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Neuropsychiatry Update

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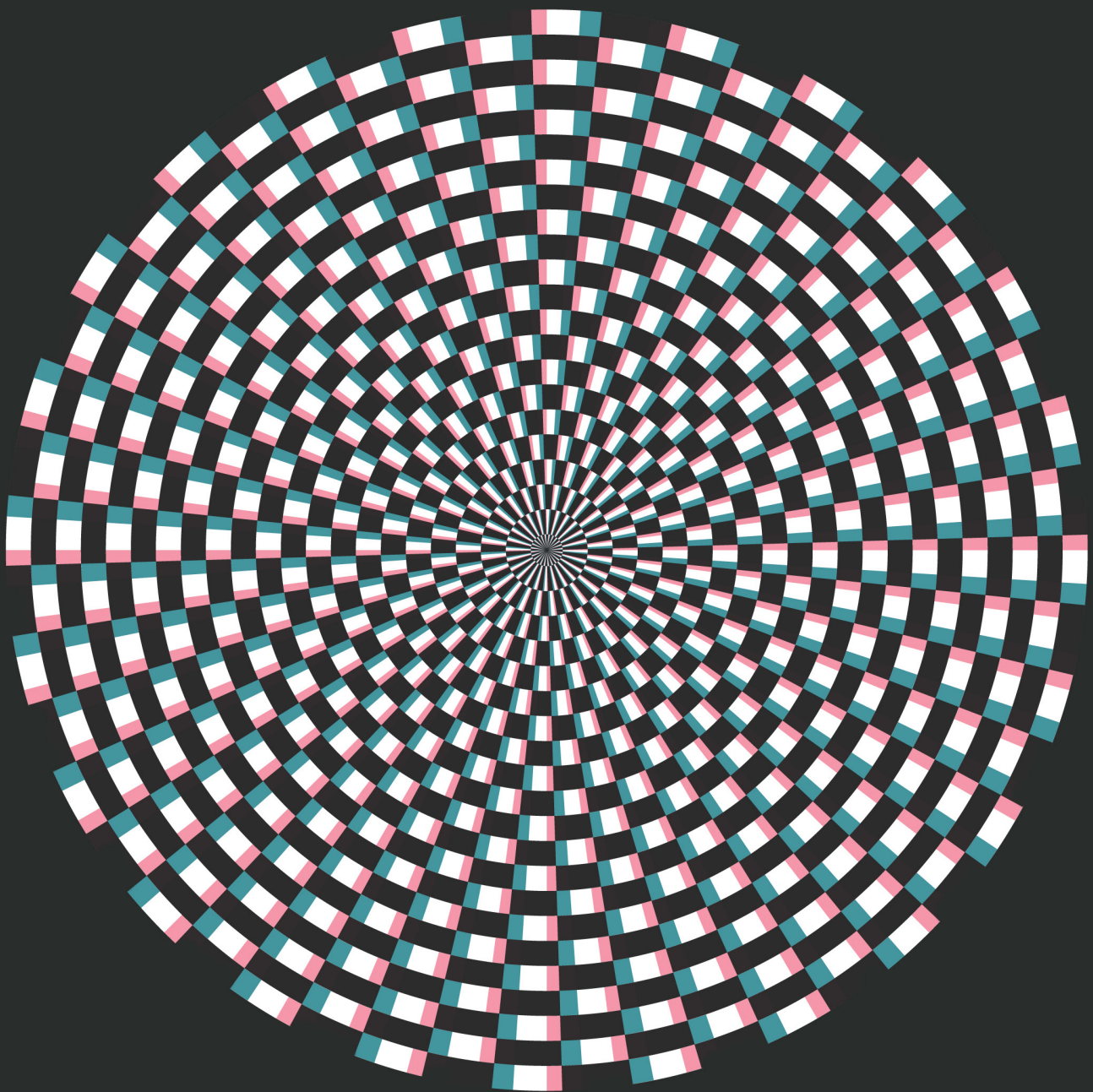

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Editors **Norman Poole**
Editorial Board **Eileen Joyce**
Address for correspondence
Norman Poole
Neuropsychiatry Service,
2nd floor Grosvenor Wing,
St George's Hospital, SW17 0QT

Email: **norman.poole@gmail.com**

Neuropsychiatry News is produced twice yearly. Articles, case-reports and service descriptions should be submitted in a MS Word format by email and should not exceed 2000 words unless agreed with the Editor. Letters should not exceed 200 words. The Editor reserves the right to edit contributions as deemed necessary. Opinions expressed in the newsletter are of the authors and not of the College.

Graphic Design **Jamie Paton – jamie@twhe.co.uk**

What do I do?

Norman Poole

Consultant Neuropsychiatrist at St George's Hospital

"What do you do?" is a question that generally crops up within moments of meeting someone new, as the questioner sizes up the other. The response, "I'm a neuropsychiatrist" is satisfyingly abstruse as most medics, let alone non-medics, have no idea what to make of it. I have developed a few stock phrases that transforms the bewildered expression to one of comprehension and, sometimes, fascination. "That sounds really interesting," I often hear, and of course it is. The range and rarity of conditions seen in neuropsychiatry is one of the many attractions of the specialism, but can also make it daunting. At times, I must have exactly the same expression of bewilderment as my interlocutor from the dinner party. Each of the articles in this edition was commissioned in response to cases seen on the wards and clinic where I work, and will hopefully assist others who face the same question, "What do I do?"

The discovery of autoimmune encephalitis associated with antibodies to neuronal membrane receptors has gripped many psychiatrists given the symptom overlap with major mental disorders. Since then the number of cases reported and variety of autoantibodies implicated has swelled. More recently, autoantibodies have been found in a significant minority of patients in the first episode of psychosis. Psychiatrists in Early Intervention Services must now be anxiously wondering how to identify those at highest risk and what to do with a positive test result. but to date, research findings and their implication for clinicians have often been contradictory and so I am grateful to Rebecca Pollard and Dr Belinda Lennox for eloquently summarising the latest developments in the field and answering my question about what to do.

An elderly patient with a very bizarre and fluctuant presentation triggered my requesting Dr Simon Ducharme write

> I'm now busy using my retro-spectoscope to diagnose other perplexing cases I've seen over the years

a paper on the C9orf72 mutation. We were caught in the classic struggle of colleagues in neurology telling us that she had a depressive stupor triggered by her dog being put to sleep, while I insisted the presentation was neurological but was unable to give a diagnosis. It was actually a neurology trainee who suggested the possibility of a C9orf72 mutation, which I have to be honest caused a wave of bewilderment to pass over me that I may not have fully concealed by nodding along sagely. I'm now busy using my retrospectoscope to diagnose other perplexing cases I've seen over the years, and I strongly recommend anyone who hasn't yet heard of the condition to read the review article. Neurosyphilis was once known as the "great mimic" and both C9orf72 mutation and autoimmune encephalitis while not so numerous can also lay claim to being fine imitators of primary mental disorders.

Talking about great mimics, Dr Sarah Cope, who I have the pleasure of working alongside, has taken a different approach to the question of what to do. Functional Neurological Disorder (FND) mimics any neurological condition, but we are now pretty good at discriminating between the two. However, there are now so many people diagnosed with FND that we need effective treatments that are deliverable to a large, and growing, population of sufferers. Dr Cope describes what we have done locally and the outcomes from multidisciplinary group interventions for FND. It's not rare but still fascinating.

"What do I do?" is not only a practical question but an existential one too. There is insufficient space in this newsletter for my own such musings but it has been heartening to observe two trainees wrestle with this question and find in neuropsychiatry a possible resolution. A very welcome European guest, Dr Joana Macedo da Cunha attended the recent three day FND conference in Edinburgh to find plenty of other visitors from around the world and different specialities. It's an exciting time for research in FND and the conference helped Dr Macedo da Cunha refine her PhD proposal on intentional binding. Dr Thomas Anderson, an FY2 in neuropsychiatry, arrived with the same look as the dinner party guest. But bewilderment passed to comprehension and, as you'll discover from his Faculty of Neuropsychiatry Conference report, to fascination. I trust yours will too.

