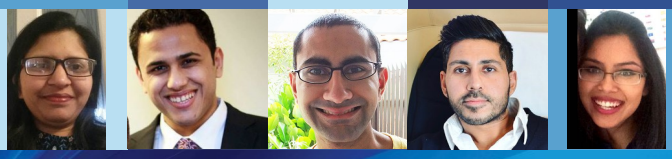


Mind the GAP

VOLUME 7 ISSUE 1 JANUARY 2018
NEWSLETTER BY WEST MIDLANDS HIGHER TRAINEES IN GENERAL ADULT PSYCHIATRY

The Genetic Link between Autism and Schizophrenia

Richard Carr Medical Student, University of Birmingham

Autism Spectrum Disorder (ASD) and schizophrenia are two serious psychiatric conditions that are widely viewed as separate clinical entities. However, there is considerable comorbidity between the two, with the prevalence of childhood-onset schizophrenia estimated at 30-50% in autistic children [1]. The clinical phenotypes of the two disorders exhibit overlap even in non-comorbid patients- the negative symptoms of schizophrenia can imitate some of those seen in autism, and misdiagnoses do occur [2].

The genetic studies have visualised this overlap. The genetic bases for both disorders are complex, and the heritability of each is high, at around 80% for both. Association studies have found that a number of the candidate genes predisposing to schizophrenia also predispose to ASD [3], although compared to the host of identified risk genes for each, this number is fairly low. On top of this, the risk genes identified so far only account for a small proportion of patients with schizophrenia and ASD and do not come close to explaining the high heritability. Certainly, they cannot explain the clinical overlap alone. One hypothesis for this is that these diseases are linked to a larger number of rare, highly penetrant alleles which might not be picked up on association studies, and there is also the possibility that other genetic mechanisms are implicated.

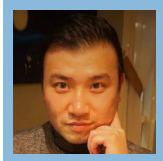
Copy number variations (CNVs), have received increasing interest in the past few years. The discovery of specific genetic hotspots where CNVs are more likely to occur has been exciting, as some of these predispose to not just ASD and schizophrenia, but other disorders as well that typically exhibit comorbidity with ASD and schizophrenia, including developmental delay and Attention Deficit Disorder/ Attention Deficit Hyperactivity Disorder. CNVs can manifest as deletions or duplications, and it has appeared that the relationship between ASD and schizophrenia in terms of associations with copy number in these hotspots has been broadly diametrically opposite. i.e., while the hotspot loci overlap, the copy numbers themselves do not [4]. This may not be the whole picture however. In one domain, DUF1220 on 1q21, deletions were thought to be associated with ASD while reciprocal duplications are correlated with schizophrenia severity. It was found that in fact, deletions were associated only with *positive* schizophrenia symptoms while the negative ones, that form the clinical overlap with autism, were associated with duplications [5].

This could suggest that divergence exists not between schizophrenia and ASD, but between the positive and negative symptoms of schizophrenia. This research has not yet been repeated for other loci. While promising, investigation into the

Upcoming Events

INTERESTING EVENTS
MENTAL HEALTH LAW UPDATE
19TH JAN 2018 @ UFFCULME

PEER GROUP MEETINGS
15TH FEBRUARY 2018
MARCH 2018 TBA
18TH APRIL 2018



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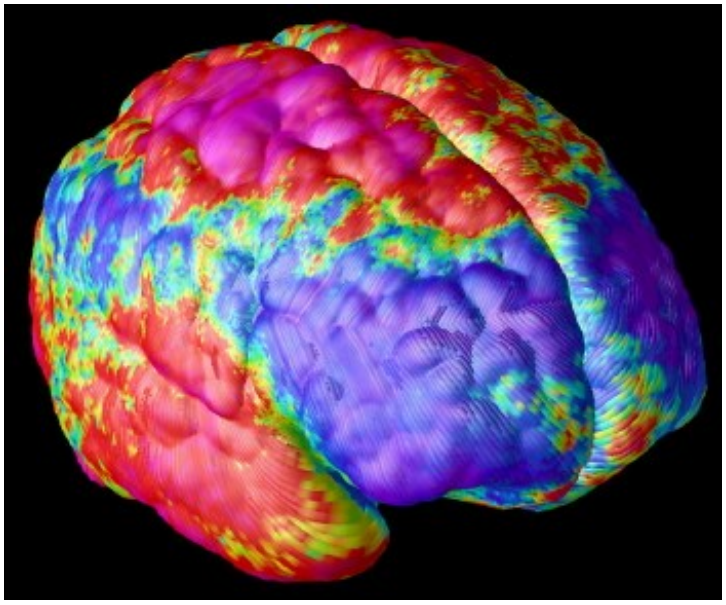
impact of CNVs as a potential bridge between ASD and schizophrenia is still in early days, and as with the association of individual genetic variants with the disease, still only explains a small number of cases.

