is capable of be updated effectively. Background details or topography (such as levels of spinal cord, actual position of tract within specific CNS structure) are not of primary importance now, but they have contextual role and can be more elaborated, developed and/or linked in any further computer presentation.

To avoid the information overload in a single figure, it was suggested to distribute the information between several figures, each showing different hierarchical levels [12]. Provided that network models are specified at a sufficiently high level of abstraction, future interactive visualization tools could interactively switch between different representations of model aspects [12]. Different from the ©Google Earth, which deals with only one background (our planet), anatomy deals with individually variable “spaces”, each subject having its own, specific “cartographic” background. In computer geographical presentation significant step is transition from one type of symbolic presentation (such as cities by circles in large scale charts), to other types of details presentation in small scale charts (such as single houses by squares). Crucial step in use of different magnifications is qualitative change of visualized details, from node (neuronal assembly) connections topology, toward synaptic interneuronal connections. This corresponds in visualization of WWW, to the transition step from network node topology to visualization of hardware details. This very advanced step is not necessary in proposed system, and even requires limitation. However, some different levels (zoom) of neuroanatomical precision are also considered here, starting from educational level for medical students, to more detailed presentations, which should correspond to higher magnifications (larger or smaller scale).

Results

Proposed examples

Beside now classical designation of red color for somatic motor systems (corticospinal tract), and of blue color for somatic sensory systems (spinothalamic tract), example of connections in limbic system is also shown here (Fig. 6).

Corticospinal tract

The presentation of this descending projection pathway, extremely simplified here for educational purposes, requires two tones of red colour, presenting upper and lower motoneuron. We propose that the first (upper motoneuron) should be darker, than the second (lower motoneuron) one (Fig. 3).

Fig. 3.

Spinothalamic tract

The spinothalamic tract as one of somatic sensory pathways, according to the tradition, generally should be presented by blue colour. Its three main neurons (peripheral or first one, central or second one, and third or cortical neuron) should be shown in different variants of blue colour. According to general principles given earlier, first neuron should be presented in darkest tone of blue colour. In Figure 3 it is defined with the numbers of RGB as label (can be used as pop-up box), ensuring that always the same colour would be used. Next neuron in this chain (pathway) is presented in lighter tone of blue colour, also defined by RGB numbers, and third neuron is the lightest one. (Fig. 4).

Figure 4:

This presentation is simplified or educational (for general medical practice) level. However, it is known that in spinothalamic pathway actually there is not triad of three neurons. For example, within the posterior horns of spinal cord there is a complex of neurons (not only the region known as the gelatinous substance) [19] and the processing of pain impulses generally involves the laminae I- VI [20]. Hence, in more advanced or even scientific level of presentation, additional tones of blue colour are to be included in order to illustrate these local, but significant connections in dorsal horns (Fig. 5).

Figure 5.

Papez circuit

As illustration of potential difficulties in realization of this proposal is given the Papez circuit presentation. To present well described and long time known [21] system of limbic connections, first requirement is to define which colour should be used for limbic system. We for example (quite arbitrary) propose here the brown colour, and as the starting point of this presentation we choose the mammillary body of hypothalamus (hypothalamus is the main effector region of the limbic system - [22]), and therefore mammillothalamic tract is shown as darkest. Every
next step is lighter in tone, opening the question if there are at disposal enough tones of brown colour which can be seen as clearly different by human eye. Other question arises, whether the “starting point” in neuronal circuits always is easy to be defined. Septo-hippocampal fibers in Fig.6 also are indicated as dark, as well as hippocampo-hypothalamic fibers are dark, which after signal processing in septal or hippocampal regions can be considered as starting fibers. Details of local hippocampal connections (as perforant and alvear paths, mossy fibers, etc.) are not presented in this picture, but for presentations corresponding to higher magnification (zoom) they should be kept in mind.

Figure 6.

Discussion

To increase the efficiency of neuroscience research, a system is needed to provide a logical and organized means to maintain and distribute data [1]. Complex systems, as networks of interactive entities, are studied through a rapidly increasing mass of data in all domains which share a lot of new and fundamental theoretical questions, what is favourable for developing the new science of complex systems in an interdisciplinary way [23]. This requires cooperative partnership of researchers from multiple disciplines and maximal level of international cooperation. In human neuroanatomy resultant scientific activity will have to catapult the field of neuroinformatics to center stage [24], and can lead to discoveries of new relations between previously unrelated parts [16]. There are two main issues in realization of this proposal, the role of human neuroanatomists and understanding of nervous pathways (maps) by the informatics engineers.

What can be the role of neuroanatomists?
Establishment of terminology in human neuroanatomy is one of most important prerequisites in realization of this project. Since development of science requires the continuous adjustment of terminology, that is the reason why it was so important to find a common international language for anatomists [5].

