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Experience of Managing COVID-19 in an Inpatient Psychiatric Setting

Dr B Harman-Jones (Psychiatry Trainee) & Dr M Aamer Sarfraz, (Consultant Psychiatrist & DME)

Abstract

The COVID-19 pandemic has presented unique challenges to psychiatric inpatient services. The Medical Education Department at Kent and Medway NHS and Social Care Partnership Trust developed specific guidance for clinicians working in this setting during the pandemic. These were distributed and presented locally, and helped to guide development of policy. In this article we present the major recommendations contained in this guidance.

Introduction

The COVID-19 pandemic has forced us to adapt to a previously unrecognisable way of life. Patients and staff have also been affected and united by this extraordinary narrative affecting every aspect of our lives. COVID-19 is the syndrome caused by human infection with SARS-CoV-2, a novel coronavirus believed to have originated in a “wet market” in Wuhan City, China, but this is as yet unconfirmed.1,2 It is likely that person-to-person transmission of the virus was occurring in December 2019, and probably earlier.3 Coronaviruses are enveloped, single-stranded RNA viruses held in a natural reservoir in bats. Some cause disease in humans such as the common cold, SARS, and MERS, and are known to acquire the ability to infect human hosts by acquiring mutations through intermediate species.1,2

The incubation period of SARS-CoV-2 infection is between 1 and 14 days, with a median of 5-7 days.3 Transmission during the incubation period is possible, and was reported in 12.6% of cases in China.3 Transmission occurs via two major routes: mucosal contact with respiratory droplets, and contact with contaminated surfaces.4 Respiratory droplets are particles >5µm in diameter produced by coughing or sneezing, and can move over short distances.4 After a surface is contaminated, viability of the virus varies depending on surface type, with one study showing this is up to 72 hours on plastic, up to 48 hours on stainless steel and up to 8 hours on copper.4 Airborne transmission has not been reported, however this may be possible via aerosol-generating procedures.3 SARS-CoV-2 has also been detected in blood, cerebrospinal fluid, urine, saliva, tears, conjunctival secretions, and faeces, but it is unclear if contact with these constitutes viable routes of infection.3

The mechanism of infection by SARS-CoV-2 is via binding to human ACE-2 receptors via the “spike” receptor, which is structurally different to the spike protein found in SARS-CoV (the virus causing SARS) and may confer greater higher binding affinity.3 High ACE-2 expression is found in the lungs, heart, oesophagus, kidneys, bladder, and ileum, which may confer higher susceptibility of these organs to the disease.3 SARS-CoV-2 may also downregulate ACE-2 which may lead to a toxic accumulation of vasoconstricting angiotensin-II, which may contribute towards the development of ARDS and myocarditis.3

Due to the complexity of the situation, it was quickly recognised by the Medical Education Department at Kent and Medway NHS and Social Care Partnership Trust that specific guidance was required to enable clinicians to work confidently, effectively and safely during the pandemic. National-level guidance was quickly devised, but was inevitably generic, and could not provide the level of detail necessary to cover the nuances and unique operational challenges presented by psychiatric inpatient work. Psychiatrists required bespoke guidance, which we set out to develop. In this article we present the major aspects of this guidance.

Method

National-level guidance for managing COVID-19 was reviewed by clinicians with knowledge of inpatient psychiatry and formulated into themes which would form the basis for our guidance. Relevant details were verified and re-presented in a slideshow format, with additional detail relevant to inpatient psychiatry researched and incorporated appropriately. After review, this document was then distributed electronically via email as a PDF file. Additionally, the Medical Education Department organised and led video conferences for consultants and junior doctors, explaining and detailing the guidance, and answering any questions. Specialist support for these videoconferences was provided by the involvement of a respiratory physician. These conferences were well-attended, well-received, have facilitated helpful information sharing between clinicians, and guided the development of formal policy by the Trust.

Results

Due to the specific implications of unmitigated spread of COVID-19 on a psychiatric ward, it is important to take precautions when assessing possible cases in this setting. These include:

- Assessing patients in a single occupancy room only. Patients should wear a fluid-resistant surgical mask while moving to the single room 5 and maintain a distance of two metres from others while doing so.
- Use of appropriate personal protective equipment must be used as if the patient has COVID-19.
- Avoiding contact with the individual as much as possible – and avoiding using a stethoscope if possible due to risk of viral contamination. Added respiratory sounds are rarely found in COVID-19 and so chest auscultation is not likely to add important diagnostic information.3

Priorities of assessment in the psychiatric setting are to determine if COVID-19 is suspected, and if the patient is acutely unwell and requires transfer to acute hospital. Additionally medical staff must review for possible red flags indicating other pathology, and consider differentials as appropriate.