The function of the genes involved in CNV hotspots and association studies can shed some light on the physiology of these diseases. Many of those identified, such as *SHANK*, *NLGN* and *NRXN* families, are involved in synapse formation and structure and some are involved in immune function. Dysfunction in both types of genes has been implicated in ASD and schizophrenia, potentially pointing to a common aetiology of the disorders. This is supported by some of the common environmental risk factors for ASD and schizophrenia, namely maternal infection, which leads to inflammation and immunological changes in the foetal brain [6]. Risk genes associated with immune function could set the stage for such problems to cause the changes necessary for the child to exhibit symptoms.

Could ASD and schizophrenia be one disease continuum?

The heterogeneity of schizophrenia patients is already substantial - an extremely negatively presenting patient will be diagnosed with the same disease as a patient presenting with mainly positive symptoms, while their condition actually might more closely resemble a spectrum disorder. This is not reflected in the diagnosis, and fairly recent changes to classification, such as abandoning the use of schizophrenic subtypes and the merging of the various autistic disorders into ASD, seems to have reinforced this. Perhaps a new system of classification is needed to more accurately represent the dizzying complexity of ASD and schizophrenia. As the field of management evolves, and therapies become more targeted, that binary structure may begin to look increasingly unrefined and ill-suited for purpose.

This article looks at only a narrow slice of the tortuous physiology underlying ASD and schizophrenia. The environment is still a major player in enriching a genetically predisposed patient into above-threshold disease. Overlap is also evident in the neuroanatomy of the two disorders that mirrors the clinical picture, with the brain areas that share common changes being those implicated in negative symptoms [7]. But the genetics are receiving most attention for now- a fascinating and rapidly evolving subject that may lead to expansive changes in the way we think about and treat ASD and schizophrenia.



False colour image from MRI of a brain showing tissue loss (red areas) in Schizophrenia (NIMH, 2006)

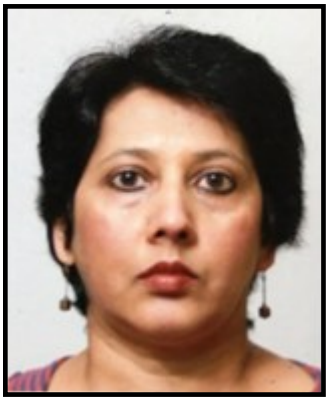
References

1. Rapoport J, Chavez A, Greenstein D, Addington A, Gogtay N. Autism Spectrum Disorders and Childhood-Onset Schizophrenia: Clinical and Biological Contributions to a Relation. Revisited. *J Am Acad Child Adolesc Psychiatry.* 2009; 48(1): 10-18.
2. Woodbury-Smith M, Boyd K, Szatmari P. Autism spectrum disorders, schizophrenia, and diagnostic confusion. *J Psychiatry Neurosci.* 2010; 35(5): 360.
3. Crespi B, Stead P, Elliot M. Comparative Genomics of Autism and Schizophrenia. *PNAS.* 2009; 107(1): 1736-1741
4. Crespi B, Crofts H. Association testing of copy number variants in schizophrenia and autism spectrum disorders. *J Neurodev Disord.* 2012; 4(1): 15.
5. Searles Quick VB, Davis JM, Olincy A, Sikela JM. DUF1220 Copy Number is Associated with Schizophrenia Risk and Severity: Implications for Understanding Autism and Schizophrenia as Related Diseases. *Transl . Psychiatry.* 2015; 15(5): e697.
6. Meyer U, Nyffeler M, Engler A, Urwyler A, Schedloqski M, Knuesel I et al. The Time of Prenatal Immune Challenge Determines the Specificity of Inflammation-Mediated Brain and Behavioural Pathology. *J Neurosci.* 2006; 36(18): 4752-4762.
7. Cheung C, Yu K, Fung G, Leung M, Wong C, Li Q et al. Autistic Disorders and Schizophrenia: Related or Remote? An Anatomical Likelihood Estimation. *PLoS One.* 2010; 5(8): e12233.

Case Report

Tics associated with Pregabalin in a patient with psychosis and fibromyalgia

Dr Nidhi Gupta MBBS, MD, DCP, MRCPsych
Speciality Doctor, Handsworth and Ladywood Home Treatment team, Birmingham. E-mail nidhi.gupta3@nhs.net



This is a case report of a woman who manifested with new onset motor and vocal tics following initiation of Pregabalin for managing her chronic widespread pain related to fibromyalgia.