An Update On Diseases Caused By Neuronal Membrane Antibodies

Rebecca Pollard and Dr Belinda Lennox

Rebecca Pollard – Research Assistant
SINAPPS research group (SINAPPS2/PPiP2), Department of Psychiatry, University of Oxford

Belinda Lennox DM FRCPsych,
Department of Psychiatry, University of Oxford

Introduction

Autoimmune encephalitis associated with antibodies to neuronal membrane receptors is now a well-established disorder in neurology. Whilst a neuroimmunological disorder, the clinical phenotype overlaps with psychiatric disorders, and patients often present initially to psychiatric services. It is therefore important for all psychiatrists to be aware of this disorder and know who to screen, and what to do if a patient has a positive result.

Discovery of autoimmune causes of encephalitis

The recognition that antibodies against neuronal cell surface targets can directly cause central nervous system disease is a relatively recent occurrence. The first descriptions were of antibodies to the Voltage-gated Potassium Channel Complex (VGKCC) in two cases of limbic encephalitis (Buckley et al., 2001). Further cases were then described, effectively treated using immunotherapy, confirming that antibodies to the VGKCC could be pathogenic. Since then, several other neuronal membrane antigenic targets have been identified and implicated in patients with encephalitis. The most common of these are against the N-Methyl-D-Aspartate (NMDA) Receptor, a glutamatergic neuronal membrane receptor which is particularly important for memory consolidation. These NMDA receptor antibodies have been demonstrated to bind to the NR1 (GluN1) subunit of NMDA receptor, and cause cross-linking and internalisation of NMDARs. Antibodies to the NMDA receptor were first described clinically by Dalmau et al. in female patients who had a rapidly progressing, sometimes fatal, encephalitis and ovarian teratomas. Resection of the tumour alongside immunotherapy such as plasma exchange, resulted in good clinical outcomes (Dalmau, 2008).

Subsequently, cases of encephalitis associated with NMDAR antibodies have been described in a range of patients; males and females, with

or without identified tumours (Irani et al., 2010; Dalmau et al., 2011). NMDAR encephalitis is now considered a mainstream diagnosis within neurology, diagnosed in several hundred patients worldwide. Clinical experience shows that when treatment is delivered early, outcomes are significantly better.

In all of the case series to date patients with NMDAR antibody encephalitis initially present with cognitive dysfunction, behavioural change, psychosis or seizures (Irani et al 2010, Dalmau et al 2008) In the initial case series 77 of 91 patients with NMDAR encephalitis initially presented to psychiatric services with their symptoms. (Dalmau et al., 2008). Screening patients when they present to services therefore might lead to earlier diagnosis, earlier treatment and better outcomes (Irani et al. 2010)

Other Pathogenic Antibodies (VGKCC)

Irani et al. (2010) discovered that the actual target for the VGKCC antibodies in limbic encephalitis are extracellular targets, namely; leucine-rich Glioma Inactivated 1 (LGI-1) and Contactin Associated Protein 2 (CASPR2). There is further evidence to show that other antibodies thought to be against the VGKCC actually bind to intracellular domains and are not actually pathogenic. Hence, this suggests screening only for antibodies that bind to these specific domains of the VGKCC (Lang et al 2017).

The clinical presentation of patients with VGKCC antibodies can differ to that of patients with NMDAR antibodies. The presentation is usually more subacute, with amnesia, seizures and encephalitis (Irani et al., 2010). Other symptoms might be seen such as hyponatraemia, autonomic instability and faciobrachial dystonic seizures, which are pathognomonic for the development of LGI1 antibody encephalitis. Psychiatric symptoms of psychosis, mood disturbance may also be seen (Prüss & Lennox, 2016).

Do antibodies have a role in purely psychiatric patients?

Whilst it is now widely accepted that antibodies to neuronal receptors may be pathogenic in cases of encephalitis, and these cases often include psychiatric symptoms of some form, there is still scepticism around the role of antibodies in purely psychiatric presentations. Currently In a mental health setting, patients who present with psychosis are unlikely to be tested for antibodies, without the presence of other neurological symptoms.(Prüss & Lennox 2016).
We have recently completed an observational cohort study The Prevalence of Pathogenic antibodies in Psychosis (PPiP1). The serum of 228 Patients with first episode psychosis were tested for neuronal membrane antibodies across 37 different NHS mental health trusts across England over two years. The patient population in this study were aged 14-35, in their first episode of psychosis and had been taking antipsychotic medication for 6 weeks or less. Importantly, none of these patients had other neurological disease, or encephalitis and all were being treated in psychiatric services. Participants' serum was tested for antibodies to neuronal membrane receptors including NMDAR, GABA A and targets on the VGKC, LGI-1 and CASPR2. Serum from a control group of 105 healthy participants with no family or personal history of mental illness was also tested for the same antibodies.

> **“These results indicate that these neuronal cell surface antibodies do exist in patients.**

Of the 228 patients with psychosis that were tested, 20 were positive for a neuronal cell surface antibody. That's a prevalence of 8.8%, compared to the healthy control group who showed a prevalence of 3.8%. Some antibodies seem to be more relevant in psychosis than others. The specific antibodies that were significantly more prevalent in the patient population compared to healthy controls were NMDAR and LGI-1 antibodies Other studies have shown similar rates, with those testing patients at first presentation finding higher rates than those with longstanding illness. A recent meta-analysis (Pollak et al., 2014) calculated an overall prevalence of 1.46% IgG NMDAR antibodies in patients with psychosis compared to 0.3% of controls using data from seven prevalence studies.

These results indicate that these neuronal cell surface antibodies do exist in patients with a purely psychiatric presentation, however we now need to establish the role of these antibodies in psychosis – some antibodies were also found in some healthy

participants. It is also necessary to determine if immunotherapy – which is effective in the treatment of antibody mediated encephalitis will also be effective in treating psychosis in psychiatric patients who test positive for neuronal-membrane antibodies.

Does immunotherapy help in psychosis?

So far there have only been small, uncontrolled/open label studies of immunotherapy treatments in patients with psychiatric presentations who test positive for antibodies to NMDA or VGKCC.
Zandi et al., (2014) demonstrated the efficacy of immunotherapy in this patient population. Eighteen patients with psychosis symptoms tested positive for NMDAR antibodies. Nine of these patients were not responding well to antipsychotics and so were given immunotherapy treatment. Eight of these nine patients showed a significant improvement in their symptoms after receiving immunotherapy. These patients showed an improvement which corresponded with decreased antibody levels. Of the patients who were not given immunotherapy, most did not improve and their antibody titre did not go down. However this was also not clear cut, some patients did improve on antipsychotic medication. Which is why we now need a randomised controlled clinical trial to help determine the efficacy and safety of immunotherapy in patients with pathogenic antibodies and psychosis.