Diagnostic features are described in Table 1. Key features include fever, cough, dyspnoea, and altered sense of smell or taste. However, the presentation can be variable and special care must be taken to spot a potentially atypical presentation in some groups, particularly the immunosuppressed.

If COVID-19 is suspected, then the patient must be immediately placed into respiratory isolation, which in a psychiatric inpatient setting will most commonly be in their bedroom. However, if on assessment the patient appears acutely unwell, then staff must consider if it is more appropriate for the patient to be transferred to an acute general hospital. In such an instance, immediate stabilising interventions such as high-flow oxygen, airway adjuncts, and nebulised bronchodilators are possible, but the use of any of these should always be in the context of escalation of care. A protocol for the process of transfer to the local acute general hospitals was developed, and is shown in Figure 1.

Key
Fever
Cough (usually dry)
Dyspnoea
Altered sense of smell/taste

Other common features
Fatigue
Myalgia
Anorexia
Sputum production
Sore throat

Uncommon features
Conjunctivitis
GI symptoms
Confusion
Dizziness
Headache
Haemoptysis
Rhinorrhoea/nasal congestion
Chest pain
Cutaneous manifestations

Bronchial breath sounds
Tachypnoea
Tachycardia
Cyanosis
Crackles/rales on auscultation

Table 1 – Diagnostic features of Covid-19.

Taken from BMJ Best Practice. Coronavirus disease 2019 (COVID-19). 2020. Available at: https://bestpractice.bmj.com/topics/en-gb/3000168#important-updat [3]