A 43 year old female who was under the care of CMHT with a diagnosis of Systemic Lupus Erythematosis (SLE), Fibromyalgia and non-organic psychosis was initiated on Pregabalin by her rheumatologist to help manage the pain associated with fibromyalgia. She was already on Quetiapine, which helped with her auditory hallucinations and paranoid delusions. Within a few days of commencing Pregabalin, she manifested with motor tics. These motor tics included- excessive blinking of eyes, twitching, shrugging of shoulders as well as jerky movements of the arms and legs. In addition to motor tics she also started to have Vocal tics which were in the form of periodic grunting and repeating the word 'no' whilst trying to have a conversation. These tics were present continually. However they were exacerbated by stress. The tics also worsened her pre-existing insomnia related to her psychosis and fibromyalgia. Additionally, the tics worsened her fibromyalgia. This again affected her mobility and cognition. Since there is a strong element of impaired cognition with fibromyalgia, she struggled to cope with her day to day activities of daily living. This in turn affected her mood and psychosis. She was reviewed by her mental health team in coordination with her rheumatologist, who suggested weaning her off Pregabalin. Her tics improved noticeably after gradual and subsequent discontinuation of Pregabalin. However they did not go away completely.

Treatment with Pregabalin is usually well tolerated in most individuals. Dizziness and somnolence are some of the most frequent adverse events at therapeutic doses. The side effect of somnolence is sometimes used to the advantage of people with fibromyalgia as they have difficulty with their sleep. Pregabalin structurally resembles GABA and binds to voltage -gated calcium channels. Certain movement disorders such as tremor, Parkinsonism and asterixis have also been reported in Pregabalin use (Perez et. al, 2009), but motor and verbal tics are rare. A possible interaction between Quetiapine and Pregabalin cannot be entirely excluded. Even though tardive dyskinesia is a rare and uncommon side effect of antipsychotic medication, it is possible that these tics were in some way manifested as a variant of tardive dyskinesia.

Management of tics includes a wide range of treatment options starting from medications to behavioural treatments. Medications include neuroleptics like risperidone and aripiprazole, clonidine, benzodiazepines like diazepam and clonazepam and Tetrabenazine. Use of botulinum toxin injections can also be beneficial in some cases especially if tics are localised to a group of muscles. However, the effect only lasts for about 3 months and injections have to be repeated.

Behavioural therapies include- psychoeducation, reduction of stress, and massed negative practice. Massed negative practice is one of the most frequently used behavioural techniques in the treatment for tic disorder. The patient is asked to deliberately perform the tic movement for specified periods of time interspersed with brief periods of rest.

Key learning points

1. Psychosis can occur in patients with chronic widespread pain (Fibromyalgia) which can be difficult to treat especially if there is an additional underlying autoimmune disease like Systemic Lupus Erythematosus

2. Unusual side effects can occur due to commonly used medication in patients with complex presentations and this might have an organic basis

3. Non pharmacological treatments can be considered as an option in some cases with complex presentations

References

Perez Lloret S, Amaya M, Merello M. Pregabalin-induced parkinsonism: a case report. Clin Neuropharmacol 2009;32:353-354

Raghavendra B. Nayak, Govind S. Bhogale, Nanasaheb M. Patil, and Sameeran S. Chate. Psychosis in Patients with Systemic Lupus Erythematosus. Indian J Psychol Med. 2012 Jan-Mar; 34(1): 90–93.

Pregabalin Case Report—MCQs

Question 1:

Neuropsychiatric manifestations of SLE include all except:

a. Depression
b. Psychosis
c. Delirium
d. Dementia
e. Nephropathy

Answers on final page

Question 2:

Antipsychotics which can be used in the treatment of psychosis in patients with SLE are all except:

a. Olanzapine
b. Quetiapine
c. Trifluoperazine
d. Aripiprazole
e. Risperidone

Differentiating Recurrent Unipolar Depressive Disorder from Bipolar Affective Disorder as a diagnostic code within the Coventry IPU 3-8 (Affective Disorders)

Dr Sazgar Hamad, Dr Yousuf Zakaria, Dr Sarita Chetri, Fola Ajekigbe, Beth Goddard
Dr Steven Marwaha (Consultant Psychiatrist IPU 3-8)

Background to the work

The IPU 3-8 (affective disorders) Unit was established 2014 specialising in the diagnosis and management of severe mood disorders and personality disorder. Differentiating between unipolar depression and bipolar affective disorder in clinical practice can be difficult but is a key task of the service, so that individually tailored effective treatment can be given to patients. Clinicians involved in the management of mood disorders need to be able to efficiently distinguish between a numbers of conditions in order to correctly diagnose bipolar disorder. A key part of this process is to be able to do thorough assessment to rule out hypomanic features as this is illness-defining in people with pre-existing depression. A key challenge is that ideally a lifetime history of hypomania should be taken.

