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Excerpt

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Structural magnetic resonance imaging in psychiatry: the functional psychoses

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Introduction

Magnetic resonance imaging (MRI) is a means of detecting a spatially localized signal which arises from the magnetic property of atomic nuclei. Although the technique for inducing magnetic resonance was developed in 1946, it is only since the work of Lauterbur over 20 years later that magnetic resonance has been used to produce images¹. Within a few years the clinical and research applications of this high resolution imaging technique were recognized. The technology is ever advancing to enable higher resolution images at faster acquisition time. MRI is now established as the gold standard in vivo technique for delineation of brain anatomy.

Principles of MRI

Magnetic properties of atomic nuclei

Mass, electrical charge and magnetism are basic properties of matter. Most mass is contained within the atomic nucleus. Each nucleus consists of protons (positively charged) and neutrons (no charge). Hydrogen is unique in having only one proton. The total number of protons and neutrons defines an isotope. Rotation of nuclei induces a magnetic field so that each nucleus becomes a dipole with north and south poles. The combined effect of the spin from multiple nuclei leads to the total spin property for each isotope. The application of an external magnetic field to an object interacts with the object's inherent nuclear spin to produce 'precession'. Precession is a cone-shaped rotating motion likened to that of a spinning gyroscope (Fig. 1). The frequency of precession is unique for each isotope, and increases in proportion to the magnetic field strength applied to it.

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P W R Woodruff

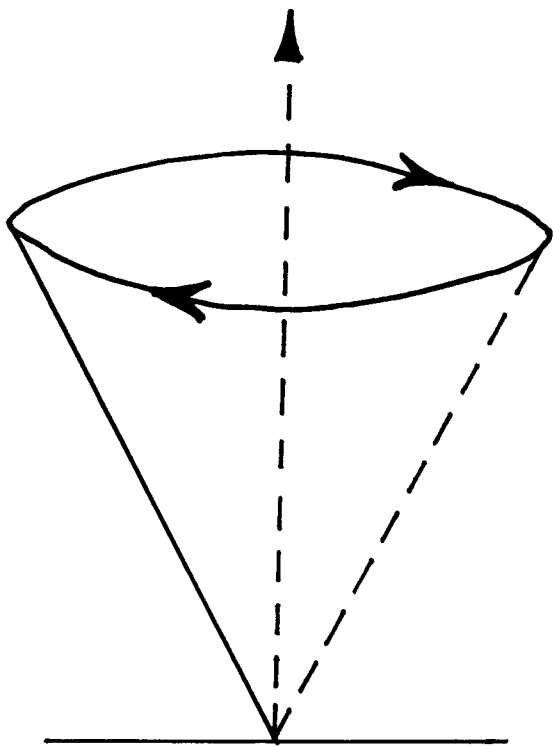


Fig. 1. Precession of an object around the vertical axis.

The MRI signal

The abundance of hydrogen in tissues makes its contribution to the MR signal particularly important. The hydrogen proton dipole is orientated either parallel or anti-parallel to the external magnetic field. Most protons adopt the low energy parallel position. When a radiofrequency impulse is applied, more protons move to the high energy anti-parallel position, a phenomenon known as resonance. Protons later resume the ‘baseline’ parallel position with the resultant release of radiofrequency energy. This energy is detected as the MR signal.

The combined magnetic effect of millions of atomic nuclei results in the measurable net magnetism of an object. The direction of net magnetism is described according to its orientation with respect to the externally applied magnetic field. The *xy* (transverse) plane is at right angles to the field and the *z* (longitudinal) plane is parallel to the external magnetic field. The *xy* plane can be considered to rotate around the *z* axis at the precessional frequency of the protons. This gives a stationary vector that describes the magnitude and direction of net magnetization in the transverse plane.