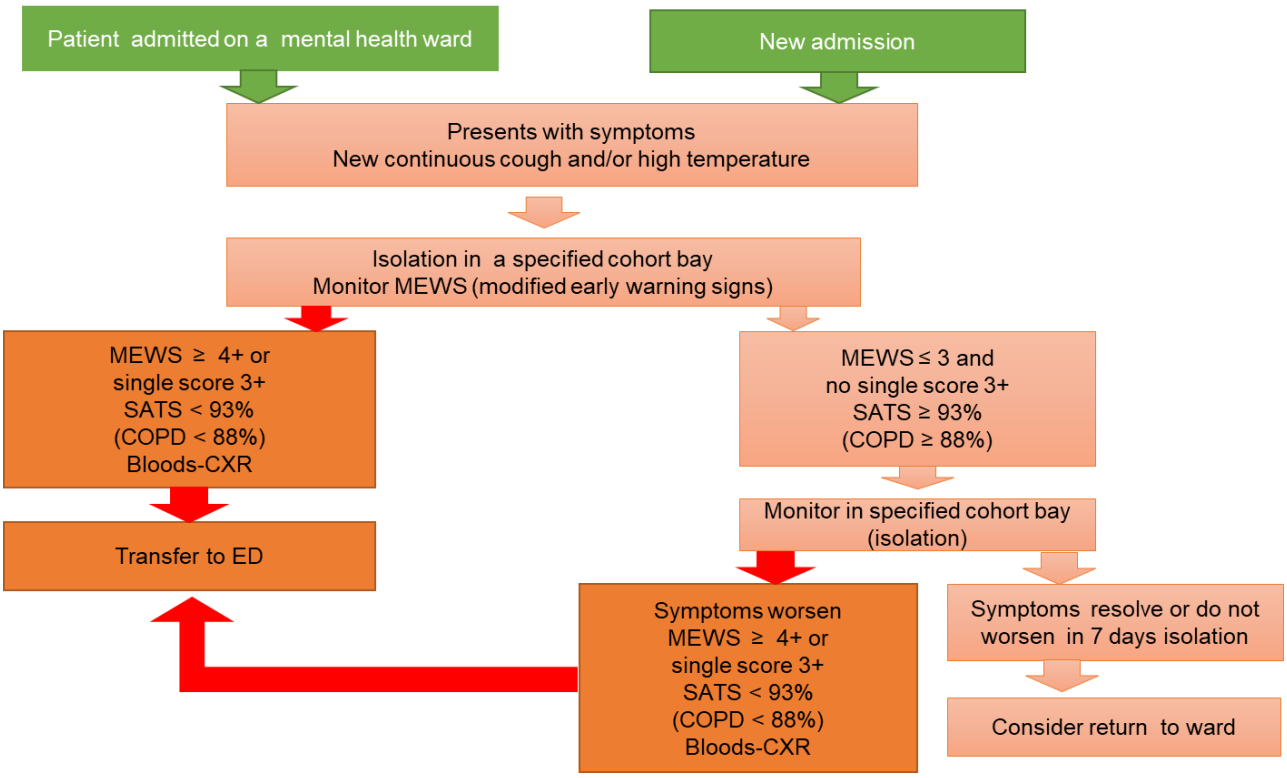

Figure 1 – Protocol for transfer to acute hospital

Infection control

Precautions against the transmission of COVID-19 work by disrupting the two major routes of transmission: respiratory droplets and contact with contaminated surfaces. Measures include respiratory isolation of cases, alterations to contact between all people (social distancing), hand hygiene at key points, and use of personal protective equipment (PPE) at key points. Guidance on the use of PPE is setting-specific and changes frequently; therefore readers are directed towards government sources for the latest guidance. Additionally the correct technique for PPE use is important, and instructional guides are available from these sources.

While it does not appear that airborne virus constitutes a viable route of transmission,3 the risk is higher when using certain "aerosol generating" procedures that are common in healthcare settings.4 These include cardiopulmonary resuscitation, and the use of continuous positive airway pressure machines. Therefore, there are additional infection control precautions that must be followed by staff when these procedures are conducted.

Certain groups in the population are being advised to "shield" from COVID-19, because they would be at increased risk compared to the general population if they were to contract the illness. In practice, this means staying at home and not leaving for any reason.6 It is important to recognise that these

individuals suffer from a wide variety of medical conditions, which could also affect inpatients admitted to psychiatric units. Therefore it would be important to explore the past medical history of all new and existing inpatients and consider what extra precautions would need to be put in place if shielding is required. The Infection Control Department should be consulted in such an instance but these measures may include provision of PPE for the patient rather than staff, and respiratory isolation even in the absence of any symptoms.

Management of COVID-19 itself

Generally speaking, COVID-19 is manageable in a home setting if there are no severe features and there are no risk factors. If severe, hospital admission is recommended as the use of high-flow nasal oxygen, non-invasive ventilation, mechanical ventilation, or extracorporeal membrane oxygenation would likely be required.

While technically constituting a "healthcare setting", inpatient psychiatric units do not have the same capacity to manage physical health problems as acute general hospitals. There is no capacity to administer oxygen on a less than emergency basis, no capacity to administer intravenous medication, it is difficult to take regular physical observations from patients and maintain continuous observation, and mental health nurses are not specifically trained in managing physical health problems. Therefore, COVID-19 patients being cared for in these settings should be considered as if they were at home, and a low threshold maintained for transfer to acute general hospital.

The management of the vast majority of cases, and certainly those appropriately cared for in a psychiatric setting, centres around alleviating symptoms of the illness, and maintaining infection control. It is sensible to encourage good hydration but it should be noted that too much fluid can worsen oxygenation.3 Patients in respiratory isolation are likely to be less mobile than usual, and the illness may specifically make patients bedbound and dehydrated due to fever. Special attention should therefore be paid to the risk of venous thromboembolism and prescription of prophylactic low molecular weight heparin if appropriate. This is something for which medical staff have a unique responsibility in a psychiatric setting, in contrast to other healthcare environments where nurses tend to be more involved in these risk assessments.

Antipyretics are recommended for reduction of fever.3 Paracetamol and NSAIDs should not be routinely prescribed to all new inpatients in the absence of the disease, because this may mask COVID-19 symptoms and lead to late identification of cases. If cough is distressing, advise patients to avoid lying on their back as this makes coughing ineffective.3 Simple measures such as a teaspoon of honey can be effective.3 Some sources recommend oral opioids to suppress cough,3 but we would suggest this be undertaken with caution in a psychiatric setting.