Aims and Objectives

This audit investigated the extent to which assessment of hypomania/ mania was carried out in patients with mood disorders newly referred to IPU 3-8 from January 2016 to January 2017

Thresholds for compliance:

Full compliance ≥ 90%

Partial compliance 89-80%

Minimal compliance ≤ 80%

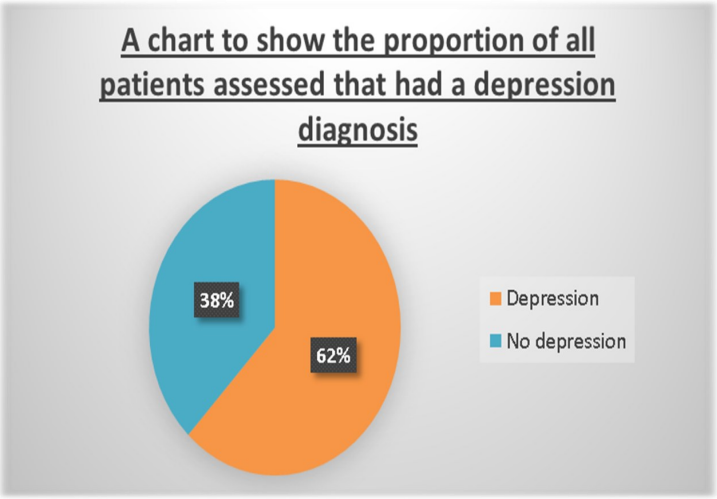
Summary of results

The audit reviewed the clinical letters of 124 newly referred patients.

77 out of 124 (62%) patients has a diagnosis of depression, the rest had other forms of affective disorders.

Assessment of hypomania was carried out in 97 (78%) patients. Only 30 patients had all symptoms of hypomania assessed, 67 patients received incomplete assessment.

Importantly 42 out 77 (50%) depressed patient were assessed for hypomania, 35 out of 77 (45%) depressed patients were not assessed for hypomania.



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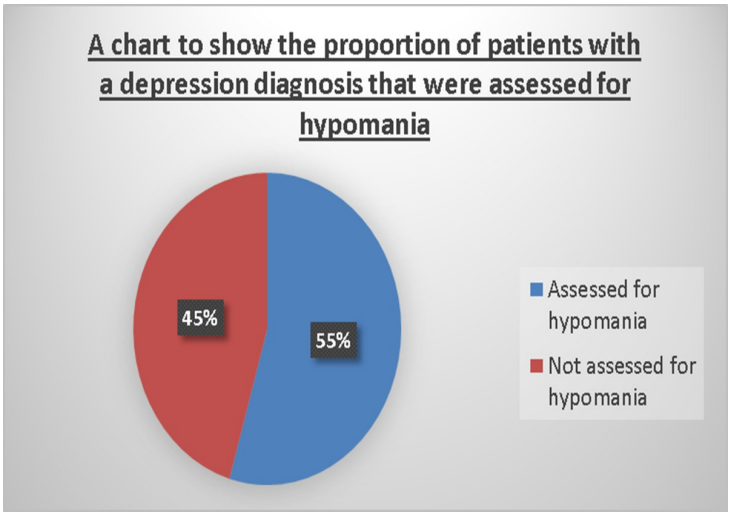
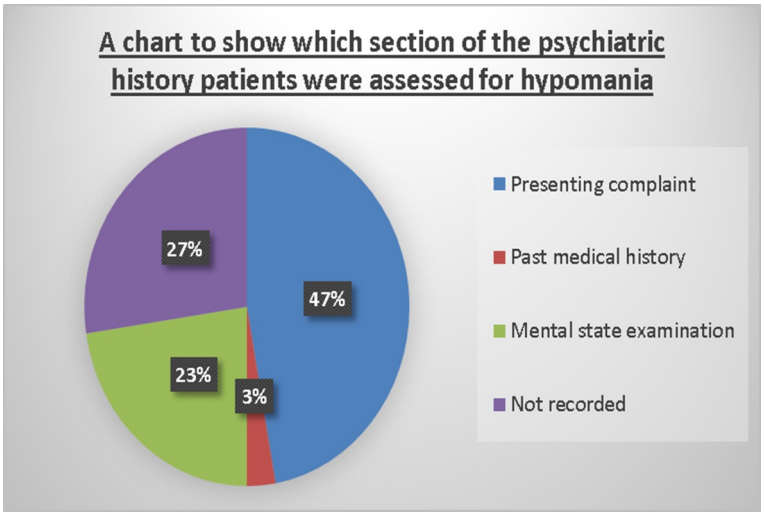
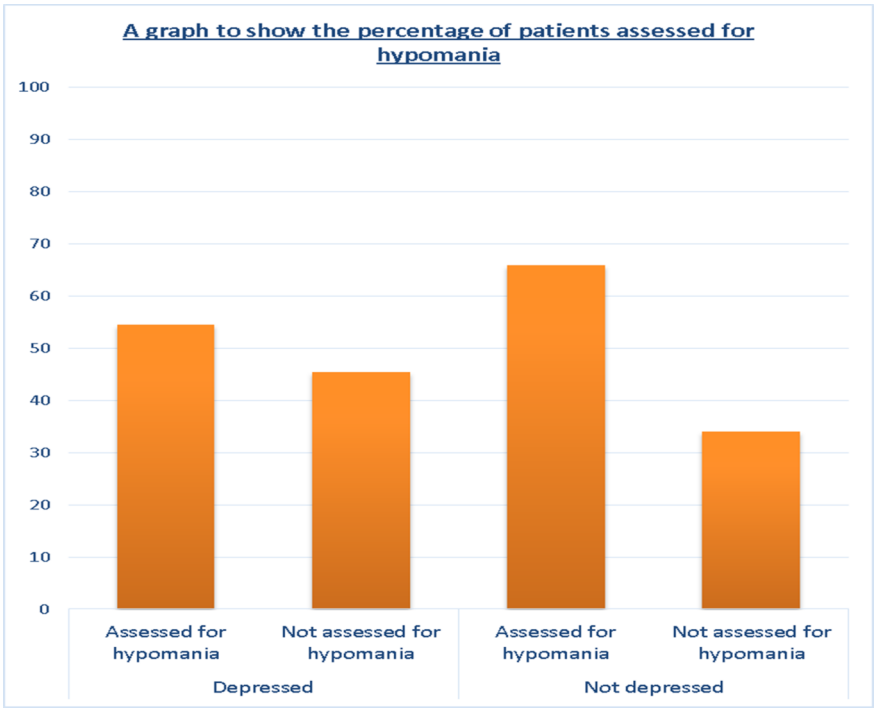






