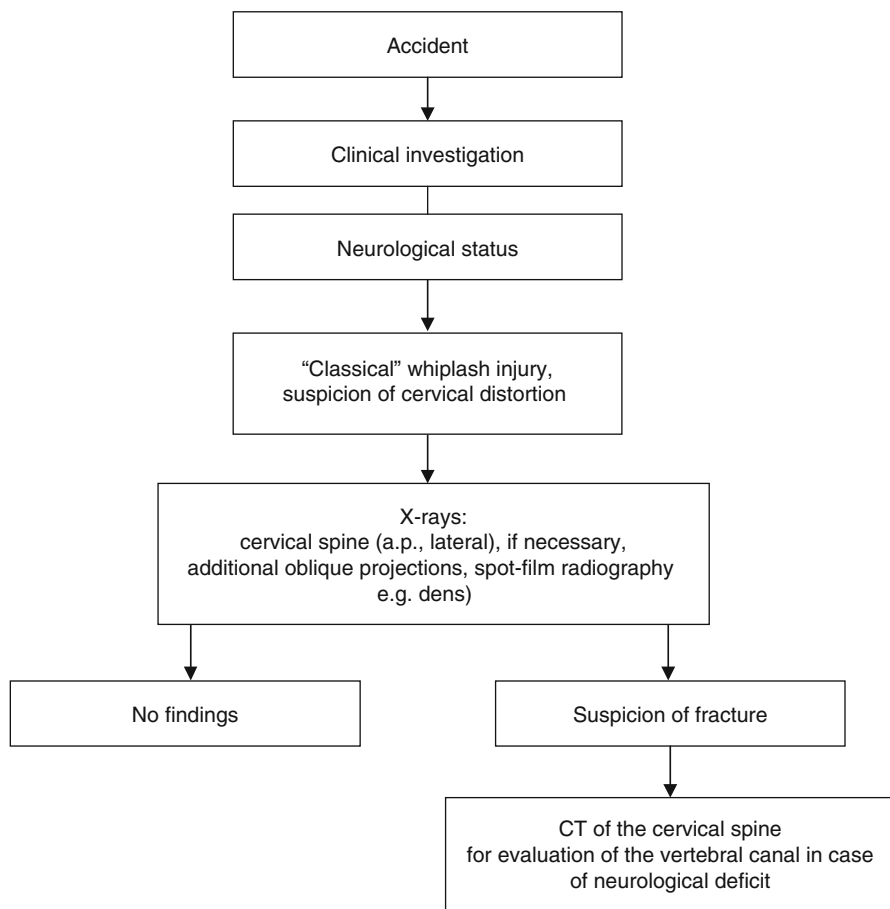


## 2.1 Diagnostic Procedure After Whiplash Injury

The usual diagnostic procedure in whiplash injury is illustrated in Fig. 2.1.

Unfortunately, methods assessing the condition of the brain are frequently not utilized. These methods are:

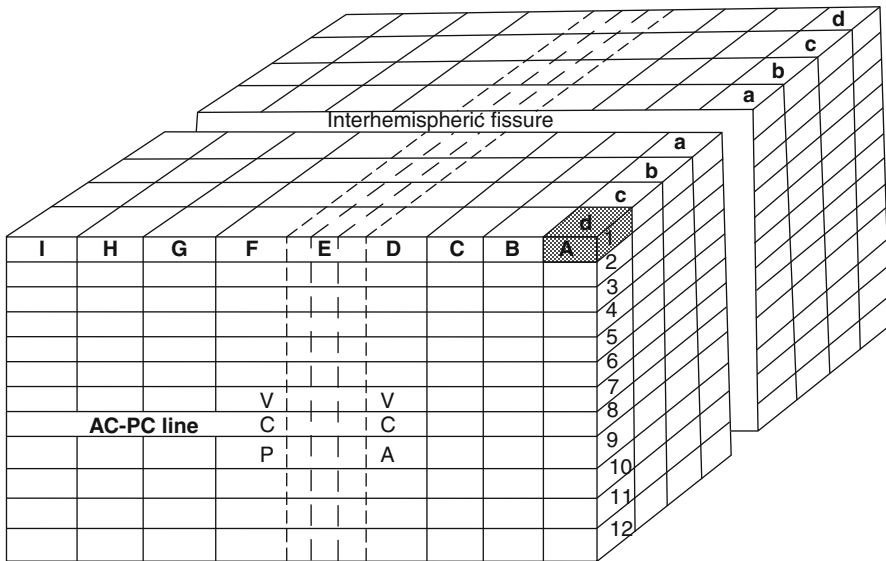
1. Computerized tomography (CT) and magnetic resonance imaging (MRI) of the brain: With these methods usually no pathological cerebral findings are found in whiplash injury.
2. Neuropsychological tests: The role of neuropsychological tests for this indication is at present still being discussed.
3. Functional neuroimaging: Functional neuroimaging devices are quite sensitive measuring instruments, which are of help in the puzzling diagnosis of the late whiplash syndrome subsequent to a whiplash injury. Especially functional neuroimaging using the nuclear medicine devices single-photon emission tomography (SPET) or positron emission tomography (PET) in combination with stereotaxic brain slice delineation (e.g., Talairach and Tournoux 1988, 1993) and statistical parametric and nonparametric mapping (SPM) software developed by Friston et al. (1991, 1995a, b) is currently of essential value. In addition, functional MRI, magnetic resonance spectroscopy, superconducting quantum interference device (SQUID) magnetoencephalography (MEG), and the new hybrid imaging technologies – such as PET/CT, SPET/CT, or MR/PET – may be future methods of functional neuroimaging interest in this indication. Due to the rapid change in the development of functional neuroimaging devices, we have excluded a detailed description of these from this book. A currently detailed and state-of-the-art review on these – including image analysis tools – can, e.g., be found in Otte and Halsband (2006).
4. Other imaging devices, such as electroencephalography (EEG) or near-infrared (nIR) spectroscopy, are important diagnostic procedures in neurosciences, but have not yet been helpful in the diagnostics of whiplash patients due to their limited spatial resolution. In these devices, future developments of medical engineering industry would be most favorable.