Breathlessness can be addressed by keeping the room cool, and by encouraging relaxation, for example using breathing techniques, and changing body positions. Psychiatric nurses are uniquely placed to use their skills here and this should be encouraged where possible and safe. Inhaled bronchodilators could be considered if there is wheeze. It would seem prudent to use inhalers in the first instance and then move to nebulised medication if necessary, because of greater availability and the closer contact required to provide nebulised therapy.

There is evidence that vitamin D supplementation is protective against respiratory tract infection.7 This may be particularly important in a psychiatric setting, as people with psychosis, for example, are known be particularly vulnerable to vitamin D deficiency. Adults are already advised to take vitamin D 10 micrograms/day from October to March, but during the pandemic adults are being advised to continue this through the spring and summer if they have limited contact with sunlight.8 It would therefore be sensible to prescribe this for all inpatients if not contraindicated. Additionally, a vitamin D level on admission bloods is valuable as if found to be insufficient or deficient, the patient would require more vitamin D than provided by this supplementation alone.

One problem that is likely to disproportionately affect medical staff dealing with COVID-19 in a psychiatric inpatient setting is patients refusing to comply with respiratory isolation. The Mental Health Act does not allow restrictive practices to be applied because of a physical health issue. Chapter 26 of the Mental Health Act Code of Practice 2015,9 which governs the use of restrictive interventions under the

Mental Health Act, should be followed wherever possible. Only where there is what is termed a "cogent reason" for departure from the Code should this be undertaken.10 It is necessary to seek specialist advice on what would constitute a cogent reason, and in our Trust a specific Ethical Advisory Committee has been devised to consider such proposals.

Implications for psychiatric treatments

Beyond the management of the disease itself, the implications of COVID-19 on the provision of psychiatric treatments are wide-reaching. The capacity for monitoring of patients is likely to be greatly reduced during the pandemic. This makes routine physical health checks, for example for patients starting antipsychotic therapy, more logistically difficult than usual. Therefore, we would encourage all clinicians to carefully consider the risk:benefit ratio in embarking on new medications during the pandemic. Clearly, there will be situations where this is not avoidable and the benefits of new medications greatly outweigh the risks. However, if a medication is likely to provide only more modest benefits, the risks of not being able to carry out physical health monitoring as readily may tip the balance in favour of delaying commencement of medication at this time.

The pandemic makes the choice of medication even more important than usual. Many psychotropics, especially benzodiazepines, can cause respiratory depression, and should be used with caution in suspected or confirmed COVID-19.10 The use of medication for rapid tranquilisation is especially risky as patients are agitated and any existing respiratory difficulties are likely to be exacerbated. Additionally the use of restraint presents another respiratory risk factor. Short-acting medication is preferred to longer acting due to the risk of rapid physical deterioration when administered. Lorazepam would be the preferred benzodiazepine as it has a shorter half-life.10

Particular care should be taken with patients on clozapine. Community titrations will be unavoidably more risky during the pandemic, therefore, we would suggest a lower threshold for inpatient titrations than usual. Clozapine should be stopped if patients are experiencing severe respiratory symptoms due to COVID-19, with particular care when restarting the medication as re-titration may be required. Patients with respiratory symptoms may reduce their cigarette intake, which may increase the clozapine level. Therefore, smoking status should be closely monitored. Additionally, serious side-effects may be missed by mistaking them as effects of COVID-19. If patients are experiencing flu-like symptoms, neutropenia must be suspected, and if experiencing symptoms of myocarditis (e.g. chest pain, shortness of breath), this is also no less likely than usual and should be suspected.

Patients on long-acting injectable antipsychotics are also affected. Capacity for community administration may be reduced, and it may be helpful to consider increasing the interval between dosing where possible. Alternatively, clinicians could consider switching to an alternative medication which allows less frequent dosing, e.g. from risperidone LAI to paliperidone palmitate 1-monthly, or from paliperidone palmitate 1-monthly to paliperidone palmitate 3-monthly.

Lithium presents additional challenges. If patients are experiencing fever, dehydration may occur which may precipitate lithium toxicity. Therefore, monitoring for symptoms of lithium toxicity should be intensified where COVID-19 is suspected or confirmed, and plasma levels obtained urgently if suspected. If confirmed, the management of lithium toxicity in COVID-19 would be no different than at other times, although involvement of general medical colleagues would be prudent due to the increased complexity of the situation.