Testing the efficacy and safety of immunotherapy in psychosis

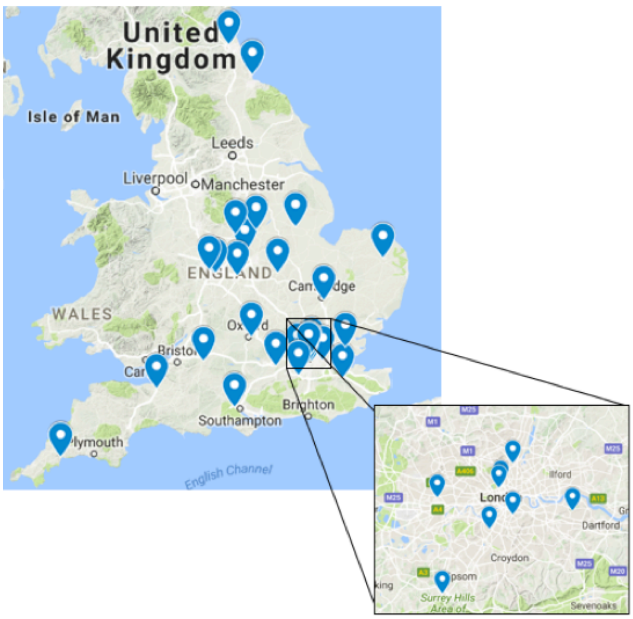
That is where SINAPPS2 comes in. SINAPPS2 aims to test the safety and efficacy of intravenous Immunoglobulin (IViG) and Rituximab in patients with symptoms of psychosis who test positive for neuronal membrane receptor antibodies (including NMDAR, LGI-1, GABA-A). We have just completed a feasibility study of immunotherapy in this patient group (SINAPPS 1) which shows that it is feasible and acceptable for patients to be treated with immunotherapy.
SINAPPS2 is a double-blind randomised controlled trial with 50% of participants receiving placebo and 50% receiving IVIG and two Rituximab infusions. All participants, in placebo and treatment groups will continue their usual antipsychotic treatment. The primary outcome measure is time to achieve sustained remission of psychosis symptoms (lasting at least 6 months). Participants will be screened for signs of neurological disease including encephalitis and they will be followed for 12 months to assess length of remission and relapses. We are setting up sites in Cambridge, Oxford, North London (UCL), South London (KCL), Nottingham, Birmingham, Newcastle, Exeter and hopefully others as well.

The trial sample size is 80 participants randomised 1:1, 40 in each trial group. Assuming an uptake rate of 50%, we therefore need to identify 160 patients with psychosis with neuronal membrane antibodies. Judging by the previous literature that estimates around 10% prevalence of pathogenic antibodies in psychosis patients; we therefore need to screen over 2500 patients with psychosis.

PPiP2 is the follow-on from our previous prevalence study which will provide this screening, and is currently underway in over 30 NHS trusts across England. We are recruiting patients aged 18-70 with at least one symptom of psychosis, receiving care from any inpatient and outpatient secondary mental health service. Patients can be at first episode, or relapse, as long as the duration of the current episode is at least 2

Inclusion criteria	Exclusion criteria
Aged 18-70	Primary diagnosis of drug-induced psychosis (concurrent drug use is OK)
Acute psychotic symptoms lasting more than 2 weeks but no longer than 2 years. If not in first episode, need at least 6 months remission prior to start of current episode.	Any other neurological disorder e.g. multiple sclerosis, epilepsy etc.

weeks and not longer than 2 years, with at least a 6 month remission prior to the current episode. Exclusion criteria are current neurological disorder or contraindications to the study medications. Patients will give a blood sample which is screened for NMDAR antibodies (using a live cell-based assay) as well as LGI-1 and GABA-A antibodies.



A map showing locations of NHS trusts involved with recruitment for PPiP2. For a full list of participating sites, please visit: www.Sinapps.org

Antibody mediated psychosis – implications for clinicians

Who to test?

For patients with acute onset psychosis clinicians can refer patients for testing directly through PPiP2 study (providing the patient gives consent) or, if not available, via routine clinical immunology testing. We advise testing for antibodies for NMDAR, LGI1 and GABAA as current research suggests that they are most relevant for psychosis.

There are further 'red flags' for clinicians, that may indicate encephalitis, and where antibodies should also be requested: rapid deterioration in mental state, loss consciousness, autonomic dysfunction, hyponatraemia, seizures, movement disorder (including catatonia) and adverse reactions to antipsychotics, including suspected neuroleptic malignant syndrome.

What to do if a patient with psychosis is positive for antibodies?

If there is a suspicion of encephalitis then patients should be urgently referred to neurology services for further assessment and possible treatment. Further less acute presentations, investigations should support the referral;

- EEG, looking for epileptic or encephalopathic changes. In more extreme cases of NMDAR encephalitis an 'extreme delta brush' pattern can be seen
- MRI, inflammatory changes in medial temporal regions would support the diagnosis.
- Lumbar puncture, looking for antibodies and inflammatory changes

How to treat patients with pathogenic neuronal antibodies

For patients showing evidence of encephalitis the first line treatment is of high dose steroids, alongside IVIG or Plasma exchange to induce remission. If a teratoma is identified this is removed. Then, to maintain remission, steroids or steroid sparing agents such as azathioprine, mycophenylate mofetil or rituximab are used.

Psychiatric management of these patients is key, and can be challenging as patients can be paranoid, aroused and confused. Compliance with the invasive treatments required can be difficult. Sedative antipsychotics, such as olanzapine are often used, as well as regular benziodiazepines, although careful monitoring is required to ensure that autonomic instability is not precipitated.

There is a particular difficulty with the use of antipsychotics whilst patients receive plasma exchange, as most antipsychotics are plasma bound, and there can be a washout and rebound arousal following plasma exchange. The timing of medication to follow plasma exchange, and the use of amisulpiride, as the last plasma bound antipsychotic, can help with this. The close involvement of psychological medicine teams in the management of these patients on neuroscience wards is vital for good treatment outcomes.

For patients with purely psychiatric presentations there is no standard treatment protocol and these patients should be treated through a clinical trial wherever possible.

Summary

Autoimmune causes of encephalitis involving pathogenic antibodies to neuronal membrane receptors are now widely recognised in neurology. The prevalence of psychiatric symptoms in the presentation of this disease means that psychiatrists need to be vigilant to the possibility of encephalitis in patients with acute psychosis. Immunotherapy is the standard treatment for this condition and outcomes are much improved when treatment is delivered quickly. Therefore, it is important that clinicians are aware of the possible autoimmune cause of psychiatric symptoms and the 'red flags' to look out for.

There is also growing evidence to suggest that these same antibodies might play a role in cases of psychosis that does not lead on to encephalitis. In these cases, immunotherapy might be a more effective treatment than antipsychotics. We are now undertaking a RCT to determine if this is the case, We are offering screening for everyone with acute psychosis who could potentially be recruited to the trial.

The research into autoimmune causes of psychosis may have important implications for both patients and clinicians: There is the potential for radically changing the way that we diagnose and treat people with psychosis.

For more information please visit: **www.sinapps.org**

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Diagnostic Implications of the C9orf72 Mutation in Clinical Psychiatry

Simon Ducharme MD MSc FRCP(C)

Neuropsychiatrist, Montreal Neurological Institute and McGill University Health Centre

Assistant Professor, Department of Psychiatry

Associate Member, Department of Neurology & Neurosurgery

Research Director, Mental Health Mission, MUHC McGill University

Introduction

Psychiatrists in clinical practice are routinely faced with atypical cases that raise concerns for an underlying unidentified neurological or metabolic process (unfortunately still too often referred to as "organic diseases"). Most clinicians feel ill equipped to identify and investigate these generally rare syndromes. Periodically a new disease with neuropsychiatric presentations is discovered (such as the anti-NMDA encephalitis), raising worries that potentially treatable cases have been missed in the past. However, testing all patients for these rare diseases is not feasible from a cost-efficiency standpoint given the high prevalence of primary psychiatric disorders.

In the last few years, increased attention has been paid to the diagnosis of frontotemporal dementia (FTD) cases in patients with late-onset behavioral changes.[1] Indeed, the behavioral variant FTD (bvFTD)[2] has significant clinical overlap with multiple primary psychiatric disorders. The prevalence of FTD is 15–22 per 100,000, with around 20–30% of cases secondary to autosomal dominant mutations. The most common mutations are on chromosome 17 (MAPT, progranulin) and the chromosome 9 open reading frame 72 (C9orf72) hexanucleotide repeat, all of which have full penetrance [3].

The C9orf72 mutation was identified in 2011 as a cause for the shared heredity of FTD and amyotrophic lateral sclerosis (ALS).[4,5] It is a GGGGCC hexanucleotide repeat expansion on the short arm of chromosome 9.[6] In healthy controls, the normal hexanucleotide repeat size is usually up to 10 and on rare occasions up to 30 repeats.[7–10] Repeat sizes between 20 and several hundreds have been identified in both healthy controls and patients.[6,9,11–16] Repeat lengths of more than several hundred are very likely to be pathogenic for ALS or FTD.[6,7,17] Although the exact function remains uncertain, both gain and loss of function mechanisms have been proposed, and related proteins could play a role in regulating endosomal trafficking.[6,18] C9orf72 is probably the most common genetic form of FTD, being present in 7–12% of subjects.[6] Of note, pathogenic repeat expansion has been identified in 2–5% of apparently sporadic FTD cases[19], i.e. in patients without family history suggestive of dominant inheritance.