Terminology is a system of terms used in a given scientific field. Nomenclature is a standardized (normalized) system of precisely defined terms, set according to certain classification principles and containing terms created within the scope of terminology [15]. Professional terminology is common place, particularly in the fields of mathematics, medicine, veterinary and natural sciences, and its use can be international, as it is with Terminologia Anatomica [5]. Anatomical concepts and terms are an integral part of not only anatomy texts and atlases, but of all discourse pertaining to the human body. Therefore, a logical and consistent representation of anatomical concepts is a requirement for knowledge sources in essentially all fields of the biomedical sciences [25]. The development of neuroanatomical ontologies (or structured vocabularies) for computer science applications is not possible without rigorous specification of relationships between concepts and terms [26], including the corresponding nervous system parts. For electronic database good foundation is Terminologia Anatomica reflecting experience and knowledge summarized by generations of anatomists. Human neuroanatomists are convenient not simply to participate, but to be an significant part of such an project, and not only because anatomy can be considered as the first exact medical field; its terminology is a crucial because effective science communication is based on an accurate and carefully defined vocabulary [15]. Different nomenclatures used currently in neuroanatomy to describe the structural organization of the nervous system lack the precision. There is a need for the development of a commonly agreed nomenclature in neuroanatomy and this fundamental problem hinders the next level of analysis of the nervous system [16].

Inspiring example for neuroanatomists is long time progress in gradual acceptance of international anatomical terminologies. The society of German-speaking anatomists (Anatomische Gesellschaft) created the first Latin anatomical nomenclature (Basiliensia Nomina Anatomica), approved after 12 years of hard work in 1895 at the society meeting in Basel (Switzerland). This work, continued for a long periods, resulted in Parisiensia Nomina Anatomica (1955; 1961) and the Nomina Anatomica (1989) [14, 27]. All this finally resulted in the new, updated, simplified and uniform terminology (Terminologia Anatomica), containing unique identifying number and terms in English and in Latin [14, 27]. However, knowledge modelers now recognize that it is very difficult to enforce the use of a standard terminology [25].

In case of neuroanatomical structural data it is difficult to have a rigorous definition of a metric space of such entities directly [2], but for specific spatial locations, calculations such as in stereotactic neurosurgery based on Talairach Atlas [28], could present individual morphology. Spatial relationships are not of primary importance in proposed system, because individual variability requires some details which in humans are not yet elucidated. Great variability present in human
neranatomy, such as the presence or absence of interthalamic adhesion, different sulcal patterns etc. [29, 30], remains unspecified, which is one factor that constrains the scope of the terminology [25], including the pathways mapping. However, this need has stimulatory and direction influence for further studies of CNS connections, by generating hypothesis and ideas for research.

Open question is how many “subsystems” (or modules) should be defined in human CNS and whether is possible to each of them to ascribe specific (“their own”) color. Even if not always color varitions visible by human eye, different RGB numbers (properties) will be error-free identified by computer. The development of maps for anatomical subsystems, such as the somatosensory or motor systems, is typically driven by the need to catalogue functional activation studies or to describe pathways of connectivity [9]. These subsystems correspond to “organs” in multi-organ organ what is the human brain [31]. We can, more or less arbitrary, identify for example, motor systems, somatic sensory systems, (or only pain system), general senses pathways (visual, acoustic, gustatory, olfactory, balance), limbic system, central autonomic network, (different) memory systems, cortical association systems, cerebellar system, food and water intake regulatory system(s), etc. Even if it seems that there is not “enough” colors, we assume that one (same) tone of one color can be applied in different very complex systems (visual and participating in memory also) showing that some fibers, originating from one system diverge, bifurcate or overlap into different pathways. Actually we expect that the main problem of neuroanatomy here will be the absence of informations, insufficient informations, or inadequately processed informations which are expected to be mapped in humans.

Why “maps”?

In general, neuroanatomy is in many aspects analogous to geography, and it is not only the coincidence that in both sciences many data were presented in printed (graphic) collections (of the earth or body maps), called Atlases [1,32]. The presentation of CNS pathways in many aspects can use geographical (cartographic) methods as kind of thematic cartography, involving maps of specific themes oriented toward specific neuroscience audiences. Like geography, neuroscience requires accepted maps, terminologies, coordinate systems, and reference spaces to allow accurate and effective communication within the field and with allied disciplines. Unlike geographic atlases, anatomic atlases cannot assume a single, constant physical reality [1]. Graphical maps provide a good method to visualize, understand and navigate a world that is too large and complex to be seen directly like the Web [33]. Many partial efforts resulted among others, in electronic atlas database applicable for anatomical targeting, structure labeling and brain mapping [34]. Question of anatomical precision or accuracy is related to the purpose of the map. For educational level (as for students) less details and main stream of impulses should be sufficient. Practically we propose creation of system of topological maps (as very general type of map), which at its first level disregards scale in the interest of clarity, what corresponds to a low magnification map. The level of detail of the connectivity may vary for complex networks where the number of lines and line-crossings increases, resulting in cluttered illustrations [12].