The emergency Coronavirus Bill makes provision for emergency amendments to the Mental Health Act, specifically: Mental Health Act assessments, extensions to periods of detention permitted under Sections 5, 135 and 136, SOAD requirements for giving medication without consent, and alterations to some forensic sections.11 However, at the time of writing, these amendments are not in force, and will only be enacted if the circumstances necessitate this.

Finally, not even the fundamentals of psychiatric practice are untouched by the pandemic. Prior to the current situation, most psychiatrists had never considered using remote consultations on a regular basis. There is a widely-held perception that this type of interaction is of lower quality than that allowed by seeing patients face-to-face, which is considered particularly important in psychiatry. However, now

"telepsychiatry" has become mainstream almost overnight, and many clinicians have been surprised at how well it can work, with even psychotherapy using this approach being well-received.12 The term refers specifically to the use of video conferencing to conduct consultations, but clinicians have also been using the telephone as it can be more accessible. For some adults with certain conditions such as PTSD or panic disorder, it may actually be preferable to face-to-face contact.12 Telepsychiatry has been officially supported as a validated and effective practice by the American Psychiatric Association, who have published the "Telepsychiatry toolkit", which although US-specific, contains many useful tips on using the approach in practice.12

Discussion

A particular focus for our guidance was on the interface between psychiatric inpatient units and local general medical hospitals, and the prompt recognition of the acutely unwell patient requiring transfer. The management of patients with COVID-19 not requiring transfer to such a setting was detailed, with guidance towards evidence-based practical measures that could be deployed considering the somewhat limited resources available. Particular guidance was necessary on the management of patients detained under the Mental Health Act and measures if these patients refused to comply with isolation measures. Finally, the implications of the pandemic on the management of psychiatric conditions and the use of psychotropic medications were discussed.

We believe our approach was innovative in a number of ways. Firstly, the Medical Education Department recognised early on in the pandemic that the application of national-level guidance was going to be problematic in a psychiatric inpatient setting. We took the initiative to commission the development of this guidance which was completed expeditiously and shared promptly with clinicians. Distribution was purely electronic in order to maximise reach and comply with social distancing requirements. Interactivity was introduced using the innovative method of video conferencing on a large scale, which also took a multiagency approach by the involvement of a respiratory physician. We also took feedback throughout the development process, releasing a number of updates to the guidance based both on clinician feedback and developments in research. Finally, because the pandemic has reduced the potential for clinicians to engage in continuing professional development activities, our approach sought to address this need by providing broad and balanced coverage on the relevant clinical, professional and academic aspects.

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Clozapine Neutropenia and the Coronavirus

Dr Chiara Buhagiar (Psychiatry Trainee) & Dr Rupa Ramesh (Consultant Psychiatrist)

Abstracts

COVID-19 is a new virus that affects the full blood count, generally causing a lymphopenia, while the white blood cell count and neutrophil count remain unchanged. Clozapine is a drug well known for causing neutropenia and low white cell counts but has no effect on lymphocytes. Not much is known about how COVID-19 and clozapine would interact. The following describes such a case, and one can see the effect on the patient's blood results as well as consider various other implications of this case.

Introduction

Neutropenia is a relatively common adverse side effect of clozapine treatment, affecting up to 2.7% of patients within the first 18 weeks of treatment.1 COVID-19 has been shown to cause lymphopenia.2 The white cell count can be either within normal range, slightly decreased in mild disease, or elevated in severe disease.3 Neutrophils are within normal range or elevated.4 The following case report describes a patient who, shortly after starting clozapine treatment, became both neutropenic and infected with COVID-19.

Methods

A 40-year-old gentleman was admitted to an acute inpatient ward after being arrested for criminal damage - arson to his own accommodation - due to a relapse and deterioration of his mental health. He had been well known to mental health services since 2001, initially due to cannabis induced psychosis, with established diagnoses of paranoid schizophrenia (diagnosed in 2013) and poly-substance misuse (diagnosed in 2012). He was aggressive, paranoid, and thought-disordered with persecutory delusional ideation. He also had a history of non-concordance with medication and multiple previous admissions, the last of which had been two months earlier. He had no known medical history, other than a having had a seizure in the past.