The most common clinical presentations of C9orf72 mutations are bvFTD, ALS, or a combination of both (FTD-ALS).[6] The bvFTD syndrome is characterized by variable combinations of behavioral symptoms including apathy, disinhibition, loss of empathy, stereotyped/repetitive behavior and hyperorality.[2] Cognitive impairment in bvFTD due to C9orf72 mutations includes the typical deficits in social cognition and executive function, but can also involve memory disturbances and parietal lobe deficits.[6, 20] ALS due to C9orf72 is often associated with early behavioral and cognitive changes, even when not meeting criteria for FTD-ALS.[21]

The language variants of FTD, referred to as primary progressive aphasias (PPA), are a more uncommon presentation of C9orf72, with most reported cases being non-fluent or semantic variants.[20, 22] Of particular interest to the neuropsychiatric community, early phenotypic characterizations of clinical cohorts with this mutation have hinted toward an unusually high frequency of predominant psychiatric presentations, sometimes many years prior to the onset of more typical FTD or ALS symptoms.[20, 23] In an effort to clarify the implications for clinical practice, the American Neuropsychiatric Association (ANPA) Committee on Research recently reviewed the literature on this topic and published clinical recommendations.[24]

Psychiatric Presentations of C9orf72 mutations
Reports of increased frequency of psychotic symptoms (delusions and/or hallucinations) in the early stages of FTD secondary to C9orf72 mutations emerged from multiple sources in 2012 [20, 23], one year after the discovery of the mutation. Unsurprisingly, most of the studies identified in our review related to psychotic symptoms (n=10). These studies have consistently reported a marked increased frequency of psychosis at the onset, or preceding more classical FTD symptoms. [20, 23, 25-31] The prevalence of psychosis ranged from 21 to 56%[24], compared to the most recent estimate of a 10% prevalence in sporadic FTD[32]. There were unexplained geographic discrepancies in prevalence, including much lower rates of psychiatric disturbances recently reported by a German consortium.[33]

Psychotic symptoms can include both delusions and hallucinations in all sensory modalities, together or separated. In terms of delusional content, there is an unusually high frequency of somatic delusions (e.g., foreign object in body, pregnancy), in addition to unexplainable somatic symptoms (e.g., pain) that do not reach delusional intensity.[20, 29, 31, 34, 35] Delusion subtypes that have been reported also include persecution, jealousy, grandiose and mystical/religious.[34] Finally, psychotic symptoms often precede the appearance of more typical FTD features by 1-5 years,[26, 34] and reports consistently describe poor response and adverse reactions to antipsychotic medications.[29, 36]

The second most commonly observed psychiatric prodrome to C9orf72 mutation cases are mood disorders. There are a few reports of well-characterized cases of late-onset bipolar disorders with manic episodes that gradually progressed to FTD, later proven to be due to C9orf72.[27, 37] Interestingly, a few patients had a family history of bipolar disorder rather than FTD. Although the numbers are anecdotal, reported manic episodes related to C9orf72 have responded to lithium.

Unipolar major depressive disorder is the most common psychiatric diagnosis preceding the recognition of bvFTD[38], however there are few reports related to C9orf72 mutations. [36, 39] A post-mortem autopsy study found two cases of C9orf72 mutation among patients with clinical diagnosis of "pseudodementia" without macroscopic atrophy.[40] At least two of these cases had catatonia components in their presentations. Of note, two cases of suicide attempts have been reported, which is a rare feature in sporadic FTD given the dense lack of insight usually seen with this disease.[41]

Very few studies were found on the topic of anxiety. In one case series of 19 patients with C9orf72 mutations, there was a 33% rate of anxiety as part of the initial presentation, but without specifying the nature of this anxiety.[42] We also identified two case reports of OCD as the initial presentation of bvFTD due to C9orf72 mutations,[43, 44] which is also a known presentation of sporadic bvFTD.[1]

It is also crucial to highlight that a third of C9orf72 cases with psychotic presentations did not have family history of FTD-ALS; therefore, in clinical practice these cases would have been considered sporadic FTD.[20, 27] They have a lower frequency of apathy [45] and greater emotional warmth at the onset of the disease than patients with sporadic bvFTD.[25, 31] Patients with C9orf72 also have a higher rate of family psychiatric history[25],

> **Results demonstrated altered body schema processing in various tasks such as two-point discrimination**

a factor that has been shown to bias clinicians toward missing FTD diagnoses.[38] In addition, these patients often do not show significant atrophy on MRI in the early stages, [27, 46] and when atrophy is present the pattern is not restricted to fronto-temporal areas, with frequent involvement of parietal regions, cerebellum and thalamus.[47] Moreover, one study showed that 18% of subjects have normal FDG-PET or SPECT scans[30], which are thought to be more sensitive for bvFTD diagnosis. Consequently, these patients often do not meet the full clinical criteria for probable bvFTD [2, 25] and clinicians need to have a high index of suspicion for C9orf72 mutations in patients with late-onset psychotic or bipolar disorders in order to identify potential cases. Indeed, it is not possible to rely solely on the absence of the usual bvFTD clinical features to exclude this possibility.

C9orf72 Mutations in Primary Psychiatric Disorders

Given the high prevalence of psychiatric symptoms at the onset of C9orf72 cases, the logical next question is to determine if the mutation is also found in patients with more typical presentations of primary psychiatric disorders. We identified 6 epidemiological studies in schizophrenia and schizoaffective disorders spanning North America, Europe and Asia.[48-53] Four of those studies did not identify a single case in a total of 1410 subjects. One study from Germany and Italy identified two cases out of 297 patients. [53] Adding all 6 studies, the prevalence of C9orf72 mutation in patients with typical schizophrenia or schizoaffective disorders is estimated below 0.1%.

A total of 4 American and European studies have investigated the frequency of the mutation in large cohorts of patients with bipolar disorder.[50, 54-56] Two cases were identified from 862 patients, which amounts to a prevalence of ≈0.1%; essentially a similar figure to the rate of the mutation found in healthy controls in one study.[9] No similar study was found for major depressive or anxiety disorders

Mechanistic Hypotheses

In C9orf72 mutations, the psychiatric disturbance could be a prodrome of FTD during the phase of functional synaptic changes and neurotransmitter instability (i.e., psychiatric features precede FTD), while in other cases it could be the result of synapse involution and cell death (i.e., psychiatric features occur in parallel to more typical dementia features).[44] The specific mechanism by which the mutation is related to psychiatric prodromes is unknown. The main hypothesis is that the atrophy pattern is more atypical in patients with C9orf72 mutation compared to sporadic cases, with more severe involvement of the cerebellum and the thalamus, two structures that could contribute to psychiatric phenotypes.[6, 47] In particular, the cerebellum has a key role in modulating thoughts, affect and behavior[57], and one study found a higher C9orf72 gene expression in the cerebellum of patients suffering from schizophrenia.[58]

While this is not a mechanistic explanation, Downey et al. (2014) have run a series of experiments of body schema perception tasks in patients with the mutation compared to sporadic FTD and controls given the high frequency of somatic complaints and even somatic delusions in these patients.[59] Results demonstrated altered body schema processing in various tasks such as two-point discrimination, body part illusions and self versus non-self differentiation.

Clinical Implications

In summary, psychotic symptoms are the most common prodrome, including various combinations of delusions, overinvested ideas, unexplained somatic symptoms and multimodal hallucinations. These symptoms are usually not responsive to antipsychotics, with frequent adverse effects. Although less common, late onset bipolar disorder with manic episodes can also be a clinical presentation, and reported cases point to good therapeutic response to lithium. Other forms of mood disturbances including recurrent depressive episodes with catatonia and depression related cognitive disturbances ('pseudodementia') are also possible.

