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Functional (psychogenic) memory disorders - a perspective from the neurology clinic

Jon Stone¹, Suvankar Pal^{1,2}, Daniel Blackburn², Markus Reuber², Parvez Thekkumpurath¹, Alan Carson^{1,3}

¹Centre for Clinical Brain Sciences, University of Edinburgh, Western General Hospital, Crewe Rd, Edinburgh EH4 2XU, UK.

²Anne Rowling Regenerative Neurology Clinic, University of Edinburgh, UK

² Dept of Neuroscience, University of Sheffield, Sheffield, UK

³ Dept of Rehabilitation Medicine and Dept of Clinical Neurosciences, NHS Lothian.

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Correspondence to: Jon Stone, ¹Centre for Clinical Brain Sciences, University of Edinburgh, Western General Hospital, Crewe Rd, Edinburgh EH4 2XU, UK

Email: Jon.Stone@ed.ac.uk

Abstract:

Symptoms of poor memory and concentration represent a common cause of morbidity amongst patients presenting to General Practitioners and may result in referral for a neurological opinion. In many cases these symptoms do not relate to an underlying neurological disease or dementia. In this article we present a personal perspective on the differential diagnosis of memory symptoms in the neurology clinic, especially as this applies to patients who seek advice about memory problems but have no neurological disease process. These overlapping categories include the following 'functional' categories: 1) memory symptoms as part of anxiety or depression; 2) "normal" memory symptoms that become the focus of attention; 3) isolated functional memory disorder in which symptoms are outwith 'normal' but not explained by anxiety; 4) health anxiety about dementia; 5) memory symptoms as part of another functional disorder; 6) retrograde dissociative (psychogenic) amnesia. Other 'non-dementia' diagnoses to consider in addition are 7) memory symptoms secondary to prescribed medication or substance misuse; 8) diseases other than dementia causing memory disorders; 9) patients who appear to have functional memory symptoms but then go on to develop dementia/another neurological disease and finally 10) exaggeration/malingering. We discuss previous attempt to classify the problem of functional memory symptoms, the importance of making a positive diagnosis for the patient and the need for large cohort studies to better define and manage this large group of patients.

Introduction

Research investigating the causes and prognosis of subjective memory impairment is dominated by studies designed to prise out those patients who ultimately progress to developing a frank dementia and target them for early intervention.

By contrast there is a remarkable lack of interest in patients who have memory symptoms, entirely unrelated to neurodegenerative disease but never go on to get dementia, or who go on to improve spontaneously.

As neurologists and neuropsychiatrists working in regional neuroscience centres, predominantly seeing a younger age group of patients, we are frequently referred patients who complain or are concerned about memory symptoms and whose symptoms can be clearly identified as unrelated to dementia. These are a neglected group of patients, at high risk of iatrogenesis. The number of patients in this group is growing alongside increased media exposure about the horrors of dementia, the need for early detection and the introduction of incentives for dementia diagnoses[1].

In this article we draw on our respective backgrounds in research of functional disorders in neurology (JS/AC/MR), neuropsychiatry (AC/PT) and the under 65 cognitive disorders clinic (SP/DB/JS/AC/PT) to: give a personal perspective regarding the differential diagnosis of memory symptoms that can be positively identified as functional; provide a narrative review of the available literature; make suggestions for a more positive diagnostic and treatment approach and suggest some directions for future research.

Terminology is always an issue in this area. We shall use the term 'Functional Memory Symptoms' to describe symptoms which are genuine but don't relate to an underlying neurological disease process. Most of the disorders we are describing may be classified in DSM-5 as Conversion (Functional Neurological) Disorder that demands positive evidence that the symptom is not related to disease (for example by demonstrating internal inconsistencies or by

identifying the symptom as one normally experienced in a healthy population). In ICD-10 the category of dissociative amnesia exists to describe isolated retrograde amnesia but other types of presentations of memory problems unrelated to neurological diseases are poorly represented.

We recognise that other terms such as psychogenic, non-organic, hysterical and ‘worried well’ have been used in the literature about these presentations. In this context functional memory symptoms are NOT synonymous with “subjective cognitive impairment” or “mild cognitive impairment” which are terms that include, of course, patients in the prodromal stages of dementia, although we argue that the patients we describe with functional memory disorders do represent a subset of those patients as they are labelled by some clinicians.

Epidemiology of Functional Memory Symptoms

Memory symptoms in the general population

Everyone knows from experience that memory is fallible. We all occasionally go in to a room and forget why we are there, lose track of a conversation or temporarily forget something familiar like a PIN – these things are all part of everyday experience. Data on this has been assembled most effectively by McCaffrey and their colleagues in their book ‘Symptom Base Rates in the General Population’[2]. They took hundreds of studies with control data and presented the frequency of symptoms in different populations. Table 1 shows some examples of this data in young healthy adults emphasising the value of considering the base rate when making any assessment of ‘normal’ cognitive function.