**Fig 2.1** Usual diagnostic procedure in whiplash injury. Imaging of the brain is routinely not performed (Strongly modified from Jörg and Menger (1998), Schmid (1999), adapted from Otte et al. (eds) (2004) Nuclear Medicine in Psychiatry, Springer, Heidelberg)

## 2.2 New Iteration Algorithms

Over the last 10 years, software technologies have helped to create iteration algorithms for SPET, which convincingly improve the signal-to-noise ratio of reconstructed images. These new iteration algorithms, such as ordered subset expectation maximization (OSEM) or depth response ordered subsets expectation maximization (DROSEM), have meanwhile replaced the conventional filtered back projection. Perfusion studies with  $^{99m}\text{Tc}$ -labeled ethylene biyldicysteinate dimer, Neurolite™ (ECD) or hexamethyl propylene amine oxime, Ceretec™ (HMPAO SPET) have become attractive and cheap in the clinical routine. For the diagnostics of potential functional alterations in whiplash injury, they are as recommendable as glucose



**Fig. 2.2** Talairach and Tournoux atlas 3D grid for the brain from 1988. AC-PC line: line between anterior and posterior commissure of the brain. The brain is “pressed” into this volume box, accurately enabling to define the coordinates of each voxel on a standardized basis (Adapted from Otte (2001) *Das Halswirbelsäulen-Schleudertrauma: Neue Wege der funktionellen Bildgebung des Gehirns - Ein Ratgeber für Ärzte und Betroffene*, Springer, Heidelberg)

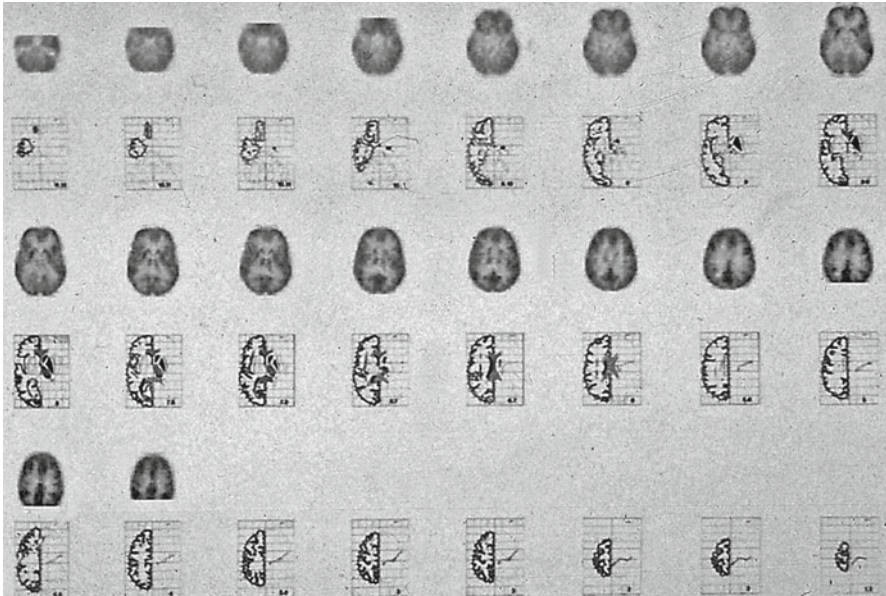
utilization studies by Fluorodeoxy-D-glucose, glucose analog; labeled with the positron emitter fluorine-18, it is used in PET as glucose metabolism marker ( $^{18}\text{F}$ -FDG PET).