The phenotypes can be indistinguishable from typical primary psychiatric disorders, without accompanying FTD symptoms. A number of factors further increase the challenge of correctly identifying cases of C9orf72 mutations in patients with late-onset psychiatric disorders. First, psychiatric symptoms can precede typical bvFTD features by up to 4-5 years. Second,

progression of symptoms can be slow over many years[25, 60]. Third, neuroimaging can be normal in the initial phase of the disease[25, 30, 61]. Finally, many subjects do not have positive family history (either no family history or only cases of apparent primary psychiatric disorders).

It should also be mentioned that, even when cognitive and neurological signs are present, they are often not restricted to the prototypical description of bvFTD or PPA.[6] Patients can have early deficits in learning and recall[20] or perceptual–motor parietal dysfunction, which is incompatible with current DSM-5 frontotemporal neurocognitive disorder criteria D requiring the relative sparing of learning and memory and perceptual–motor function. There are also cases with parkinsonism (usually a late feature), Huntington disease–like phenotypes, and cerebellar dysfunction.[6, 9, 25, 62]

The other clear finding from this review is that C9orf72 mutations are very rare in patients with typical DSM-5 schizophrenia or schizoaffective disorder (<0.1%) and bipolar disorder (≈0.1%). It is therefore not advisable to test patients with these disorders at random. The prevalence of C9orf72 mutation in cases of late onset psychotic disorder or mania remains unknown, but based on epidemiology of late onset psychotic disorders (estimated incidence ≈12.6/100,000)[63], C9orf72 mutations would only explain a minority of cases. However, restricting testing to patients meeting diagnostic criteria for bvFTD or with family history of FTD–ALS will clearly miss cases over periods of many years until the dementia becomes more evident.

Although there are currently no curative treatments, establishing a diagnosis of neurodegenerative disease is important for families to plan personal and financial affairs prior to severe cognitive decline, in addition to familial counseling. It is also important to avoid potentially deleterious interventions such as high dose antipsychotics in psychosis due to C9orf72 mutations. It will be even more crucial to identify these patients when potential therapeutic interventions come along, while not causing prohibitive costs by testing patients at large.

In all patients with late onset mania, psychosis and mood disorder with catatonia or unexplained cognitive deficits, a detailed family history should be obtained including screening for early onset dementia, FTD, ALS, parkinsonism and unexplained neuropsychiatric syndromes. Patients should have at minimum a screening cognitive assessment (e.g., MoCA) and elemental neurological examination. Clinical symptoms of dementia including symptoms of bvFTD and PPA should be elicited from patients and relatives. Neuroimaging minimally should include a cerebral CT-scan, but ideally a brain MRI to assess for early signs or cortical and subcortical atrophy. If there is a suspicion of bvFTD or other early onset dementia, a consultation in behavioral neurology or neuropsychiatry should be obtained. If structural imaging does not provide a definite diagnosis, there should be considerations for an FDG–PET scan, however one needs to keep in mind the high rate of abnormal findings in patients with primary psychiatric disorders.[61] If an Alzheimer's disease pathophysiology is part of the differential, a lumbar puncture for diagnostic biomarkers is an option in patients with young onset dementia.

In patients with late onset psychiatric presentations but without further clinical evidence of FTD, the question of who should be tested for C9orf72 mutation remains open. There are various criteria for genetic testing in patients with FTLD spectrum syndromes[64], but currently no agreed upon guidelines on who should be tested for the mutation in patients with late onset psychiatric disturbances. The ANPA committee on research proposed the following approach for C9orf72 testing in patients presenting with late onset (after 40 years of age) psychosis, bipolar disorder, or major depressive disorder with catatonia or unexplained cognitive deficits

Testing should be obtained if:

1. There is a history of first degree relative with confirmed C9orf72 mutation, FTD or ALS
2. They meet criteria for the high risk category of Wood et al. (2013)[64]

Testing should be considered and discussed with the patient if:

3. There is a first-degree family history of late onset bipolar or psychotic disorder, or other unspecified progressive neuropsychiatric disturbance
4. There is progressive deterioration with cognitive decline and/or emerging features of bvFTD and/or parkinsonism

Genetic consultation and counseling prior to proceeding to testing should always be obtained.

Based on the current literature, testing should not be obtained in patients with DSM-5 diagnosis of schizophrenia, schizoaffective or bipolar disorder with onset prior to the age of 40 unless there is a proven genetic mutation in a first degree relative.

Conclusions

Psychiatrists need to be aware that late onset psychosis and bipolar disorder can be the initial prodromal phase of C9orf72 mutations, as they are the most likely to be the first specialized physicians to encounter these patients. The presentations are heterogeneous and can be difficult to identify given their homology to primary psychiatric disorders, frequently normal imaging and delayed appearance of more typical FTD features. Physicians need to have a high index of suspicion and elicit detailed family history of neurodegenerative diseases in those patients. We encourage clinicians to refer potential cases to neurocognitive clinics specialized in FTD for diagnostic work-up, including genetic testing.

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Group Hysteria: Evidence-base and experience of using group treatments for Functional Neurological Disorder

Dr Sarah Cope

Clinical Psychologist, Neuropsychiatry Service 2nd Floor, Grosvenor Wing, St

A patient with functional neurological disorder (FND) has neurological symptoms that are incongruent with symptoms caused by typical neurological disease. It can be demonstrated that normal function is possible, but the patient is unable to access this normal function (Edwards et al., 2012). FND is classified as Functional Neurological Symptoms Disorder (conversion disorder) in DSM-V and within Dissociative (conversion) Disorders in ICD-10. FND is a common presentation in Neurology clinics, but recommended treatment is still being developed (Carson et al., 2012). There are common misconceptions held about FND, such as "Only long-term treatment can help"; "FND is always due to trauma"; and sometimes even "It's untreatable". These may not be as ridiculous as previous misconceptions, such as Plato's idea that it was due to a wandering womb, or Galen's view that it was due to sexual deprivation in particularly passionate women, but these types of erroneous beliefs can have negative consequences for patients' treatment.

There are many aetiological pathways to FND, and a wide range of heterogeneity in presentations. Like any other illness, there is a range of severity and complexity, with different levels of need. And arguably when treating FND, you should approach it like any other mental health or physical health problem, by giving the appropriate level of treatment. In terms of guidelines, NHS Scotland has published guidelines recommending that treatment for FND follows a stepped care approach (NHS Scotland, 2012). Firstly, FND should be diagnosed and appropriately explained by a neurologist. If explanation alone is unsuccessful, brief and effective treatments, such as individual guided self-help, should be offered. And for patients with severe FND, specialist multi-disciplinary treatment should be offered.

Within our Neuropsychiatry Service, we became interested in whether group treatments could be delivered as part of the treatment pathway (Agrawal et al., 2014).

Evidence-base of group treatments for FND. There have been a number of studies published on group treatments for FND (see Table 1).

Table 1: Published studies on group treatment for FND

Target symptoms	Published study	Setting	Sessions	Treatment approach
Functional non-epileptic attacks (FNEA)	Prigatano et al. (2002) Zaroff et al. (2004) Barry et al. (2008) Metin et al. (2013) Chen et al. (2013) Cope et al. (2017)	Epilepsy Centre Epilepsy Centre Epilepsy Centre Psychiatry Epilepsy Centre Neuropsychiatry	24 10 32 12 3 3	D, PP D, PP PP D, PP, BT D D, CBT
Mixed FND	Conwill et al. (2014)	Neuropsychiatry	4 or 5	D, CBT
Functional memory disorder (FMD)	Metternich et al. (2008)	Memory Centre	13	D, CBT

D = Psychoeducation regarding diagnosis and basic management
CBT = Cognitive behavioural therapy
BT = Behavioural Therapy
PP = Psychodynamic psychotherapy

The number of sessions have varied, and all but one included psychoeducation regarding diagnosis and basic management. They were all delivered in a specialist setting. Many have had a cognitive-behavioural or behavioural orientation. Some of the groups for functional non-epileptic attacks (FNEA) were psychodynamic in their approach and were of longer duration.