For complex or specialists studies, as well as for complex analytical and projecting purposes, detailed maps including local circuits, collaterals and parallel streams should be necessary. Links to other databases connected as modules, such as Visible Human, Connectivity Pattern Tables [12], Brain Architecture Knowledge Management System [16] or Foundational Model of Anatomy [4] can be used. Parallelism of neural networks and internet

Here we discuss some similarities or even analogies in design and in studies of neural pathways and of Internet, as the reason why neuroinformatics engineers should participate in this project. While the construction perspective to a large degree builds on terminology from neuroanatomy, the connection view of networks seems to have received little attention in thepast, whence there is no established terminology [12]. The informatics community faces with the unification of existing large, heterogeneous neurodatabases in a user-transparent manner, what goes above and beyond data sharing, [2] what is very much like the WWW, where there is an interconnection of data processing and storage nodes in a decentralized network. However, an alternate parallel goal complementing these efforts is the ability to graphically navigate, browse and query such aggregations of repositories [2].

A kind of complex idea (information) which becomes a distinct memorable unit capable of spreading itself is called meme [35], and can be stored in brains, computers, etc. [36]. The storage of memes in brain has a neuroanatomic substrate and is related to synaptic structures, constellation and configurations. Other very powerful system for storing and spreading memes is the World Wide Web [see in 36]. Term mapping is widely used in research of Internet and significant research and technical challenge in the study of large information networks is related to the
lack of highly accurate maps providing information on their basic topology [37]. The general phenomenon of spreading over a network is ubiquitous. Since spreading takes place over the links of a network, it is clear that the topology of the network can have a profound influence on spreading process [38]. It is well known that stimulation based neuroscience is ideal for integrating data from otherwise currently under-connected realms [24]. Analogous to the stimulation studies in brain research, the study of the topological properties of the Internet, using special active probing techniques and the methods of network tomography, inform about the key state parameters of Internet paths [39].

For neuroanatomists is interesting the statement that the Internet can be modelled on two levels: microscopic (zoom) and macroscopic. This means that adequate models for the propagation medium – the internet, can define two abstractions of the Internet topology: the Microscopic Internet graph and the Macroscopic Internet graph [40]. Spreading on networks can be presented in a spatial resolution which is not microscopic, but rather at the level of „neighbourhoods” connected subgraphs with roughly the same spreading power. Network structure analysis suggests a method of graph visualization [38] where different other frame works modules can be inserted as links.

Conclusion(s)

Important is that here considered system is open for further addition and changes of data, for development, interoperability, for integration of information from multiple sources, and by this way, for increase in its complexity. One of most expected potential advantages of this system of standardized mapping is its use in computer processing. Computers can automatically identify the colours of screen, and this feature can be used in different ways by software (CAD and other specialized illustration software) to create dynamic, interactive maps of nervous connections that can be manipulated digitally, enabling information richness of the map. Finally, this article should be seen only as a proposal open for change and further discussion. We are sure that it opens a promising and new field, not only for presentations, but also for further studies of human CNS. Its value should be not only educational one by contributing to clarity and simplicity, but also it should point to gaps in our knowledge which demand more specific elaboration. Propelling role of this enterprise is in showing what of key data are missing for integrate informations about human brain. *These concepts were presented in part at VII International Symposium of Clinical Anatomy. Varna, Bulgaria, October 12th - 15 t, 2006. Scripta Scientifica Medica Vol. 38, 2006, Suppl. 2. p. 68

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[11]Nolte J. Human Brain. St. Louis, Mosby. 2002; Figure 19-6 (With permission of Elsevier, B/Malobabic_BG10-06)


Illustrations

Illustration 1

Fig. 1. CNS pathways. Years: A. 1921 [6]; B. 1946 [7]; C. 1958 [8] (red- touch; blue- pain)

Illustration 2

Fig. 2. Colors as in traffic (red-stop; green-go); Year 2000 [11](permission of Elsevier)
Illustration 3

Fig. 3. Corticospinal path defined by RGB system numbers ensuring use of standard red color tones

Illustration 4

Fig. 4. Spinothalamic tract, overview. Box indicates posterior horn details magnified in Fig. 5.
Illustration 5

Fig. 5. Spinothalamic tract (box in Fig. 5). Details analog to light microscopy high magnification

Illustration 6

Fig. 6. Difficulties (Papez circuit): long neuronal chain needs larger color scale
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Reviews

Review 1

**Review Title:** Standardized Digital Mapping Of The central Nervous System Connections in Humans

Posted by Dr. Goran Spasojevic on 16 Nov 2010 02:45:37 PM GMT

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**Rating:** 7

**Comment:**
Paper is related to an interesting and actual problem of presentation of pathways of central nervous system in humans. Various ways of these presentations can be a limiting factor in neurosciences. Interesting is also author's suggestion to the standardized presentation of nervous pathways, as well as pointing to the parallelism to internet studies. History of anatomical nomenclature suggests to possible solution for similar standardization of visual presentations in neuroanatomy. Interesting paper full of information, congratulations to author.

**Competing interests:** No

**Invited by the author to make a review on this article?** No

**Experience and credentials in the specific area of science:** neuroanatomy

**Publications in the same or a related area of science:** No

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