Structural MRI in psychiatry

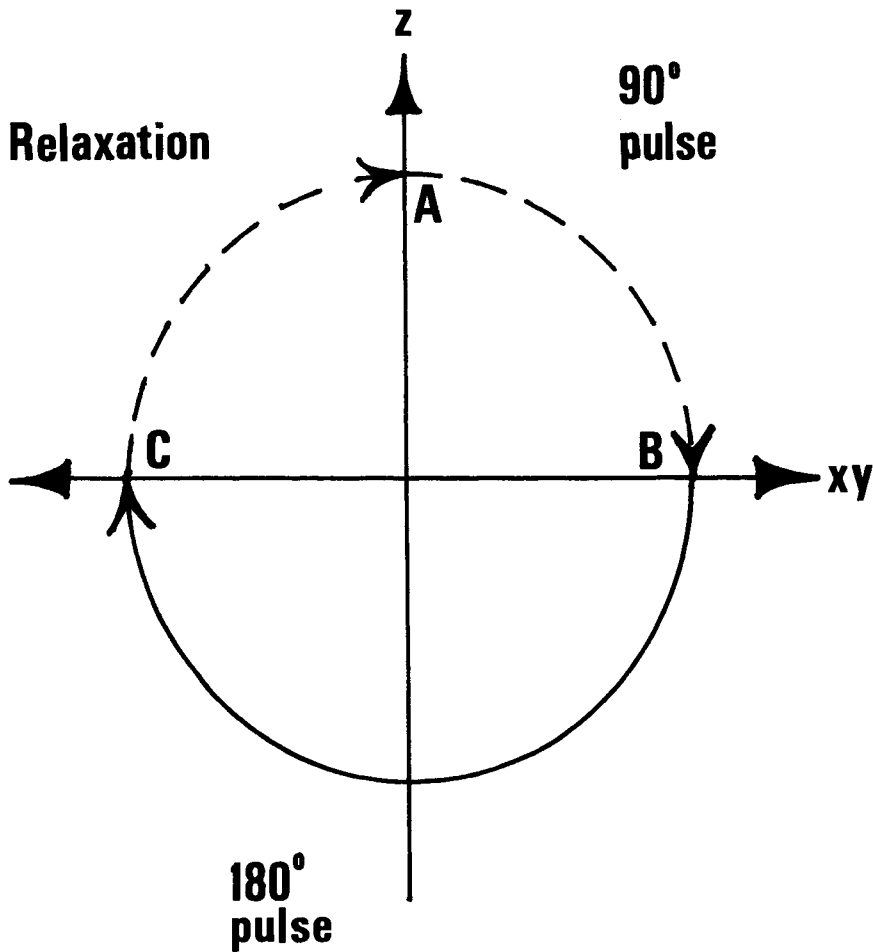


Fig. 2. Application of a radiofrequency pulse at the proton resonant frequency moves the net magnetization vector in the xy direction (A to B). A 180° spin-echo pulse refocuses the vector in the xy plane (C). Relaxation results in the magnetization vector then returning to the original position (A).

At rest, in an external magnetic field, net magnetization lies in the longitudinal z direction with none in the transverse xy plane. Application of a radiofrequency pulse (RF) at the proton resonant frequency in the transverse direction changes the net magnetization from the z to the xy direction (Fig. 2). A spin-echo pulse allows refocusing of the spins (see below). After the RF pulse stops, the magnetization vector returns to its original z direction by the process of relaxation. For a given tissue, relaxation in the longitudinal and transverse planes occurs at different rates described by the time

P W R Woodruff

constants T-1 and T-2. T-1 denotes relaxation in the longitudinal direction and T-2, relaxation in the transverse direction. T-1 relaxation results from loss of nuclear energy to the local environment or lattice. T-2 relaxation occurs because of 'dephasing' of proton precession causing net cancellation of the transverse magnetic vector (spin-spin effect). Both T-1 and T-2 relaxation for fluids like cerebrospinal fluid (csf) are much longer than for other tissues with higher fat content like white matter. The RF pulses can be altered so as to weight T-1 or T-2 relaxation times in such a way as to optimize contrast between the tissues of interest.

Imaging parameters that can be altered to maximize the contrast required include echo time (TE), pulse repetition time (TR), inversion time (TI) and flip angle of the magnetization vector. Different pulse sequences will be discussed first, then, the way in which these parameters can be modified to weight images to achieve the required contrast.