Table 1: Published studies on group treatment for FND

Published Study	FND	Sample Size	Control Group	Sessions	Main Outcomes
Prigatano et al. (2002)	FNEA	9	No	24	FNEA frequency: 6 (decrease), 2 (no change), 1 (increase)
Zaroff et al. (2004)	FNEA	7	No	10	Sig. decreases in post-traumatic and dissociative symptoms. FNEA frequency: 4 (no change), 2 (decrease), 1 (increase).
Barry et al. (2008)	FNEA	7	No	32	6 patients experienced decrease in FNEA, of which 4 ceased having them. Sig. decrease on BDI.
Metin et al. (2013)	FNEA	9	No	12	Sig. reduction in FNEA, but median FNEA had already reduced considerably by the 1st session of group.
Chen et al. (2013)	FNEA	43	Yes	3	No sig. difference in FNEA frequency between groups. Sig. improvement on functioning for treatment group.
Cope et al. (2017)	FNEA	19	No	3	Sig. decrease in FNEA frequency. Sig. improvements on psychological distress, illness beliefs, and understanding of FNEA.
Conwill et al. (2014)	Mixed	16	No	4 or 5	Sig. improvements on 'emotional wellbeing' and 'role limitation due to emotional problems' on SF-36.
Metternich et al. (2008)	FMD	31	Yes	13	Treatment group had sig. increase in memory-related self-efficacy.

Outcomes following group treatment are varied (see Table 2), and most reported research has had small sample sizes and no control groups. Primary measurement of outcome for groups for patients with FNEA tends to be FNEA frequency. Four studies provided group treatment for FNEA based around a psychodynamic approach. The number of sessions ranged from 10 to 32, and the sample sizes were small (7–9 patients). By the end of treatment, some of the patients had reduced frequency of FNEA (Prigatano, Stonnington and Fisher, 2002; Barry et al., 2008; Metin et al., 2017; Zaroff et al., 2017). Chen et al. (2014) had the largest sample size and a control group. They examined the effectiveness of a 3-session psychoeducation group treatment for FNEA.

The sessions were monthly and each lasted 90 minutes. They found that whilst there was not a significant difference in terms of reduction in FNEA, the treatment group did demonstrate a significant improvement in functioning at follow-up, when compared to the control group of routine care.

In terms of outcomes of group treatments for other FND presentations, there have been fewer studies published. Conwill and colleagues evaluated a psychoeducation group for patients with FNEA or other functional neurological symptoms. They offered 4 or 5 CBT-based group sessions. And they achieved significant improvements on the domains of 'emotional wellbeing' and 'role limitation due to emotional problems' on the SF-36, a quality of life measure (Conwill et al., 2014). Metternich et al. (2008) evaluated a 13-session CBT group for functional memory difficulties. They found patients who had attended the group reported significantly increased memory-related self-efficacy compared to the waiting-list control group. In conclusion there is a small, but growing evidence-base that supports the use of group treatments for FND.

Outcomes of group treatments trialed within our service, and treatment pathway.

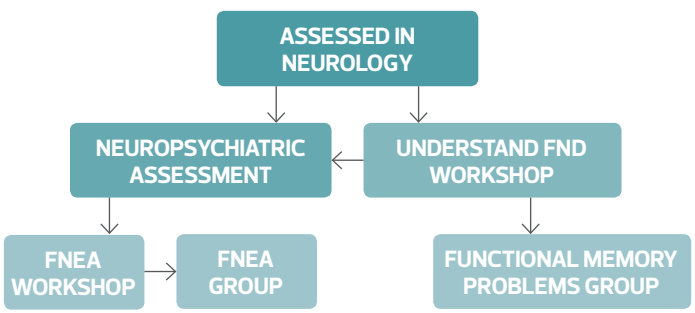
We have recently published on data from our 3-session FNEA CBT-informed group (Cope et al., 2017), which we have since redesigned to make it a longer group intervention. The FNEA group in our service was developed to help patients understand their diagnosis, to enable them to meet others with the same diagnosis, and look at what may be contributing to the maintenance of their FNEA, with the aim of improving patients' self-management. The patients were not only newly diagnosed patients (the average length of time experiencing FNEA was 7 years (with a range of 1–25 years). 36% of patients had comorbid epilepsy. The group covered explanation of diagnosis; possible predisposing, precipitating and perpetuating factors; the CBT model; grounding strategies; reducing avoidance behavior; thought challenging; and relaxation strategies.

Patients were given handouts for each session, and patients had homework tasks between-sessions, which were then reviewed at the beginning of the next session. We collected data on FNEA frequency, attitudes to FNEA, mood, impact on functioning and illness beliefs. In the first session only, we administered the dissociative experiences scale, and part of our analysis compared patients grouped as "high dissociators" vs patients grouped as "low dissociators". We found that a significant proportion of patients experiencing FNEA decreased, with 40% of patients at the end of treatment attack-free for the preceding 4 weeks. We also found significant improvements on measures of psychological distress, illness beliefs and understanding of diagnosis. There were no significant differences in terms of outcomes for patients with epilepsy versus patients without epilepsy, and the length of time patients had experienced FNEA was also not significantly associated with outcomes. This suggests that those with comorbid epilepsy and/or long-term FNEA could still potentially benefit from a brief group intervention. The high dissociative group of patients had significantly higher scores on all the measures compared with the low dissociative group. This indicates that the FNEA patients who experienced higher dissociation experienced greater mental health difficulties and had poorer functioning. Nevertheless there were no significant differences in terms of outcomes for the high vs. low groups, which indicates the intervention was beneficial for both low and high dissociators. Patient feedback was positive, and high satisfaction was reported by most. There were of course limitations to our study, namely the lack of control group or follow-up data. We plan to address these limitations in future studies. Based on these results and patient feedback, we have restructured the group and it is now 6-sessions long, including a stand-alone FNEA workshop session, 4 CBT-informed group sessions, and a follow-up group session.

We have built on the promising results of the FNEA group treatment, and have trialed other groups for FND presentations. Our group treatment pathway is shown in Figure 1. The Understanding FND Workshop was developed in order to: explain the diagnosis and introduce potential treatments of FND; give patients the opportunity to hear from multiple professional groups who may be involved in their care, as well as hear a patient's experience of treatment; allow patients to see that FND is common; and increase patients' carers' understanding of FND. Both neurologists and neuropsychiatrists can refer into the workshop.

The workshop is facilitated by Professor Mark Edwards (Consultant Neurologist), Dr Niruj Agrawal (Consultant Neuropsychiatrist), a physiotherapist, me, and a patient who has been through treatment. We have not published the results from the workshop yet, but we have examined data from six workshops. A total of 110 patients and 87 family members (or friends or carers) attended. At the beginning and end of each workshop, patients and their guests were asked to rate, on numerical rating scales ranging from 0 to 100, how much they: understood the FND diagnosis; agreed with the diagnosis; were hopeful regarding recovery; and believed FND is treatable. We found significant differences between the pre and post ratings on all scales, for both patients and guests. Understanding of diagnosis showed the greatest increase. The workshop has been well-received, and high patient and guest satisfaction reported. In particular, people like hearing from a patient who has been through treatment. We have also found our neurology colleagues appreciate having the workshop to refer into, particularly for patients who may not be referred to Neuropsychiatry.

