



# Alzheimer's disease: Oxford Project to Investigate Memory and Ageing (OPTIMA)

## Introduction

The Project examines how the use of brain scans can contribute towards an accurate diagnosis of Alzheimer's disease and aims to lay the foundations for the development of new forms of prevention and treatment.

## Let's look at the science:

### How is an Alzheimer's disease diagnosis made and how accurate will it be?

A definite diagnosis of Alzheimer's disease and other forms of dementia such as dementia with Lewy Bodies (DLB) can only be made through the examination of brain tissue under a microscope, usually after death.

Studies have shown that when a doctor is certain that Alzheimer's disease is the probable cause of a patient's problems, and there is no other disease present, diagnosis proves to be correct in over 75 per cent of cases.

However, some cases are not so easy to diagnose. It may not be possible to diagnose Alzheimer's disease in these people with certainty. When such cases were followed up after death, OPTIMA found that a quarter of all the clinical diagnoses made were incorrect.

### What brain scans were used and how can they help in making a diagnosis?

The Project used CAT scans (computerised axial tomography). These are X-rays which show the brain's structure and which can show the changes in the brain that accompany the development of Alzheimer's disease. If these

changes were taken into account when making a diagnosis, the Project found that the accuracy of the diagnosis improved and inaccurate diagnosis occurred in one in five cases instead of one in four as above.

The Project also used SPECT scans (single photon emission controlled tomography) that give pictures of blood flow through the brain. These pictures can show characteristic changes in the parts of the brain that are concerned with thinking and processing information. Using these scans the Project was able to reduce the rate of error below one in five. When both scans were used the error rate fell to less than one in 20.

However, neither of these scans, either individually or together, can be used to confirm with 100 per cent certainty the presence of Alzheimer's disease in an individual during life. This is also the case with another more recent form of scan, MRI (magnetic resonance imaging), which creates pictures using a powerful magnetic field rather than X-rays.

### What else have the brain scans shown?

The CAT scans showed that tissue in the medial temporal lobe of the brain was shrinking at least ten times faster in people with Alzheimer's disease than in other elderly people.

In people without Alzheimer's disease the rate of tissue loss in this area of the brain is about 1.5 per cent per year. However, the Project also showed that some normal elderly people lose tissue at a faster rate. At this stage of the research it is not possible to say whether tissue loss as measured by these scans is an early sign of Alzheimer's disease.

The scans used by OPTIMA, and MRI scans, will have to be given to many more people over several years and the results confirmed after death before firm conclusions can be drawn.

## **Diagnosis: Questions & Answers**

**I have been caring for my wife for several years now. The Consultant has said that she has Alzheimer's disease but she hasn't had a brain scan. Should we ask for one in case the doctor is wrong?**

If the doctor is quite certain of the diagnosis then, in the majority of cases, he or she will be correct and a scan is unnecessary. Doctors also regard it as impractical to scan everyone. However, if there is uncertainty about the diagnosis, brain scans can help a great deal. For example, a scan showing tissue loss in the medial temporal lobe in a person complaining of significant memory difficulties makes a diagnosis of Alzheimer's disease more likely.

### **Which scan should be done first?**

The CAT scan is usually the first to be done since this allows the doctor to exclude problems such as tumours, strokes and other structural changes in the brain that might have caused the memory loss.

The SPECT scan should only be carried out first if the doctor is concerned about whether the patient might have a more rare frontal lobe dementia such as Pick's Disease. In such cases the changes in blood flow in the frontal regions of the brain will be quite clear and can help make the diagnosis more exact.

### **If a brain scan is necessary will we have to go to a special centre?**

No. Most hospitals have CAT scanners and almost all now have SPECT scanners. However, it is important that a consultant who understands how to interpret scans of the brain is involved. The OPTIMA Project also identified the importance of using a certain angle of measurement when using CAT scans so this expertise will be required.

## **What about dietary risk factors?**

The Project found that, in the patients who had Alzheimer's disease, and in some of those with other dementias, the level of an amino acid called homocysteine found in blood plasma was significantly higher than in other people. They also found that the levels of the B vitamins, folic acid and vitamin B12 were significantly lower in the same patients. High levels of homocysteine are known to be associated with strokes, heart disease, and some cancers.

### **Does this mean that high levels of homocysteine actually cause Alzheimer's disease?**

The true answer is that at present we simply do not know. Many other researchers have now found that the levels of folic acid and vitamins B12 are reduced in dementia, and specifically in Alzheimer's disease, and others have shown high levels of homocysteine, not only in Alzheimer's disease but in other diseases too. The high levels of homocysteine in the research could be the result of Alzheimer's disease rather than the cause.

### **What is different about the OPTIMA study?**

In this study the patients had received a postmortem examination so the diagnosis of Alzheimer's disease was accurate. Those patients with higher levels of homocysteine than others were four times more likely to have Alzheimer's disease.

### **Can you treat high levels of homocysteine?**

Yes. High levels can be brought down to normal by taking folic acid or vitamin B12 supplements. These vitamins are also found in vegetables such as broccoli, fruit, soya flour, meat and fish. But someone with a serious deficiency would need to eat a very large quantity of these foods to equal the supplements required.

### **Does this mean that if a person has Alzheimer's disease or if they are worried that they are developing the condition**

**they should start taking folic acid or vitamin B12 supplements?**

No. The truth is that no one knows whether taking supplements will make any difference at all. If a person's blood levels are normal there should be no need to take supplements. A GP will advise if they are necessary.

No one knows whether taking supplements will help to prevent the disease or whether it will affect the rate at which the disease progresses. The only way that this will be discovered is by doing further studies on many more patients over a long period of time.

**Are there any harmful effects from taking these vitamins?**

At high doses some vitamins can be dangerous and toxic. However, at the doses found in normal vitamin supplements that can be bought over the counter at the chemist or in health food shops they are quite safe. Of course, it is always wise to discuss taking vitamin supplements with your GP in the first instance. For example, very rarely, taking folic acid when the level of vitamin B12 is very low can give rise to nerve cell damage.

**What does all this mean for me?**

It is not possible to give general advice to specific individuals in this situation. A great deal of research into Alzheimer's disease is currently taking place and many promising leads may take many years to confirm.

However, if you are concerned about yourself or a close relative, you should first discuss the situation with your GP who may decide to refer you to a specialist such as an old age psychiatrist or neurologist.

You can also contact Alzheimer Scotland's 24 hour Dementia Helpline for information, support or just someone to listen. Call freephone 0808 808 3000.

OPTIMA research has been published in medical journals and has been extensively confirmed around the world. The first report in Archives of Neurology in 1998 has now been cited more than 300 times in the medical and scientific literature. OPTIMA has received funding from The Medical Research Council to carry out a pilot trial of B vitamins in the elderly with mild cognitive impairment. This trial will use MRI scans to monitor the rate of shrinkage of the brain to see if the vitamin treatment slows it down. It started early in 2005 and will take place in Oxford and Bristol.

For more information about the OPTIMA Project contact: Professor A David Smith, Department of Pharmacology, University of Oxford. david.smith@pharmacology.ox.ac.uk and www.pharm.ox.ac.uk/optima.htm

This information sheet is based on information from OPTIMA collaborators and approved by Professor A David Smith.



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