Predictably, there is also evidence that these cognitive complaints increase during the lifespan. A Dutch study of nearly 2000 healthy subjects found that as many as 29% of people aged 25-35 considered themselves forgetful, rising to 34% (40-50 years), 41% (55-65) years and 52% between 70-85 years[3]. High proportions (47-60%) of these respondents said they were

'worried' to some extent about their forgetfulness. Complaints of forgetfulness were correlated with depression and poor subjective health. Although some attributed them to emotional problems or lack of interest the most commonly cited cause after age was 'unknown'. Such data needs to be put in the context of changing frequencies of mental disorder across the lifespan. Anxiety and depression also increase with age with most studies finding an increase in frequency until the 40's and 50's when the frequency levels off or drops[4].

Studies of memory clinics

Early studies of memory clinics found high proportions of patients without dementia. A cross-sectional study of 418 consecutive patients seen at the Institute of Psychiatry in London in the 1980s 24% received a diagnosis of 'memory complainers (no diagnosis)' and a further 6% were found to be 'neurotic' or have a mood disorder. Three more recent studies of memory clinics run by neurologists in the UK (which usually have a strong bias to seeing patients under 65 years of age) give indicate how commonly dementia is *not* diagnosed now in patients with primary cognitive complaints. A study from Liverpool reported rates of 40% in 2006 (n=183) dropping to only 24% (n=252)(Figure 1) [5]. They attribute this to raised awareness of referral guidelines and increasing referrals and suggest that many of those without dementia were 'the worried well' or had depression.

Similarly a centre in Sheffield reported that the frequency with which presentations in the memory clinic were related to neurological or neurodegenerative disorders dropped from 65% in 2004 to 45% from 2012 and that functional memory disorders were common in the remaining patients [6](Figure 1). A third study published in this issue of Journal of Alzheimer's Disease from Bristol reported that 12% of their patients had this diagnosis with the figure rising to 33% in the under 60s.[7]. Functional memory disorder was diagnosed twice as often in women as men and 9/19 patients were thought to have invalid neuropsychological results on the basis of effort testing. .

Cohort studies of Subjective Cognitive Impairment (SCI) and Mild Cognitive Impairment (MCI)

Epidemiological data on SCI and MCI predominantly relates to adults over 65 and even then the focus is more on the risk of dementia rather than explaining what is wrong with the other patients in the cohorts. It is outwith the scope of the article to discuss definitions and problems with the concept of MCI but this usually signifies the presence of memory complaints which are abnormal for age but no dementia in combination with normal activities of daily living[8]. Nonetheless studies in this area show that up to 40% classified in either category improve rather than deteriorate over time.[9][10][11]) Even in this older age group (typically over 65), SCI has been found to be associated with anxiety and depression and physical health complaints. In a younger age group (age 45-64) psychological distress was the biggest factor related to SCI[12] However, the lack of research focus on functional cognitive symptoms means that their epidemiology is poorly understood.

In addition to changes across the lifespan there is some evidence that concern and awareness of memory complaints are increasing over time as well. A study examining data from three iterations of the British National Survey of Psychiatric Morbidity found evidence that the frequency of complaints has been creeping up from 1993 to 2007 (Figure 2)[13]

Differential Diagnosis of ‘Non-Dementia’ Memory Symptoms in the neurology clinic

The following list is not presented as a nosology of mutually exclusive diagnoses, but as a description of the most common clinical profiles encountered in memory clinics when no evidence of neurodegenerative disorder or neurological disease can be found to explain the patient’s memory symptoms. These typologies may overlap with one another but benefit from conceptualisation because they are likely to differ in terms of causation and outcome and because they are treated differently. We are not aware of any previous study that has attempted to break down these types of complaint among patients attending a memory clinic.

1. Memory symptoms as part of Depression or Anxiety

Case: A 58-year-old woman presents with a 6-month history of pervasively low mood and anhedonia with suicidal ideation and feelings of worthlessness and guilt. She has also noticed a marked decline in her memory, forgetting what people have told her and important appointments. Her general practitioner has started an antidepressant but refers her because he is concerned she may be developing dementia.

Complaints of poor memory and concentration are symptoms that forms the basis of diagnostic criteria for both major depression and generalised anxiety in DSM[14]. In patients with depression, deficits in executive function, attention and memory occur not only during periods of low mood but are also detectable during apparent remission [15][16]. Subjective memory complaints in depression do not correlate well with objective findings in neuropsychological testing. This may mean that depressed individuals have a different concept of “memory problems” from neuropsychologists or reflect the limited ecological validity of neuropsychological tests. Among the more consistent objective findings are a failure of executive organisation of memory and overgeneral autobiographical memory [17] (the inability

to remember precise details but rather just general impressions ie I went on holiday as opposed to I particular enjoyed a specific event whilst on holiday).

2. “Normal” memory symptoms that become the focus of attention/anxiety

Case: A 25-year-old philosophy student presents with a 6-month history of worsening memory complaints. He reports that he always had an excellent memory which was better than that of most of his peers. Recently however, he has been somewhat alarmed and puzzled by episodes where he has forgotten that he left the tap running, times when he has gone to another room and forgotten why he is there and has put unusual objects in the fridge. On questioning, the frequency and nature of these episodes appear to be occurring in a range that is normal for the population. He is not particularly anxious or depressed, but appears introspective and puzzled.