## 2.3 Stereotaxic Atlas of Talairach and Tournoux

The basis for SPM analysis of brain alterations is the coordinate system according to Talairach and Tournoux. We would, therefore, like to describe this atlas and the idea behind it in more detail.

Talairach and coworkers had already finished an atlas for the basal ganglia of the human brain in 1958. The first edition of the whole brain was published in 1967 entitled *Atlas d'Anatomie Stéréotaxique du Télencéphale*.

In this atlas, a new idea was proposed: a proportional stereotaxic grid showing the anatomy of the brain in a standardized coordinate system. For this atlas, Talairach studied in total 20 full brains and 100 hemispheres, which he compared with 400 neuroradiological assessments. For the anatomical sections, the AC-PC line (line between anterior and posterior commissure) determined by the neuroradiological image data was taken as the reference line and anatomical slices were cut in parallel to this line. From this, a 3D grid was created, which is defined by three main lines and 6 reference voxels (Fig. 2.2).



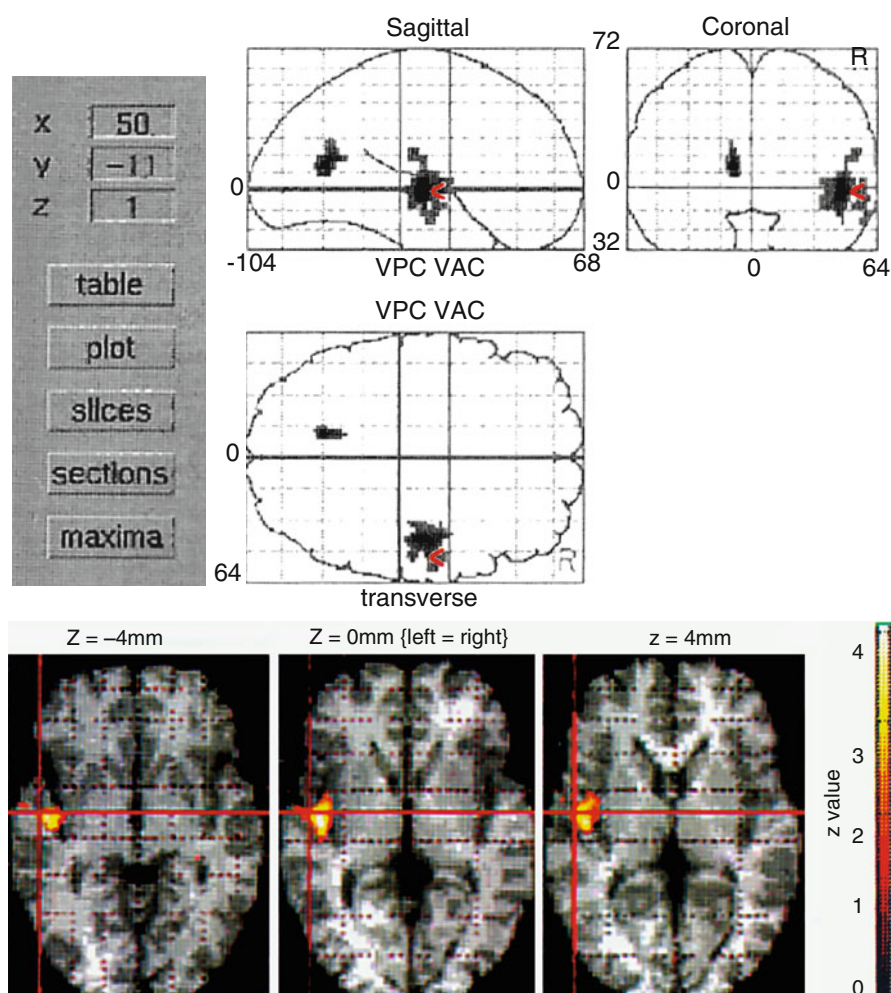
**Fig. 2.3** Example from the *Talairach and Tournoux* atlas. Transversal slices from the digitized atlas are exhibited with the corresponding PET slices, which are normalized according to the *Talairach* atlas (Modified from Otte (2001) *Das Halswirbelsäulen-Schleudertrauma: Neue Wege der funktionellen Bildgebung des Gehirns - Ein Ratgeber für Ärzte und Betroffene*, Springer, Heidelberg)

According to this coordinate system, the Talairach reference brain was defined.