After 3 months on an acute inpatient unit he was discharged to a rehabilitation ward on olanzapine depot 300mg every 2 weeks and semi-sodium valproate 1000mg in the morning and 750mg at night. After a week on the rehab ward his mental health appeared to deteriorate once more, and he had a relapse where he was aggressive to staff. The rehabilitation ward was unable to support his behaviour. He was therefore transferred back to the acute ward.

Given the relapsing and remitting nature of his illness, and the fact that he had previously tried

aripiprazole, risperidone, paliperidone and olanzapine (which had seemed to be the most effective for him), it was felt that clozapine was a better option moving forward. The patient had, in the past, been reluctant to switch to clozapine. On this occasion, however, he agreed, in order to try to prevent further relapses with their attendant readmissions to hospital.

Prior to clozapine initiation, his baseline bloods showed a total white blood cell (WBC) count of 7.9 x109/L, with a neutrophil count of 4.3 x109/L and lymphocytes of 2.6 x109/L (see Table 1, along with the reference ranges).

	11/11/2019	**01/04/2020 (pre-Clozapine)**	**08/04/2020 Clozapine Day 4**	**12/04/2020**	**13/04/2020 Clozapine stopped**	**14/04/2020**	**15/04/2020**	**21/04/2020**	**29/04/2020**	**Units**	**Normal Range**
WBC	7.3	7.9	4.9	2.7	2.9	3	3	6.6	6.5	10^9/L	4.0 - 11.0
Automated Neutrophil Count	5.1	4.3	2.1	1.2	1.6	1.4	1.5	4.1	3.4	10^9/L	2.0 - 7.0
Automated Lymphocyte Count	1.6	2.6	1.7	1	0.9	1.1	1.2	1.6	2.3	10^9/L	1.0 - 4.0

Table 1: *Table showing the patient's blood results for white blood cells (WBC), neutrophils and lymphocytes*

On day 4 after starting clozapine, his bloods were taken and showed that his WBC had dropped to 4.9 x109/L, neutrophils to 1.6 x109/L and lymphocytes to 1.7 x109/L. Although there was a clear drop in his white cell and neutrophil counts, it was still considered safe to continue with clozapine treatment (CPMS) (see Table 2).

Date Blood Taken	WBC (x 10^9/L)	NC (x 10^9/L)	PLTS (x 10^9/L)	EOS (x 10^9/L)	MXD (x 10^9/L)	Total Daily Dose (mg)	Name of Laboratory	Blood Alert
10/12/2018	8.50	4.80	212	0.10	0		CPMS Fax	Green
01/04/2020	7.90	4.30	187	0.20	0		CPMS Fax	Green
08/04/2020	4.90	2.10	149	0.10			Darent Valley Hospital DA2 8DA	Green
13/04/2020	2.90	1.60	134	0.00			Darent Valley Hospital DA2 8DA	Red
14/04/2020	3.00	1.40	146	0.00			Darent Valley Hospital DA2 8DA	Red
15/04/2020	3.00	1.50	152	0.00			Darent Valley Hospital DA2 8DA	Amber
21/04/2020	6.60	4.10	347				Darent Valley Hospital DA2 8DA	Green
16/05/2020	7.80	3.70	200	0.60			Darent Valley Hospital DA2 8DA	Green

Table 2: *Table from the Clozapine Monitoring Service (CPMS) showing the safe green results and red alerts*

