# New Techniques in the Study of Headache

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## Introduction

As a symptom, headache must be classified as part of a syndrome. Accordingly headache can be caused not only by pathologic processes, but also by functional disorders. An exact neurologic examination supported by orthopedic, ophthalmologic and otorhinolaryngologic findings should precede the examination of cranial and extracranial structures by means of refined techniques.

From a clinical and phenomenological point of view, headache may be classified into different etiologic types. Thus, four categories of headache can be differentiated according to the type of structural dysfunction involved: (a) "dolor localisatus", which is related to some pathologic process in the head; (b) "dolor projectus", caused by lesions or irritation of neural structures in the head region; (c) "dolor translatus", produced by functional mechanisms in order to create a resting state in the locomotor apparatus of the head; and (d) "central pain", arising from a dysfunction of the pain perception system.

Headache may be caused by disorders of extracranial brain vessels, as in migraine and other "vascular" headaches. "Blockade" of the cervical joints is also a presumed cause of headache. Headache attributable to local processes of the skull or the face may be accompanied by spasms of autochthonous muscles of the cervico-occipital region caused by joint-blocking reflexes. Dolor translatus (in the pseudoradicular or referred pain form) is mediated by nociceptive afferents which refer to the dermatomes C2 and C3, producing the characteristic "vertebrogenic headache". Central pain, which shows completely different etiologic aspects, may have its origin either in the posterior thalamus or in the thalamocortical pathways.

This range of possible causes gives some idea of the difficulties involved in arriving at a diagnosis of the causes of headache and the necessity of using modern techniques of investigation. With methods of neuroimaging, we are able to diagnose pathologic processes and functional disorders of the head and, to some extent, of the cervical spine. As mentioned, because of its various causes, headache as a symptom requires exact diagnostic differentiation based on an exhaustive examination. Only with the results of a clinical examination that includes neurologic, neuro-orthopedic and psychiatric findings can a diagnostic programme be outlined. New neuroimaging techniques can be used in the examination programme to clarify the underlying causes of headache syndromes.

The examination of the brain vessels by means of invasive catheter angiography was a very important diagnostic method until recently. However, the relatively frequent incidence of severe allergic or angiospastic side effects and other accidents occurring with such techniques was an incentive to invent new methods of vessels examination.

## Historical Development of Subtraction Methods

Photographic subtraction methods were described as early as 1935 by the Dutch neuroradiologist Ziedse des Plantes [14]. The real breakthrough in medical diagnosis, however, was accomplished only a few years ago with the development of digital subtraction angiography (DSA), which makes use of modern computer techniques [2]. As in the photographic analogous subtraction method, preliminary images without contrast are obtained with DSA. This represents the "background noise" of vessel representation.

After administering contrast material, the picture without contrast and the angiographic pictures are digitalized, and subtraction images are obtained from computer processing of the available data. The advantage of this method lies in its use of electronic picture amplifiers which, by allowing image contrast to be substantially heightened, means that only small amounts of contrast material are required. To represent smaller vessels and especially small intracranial aneurysms, intra arterial application of contrast material through a catheter is necessary.

Larger extracranial vessels, such as the carotid and vertebral arteries, can be examined with ultrasound and Doppler procedures [15]. The Doppler method measures the velocity of blood flow. By means of colour coding and simultaneous $x$-$y$ registration performed while a probe is moved along the vessel, a picture of the blood velocity in the vessel examined can be obtained.

B-mode sonography, in which the probe is held without being moved, provides anatomical information concerning the examined portion of the vessel. In this case, the representation is continuous and in real time and even makes possible the visualization of movements and pulsation. Thus, whereas the Doppler procedure supplies physiologic information concerning vessel dynamics, B-mode sonography provides information about vessel statics and anatomy.

In contrast to i.v. DSA, sonography gives information about the haemodynamics of extracranial vessels, including the degree of functional impediment through a stenotic portion of a vessel, anatomical wall structures, and the extent and consistency of plaques.