Figure 1: Group treatment pathway



Dr Norman Poole and I have piloted a 6-session CBT group for functional memory problems. It was very small, as although we invited 6 patients, only 3 attended. In the group we covered information about memory; introduced the CBT model and rationale; introduced and practised mindfulness exercises; planned behavioural experiments; taught thought-challenging; and encouraged patients to set goals based on their values. Although we used the CBT health anxiety model (Warwick, 1998) as a guide for the treatment, we found it did not fully represent the presentation of functional memory problems. Maintaining factors like selective attention, worrying about memory failures, and seeking reassurance were relevant, but did not provide the full picture. Within the treatment, we also used ideas from Acceptance and Commitment Therapy (ACT), a type of CBT (Hayes et al., 2006) that we think may be a potentially useful treatment for FND (Cope, Poole and Agrawal, 2017). We found that the ACT ideas around acceptance of their difficulties, and living life despite them were useful. There were no differences on memory functioning at the end of the group, but patients did report more acceptance of their condition. Two out of the three patients were able to be discharged from the service after the group, which suggests it is useful to offer. We need to run more functional memory groups in order to develop the treatment.

Benefits and limitations of group treatments

There are a number of potential benefits associated with group treatments. These include it being cost-effective as it offers help to a number of patients at the same time, and that patients can also support and learn from one another. A key potential benefit is that it increases the credibility and acceptance of the diagnosis, and reduces stigma. Patients often comment on how it helps them to see that others are experiencing similar difficulties, which helps them to feel they are not "mad" or "a medical mystery". This may serve to reduce the potential threat associated with the diagnosis, helping patients to reduce their focus on the unwanted symptoms. Another potential advantage is that it is possible to include family members or friends in a group setting. We think this must help in acceptance of the diagnosis, as family members' and significant others' doubts and misunderstanding can feed into patients' own doubts and misunderstanding.

Of course there are limitations with a group approach. Firstly, you cannot base group treatment on a patient's individual formulation. Although aspects of group treatment can be individualised slightly if it is a longer treatment, for example in a CBT group there is discussion of a patient's homework. Secondly, groups can be intimidating for some people, which is difficult to resolve. But we have found that having the FND workshop first aids openness to attending other groups. Finally, a group can be dominated by 1 or 2 members, but effective group facilitation can overcome this issue.

Conclusions

Groups can offer something that individual treatments cannot, namely meeting others with the same diagnosis. It appears that facilitation of FND groups in specialist settings is important for the credibility of the intervention. Group treatment, of course, does not replace the need for individual therapy, as some patients require individualised treatment. Future research should try to establish what the active components of group treatment are, as it is not clear which aspects are the most important, such as, is it simply the group setting, the psychotherapeutic model, and/or increasing understanding of diagnosis.

This article is based on a presentation given at the Royal College of Psychiatrists International Congress 2017.

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Faculty of Neuropsychiatry, Sept 2017

Dr Thomas Anderson

FY2 in Neuropsychiatry, St George's Hospital

What is neuropsychiatry? This is the question I asked myself when South Thames Foundation School offered me a four-month placement at St George's. At first, I thought this reflected my own lack of knowledge, but since then I have discovered that a most of the medical community seems to be unaware of this secretive and mysterious sub-specialty.

I am an FY2 trainee who is currently out of sync with the regular training scheme. As a consequence, each summer STFS provided me with a list of vacant foundation rotations that needed filling. I would like to claim that I made this year's choice on academic grounds, but the benefits of being in Greater London seemed to outweigh the potential hazards of spending four months in an unknown mental health sub-specialty.

Two months in, I'm pleased to say that this has proved much more than just a geographical convenience. Although I still have my hopes set on a career in the Orthopaedic department, I am enjoying both the academic challenge of exploring something new and the supportive nature of the department. Encouraged by one of my supervising consultants Dr Niruj Agrawal, I attended day one (14th) of the Royal College of Psychiatrists Faculty of Neuropsychiatry Annual Conference, unsure of what to expect but content with a day trip out of the hospital and something to stick on my CV.

> I have always been intrigued by the human mind and the mechanisms behind human thought, so the first plenary Image, Imagery and Imagination was an ideal start to the day

The conference began with a formal welcome and introduction from Professor Eileen Joyce, the Faculty Chair. Professor Wendy Burn followed with a roundup of work within the college with a focus on the efforts to incorporate neuroscience and neuropsychiatry into the membership exams.

I have always been intrigued by the human mind and the mechanisms behind human thought, so the first plenary Image, Imagery and Imagination was an ideal start to the day. Professor Adam Zeman spoke on Aphantasia (loss of the mind's eye). He told the story of how a man unable to imagine his grandchildren's faces had lead him and his team in Exeter to classify a condition that now resonates with many thousands around the world. Interestingly, they have found that individuals with Aphantasia could still recall details of memory despite the inability to recreate images in their mind.

Professor Giacomo Rizzolatti then spoke on mirror neurons, explaining the concept with a series of videos of monkeys being given and subsequently not given items of food. He hypothesised that mirror neurons could explain how empathy is built into the observation of action and went on to describe how perhaps mirror neurons could explain the tolerance of the Nazi regime in world war two.

The final speaker Professor Dennis Velakoulis changed tack, speaking of his work on the neuropsychiatry of younger onset neurodegenerative disorders. He hypothesised that the shared phenotype of chronic schizophrenia and FTD could perhaps explain a common pathological process. What I liked about Velakoulis' talk was his willingness to challenge current theories on disease process. Given that much of mental health knowledge lacks the support of scientific facts, there is still significant potential for discovery.

Plenary two – titled Mild TBI and the Post-Concussion Syndrome – focused on what appears to be the hottest topic in current neuropsychiatry debate: what is mild TBI?

Having just moved from the T&O department, I have been very reflective on the outcome of trauma patients. Previously, I thought that if a patient achieved a PTA of 12/12 and their anatomical deformities were corrected, we'd done a good job. But unfortunately, time and again patients with ''mild'' TBI turn up at the neuropsychiatry outpatient clinic with significant mental health complications, and it seems clear to me that the work done by the orthopedic department fails to consider the full spectrum and non-mechanical sequelae of trauma.

The talk started with the neurological perspective from Professor David Sharp, who spoke about the importance of differentiating post-concussion symptoms to allow a more accurate diagnosis and subsequent focus for treatment. He also discussed the use of diffusion imaging to identify diffuse axonal injury and recommended its use as a predictor of post-concussion symptoms. Unfortunately, not everyone who reports post-concussion symptoms has identifiable axonal injury, and Dr Nigel King's words on the neuropsychological perspective of mild TBI hoped to unpick the spectrum of disease. He focused on features of chronic and persisting symptoms and the role of psychological intervention in treatment.

Lastly, Dr Robin Jacobson discussed the neuropsychiatric perspective and medico-legal dilemmas. He proposed duration of PTA as a useful and valid tool for categorising mild TBI and predicting outcome. Jacobson was the only speaker to touch on the highly sensitive topic of malingering and stated that effort tests provided a crucial role in accurate assessment. Despite the lack of clear consensus between the speakers, there was at least agreement that mild TBI was real. But, even this was thrown up in the air when a member of the audience pointed out that cognitive symptoms in other neurological diseases are rarely seen in the absence of radiological changes and that for a significant number of individuals with mild TBI, brain imaging will be normal.

In the afternoon, I attended a seminar on smart technology and epilepsy management by Dr Rohit Shankar and Professor Stephen Brown. They discussed the ignored tragedy of sudden unexpected death in epilepsy (SUDEP) and their efforts to tackle this mortality burden. They described their work in partnership with major tech firms, where they aim to design wearable technology that can identify seizures and automate response. Their great success however, has been in the development of EpSmon – a patient controlled app that allows self-monitoring of their condition and encourages engagement with services if certain high-risk features are recorded. They very eloquently stated that while major tech firms look for the "slam dunk", they have managed to almost eliminate SUDEP in their local area with a simple and free app.

The final plenary – titled Epilepsy and the Mind: What the Humanities Can Teach Us – looked at three different mediums: film, music and literature. The first talk by Dr Ken Barrett focused on the 1946 war movie A Matter of Life and Death, in which the main protagonist experiences temporal lobe seizures and peri-ictal psychosis. Professor Steve Brown spoke on music and epilepsy, including its role as a trigger in musicogenic epilepsy, as a protective factor in general cognitive development and as a possible treatment mechanism. Lastly, Dr Maria Vaccarella talked about epilepsy and its role in contemporary fiction and how literature can help clinicians better understand the patient experience. Discussing the humanities at a medical conference seemed novel, but given the arts provide such an important access point to the general public, they clearly have a role to play in health education for both the clinician and the patient.