Since nearly one third of the population regard themselves as ‘forgetful’, it is perhaps surprising that patients with these ‘normal’ memory failures don’t present more often to health professionals. Patients who do find their way to a clinic with symptoms like this often appear to have an excessively high expectation of their own memory, an excessively high expectation of health services or they have been referred by an inexperienced healthcare practitioner (who may be more anxious than the patient!). These complaints about ‘normal’ cognitive failures are arguably a subset of patients with functional memory symptoms and overlap with more general health anxieties. However, some patients attend memory clinics whose day-to-day experience cannot be categorised as anything other than ‘normal’ and who benefit from having this explained to them.

3. Functional Memory Disorder (as a relatively isolated disorder)

Case: A 37-year-old woman is referred by her GP because she has noticed increasing problems with her memory. She has cognitive symptoms such as losing track of the conversation, losing objects in the house, forgetting where she had read to in a book etc but they appear to be happening much more frequently than anyone would expect. She has also noticed some word finding difficulty and

occasional spoonerism/neologisms. She explained how she had forgotten her PIN number and went completely "blank" and "spaced out". On another occasion she forgot a whole car journey home even though she was driving. She can, however, enjoy complex crime dramas and is able to relate her history in detail. She is more concerned than her family, although they have often noticed the problem.. She has some anxiety about what is wrong but not enough to make a diagnosis of an anxiety disorder.

In the above example the patient's employer and family seem to think there are problems with cognitive performance. It would not be appropriate in this case to say that the cognitive failures described are 'normal' or that the patient belongs to the 'worried well'. The patient is not 'well' as the problem is impacting on social and occupational functioning, and although some of the examples of suboptimal cognitive performance themselves are 'normal' the extent and frequency of them are not. The extent of memory symptoms is also disproportionate to the degree of anxiety perceived by the patient and cannot be explained away simply by labelling this problem "anxiety-related". In this scenario that another diagnostic label or formulation is required in order to explain to the patient what has happened and to facilitate treatment – a functional memory disorder.

In our view the core of a functional memory disorder (FMD), like any other functional disorder, depends on showing positive features which allow its identification and ensuring that the symptoms cannot be explained by another diagnosis. Like in other functional neurological disorders, substantial internal inconsistency is an important pointer to the diagnosis of FMD (e.g. this patient complains of poor memory function but is able to give a detailed description of many memory failures). In addition external inconsistency with what we know happens in pathological diseases affecting memory allows greater confidence in the diagnosis. For example, consistently forgetting family names but recounting those of doctors seen in detail or notable preservation of praxis in the context of severe 'Alzheimer's like' memory impairment. We discuss the status and potential clinical features of functional memory disorder below.

4. Health Anxiety about Dementia

A 47-year-old man presents with some relatively minor sounding cognitive symptoms such as forgetting where he had got to in a book, forgetting what he had for breakfast. He also had an episode where he drove home for 30 minutes but then couldn't remember any of the journey. He has become terrified that these symptoms represent dementia. His uncle died of Alzheimer's at the age of 71. He has been reading about dementia online and admits reluctantly that he has been worrying constantly about dementing himself soon.

Dementia has an increasingly public profile. Heads of state convene meetings about dementia. GPs are paid additional fees for diagnosing dementia. In this context it is reasonable to ask whether the downside for all this publicity is the induction of health anxiety about dementia in a proportion of the population. The confusing term 'anticipatory dementia' to describe a specific fear of dementia was coined in 1996 in the adult children of affected parents [18]. More recently scales to assess 'Dementia Worry' [19][20] and "Fear of Alzheimer's disease" have been described [21] which, unsurprisingly, find that these problems are more common in dementia clinic patients without dementia than healthy controls. Health anxiety is defined as anxiety about a health condition that only responds temporarily, if at all, to reassurance and is associated with some insight. Normal investigations may have the paradoxical effect of worsening the condition- 'there must be something if they need to do a scan – they just haven't found it, yet'.

A Cochrane review concluded that psychotherapy for health anxiety in general (hypochondriasis) showed significant improvement on average across studies [22]. When identified treatment of health anxiety is therefore often clinically rewarding. Effective internet delivered CBT treatments for health anxiety have also been developed to help improve access [23]. However, there is as yet, no specific trials regarding the effectiveness of psychotherapy for specific "dementia health anxiety".

5. Memory symptoms as part of another functional disorder

A 39-year-old woman presents with a four-year history of fatigue and a two-year history of left-sided weakness, pain and memory symptoms. Clinical examination including a positive Hoover's sign demonstrated that her weakness is functional in nature and appropriate investigations have excluded comorbid disease. She has responded well to explanation and rehabilitation and there is no ongoing anxiety or depression. On returning to clinic she complains that although her weakness has improved, she still has a lot of fatigue and pain and has noticed increasing memory symptoms such as forgetting appointments.

Functional disorders such fibromyalgia, chronic fatigue syndrome and irritable bowel syndrome are common in primary and secondary care. The core symptoms of all these disorders include sleep disturbance fatigue and, impaired memory and concentration. Studies highlight problems with attention, memory and reaction time [24,25]. Other diagnostic entities such as “post-concussion syndrome” or chronic whiplash have been associated with similar symptomatology and findings on testing.