Imaging sequences

The most commonly used sequences for structural imaging are those called spin-echo and inversion recovery.

Spin-echo After the application of a radiofrequency impulse (RF pulse), the transverse signal decays due to dephasing of protons precessing in the xy plane. This decay is due to interference between neighbouring spinning protons (spin-spin effect) as well as inhomogeneity of the external magnetic field. The observed time of decay in transverse magnetization due to both of these effects is called T-2*. The spin-echo sequence maximizes the signal (otherwise lost due to dephasing) by 'refocusing' spins that are out of phase. An initial 90-degree pulse tips the magnetization vector from the longitudinal to the transverse plane (Fig. 3). This is followed by a 180-degree refocusing pulse which produces a recordable spin-echo at the time interval equal to that between the 90-degree and 180-degree pulses.

Inversion recovery spin-echo An initial 180-degree pulse inverts the magnetization vector in the z plane followed by the conventional spin-echo sequence of a 90-degree and 180-degree pulse sequence. The inversion time (TI) is the interval between the initial 180-degree pulse and the 90-degree pulse that follows. The signal largely depends on the extent of T-1 relaxation that has occurred during the inversion time and is therefore highly T-1 weighted. The disadvantage of inversion recovery is long imaging time and hence the potential for movement artefact. Reducing imaging time by lessening the number of data acquisitions is at the expense of the signal-to-noise ratio. Physiological movement can be taken into account by cardiac or respiratory gating. Faster imaging techniques, e.g. gradient echo pulse sequences, have particular uses in blood flow angiography and for detecting csf pulsation.

Structural MRI in psychiatry

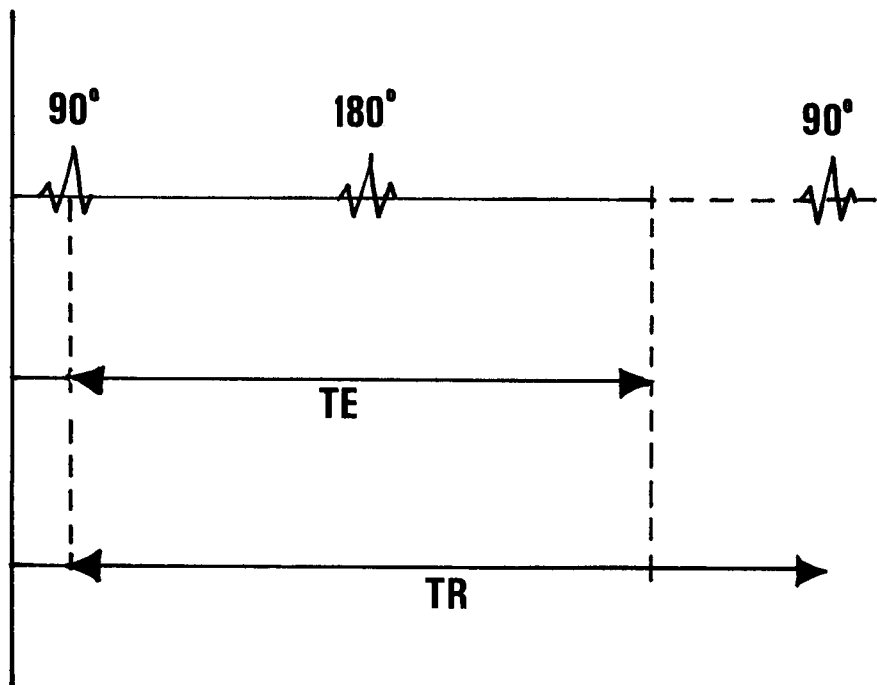


Fig. 3. The pulse sequence of the spin-echo. TE = echo time; TR = pulse repetition time.

Ultra-fast techniques like echo planar imaging are increasingly being applied for functional imaging.

T-1 and T-2 contrast The T-1 and T-2 values for csf, white and grey matter are shown in Table 1. Signal changes due to variations in TR are dependent on T-1 relaxation rates. As seen in Fig. 4, tissues with short T-1, e.g. white matter (WM), give a bright signal at short TR intervals. At long TR, the signal depends increasingly on proton density, and so the csf signal becomes more prominent. Signal intensity also varies with TE. The interrelationship between the effects of TR on the signal are shown in Fig. 5.