Reference

The Mood Disorders Questionnaire
Prim Care Companion J Clin Psychiatry. 2002; 4(1): 9–11.

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC314375/

The Mood Disorder Questionnaire is a brief, self-report screening instrument that can be used to identify patients most likely to have bipolar disorder.

Recommendations

- Discuss results of the audit at the team's clinical governance meeting. Agree further recommendation with IPU 3-8 clinicians
- Discuss results of the audit in local academic teaching and junior/ senior meeting. Protocol for side effects monitoring and physical investigations are introduced in Feb 2014 as part of doctor's induction pack.
- Display a poster or card in IPU 3-8 clinic as a reminder
- Set up a process by which a standardized questionnaire for bipolar disorder can be to be completed by the patient before clinical assessment. E.g. Mood Disorders Questionnaire
- Re-audit in 6 months

Reflective Practice Group for GP and Foundation Trainees: Setting Up and Evaluating a Group

Dr G Madhavan, ST5, Dr C Cooper, ST6, Dr A Albeniz, Consultant Medical Psychotherapist
Coventry and Warwickshire Partnership Trust.

Background

Balint and/or reflective practice groups are compulsory for core psychiatry training.

Development of reflective practice is an objective of both RCGP and Foundation Curriculae.

Methods

From June 2016 to October 2016, a regular reflective practice group (2 groups of 8 sessions) for GP and Foundation trainees was initiated at the Coventry & Warwickshire Partnership Trust with two higher trainees acting as co-facilitators, with regular supervision by the local Consultant Medical Psychotherapist. A Pilot group ran initially during June and July 2016 and a second group was established shortly after the new doctor intake in August 2016 which built on feedback gained from the pilot group.

Feedback was obtained via email correspondence for the pilot and from the use of a short online survey for both attendees and non-attendees for the second group.