Functional Neurological Disorders are characterised by internally inconsistent clinical manifestations, such as the left-sided weakness and the positive Hoover's sign described in the case example. Studies in patients with functional movement disorder[26,27] and dissociative (non-epileptic) attacks [28][29,30] have highlighted a similar range of cognitive findings to other functional disorders..

Just as it may be appropriate for some patients to consider an anxiety or depressive disorder as the predominant cause of their memory symptoms, it may be clinically more appropriate in some individuals to consider that memory symptoms are best seen as part of their functional somatic disorders. This judgement depends primarily on whether the symptom appears proportionate to the functional syndrome previously diagnosed.

6. Retrograde dissociative (psychogenic) amnesia

A 41-year-old university lecturer presents with a dense retrograde amnesia. His family bring him to hospital because he had woken up one morning believing that he was 19 years old. He seems unable to recognise his wife or children. He was able to acquire new memories but could not recall any events from his life after the age of 19. He looked bewildered but was able to use objects such as his phone which he would have learnt to use more recently. Over the next few weeks his memories gradually returned. He denied any recent stress although admitted to fatigue. He returned to work but re-presented a year later with more short-lived episodes lasting a few hours in which he felt 19 again.

The hallmark of a “psychogenic” or “dissociative” amnesia is the presence of dense retrograde amnesia predating a particular time point usually associated with well-preserved anterograde memory and loss of personal identity [31]. This type of memory loss, probably seen as commonly in TV and film as it is in clinical practice [32], is usually quite distinct and does not show much overlap with the presentations described above. Neurological disorders such as brain injury, transient global amnesia or transient epileptic amnesia may also present with retrograde amnesia although here there is nearly always anterograde amnesia as well as a temporal gradient in which older memories are better preserved without a sharp temporal ‘cut-off’. Loss of personal identity, especially in the presence of legal proceedings may particularly be associated with malingering which is an important differential diagnosis of this presentation.

7. Memory Symptoms secondary to prescribed medication or substance misuse

Case – A 35-year-old man with a ten-year history of chronic back pain was referred because of concerns about his memory. He complained of constant ‘brain fog’ with frequent ‘absent mindedness’ leading to missed appointments, forgetting why he had gone to the shops and inability

to read a novel. He was not depressed or anxious. His medication including MST (long acting Morphine) at a dose of 160mg twice daily as well as Amitryptiline 150mg, Diazepam 5mg twice daily and Gabapentin 900mg three times a day.

A considerable proportion of patients presenting to under 65 memory clinics and not found to be experiencing memory symptoms of neurodegeneration or neurological disease take prescribed, over-the-counter or illicit drugs capable of exacerbating cognitive symptoms. In the UK many patients with chronic pain syndromes are placed on high dose opiates even when no clear cause of the pain can be identified. Evidence is mounting against this approach, considering issues such as dependence and tolerance [33]. Surprisingly, there is no consistent evidence that opioids adversely affect cognition in chronic non-cancer pain with some studies even suggesting an improvement [34]. There seems to be stronger evidence that pain itself is associated with impaired cognition [35][24]. However, common-sense does suggest that combinations of drugs as above drugs including those with more legitimate roles in functional disorders such as pregabalin, gabapentin, topiramate and tricyclic antidepressants can significantly impair cognitive function. Sodium valproate, and its potential for hyperammonaemic encephalopathy as well as anticholinergics used for bladder symptoms are worth a special mention.

8. Diseases other than Dementia causing Memory Disorders

There are of course numerous other diseases which cause memory disorder that are not one of the primary “dementias”. These include cognitive impairment and dementia associated with multiple sclerosis, autoimmune encephalitis, paraneoplastic disorders, CNS infections including HIV, metabolic disorders such as vitamin B12 deficiency states, transient epileptic amnesia and transient global amnesia to name but a few. Some non-neurological disorders such as obstructive sleep apnoea may also have effects on memory and concentration.

9. Patients who appear to have functional memory symptoms but then go on to develop dementia/another neurological disease

The clinician in the memory clinic must of course be aware of the limitations of any clinical diagnosis. Many types of dementia begin with mild symptoms in the prodromal stages, commonly anxiety and depression which are more common in the early stages of most neurodegenerative disorders than in the general population. Neurological or medical disorders may also be complicated by additional functional symptoms.[36,37] The discovery of such symptoms (for instance through internal inconsistencies) should not stop the clinician from considering whether another disease process is also present [38]. Patients may also develop functional symptoms such as paralysis as part of a prodrome of dementia. A balance must be struck between making a positive diagnosis of a functional memory disorder to enable treatment to take place, and not missing an underlying progressive disease using judicious follow up. It remains to be seen whether advances in neuroimaging and CSF analysis will aid this separation, given the likelihood of false positive findings in some of these techniques, such as amyloid imaging.

10. Exaggeration/ Malingering

Case – A 42-year-old woman presents for medicolegal assessment seven years after a head injury. She has had a psychometric assessment that suggested results compatible with a moderate to severe brain injury. Review of the notes indicated that her cognitive symptoms had worsened over time and that the initial head injury was not associated with any amnesia or focal deficit. At interview she presented in a childlike way, was barely able to interact socially and used a wheelchair. She and her husband claimed this was always her level of function. Covert surveillance on holiday demonstrated that she could cycle one-handed and was interacting in a normal way with friends.