Table 1. *T-1 and T-2 relaxation times for the three main brain tissues are shown in seconds*

Tissue	T-1	T-2
Cerebrospinal fluid	4.0	2.0
Grey matter	1.0	0.08
White matter	0.6	0.03

P W R Woodruff

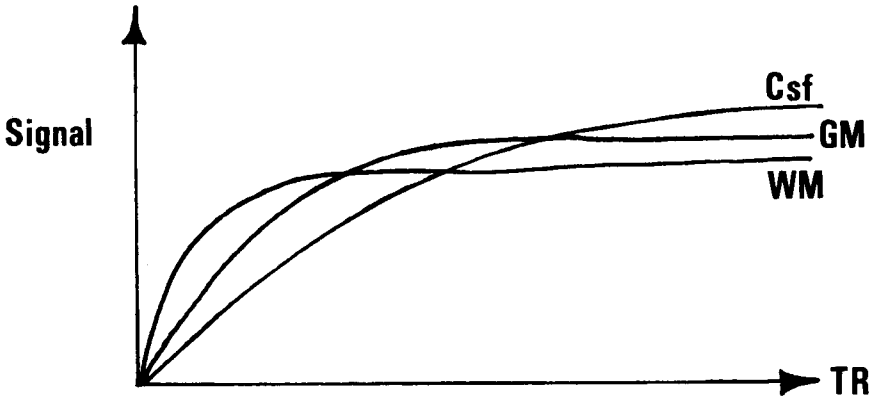


Fig. 4. Signal changes for cerebrospinal fluid (csf), cerebral grey matter (GM) and white matter (WM) at varying pulse repetition times (TR).

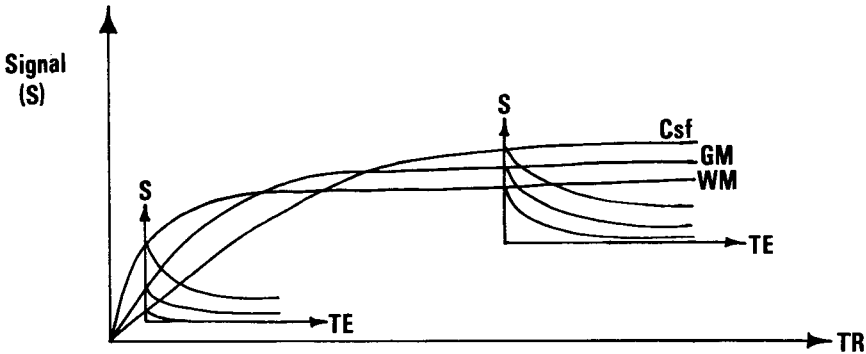


Fig. 5. Signal changes for cerebrospinal fluid (csf), cerebral grey matter (GM) and white matter (WM) at varying pulse repetition times (TR), both at short and long echo times (TE).

At short TR and TE, signal contrast is T-1 weighted, being greater from tissues with short T-1 characteristics. At long TR and TE the signal is T-2 weighted, so tissues with longer T-2 characteristics give a brighter signal. At long TR and short TE the signal depends on proton density, hence the prominent signal from csf.

Thus in T-1 weighted images, tissues with short T-1 values give high signal density (white matter > grey matter > csf). In T-2 weighted images, tissues with long T-2 values give high signal intensity (csf > grey matter > white matter). In proton density images, tissues with high water content give a large signal.

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Volumetric analysis

Many studies using MRI in psychiatry measure volume or areas of anatomical regions. High resolution plus appropriate imaging sequences are required to maximize contrast. In general, resolution has improved considerably in recent years with the use of more powerful magnets and more refined hardware. Early studies using planimetry and simple linear or area measures have evolved to more accurate volume measurements with computer-outlining techniques. Usually slices of 1–10 mm thick are taken, and the anatomical region is outlined and volume estimated from the area multiplied by slice thickness. The thinner the slice, the better the estimate of volume as long as resolution is adequate. However, as the slice becomes thinner, the signal/noise ratio is reduced. There is, therefore, the need to balance these factors which depend on the technology available.

