CFU Carers' Support Group

For carers and relatives of people with fronto-temporal dementia and semantic dementia

Newsletter

JUNE 2007

www.cfucarers.org.uk
Welcome

A warm welcome to the June edition of our CFU Carers Support Group Newsletter! A big thank you to all of you who came to our Carers’ meeting on 24th May. Professor Neary, Head Consultant Neurologist at the CFU, gave a fascinating scientific overview of the clinical aspects of frontotemporal dementia and semantic dementia, as well as an up-to-the-minute account of genetic and molecular research into the causes of these conditions. We’ve provided a quick summary of his talk in this newsletter for those of you who weren’t able to attend. Don’t forget you can also log onto our carers’ website at: www.cfucarers.org.uk to read previous newsletters and summaries of invited talks. We hope you have a great summer and hope to see you at our next support meeting on 26th July!

Contents

Welcome 2
Fronto-temporal Lobar Degeneration: A Scientific Overview 3
Carers’ Questions 11
Did you know? 9
Fronto-Temporal Lobar Degeneration (FTLD)

Fronto-temporal dementia and semantic dementia form part of the same disease, known as ‘fronto-temporal lobar degeneration’ (FTLD). FTLD typically affects people between the ages of 45 to 65. It is the second most common cause of dementia in younger people. Symptoms progress insidiously and may be very subtle at first, so that they only become apparent to relatives and partners after some time. It affects men and women to an equal degree. The average duration of the illness is 8 years although it can vary widely from 3 to over 20 years. In some cases, there is a history of similar disorders in the family. FTLD affects the anterior parts of the brain. When the frontal lobes are predominantly affected, this gives rise to the clinical syndrome of fronto-temporal dementia. Selective dysfunction of the temporal lobes gives rise to semantic dementia.
Fronto-temporal dementia

Fronto-temporal dementia (FTD) is a behavioural disorder, characterised by a profound change in personality.

**Behaviour**

The most common behavioural symptoms are:

- Affective change (e.g. loss of empathy or feeling towards others)
- Loss of insight (the person is not aware of any changes within himself)
- Repetitive behaviours / stereotypies (e.g. tapping fingers, hoarding possessions)
- Change in eating / oral behaviours (e.g. preference for sweet foods)
- Reduced response to pain

Symptoms are not exactly the same for all sufferers, and depend on which part of the brain is most affected. Generally speaking, there appear to be two different patterns:

*Apathetic*: Patients are inert and inactive, and act as if they are depressed. However, they do not complain of feelings of depression, and remain unconcerned about their lack of motivation and drive.

*Disinhibited*: Patients are overactive and act inappropriately in social situations. They show a lack of concern for the feelings of others and are often restless and irritable.

**Cognitive symptoms**

People with FTD do not have any primary problems in language. However, because of their reduced social awareness, conversation becomes severely limited and patients may eventually become mute in the later stages. By contrast, patients retain good visuo-spatial skills and can negotiate their environment without getting lost. Their memory can seem impaired, however this tends to occur as a result of poor attention and concentration, and patients often remember information that is personally salient to them.

**Physical symptoms**

Patients are typically physically fit. Initial changes are apparent in mental function only. As the disease
progresses, reduced activity and physical slowing may occur. In some rare cases, people with FTD can develop physical signs of Motor Neurone Disease (e.g. twitching and wasting of the muscles.

**Brain imaging**
FTD predominantly affects the anterior parts of the brain. We can use 2 types of scans to see whether these parts of the brain are affected A structural scan (e.g. MR scan) shows the overall structure of the brain from different angles. A widening of the black spaces between the ridges of the brain tells us that this part of the brain is shrinking. A functional scan (e.g. SPECT scan) reveals the function of the brain. This is particularly useful if a patient is in the early stages of a degenerative disease: the brain may not be shrunken but certain parts of it are not working properly. On the SPET scan, yellow/orange indicates that this part of the brain is working normally, while purple/blue indicates a loss of function. As you can see on p.5, the MR scan shows shrinkage of the frontal lobes, while the SPET scan shows reduced activation in the anterior parts of the brain.

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**Semantic Dementia**
Semantic dementia (SD) is another clinical manifestation of frontotemporal lobar degeneration, associated with shrinkage of the temporal lobes. SD is a relatively rare disorder and is much less common than FTD.

**Cognitive symptoms**
**Language**
Problems in language tend to occur first. People with SD have difficulty naming and often use the incorrect word in conversation (e.g. calling a lion a “dog” or saying “water” for milk). They have difficulty understanding the meaning of words and may fail to recognise relatively simple words in conversation. Nevertheless, their speech is generally fluent and effortless, which may initially give relatives the impression that they do not have any primary difficulty with language. Moreover, their repetition is good,
and they can generally read and write words they do not understand.

**Visual recognition**
The disorder may also affect the ability to recognise objects and faces. The sufferer sees normally (and so can distinguish when two objects or faces are the same or different), but is no longer able to attribute any meaning to what they see. This is why sufferers may still be able to draw accurately objects that they no longer recognise. Occasionally, difficulties in visual recognition may occur before language problems.

**Behaviour**
Difficulty in comprehension is by far the most important feature of SD, however, sufferers do also show changes in their behaviour. These changes are generally more subtle than those observed in FTD, and have a more obsessionnal quality. Sufferers tend to focus on a restricted range of activities (e.g. house work, sewing, walking), which they pursue obsessively. They develop a preference for fixed routines and often become preoccupied by time, so that certain activities are always carried out on set days and at fixed times. Sufferers generally become more self-centred although they rarely show the marked loss of empathy and lack of self-care typical of FTD.