A comprehensive discussion of this is beyond the scope of this article. The hallmark of malingering or exaggeration is the presence of a marked discrepancy between reported and

observed function as described here. Someone who has a functional memory disorder should be able to report with reasonable accuracy what their normal day to day function and interactions are like. Considerable data exists on validity/effort testing mainly in the context of medicolegal assessment after brain injury[39].

Existing data suggests that effort testing should be a standard part of psychometric assessment, (if psychometric assessment is required). Failure of effort testing is not however synonymous with deliberate deception. Below chance performance does not necessarily mean that the person is wilfully and consciously failing even if it does invalidate other measures[40]. It may even be a marker of a functional memory disorder [27].

Clinical Approach to Assessment and Treatment

Some clinical features of encounters with patients with functional memory symptoms include those seen in Table 2. A recent study using conversation analysis of 25 recorded consultations (16 of which were considered to be with patients independently diagnosed as having a functional memory disorder) examined some of these discriminating factors formally for the first time [41]. This exploratory study suggested that the following five factors were of the greatest discriminating value: (1) whether the patient is able to answer questions about personal information (for example 'how old are you?' or 'where do you live?'); (2) whether they can display working memory in interaction (for example the patient who can recall something they said earlier in the consultation); (3) whether they are able to respond to compound questions; (for example answering a two part question given by the neurologist)(4) time taken to respond to questions (generally being quicker); and 5) the level of detail they offer when providing an account of their memory failure experiences (offering more elaboration and detail in their responses).

An additional feature suggestive of the diagnosis of functional memory disorder highlighted by Schmidtke et al was the presence, in the history, of episodes consistent with dissociative lapses, for example 'I arrived home and couldn't remember any of the journey' [42].

Neuropsychological Testing

In the right hands, neuropsychological testing can be an elegant way to demonstrate some of the internal inconsistencies that are the hallmark of a functional memory disorder. Ideally, this should be done with a focus on reporting the whole style of interaction and the way the patient responds to testing and not just focusing on scores. Neuropsychological tests results in the normal range may also help to reassure patients about their cognitive function. Symptom Validity Testing (or Effort testing) may have particular value in legal scenarios

There is a clinical argument, however, when multiple positive indicators of a functional memory disorder are clinically apparent that formal neuropsychometric testing may be unhelpful and can sometimes lead to iatrogenic worsening of symptoms. Cognitive assessment may not provide a "clean bill of health" but produce findings such as "patchy deficits affecting executive, attentional and memory function". Such results may be interpreted as evidence of possible neurodegeneration, especially when anxiety, depression and effort are not considered. Repeat testing after six or twelve months may be recommended. Alternatively referral to dementia or head injury self-help groups. may strongly perpetuate the idea that memory symptoms relate to brain damage.

Treatment

Identification and Diagnosis

We recognise that distinguishing Alzheimer's disease (AD) and other neurodegenerative disorders from non-degenerative memory problems may be hard, especially at a stage when symptoms are relatively mild.. However, in our experience it is often possible to recognise and diagnose functional memory disorder at their first visit. Patients with a functional memory disorder should be told as soon as possible what the most likely diagnosis is and why they do not have a dementia or are unlikely to be developing it. This approach accepts that dementia, usually prodromal dementia, will sometimes be mislabelled as a functional disorder.

We find the 'archetypical presentations' described above helpful in guiding our recognition and treatment of memory symptoms unrelated to neurodegenerative disorders. Most patients are not 'pure' examples of one of the subtypes we have described, but a framework such as this may allow more targeted treatment and remind clinicians to look, for example, for treatable problems such as health anxiety.

Explaining the diagnosis

As for any explanation we would recommend that the doctor should make it clear where possible that:

(1) That they are taking the problem (and associated disability) seriously both during the history-taking and during the discussion of the diagnosis.

2) There is a diagnosis – the precise term, e.g. functional memory disorder, may not be as important as the principle of applying a diagnosis. Simply telling a patient that there is 'no dementia' is not sufficient since that does not offer an explanation for the complaints the patient has. Some clinicians may be tempted to use the term "mild cognitive impairment" (MCI) in this situation. Whilst it is recognised that patients with MCI are at increased risk of progressing to a dementia it is an accepted part of the MCI concept that it may not progress or, indeed, improve[9][10][11][43]. However, we have significant concerns about the anxiogenic effects of

the MCI concept particularly when associated with the language of 'converting' to AD. At the current time the risk is that more harm is done by the over-diagnosis of (presently) *irreversible* neurodegenerative processes than by the early recognition of a possibly *treatable* disorders causing memory impairment listed above .

3) There is a rationale for the diagnosis, i.e. it has been made on the basis of positive evidence of symptoms and signs that are characteristic of a functional memory disorder. There is no reason why the features described above could not be discussed openly with the patient as evidence of internal inconsistency that is the hallmark of the diagnosis. For instance, pointing out that the patient's memory obviously worked well in the clinical interaction because they were able to give a very detailed account of their concerns can provide a basis for the reassurance that patients developing a dementia would not have been able to produce a similar report. This would be equivalent to using an explanation of Hoover's sign of functional (psychogenic) leg weakness (where hip extension is weak during voluntary movement but improves when movement is directed to the contralateral leg) as a therapeutic intervention [44]

4) Some explanation of 'how' the symptom arises (even if 'why' is more complicated) – for example a discussion about how the symptoms may arise due to poor concentration. Some patients appear to develop an unrealistic view of how normal memory performs.