When searching for the causes of headache, brain structures are also of great diagnostic value. Until only 0 years ago, information about the brain was possible only by means of indirect and invasive methods like the pneumoencephalogram (PEG), which furthermore produced only a blurred representation of the material.

With Hounsfield's introduction of "reconstructive tomography" into medicine in 1973 [7], the goal of obtaining images of horizontal body sections for medical diagnosis was at last realized. Interestingly, this method had already been known and applied in various branches of science [8]. Thus, in 1956, Bracewell [4] developed a radioastronomical technique of image reconstruction useful for identifying sun regions by means of microwave radiation. Independently of Bracewell's work, researchers found other uses for picture reconstruction as well. In 1968, De Rosier and Klug [5] applied image reconstruction to investigate the structure of complex biomolecules through electron microscopy. Rowly [11] also implemented this technique in 1969 for optical purposes.

In medicine, reconstructive tomography developed mainly from conventional tomography without employing knowledge from other fields and is based on the work of Takahashi dating from 1957 [10] and the results of Oldendorf's research published in 1961 [9]. Early laboratory techniques of picture reconstruction functioned according to the principle of back projection and were only capable of producing blurred pictures. A big step forward was made in 1963 by Cormarck, who developed a mathematical algorithm for the exact construction of images. He developed X-ray projections and applied them to simple phantom studies.

The historical development of reconstructive tomography shows how limited the exchange of experience among the various sciences is and how long the path from laboratory to routine methods in medicine can be.

## Topographic Methods of Neuroimaging

To arrive at a two-dimensional distribution of a signal in a section of the body, the sum of the various angles in that section level has to be calculated. The sum signal, consisting of the sum of all the signals on this line, can be transformed into a two-dimensional signal distribution for the desired section. This basic principle, applied to various kinds of signals, is the basis for several tomographic methods of neuroimaging.

*Transmission-computed tomography* (CT) uses X-rays as signals in the form of a thin beam, arranged diametrically against the detector and mechanically around the section to be examined. In this way, it is possible to receive sum transmission signals from various angles. Since the strength of X-rays is inversely proportional to tissue density, the sum transmission signal corresponds to the total attenuation at the corresponding section angle. By means of the above-mentioned reconstruction algorithm, the attenuation and, therefore, tissue density can be identified at every point of the slice. A picture of the density distribution corresponding to the anatomy of the section thus emerges. By providing contrast, the density distribution can raise the proof probability of pathologic changes, thereby facilitating the diagnosis of tumors and vessel malformations like angiomas or aneurysms.

*Single-photon emission tomography* (SPET) is a neuronuclear medical investigation technique, in which the signal used for image reconstruction is gamma radiation emitted by the patient himself [13]. This method makes use of a radioactively labelled substance, administered intravenously, which enriches itself primarily in the organ being examined. The gamma radiation emitted by the tracer in the organ is then registered by a rotating gamma camera.

The point distribution pattern of the radioactive tracer is the result of the sum signals of the various angles. While tracers long in use like technetium-99m have been overshadowed by the advantages of CT, a family of radioactive substances which fulfill the two requirements for brain imaging, i.e., blood-brain barrier permeability and retention in the brain parenchyma, has come into use during the past 2 years.

The most promising of these $N$-isopropyl-$P$-iodoamphetamine tracers has been labelled with iodine-123 (IMP) [6]. This lipophilic compound is concentrated in the brain, primarily because of the presence of high-capacity, relatively nonspecific binding sites for amines. The initial distribution of IMP correlates with regional cerebral blood flow.

*Positron emission tomography* (PET) is another neuronuclear medical investigation method. Positron-emitting radionuclides are produced by a cyclotron. Either the radionuclide or a compound labelled with the radionuclide is given to the patient immediately. The decay of the radionuclides and the subsequent positron annihilation give rise to two antiparallel gamma rays in the tissue which are recorded by rotating detectors, as in CT.