**Physical symptoms**
Sufferers are generally fit and physically healthy although they may become slowed down in the later stages of the disease.

**Brain imaging**
As you can see below, the MR (structural) scan shows severe shrinkage of the temporal lobes. Although both sides are affected, one temporal lobe tends to be more affected than the other. In this scan, the left side (imagine the person is facing you) is more shrunken. The SPET (functional) scan shows reduced activation in the temporal lobes, again more marked on the left side.
MR scans in FTD

Shrunken

Anterior cut

Posterior cut

SPET scans in FTD

Anterior cut

Reduced activation

Front

Back

MR scan in semantic dementia

Shrunken

Reduced activation

SPET scan in semantic dementia
Frequency of clinical syndromes in FTLD

Fronto-temporal dementia (FTD) is by far the most common disorder, followed by semantic dementia (SD). Fronto-temporal dementia with motor neurone disease occurs in 14% of FTLD cases, while 11% have progressive aphasia, a selective disorder of language production.

What causes FTLD?

The full answer to this question is not yet known, however researchers are continually uncovering new leads. The disease process affects nerve cells in the upper layers of the cortex (the outer layer of our brain known as the grey matter). By looking through the microscope at the cortex of brains, researchers have identified 2 main types of disease process in Fronto-temporal lobar degeneration. The first main type is called Tau positive pathology. Each nerve cell in the brain contains a microtubule network, whose role it is to maintain the structure of the cell by transporting proteins to parts of the cell that need them. Tau acts as the glue which binds these microtubules together. In FTD, there is a dysfunction in the production of tau, which means that the microtubule networks disintegrate, leading to progressive starvation of the cell. Looking through the microscope, it is possible to see the accumulation of tau in the cells. Some forms are referred to as Pick bodies, which is why fronto-temporal dementia was originally known as Pick’s disease. However, these Pick bodies are only observed in a small minority of FTLD cases. The second main type of disease process is called Tau negative pathology. In this type, the disease is caused by a dysfunction of a protein called TDP-43. In normal cells, TDP-43 is
transported into the cell’s nucleus (or centre) where it interacts with other proteins involved in cell regeneration to promote cell survival. In tau negative cases however, this TDP-43 protein remains trapped in the cell’s periphery and cannot get into the nucleus, leading to a progressive deterioration of the cell.

It is as yet unclear what causes these key proteins to stop working suddenly in mid-life. To date, the most promising leads for research have come from cases of FTLD where the condition is inherited. In 1998, researchers from Manchester and America identified one of the genes associated with tau positive pathology. They worked out family trees of patients with FTLD and retraced the condition back through generations to the originating family. They then analysed the DNA of all affected members of this family and found that they all carried a defect (or mutation) in a gene that was associated with the regulation of the protein tau. In 2006, the same group identified another gene mutation, which is associated with the tau negative type. The discovery of these 2 genes has been a real scientific breakthrough, but still only accounts for a small number of cases with FTLD. Researchers are continuing to look for other genes which may be involved in cell degeneration in FTLD.

Did you know?

Brenda recently won a Community and Social Care award for her outstanding practice and achievement in setting up the CFU Carers’ group, which was recognised as the only service of its kind in the North West. The carers’ group was also awarded a prize by the Manchester Neurosciences Clinical Development Directorate for its role in supporting patient families and carers. Thanks to your continued support and commitment, the group has grown from strength to strength and has attracted interest from many medical and health professionals, helping us to improve understanding of fronto-temporal dementia and semantic dementia.
Q. What is a gene mutation?
A. A gene mutation is an altered gene. A gene can be thought as a code which contains information necessary to perform a specific function in a cell. If the gene is mutated, then the information it carries becomes altered and can change the specific function it regulates in the cell.

Q. Can gene mutations be caused by emotional factors?
A. No. Although symptoms may only appear in mid to later life, the mutation in the gene is present from the day we are born and cannot be altered by any environmental or emotional factors.

Q. Do people with FTD develop problems in language?
A. People with FTD do not have any primary difficulties in language. They have no problems in articulation or expression and speak in grammatically correct sentences. However, their conversation often becomes reduced because they have lost their social awareness of others and are unable to appreciate the value of talking to people. Conversation may be limited to a few set phrases which people will repeat over and over (e.g. ‘It’s one of those things’). In the later stages of the disease, people may become mute or only use speech to communicate their needs rather than make conversation.

Q. Do people with FTD and SD become aggressive?
A. People with FTD or SD can get more irritable and rigid in their behaviour. They often act in an ‘asocial’ way, as if other people do not exist, but they are rarely antisocial and deliberately causing harm. Patients can become very attached to a set routine, doing the same things at the same time, and can get upset and agitated if their routine is changed.

Q. Are headaches a common symptom in people with FTD or SD?
A. Not really. Headaches are very common in the general population, but there is no medical link between headaches and degenerative brain disorders. If a person with FTD or SD is repeatedly complaining about headaches, it may be part of their behavioural routine and may not be related to an actual sensation of pain. People with FTD and SD often engage in repetitive, stereotyped behaviours, such as doing something or talking about the same thing over and over again. Some patients will focus on medical complaints and talk about them repetitively, even if they are not actually physically experiencing the symptoms at the time.