The importance of MRI in psychiatry

Clinical applications

Clinical applications of MRI include: 1) diagnosis of organic brain disorders; 2) monitoring progress of chronic disorders; and 3) assessing prognosis. MRI is more sensitive than computerized tomography (CT) at detecting non-calcified intracranial lesions and gives much better anatomical detail. MRI complements CT in aiding diagnosis of physical brain disease that underlies organic psychoses, e.g. cerebral infarction or tumour. Clinical indications for MRI in psychiatric patients are similar to those for CT and include: 1) history of head injury or other neurological disease; 2) presence of neurological signs including movement disorder of unknown cause; 3) acute confusion or gradual cognitive decline; 4) dementia; and 5) first psychosis or major personality change in patients over 50 years old².

MRI is the most sensitive technique for detecting small lesions such as hyperintensities or microinfarcts as may be seen in temporal arteritis or systemic lupus erythematosus. White matter lesions on T-2 weighted images may be important in the clinical assessment of multiple sclerosis. Plaque count relates to prognosis in this condition. Diffuse white matter changes such as leucoencephalopathy in AIDS can be seen clearly using MRI. Because of its sensitivity, MRI may demonstrate cerebral atrophy before obvious cognitive decline in patients with dementing illnesses including AIDS. Specific regions may be more easily identified with MRI than CT, like the pituitary gland in neuroendocrinological conditions. It may be preferable to use MRI on patients with conditions like AIDS when multiple pathology is suspected like atrophy, leucoencephalopathy and intracranial lesions like lymphoma or toxoplasmosis.

MRI does not expose patients to X-ray radiation, and, as long as there are no contra-indications, is safer than CT. Contra-indications to MRI

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P W R Woodruff

include: 1) metallic implants, e.g. aneurysm clips or orthopaedic screws; 2) metallic foreign bodies, e.g. metal lathe eye injuries or shotgun injuries; and 3) pregnancy.

Research applications

The importance of MRI in psychiatric research is to enable expansion of post-mortem and CT brain studies by providing the means to measure neuroanatomical regions in vivo. Furthermore, MRI can detect boundaries between grey and white matter within anatomical regions. Combining structural MRI with information using clinical, neuropsychological, neurophysiological and functional neuroimaging techniques provides a powerful means of detecting important relationships between brain structure and function in psychiatry.

Subject selection in MRI studies

Much has been learnt about normal brain morphology from MRI studies in psychiatry that use a normal control group for comparison. Brain abnormality can be defined by significant deviation from a normal control range. Therefore, it is important to: 1) determine normal brain morphology; and 2) identify features of subject groups that may influence the brain structures being studied. For instance, schizophrenia may be a heterogeneous condition in which only subgroups of patients have brain abnormalities. The finding of statistically significant differences in size of brain structures between schizophrenics and controls may therefore depend on the criteria used to select the two groups. The choice of control subjects is therefore crucial to MRI studies which draw conclusions often from small differences between groups.

The normal brain

Normal brain asymmetry

The left occipital pole is larger and extends more posteriorly than the right, whereas the right frontal region is often larger and protrudes more anteriorly than does the left. The right temporal region is usually larger than the left. Compared with the right, on the left side, the planum temporale is larger and the Sylvian fissure ascends more steeply and extends more posteriorly³.

In general, men show more hemispheric asymmetry than women⁴. The corpus callosum is possibly larger and more bulbous posteriorly in women and non-right-handers^{5,6}. Right-handed persons may have more cerebral asymmetry than left-handers⁷. Cerebral size in women is less than men. This difference is probably related to factors determining height⁸.

Structural MRI in psychiatry

Age

Brain shrinkage, in the absence of cognitive deficit, is more noticeable as age advances. This shrinkage becomes more prominent after the age of 55. Studies using MRI have demonstrated age-related decreases in volume of cerebral cortex, cortical grey matter, basal ganglia and anterior diencephalic grey matter^{9,10}. Murphy¹¹ compared two groups of subjects aged < 35 and > 60 and found specific reduction in lenticular and caudate nuclei, after taking reduced cerebral size into account. Volume of lateral ventricles, third ventricle and csf were all greater in the older group. Normal brain asymmetry was preserved. Similar results have been described in other studies¹².