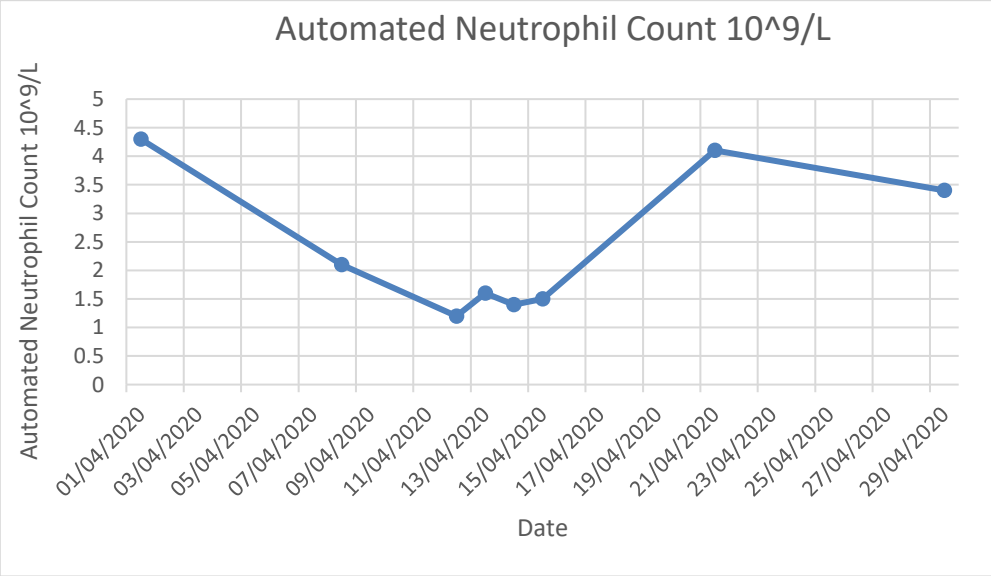
On day 8 of treatment, the patient developed a fever (38.1°C). At the time, the differential diagnosis was neutropenic sepsis or COVID-19, so bloods and a COVID-19 swab were done to investigate further. His bloods showed a CRP of 7mg/L (Ref. range <10), WBC 2.7 x109/L, neutrophils 1.2 x109/L and lymphocytes 1.0 x109/L. His COVID-19 swab came back positive and he was therefore diagnosed with coronavirus. Neutropenic sepsis was ruled out due to his low CRP and the clinical presentation (he presented only with a fever and no other signs of sepsis). Due to the neutropenia (neutrophils <1.5) his clozapine was withheld and his blood counts were monitored daily (see Table 1). The following day (13/4/20) repeat tests showed total WBC 2.9 x109/L, neutrophils 1.6 x109/L and lymphocytes 0.9 x109/L and he had a red alert from CPMS (Table 2).

The patient was restarted on olanzapine. He remained in isolation, taking regular paracetamol to control his fever, and was transferred to the COVID-19 ward. His bloods began to normalise, as seen in the tables, and, 3 to 8 days after cessation of clozapine, they had returned to his admission levels. His only symptom from the virus was a fever. 15 days after the start of his isolation period, he was transferred back to his acute ward, being symptom-free and testing negative on a repeat swab.

Case Discussion

Neutropenia is an uncommon (between 0.1% and < 1%) side effect of olanzapine.5 The risk of agranulocytosis is significantly lower with olanzapine than with clozapine. The exact mechanisms by which olanzapine causes neutropenia are not well established but are thought to be similar to those of clozapine.5 In this case the patient had been on olanzapine for over ten years and during that time there had been no documentation or evidence of neutropenia. Also, neutropenia did not persist once the patient was restarted on olanzapine; in fact, his blood results resolved to pre-clozapine levels.

The patient had also been on semi-sodium valproate since 2018, and previously between 2014-2016. It had been stopped in the first instance as it was felt that he did not need to be on both valproate and olanzapine as his mental state had been stable. Throughout the time that he was taking valproate, there were no haematological changes noted on his blood tests. The main haematological side effect that valproate is known to cause is thrombocytopenia. This occurs in 5 to 18% of patients on valproate, with females and the elderly being at increased risk.6 Leucopenia, and by extension neutropenia, is also a rare side effect of sodium valproate;7 however his blood levels were well within range throughout. It should be noted, however, that concurrent use of valproate increases the risk of, and has been associated with, clozapine induced neutropenia.8