Neuropsychiatry continues to surprise me. The breadth of topics discussed – from hard science to the humanities and philosophy – is rare in medicine. Not only this, but mental health and physical health are too often viewed as two distinct entities, and I feel that neuropsychiatry provides a platform where these two realms can be discussed in a progressive manner. Although I'm not quite ready to alter my career plans, so much about neuropsychiatry appeals to my innate interests and I think I'll return to the conference next year for more.

The 3rd International Conference on Functional (Psychogenic) Neurological Disorders (FND), Edinburgh, Scotland, September 6th – 8th 2017.

Joana Macedo da Cunha

St George's, University of London & Faculdade de Medicina, Universidade de Lisboa
Departamento de Psiquiatria e Saúde Mental, Centro Hospitalar, Universitario do Algarve

Before a multidisciplinary crowd of over 500 professionals, international experts explored topics relating to phenomenology and classification (day 1), mechanisms and etiology (day 2) and treatment (day 3) of FND. The multiplicity of backgrounds represented at the conference, including psychiatry, neurology, physiology, psychology, physiotherapy, and ethics, allowed a fresh revisit of some of the centuries-long controversies surrounding FND, supported by current clinical and neurobiological research regarding these disorders. With its roots on the concept of hysteria, what is now known as FND can be found described in the medical literature since ancient Greece. It presents with neurological signs and symptoms that are inconsistent with recognized "organic" neurological or medical conditions, and arising without any clear structural brain lesion. This classic neuropsychiatric entity was for many years conceptualized as a pure "psychogenic" disorder in which, according to Sigmund Freud and his contemporaries, an "(intolerable) affective idea" was converted into a physical phenomenon. Hence, the fall of the "neurological" hysteria of Charcot, that hypothesized a brain malfunction underlying what we now know as functional neurological symptoms, led to a decrease in neurobiologically-based approaches, both from clinical and research perspectives.

During World War I, an unprecedented number of soldiers were diagnosed with shellshock: a controversial

diagnosis characterized by an array of functional neurological symptoms such as blindness, weakness, tremor and gait disturbance. It was conceptualized as being directly associated to battlefield trauma, and quickly raised many controversies and debates in neuropsychiatry.

Today, most of those issues such as the role of physical/psychological trauma, the cultural modulation of symptoms, and the problem with malingering, still apply to FND, as presented by Professor Sir Simon Wessely in his talk "Lessons from Shellshock". Although a debate about neurobiological causes for these neurological symptoms ensued, an emphasis was put on the psychological factors and mechanisms such as conversion, dissociation, and suggestibility. The role given to personal trauma, both recent and early life/childhood traumatic experiences, was of a causal nature. This was widely discussed in the conference, albeit within a refreshed and contemporary framework as presented by Dr. Selma Aybek in her talk, "Early Life Experiences and Life Events". While presenting the extensive research work of her group in the role of

emotional processing and trauma in patients with FND, Dr. Aybek emphasized that what was once thought as the only possible cause for FND should be thought as an important predisposing and possibly perpetuating factor in some patients.

After the fall of psychoanalysis, and a brief period through wherein some authors claimed the disappearance of hysteria, the noted high prevalence of FNS amongst patients referred to neurology clinics (16%, second only to headache), together with the new and advanced neuroscience based techniques, induced a rebirth of the academic and clinical interest in FND over the last few decades, as reflected in the topics presented throughout the conference. One of the main shifts in this area was in diagnosis, as explored by Professor Anthony Lang and Dr. David Perez at the first day of the conference. Current diagnostic criteria, as echoed in the DSM-5, focus on positive clinical features, removing the need to identify an acute precipitating stressor. Similarly, doctors no longer need to actively exclude malingering to establish a diagnosis of FND.

As observed by Professor Anthony Lang, from a neurological perspective there are still many challenges such as the absence of a gold standard, leaving the diagnostic accuracy to rely heavily on the expertise of the assessor; and the potential, fairly common, superimposing of functional neurological symptoms on "organic" disorders with often blurred boundaries, and a significant overlap with conditions with their own diagnostic uncertainty and lack of biological markers, such as focal dystonia. He highlighted that structured composite scores could possibly provide more accurate diagnostic tools and thereby improve patient care.
The shift from a diagnosis of exclusion to a "positive" neurological diagnosis was a paramount step in the care of these patients, allowing an early and accurate diagnosis. Nonetheless, as Dr. David Perez emphasized, the psychiatric, psychological and psychosocial factors still play a crucial role in treatment and prognostic individualized approaches to patients. Albeit a high rate of psychiatric comorbidity in patients with functional neurological disorders, it is well known that this is not always the case. Nonetheless, as Dr. Perez pointed out, sub-threshold symptoms are usually overlooked in categorical approaches to psychiatric comorbidities. The presence of alexithymia, maladaptive coping strategies and personality traits in FND should be explored and efforts in developing tools to evaluate such symptoms in these patients could provide excellent value on improving patient care. The clear overlap between functional neurological disorders, somatic symptom disorders and dissociative disorders suggesting that a transdiagnostic approach versus a comorbidity view of these situations should be considered and further investigated. Furthermore, different sub-types of FND also overlap, with many patients presenting with an array of symptoms, ranging from the most common types such as movement symptoms and non-epileptic attacks, to also visual, auditory, cognitive and speech symptoms. The phenomenology of the different sub-types was explored by different experts during the first day of the conference, from which I would like to highlight the talk by Dr. Jeffrey Staab, "Dizziness and Persistent Postural-Perceptual Dizziness". In his model, he emphasized the role of abnormal body-monitoring involved in acute high-risk postural control strategies, that by persisting beyond the acute phase, can lead to symptom manifestation.

The role of attention in FND is consensually considered to be one of the most important pathophysiological clues. Given that FND symptoms are almost always distractible, it is considered that an abnormal body-focused attention is involved in the generation and perpetuation of symptoms. Modern computational-based models of brain functioning propose that perception is the result of the interplay between prior beliefs about the world and sensory input. The weight of each one in percept generation is thought to be modulated by attention, as brilliantly explained by Professor Mark Edwards in his talk. Attention and its manipulation is also on the central to many of the treatment approaches discussed, such as cognitive-behavioural therapy, and most recently physiotherapy based approaches.

On the final day of the conference, the talks given by Dr Jon Stone, Professor Laura Goldstein, Professor Richard Brown, Mr Glenn Nielsen made clear that an individualized approach, beginning with a correct (and understandable) explanation of the diagnosis, and ending in a clinical multidisciplinary approach is the right way to go, when treating patients with FND.
This conference exposed the dynamic and multidisciplinary clinical and scientific community surrounding FND. It is a very exciting time for FND research, promising to unravel of one of the most enigmatic mind-body disorders of all times.

Phillip Slack

Request For Help

Dear Colleagues,

The Old Age Psychiatrist (the newsletter for the Faculty of Old Age Psychiatry, RCPsych) is running its annual writing competition for doctors (ranging from foundation trainees to consultants). The prizes are £150 for the winner and £50 for the runner up! Also the 5 short-listed entries (including those of the winners) will be published in the Old Age Psychiatrist.

The topic is A world without dementia: where would old age psychiatry be?

If dementia were cured tomorrow what would be the role of the old age psychiatrist? Creative or original writing welcome (including essays, short stories, personal accounts and poems) with word limit up to 1000 words.

Please email your submissions to Anitha Howard at dranithahoward@gmail.com by 31st October 2017 along with your name, grade, work address and contact phone number.

Last year's shortlisted submissions can be seen at **www.rcpsych.ac.uk/workinpsychiatry/faculties/oldagepsychiatry/newsletters/enewslettermay2017/2016writingcompetition.aspx**

Kind regards
Philip Slack

ST5 Old Age Psychiatry
Trainee Editor
philip.slack@doctors.org.uk