5) That it is potentially reversible and treatment may help.

6) There is written information to spend longer understanding the problem – as suggested by a Dutch population-based cohort study of subjective forgetfulness [3]

7) There is a willingness to triage the patient for further treatment and/or follow up the patient as required if the symptoms are causing significant disability.

Further Treatment

1. *Treatment of Anxiety or Depression.* Where present, anxiety or depression should be treated using either pharmacological and/or psychological therapies depending on circumstances. Significant health anxiety symptoms should be managed with cognitive behavioural therapy, other psychotherapeutic or psychoeducational approaches. Other disorders such as agoraphobia or obsessive compulsive disorder may become apparent as treatment progresses.

Where the patient seems to have genuine dissociative (psychogenic) retrograde amnesia our impression is that more interpersonally directed or trauma related treatment may be more efficacious.

2. *Specific issues relating to treatment of functional memory symptoms.* A common clinical feature of functional memory symptoms are avoidance of using memory and the association of memory utilisation with the experience of failure.. A core part of the management of any patient involves a graded return to the normal utilisation of memory. Patients' avoidance tends to be subtle. For instance they may exhibit an increased dependency on family members and the concerned relative will often have to be part of the intervention process.

These unhelpful thoughts and avoidance can be challenged using typical cognitive therapy techniques focusing on inconsistency, (i.e. its works sometimes and not at others) and also education about the normal experiences of forgetting. A more detailed guide to challenging unhelpful thoughts in functional neurological symptoms disorders can be found elsewhere [45].

3. *Reduction or avoidance of medications impairing cognition*

4. *Regular clinical review* is important both to ensure adequate clinical management but also to pick up the small number of patients who are in the early stages of a degenerative disease.

Previous attempts to define functional memory/cognitive disorders

Two groups have attempted to define and study this group of patients. In a series of important studies Schmidtke et al described patients attending a memory clinic with 'Functional Memory Disorder' (FMD) in whom it was felt that the symptoms were not explained by dementia or depression (although they did not exclude anxiety disorders)[42]. They defined their patients on the basis of having an impairment in functioning, having some evidence of a psychological stressor, falling within 1.5 standard deviations of population norms on psychological testing and not having dementia or depression. The data highlighted how frequent the problem is in clinical practice and also provided interesting follow up data. At a mean of 46 months follow up, one patient developed dementia, but only six had improved, lending weight to the idea that most of these patients are not 'worried well' who return to normal when reassured by a doctor. The authors tested a functional memory disorder scale which has many items that appear typical of this patient group (Table 2). They subsequently went on to show that cut off scores could distinguish healthy controls from these subjects[46]. There is no evidence, however, that it has sensitivity or specificity for use against subjects with early onset dementia.

Delis and Wetter defined a similar patient group as having a 'Cogniform Disorder'[47]. Their paper drew evidence primarily from the large literature surrounding effort/validity testing and was biased towards the neuropsychological assessment of claimants after mild head injury. They distinguished, between patients with 'normal' cognitive symptoms with and without social and occupational impairment. They proposed diagnostic criteria based heavily on inconsistencies, either or test scores with each other, or of symptoms and test scores with day-to-day function, something that is missing from the Schmidtke criteria (Table 3). They also accounted for the presence of variable intentionality, and the fact that these symptoms may or may not cause occupational or social impairment.

The original description of “pseudodementia” encompassed all of the types of patient described here, even if that term is now reserved for patients with severe depression [48]. Subsequent scattered reports of “functional dementia” show that this is not a new problem even if it has only rarely been grappled with [49].

Is there a neuroanatomy of functional memory disorders?

The answer, inevitably is likely to be ‘yes’ although this is outside the scope of this review. However, it is likely that the different “archetypes” of functional memory disorders differ in terms of their neurobiological underpinning. There has been consistent evidence linking depressive disorder to reduced volumes in prefrontal cortex and hippocampus [50]. Whilst it is tempting to link these structural deficits and memory problems together studies so far have demonstrated rather inconsistent findings. Lack of precision in both depression phenotypes and cognitive phenotypes may be the issue rather than the absence of any true association. Several studies of patients with dissociative /retrograde amnesia have examined potential neural mechanisms [31] including dysfunction of temporal lobes and in one of the largest studies of 14 patients, right inferolateral prefrontal hypometabolism [51].