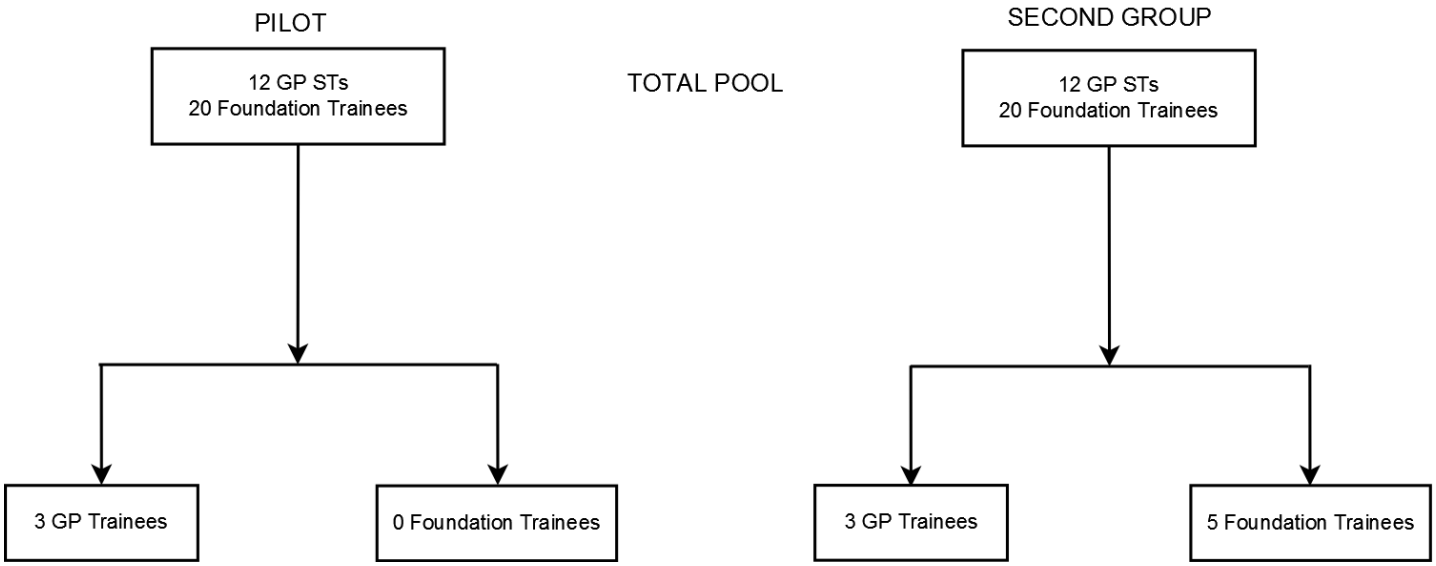
Results

There was limited attendance to the pilot group; however, feedback gained was used to develop the second group which showed a surge of interest early on. This was not sustained and feedback suggested various issues, including timing and location, appeared to impact on attendance.

Feedback also reported benefits gained by trainees who attended the groups and who appreciated the opportunity to attend.

"A good forum to discuss any issues I was having as a newly qualified doctor."

"It's a great skill to learn to explore rather than criticise your thoughts and feelings."