Social class

A negative association has been found between socioeconomic status and brain size¹³. It has been suggested that this association may be due to poor nutrition adversely affecting brain growth. The association may also be due to the fact that people with conditions that result in brain shrinkage 'drift' down the social scale as a result of their condition. Using paternal social class to match subject groups may take account of social drift.

Intelligence and education

Intelligence accounts for about 12–30% of the variance in brain size of normal individuals, being greater the higher the IQ. Andreasen¹⁴ found IQ correlated with volumes of cerebrum, cerebellum, temporal lobe, hippocampus and grey matter. There was no such correlation with white matter, cerebrospinal fluid, caudate or lateral ventricular volume. The finding of decreased frontal lobe size in schizophrenics was later attributed to the choice of a control group with more years of education⁸. Comparison of the same patient group with a control group matched for education did not reveal differences in frontal lobe size¹⁵.

The abnormal brain

Factors affecting brain structure

Injury MRI is very sensitive to lesions which may persist after full clinical recovery from trauma. There may, for example, be distinct foci or more generalized atrophy observed. Special care needs to be exercised in evaluating individuals likely to have such lesions before including them in research study groups.

Pre-existing neuropsychiatric disease Many neuropsychiatric diseases are associated with significant brain abnormalities detectable using MRI. Common

P W R Woodruff

examples include: Parkinson's disease, Alzheimer's disease, multi-infarct dementia, AIDS, systemic lupus erythematosus and multiple sclerosis.

Alcohol Psychiatric disorder amongst alcoholics and drug abusers is common. One study of alcoholics demonstrated that 65% had a current psychiatric disorder including antisocial personality disorder (36.5%), affective disorder (27%), schizophrenia (4.3%)¹⁶. It is, therefore, particularly likely that studies on psychiatric patients will include alcoholics and drug abusers¹⁷. From an emergency clinic sample, 47% of schizophrenics had a lifetime risk of alcohol abuse-related disorder¹⁸.

Post-mortem studies have demonstrated loss of cerebral and cerebellar cortical neurones and white matter in alcoholics. Female alcoholics are more likely to develop these changes^{19,20}. However, it was demonstrated in a recent post-mortem study that, although compared with controls, alcoholic male brains were smaller, they contained the same number of neurones²¹. MRI studies in alcoholics demonstrate reversible and irreversible brain shrinkage. Zipursky et al²² demonstrated reversibility of ventricular enlargement after abstinence.

Raised T-1 level was related to cognitive impairment in some alcoholics²³. More detailed studies in alcoholics have demonstrated volume reductions in cortical and subcortical cerebral structures. These structures include: diencephalon, caudate nucleus, dorsolateral prefrontal and parietal cortices and medial temporal lobe regions. Cortical and ventricular csf was increased. Cerebral grey matter was reduced²⁴. Generalized grey and white matter loss was more marked in older than younger alcoholics with equivalent drinking history. This was interpreted as an age-related increase in vulnerability of the brain to effects of chronic alcohol abuse²⁵.

Other substances Opiates, cocaine, solvents, benzodiazepines and other drugs or chemicals may also be related to brain abnormalities²⁶⁻²⁸. It is, therefore, prudent to take account of drug abuse in studies designed to investigate brain abnormalities from other causes.

Previous treatment There is little evidence that neuroleptic medication per se alters brain structure detectable using MRI except perhaps the basal ganglia. Studies in psychotic patients do not generally find correlations between brain size and length of exposure to, or dose of, anti-psychotics²⁹.

Structural brain abnormalities in patients referred for ECT include lateral and third ventricular enlargement, atrophy of frontal and temporal lobes, amygdala and hippocampus. On the evidence available it seems unlikely that ECT itself results in progression of these abnormalities³⁰. T-1 values may rise acutely after ECT and return to normal within hours. The rise