Research Priorities

Despite notable attempts to define the nature of the clinical problem in this area, this is a topic that is hugely under-researched given how much time and clinical resources appears to be going in to providing assessments for these patients. In addition there are likely to be substantial societal costs from lost time at work and provision of state related benefits. We suggest the following important research questions:

1. What is the extent of 'non-dementia' cognitive complaints which give rise to occupational or social impairment at a population, primary care and secondary care level?
2. Is it possible to define a group of patients using positive diagnostic criteria based on typical symptoms, psychosocial variables with normal test scores (as suggested by Schmidtke et al[42]), an approach that positively identifies inconsistencies between symptoms, symptoms and performance and within psychometric test scores. (as suggested by Delis and Wetter[47]) or perhaps a combination of the two approaches
3. If we can identify a group of such patients is it possible, and is there clinical value, in attempting to separate out the seven types of presentation we have described in this paper or in characterising different patient groups using a dimensional approach?
4. What is the prognosis of these presentations in primary and secondary care and do they vary according to the clinical emphasis? For example do those patients with specific dementia phobia do better or worse than patients with little health anxiety?
5. Would making a positive diagnosis of a functional memory disorder enable more specific and effective treatment and would this improve prognosis?
6. Can biomarkers in dementia diagnosis, such as amyloid imaging, PET/SPECT imaging, and CSF tau/amyloid be developed to predict a diagnosis of functional memory disorder as well as a diagnosis of dementia.

At this stage we suggest that it is premature to attempt to define diagnostic criteria for a problem which has been so poorly studied. Large cohort studies are required to define more carefully the clinical characteristics and prognosis of these types of presentations.

Conclusions

Functional memory disorders are common in any neurology service but especially in the cognitive or memory clinic. They have traditionally been ignored both by clinicians and researchers more interested in dementia. Patients with functional memory symptoms are not

just the 'worried well' or people with "just anxiety and depression". They represent a variety of overlapping phenotypes some of which are associated with significant social and occupational impairment and may have different clinical approaches. Data is beginning to emerge to allow a positive diagnosis of a functional memory disorder, with an emphasis on internal inconsistency but also other features of the presentation such as dissociative symptoms. Large cohort studies are required to take this work forward to a point where the "memory clinic" can help everyone with a memory symptom, and not just those with dementia.

Figure 1. Proportion of patients in neurology led clinics with a diagnosis of dementia is surprisingly low. [5][6]

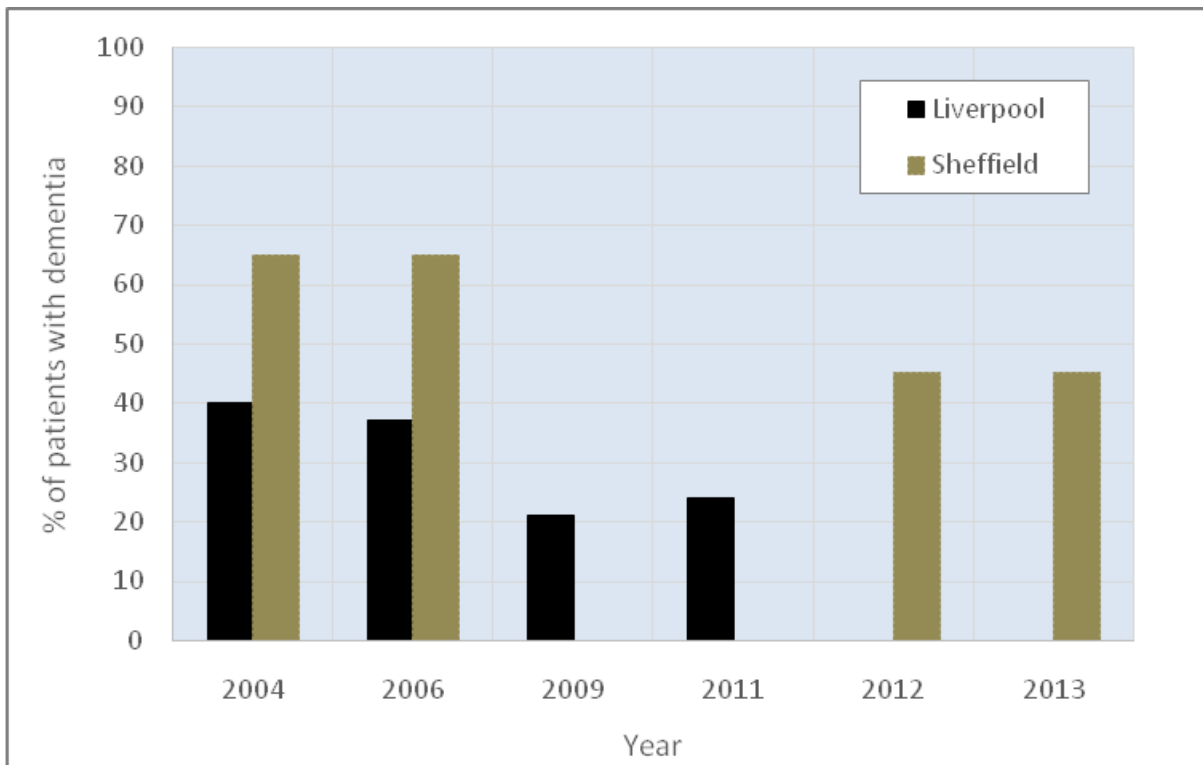


Figure 2. Subjective memory impairment appears to increase over both the lifespan and over time. Figure reproduced with permission from Begum et al based on 1993, 2000 and 2007 English Psychiatric Morbidity Surveys[13]