The most promising tracer employed with this technique is glucose labelled with fluorine which produces functional images that show regional cerebral blood flow or regional cerebral metabolism, depending on the kind of tracer chosen [10]. This method of investigation, which requires a cyclotron, is presently used in only a few research centers because of the high expense involved.

*Nuclear magnetic resonance* (NMR) is the newest technique in image-producing procedures. Rather than ultrasound or radioactive radiation, high frequency electromagnetic fields are used as signals. Nuclear magnetic resonance, developed by Bloch and Purcell in 1946 [3], exploits a recently discovered physical effect. When excited by a high-frequency electromagnetic field, all magnetic atom nuclei, which includes the nuclei in over half the atoms of all natural elements, send out additional high-frequency electromagnetic radiation in an homogeneous magnetic field. The force of the electromagnetic radiation emitted is proportional to the number of magnetic atom nuclei.

When this principle is applied to medicine, the quantity of protons in the body can be determined. To determine the proton distribution in a certain body layer, sum signals can be generated by superimposing a nonhomogeneous magnetic field at different angles, which allows the proton distribution in a section of the body to be reproduced according to the reconstructive algorithm described earlier. Through their interaction, magnetic protons interfere with the magnetic fields of various types of tissues, thus furnishing two further diagnostic parameters which are to some degree characteristic for each type of tissue [1]. In this way, three different parametric pictures are available:

1. A spin-echo picture (SE), which corresponds predominantly to the interaction of protons with each other
2. An inversion-recovery picture (IR), which corresponds predominantly to the interaction of protons with tissue and provides a sharp contrast in the gray and white matter of the brain
3. A repeated free induction decay picture (RFID), which shows changes in proton density and supplies a very low gray-white matter contrast

## Discussion

These parameters can be used to create images that supply information otherwise unavailable. Body parts containing a high percentage of water appear as light areas; air, bones, and vessels are visible as dark regions. Together, these parameters produce images that are easy to interpret. In a single picture, each of these parameters can be given more or less emphasis, which means that NMR images provide information that is not only distinct from that available with other techniques, but also complex in character. While RFID pictures alone are of limited diagnostic value, acute infarcts, demyelinating processes, cerebral edema, and tumours can be clearly depicted with IR images. After technical modification, SE pictures are also of importance for diagnosing neurologic diseases.

The use of special contrast seems to be a promising approach because even very low doses of paramagnetic substances lead to a significant decrease in magnetic interaction. Since NMR shows both atomic nuclei and their bonds to surrounding atoms, biochemical information can be obtained with this technique. In the future, it may be possible to use body particles other than protons for this purpose. Since the total concentration of elements in the human body is lower than that of hydrogen protons, extremely long measurement times and higher magnetic fields are required for images of this kind. Through the use of supraconductive magnets, experiments have already shown that it is possible to gain additional biochemical information relating to assimilation, e.g. concentrations of creatinine, phosphate and inorganic phosphorous acid in living tissue.

## Conclusion

Headache is a symptom that can have a number of underlying causes. Hence, an etiologic evaluation of headache should be carried out only after correlating other clinical information, including case history and neurologic, psychiatric and neuro-orthopaedic findings.

In the past few years, a number of mutually supplementary investigative methods for examining the head, brain, neck and spinal cord have been developed which can aid in determining the causes of headache. These new techniques of neuroimaging not only provide an abundance of structural, vascular and metabolic information, but also have the additional advantages of being innocuous, precise and reproducible. Because the imaging procedures described here have great potential importance in the diagnosis of both pathologic processes and functional disturbances, we must keep abreast of future developments in the field of neuroimaging. The clinician will increasingly find himself in need of the insights and tools of physics and computer science.

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## Updating in headache : [proceedings of the 1st Interna ional Headache Congress, 14-16 September, 1983]

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Zusammenfassung: In September 1983 the First International Headache Congres took place, the founding congress of the International Headache S ty (IHS). The fact is that differential diagnosis and treatment of recurrent and chron- ic headaches represents a broad field that cuts across many disciplines. Read less

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