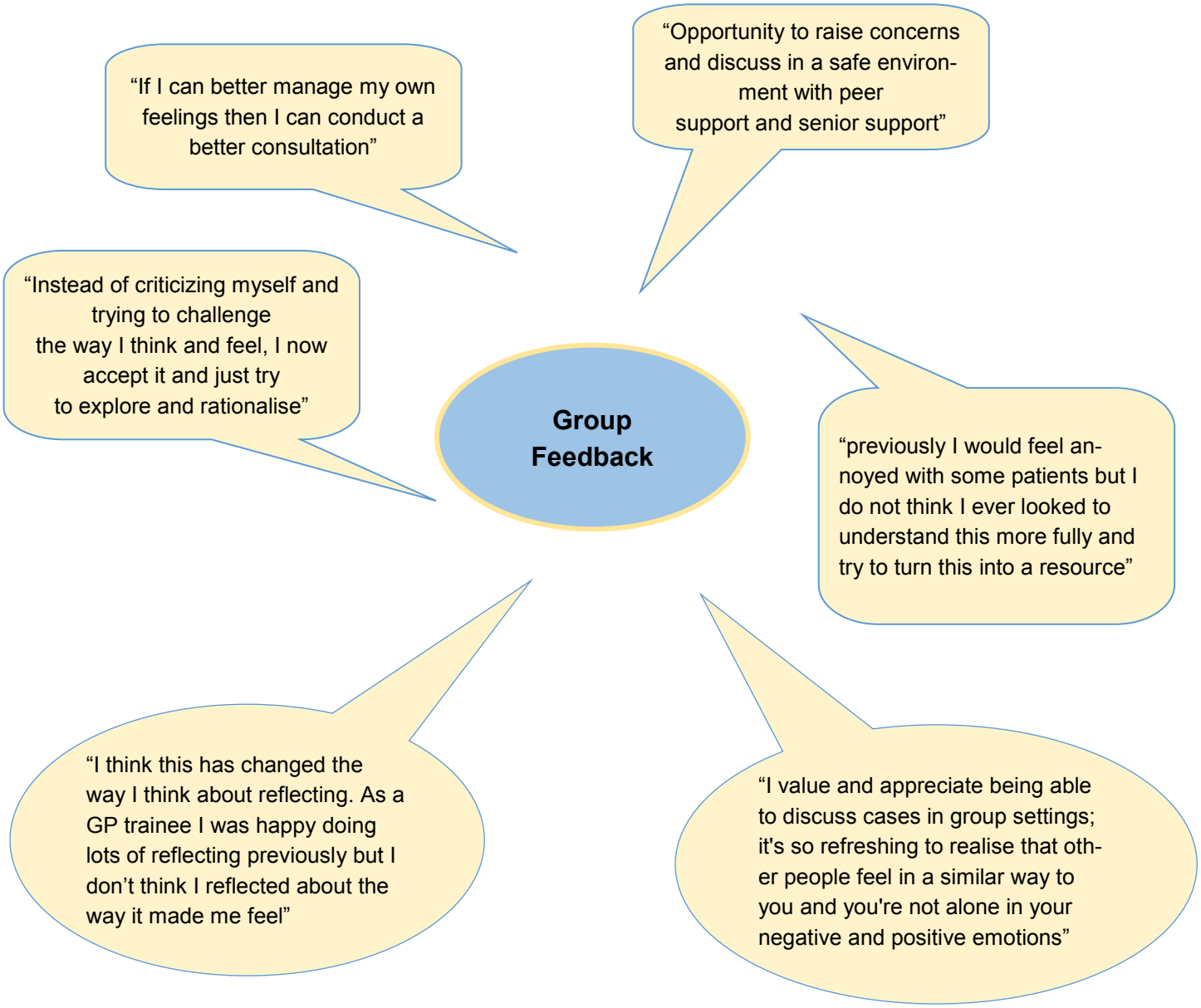


Themes

Themes that emerged in the groups included seeing patients in non-clinical settings (e.g. living near patient or coming across patient when with doctor's own family), dealing with strong emotions that arise within self and team including "splitting" when treating patients with personality disorders, conflict with seniors regarding management plans, managing patients that show attraction towards the professional, dealing with the death of a patient seen when on-call and the responses of those around. The participants would often be keen to bring a topic to discuss, such as the themes above. They would be encouraged to relay what happened and share other experiences that reflect their emotional responses to similar narratives.

Conclusions

This article outlines setting up a reflective practice group, issues encountered and outcomes. Reflective practice groups can be a useful resource for Junior Doctors to discuss various difficulties encountered in clinic practice, though they often did not attend due to clinical responsibilities. Incorporating group timings into local teaching programmes with the compulsion to attend could improve attendance and therefore benefit the developing new doctor. Further establishment of student groups may aid in influencing uptake for future postgraduate groups although further research is required.



Case Report

A case of mood changes due to anabolic steroid use

Dr Rajan Bhambra Foundation Year 1
Handsworth CMHT, Birmingham and Solihull Mental Health Trust

A 48 year old male presented for a follow-up outpatient appointment with his wife.

03/11/2017

His main complaint was difficulty sleeping, as his thoughts were keeping him up late into the night. In addition to this, he was becoming agitated when around crowds of people and he would need to leave to go home immediately. The reason for this became clear when the wife revealed his agitation led to anger, which manifested itself through the patient hitting and head-butting walls. His coping mechanism for this anger would be to lift weights when he got home. Tying into this anger, his wife stated that his mood swings were terrible and he struggled to complete small tasks such as making tea. The patient also stated that he had been having suicidal thoughts for years, although his wife and his daughter aged 16 were his protective factors. He did not want to go over his past psychiatric history.

Mental State Examination

Appearance + Behaviour: Well kempt. Very muscular. No eye contact, mainly looking at floor, occasionally at computer or wife. Visibly agitated and upset, especially with any mention of past thoughts/history. Fidgeting. Sweating profusely.

Speech: Quiet voice, normal tone and rhythm.

Mood: Subjectively-Low. Objectively-Low.

Thought: No formal thought disorder. Thought content - suicidal, ruminating on past events, paranoid.

Perceptions: No abnormal perceptions in any modality.

Cognition: Intact.

Insight: Good insight into illness and compliant with medication.

Orientation: Orientated to time, person and place.

So now that we have a snapshot of the patient at this point in time, next we see how he originally presented when referred by the GP.

Original Presentation — August 2013

Referral received from GP stating patient presented with depression and suicidal ideation. This depression has been present for the past 20 years following his partner having an extra-marital affair with his cousin. They still remain together. The patient has constant thoughts about his wife's past infidelity but has never sought counselling or help. 5 weeks ago he confronted his partner about the incident again and has been planning ways to end his life since. He calls the Samaritans helpline 5 times a day. His last attempt on his life was 10 years ago when he slit his wrists in the bath and was only saved by his mother-in-law.

What is interesting from this is that the patient has been suffering from low mood for 20 years but chooses now to present for help. What could the triggering factor for this be?