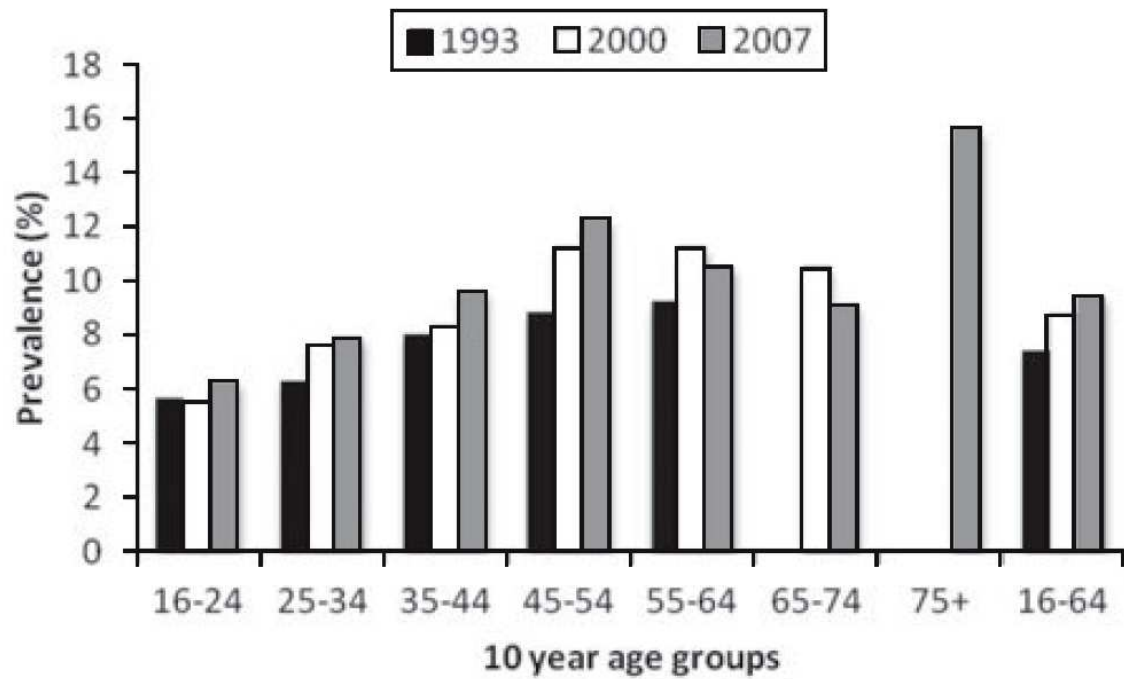


Table 1. An example of a study of 'base rate' memory symptoms in young healthy controls[2]

Cognitive Symptom	Frequency Reported
Community Controls - n=223 mean age 30	
Forgets recent telephone conversation	9%
Forgets why they entered room	27%
Forget yesterday's breakfast	27%
Forgets where car was parked	32%
Loses car keys	31%
Forgets where they went today	5%
Forgets appointment dates	20%
Loses items around house	17%
"Concentration difficulty"	14%
College Students - n=620, age range 17-26	
Memory Gaps	10%
Speech problems	17%
Word finding lapses	27%
Unrecalled behaviour	9%

Table 2. A selection of clinical features which may help with the discrimination of functional and neurological disease causes of memory disorders.

Functional	Neurological Diseases
Young	Older
Attends alone	Attends with someone
Patient more aware of the problem than others	Others more aware of the problem than patient
Able to detail list of drugs, previous interactions with doctors	Less able
Watches TV dramas	Stops following drama
Marked variability	Less variability
Types of memory symptom are usually within most people's normal experience	Types of memory symptom are often outwith normal experiences
'I used to have a brilliant memory'	Does not highlight previous 'brilliant memory'

Table 3. Comparison and appraisal of previously suggested diagnostic criteria proposed for patients with functional memory symptoms[42] [47]

Functional Memory Disorder[42]	Cogniform Disorder[47]
Complaint of memory symptoms >6 months	Complaints of memory symptoms (outwith normal range) OR low scores
Presence of psychological stress	Inconsistencies (two of nine specified) covering: Symptoms/scores vs nature of pathology; Variability over time; Evidence of poor effort / invalid results; Symptoms vs everyday functioning; Delayed onset or worsening after injury
Verbal memory and attentional capacity above 1.5 SD lower limit of normal	No specific cut off specified
No organic disease or major psychiatric disorder (major depression, psychosis, dissociative disorder) found	Disproportionate to any neurological or neuropsychiatric disease present
	Not intentional (or specify if features of malingering or factitious disorder)
Problems	Problems
Not all patients may have psychological stress, or if they do it may revolve around the memory symptoms	Complicated criteria with uncertain validity
Some patients may score below 1.5 SD but still have a functional memory disorder	Criteria weighted towards medicolegal brain injury scenario
Severe anxiety not included. Functional somatic disorders not specified. No mention of drug effects	No mention of other supportive features of functional memory disorder – e.g. attending alone, dissociative ‘absences’
Functional Memory Disorder scale unlikely to discriminate between functional disorders and dementia	Unclear how to apply in context of anxiety , depression or other somatic symptoms

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Authors, Contributors and Guarantors

JS wrote the first draft of the paper. SP, PT, MR and DB and AC made revisions and suggestions.

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