The Talairach atlas shows all brain slices of the three dimensions of the Talairach coordinate system. In its version from 1988, it has become a European standard. In the first edition (1967), the atlas was produced from six brains of different sizes in order to demonstrate the validity of the stereotaxic coordinate system. This atlas comprised 32 sagittal slices from the hemispheres of two brains, 22 and 24 coronal slices from two further brains, and each 18 transversal slices from a third pair of brains. By contrast, in the 1988 version of the Talairach atlas, only one brain of a mid-European woman is taken as the anatomical reference. In Fig. 2.3, an example from the Talairach atlas is shown along with the corresponding PET slices in transversal projection.

## 2.4 Statistical Parametric Mapping (SPM)

Over now nearly two decades, the freely available software package from the Wellcome Department of Cognitive Neurology, London, known as SPM (versions SPM'94 up to SPM'99, and SPM2 up to SPM8, which are all based on SPM'94 and use MATLAB (The MathWorks, Inc.) functions and subroutines), has helped in the standardization of measurement and data analysis in



**Fig. 2.4** Example of statistical parametric mapping (SPM) used in PET (Adapted from Otte (2001) *Das Halswirbelsäulen-Schleudertrauma: Neue Wege der funktionellen Bildgebung des Gehirns - Ein Ratgeber für Ärzte und Betroffene*, Springer, Heidelberg)

functional neuroimaging comprising analysis of fMRI, PET, SPET, EEG, and MEG data. Generally, its idea is based on the region-of-interest (ROI) technique with the difference that the regions-of-interest are now voxels in a standardized stereotaxic room. This software not only spatially normalizes PET, SPET, or fMRI images to the standardized stereotaxic Talairach and Tournoux atlas (1988) but it can also perform statistical analyses on study groups on a voxel-by-voxel basis (Friston et al. 1991, 1995a, b); this allows for reliable and objective image handling that could improve interstudy variability due to the

analytical process itself. An example of SPM used in PET taken from Otte (2001c) is given in Fig. 2.4.

The various versions of SPM and a detailed description of the procedure can be retrieved from the following internet homepage for free: <http://www.fil.ion.ucl.ac.uk/spm/>

This method is described in detail under the aforementioned link. In brief, after interfile conversion of the reconstructed transaxial brain files into ANALYZE format, images are transformed to the stereotaxic coordinate system of Talairach and Tournoux using SPM. Then, the normalized images of patients and healthy subjects are compared by computing a voxel-by-voxel  $t$ -statistic. The  $t$ -statistic is transformed to a normal statistic yielding a Z score for each voxel. Voxels exceeding the significance level are then displayed in a “glass view” of transverse, sagittal, and coronal projections of a statistical parametric mapping.

## 2.5 Control Group

Any quantitative image analysis in functional neuroimaging is based on interindividual comparisons of data from a single patient or a patient group with data from a (normal) control group (Otte 2000c). This applies to both the ROI analysis and the SPM method (Friston et al. 1991, 1995a, b).

The recruitment of healthy volunteers is rather easy in some countries, but in many European countries, it is difficult, as most ethical committees do not allow studies with exposition of radioactivity to healthy volunteers without any indication. If they do so, then it is only under strict regulation. Besides, the payment and offering of incentives to healthy volunteers has become a contentious issue today.

Many institutions try to resolve this challenge by allowing for data from patients without brain alterations on previous scans or from oncological cases outside the brain having an additional (“normal”) brain scan without the need for a further radioactive injection. However, especially in functional neuroimaging, this can cause potential pitfalls: Firstly, such additional scans often follow other methodological protocols as compared with standardized brain scans; secondly, oncological patients may have brain alterations (e.g., Tashiro et al. 2000). Taking such oncological patients as a “normal control group” is, therefore, dangerous and may cause conflicting challenges in the evaluation of brain lesions not only in patients who are involved in compensation cases.

It is, of course, permissible to choose a group of patients with a known brain disease as a differential diagnostic control group. Furthermore, it is important to match the control group in age and gender and to perform a substantiated statistical power calculation for the number of control subjects needed.

Hence, caution is required, since the control group plays the most important but, at the same time, the most sensitive and vulnerable role in the quantitation of functional neuroimaging.

We will encounter this problem in some of the functional neuroimaging studies in whiplash injury (see Sect. 3.2).

Whiplash Injury

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