He did reveal that 4 months prior to the referral his wife found out he had been in an affair. Or is there another underlying reason? Also, there is no mention of agitation or anger, which is one of his major symptoms at the follow-up in November 2017. After this initial referral, a full assessment was completed which revealed the following:

The extramarital affair he has been ruminating on occurred in 1996. It was between his wife and his cousin, and lasted 'a few months'. His cousin was murdered 2 years after the affair and the patient described celebrating with champagne on hearing the news.

Past Psychiatric History

Not known to mental health services.

Social History

Has been with his wife since the age of 12 and they married 18 years ago. They have 5 children, 3 of which live at home and they are aged between 11-28. No issues with accommodation and receiving benefits. The patient previously worked in a factory aged 16, and then small jobs such as chrome plating since then. He stopped working approximately 10 years ago when he was sacked due to his attitude.

Case report continued..

Personal History

The patient described a difficult upbringing in which he received physical and emotional abuse from his parents. His father left when he was 7. His siblings include a younger sister and an older brother. As his mother could not cope with his behaviour, the patient went into care at the age of 11, however neither of his siblings did. The patient believes one reason for this was he looked very much like his father and this led to his mother not being able to cope, often saying to him 'you are an evil little boy, you are just like your father'. Whilst in care he was sexually abused and also physically abused by staff. At the age of 14 his partner (his current wife) became pregnant he and left school at the age of 16.

Drug History

Nil. No allergies.

Family History

Both father and nephew had 'psychotic illnesses'.

First psychology review revealed the ruminating thoughts centred around the patient being unable to accept the affair was with his cousin, he still remained concerned if she loved him. Also of note was his extensive forensic history, in the past he was performing organised robberies in order to fund his drug habit. He reflected on his need to feel in control, and his destructive behaviours. In the past, he had gone to football matches with the intention of starting fights. As such, could the patient be presenting with an undiagnosed personality disorder? Subsequent psychology reviews unearthed an underlying anger which became more prominent when the patient felt let down. He had also had multiple affairs with women for the purpose of seeking reassurance and praise. In addition to this, there was a growing baseline of anxiety which had resulted in a number of panic attacks in public situations, with his wife having to take him home immediately. Although the suicidal thoughts remained, there was no active intent and the patient remained stable on Fluoxetine 60 mg O.D.

Initial impression (August 2013)

Depression secondary to social circumstances.

An urgent referral to the Home Treatment Team and medications prescribed were Fluoxetine 20mg O.D, Lorazepam 1mg PRN use and Zopiclone 7.5mg O.D.

Update (September 2013)

Telephone call from wife reveals patient has been abusing steroids for the last 2 years. He reveals he has been taking Oxybol 50mg, Enanthal 250mg and Testobolin 250 mg. However, he states he has been off steroids now for 8 weeks. When he stopped his mood and libido dropped, he became irritable, had fearful dreams and his testicles shrunk.

Could this be the triggering factor for the patient's deterioration in mental state?

Anabolic steroid use on mental health

It seems the abuse and following withdrawal of the steroids was the triggering factor for the patient's presentation. This could have been secondary to an underlying personality disorder, suggested by the patient's long history of aggressive, impulsive and antisocial actions on a background of major childhood trauma. Supporting evidence for this assumption is as follows:

- 'Major mood disturbances associated with anabolic-androgenic steroids may represent an important public health problem for athletes using steroids and sometimes for the victims of their irritability and aggression'. [1]
- 'Anabolic-androgenic steroids also show mood destabilising effects, with long-term use inducing depression and short-term hypomania; withdrawal/discontinuation may be accompanied by depression'. [2]

References

1. Pope HG, Katz DL. Psychiatric and Medical Effects of Anabolic-Androgenic Steroid Use. A Controlled Study of 160 Athletes. Arch Gen Psychiatry. 1994;51(5):375–382.

2. Piacentino, Daria et al. "Anabolic-Androgenic Steroid Use and Psychopathology in Athletes. A Systematic Review." Current Neuropharmacology 13.1 (2015): 101–121. PMC. Web. 7 Nov. 2017.

Current General Adult Psychiatry Peer Group Committee

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Mind the GAP Vol 7 Issue 1

Events and Conferences

RCPSYCH EVENTS

West Midlands Division Spring Academic Meeting **May 2018**
General Adult Psychiatry Faculty Annual Conference **Oct 2018**

WEST MIDLANDS DIVISION

Research Presentation Prize
Entrants must submit an abstract of 300 words to ***westmidlands@rcpsych.ac.uk*** by 31st March 2018

Mental Health Law update

19th January 2018

With Paul Barber mental health solicitor and Rob Brown, AMPH

£30 for trainees

Contact
gapeergroup@gmail.com

MCQ Answers

Tics associated with Pregabalin article
Page 3

Question 1 — (e)
Question 2 — (c)

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