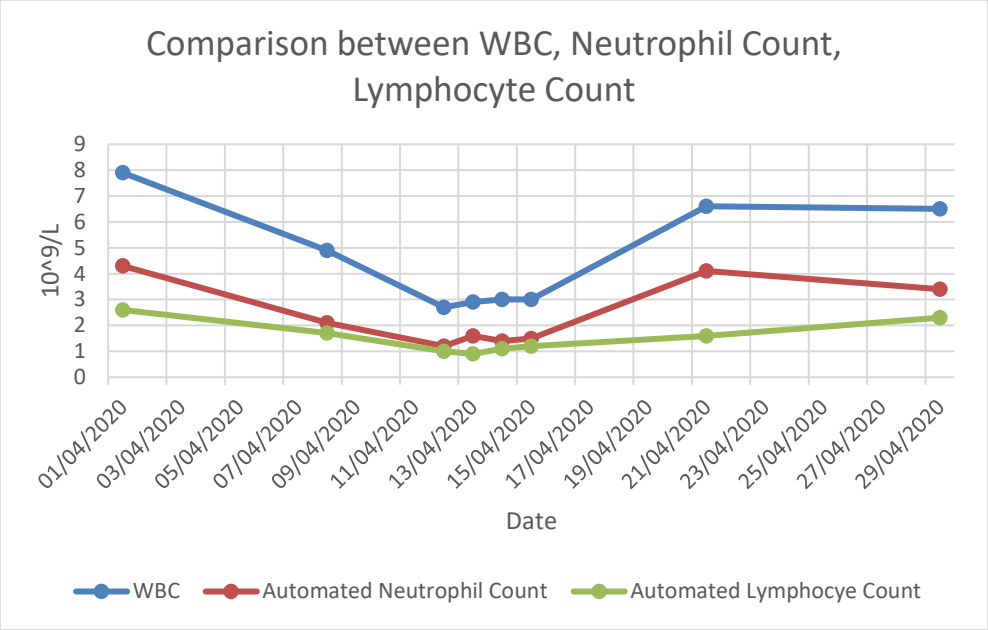


Graph 1: *Graph depicting the neutrophil count*

Clozapine carries a significantly increased risk of neutropenia compared to olanzapine, affecting close to 3% of patients.1 Although still unclear, a number of mechanisms for this effect have been postulated, including direct bone marrow suppression, toxicity by the drug itself or its metabolites, or by causing immune-mediated destruction of the granulocyte line.1 Risk factors include having a lower baseline white cell count, being Afro-Caribbean, and being younger in age. This patient did not have any of the risk factors; however, he did become neutropenic within the first 18 weeks of treatment, which is the most common time to get this side effect.1

A policy has been released to show that patients on clozapine who develop a low WBC count in the context of COVID-19 infection can generally continue their treatment with the drug, as the low count is due to the virus causing a decrease in the lymphocytes while neutrophils generally remain within range.7 This case, however, described a neutropenia which is out of keeping with the blood picture of COVID-19 and is more consistent with the usual adverse reaction of agranulocytosis that clozapine is known to cause. 9

It is important to note that this patient's lymphocytes were also on a downward trend; however, they were only below normal range (1.0-4.0 x109/L) on one occasion (0.9 x109/L). Lymphopenia has been reported in most studies of COVID-19, in up to 85% of patients.10 It is likely that this downward trajectory of the lymphocyte count is a result of the viral infection as clozapine is not known to affect lymphocyte count.11



Graph 2: *Graph depicting the comparison between WBC, neutrophil count and lymphocyte count*

In this case it was highly important to rule out neutropenic sepsis as up to 60% of patients with severe drug induced neutropenia can develop septicaemia.12 His bloods were monitored daily as close monitoring of blood counts has been found to reduce the incidence of fatal neutropenia to 0.03% during clozapine treatment.12 Any neutropenic patient who presents with signs and symptoms of septicaemia or who is at high risk of infection should be treated aggressively and broad-spectrum antibiotics should be initiated empirically.13 This patient presented with a fever only and was not septic. Although the patient did have a high fever and a positive COVID-19 swab, he did not have a severe illness. The degree of lymphopenia, which has been linked to disease severity in COVID-19, was only mild and his CRP was normal.

Another independent marker of severity, morbidity and mortality found in association with the coronavirus is the neutrophil-to-lymphocyte ratio (NLR).14 An increased NLR holds a worse prognosis for the positive COVID-19 patient and, even given what we have seen with our patient, it would be important to keep this in mind in the future with patients whose medication, such as clozapine, may be affecting their blood levels.15

The authors of this case report acknowledge that a false positive swab test for COVID-19 cannot be ruled out and, in the future, when accurate antibody testing is more widely available, this can be looked into.

This case also reveals the potential to detect neutropenia at an earlier stage than is routinely practised. This patient went from a situation of 2 acceptable (green) results from CPMS to an established state of neutropenia (red result). This happened in the middle of the COVID-19 epidemic and, fortunately, his immuno-compromised state did not translate into any opportunistic overwhelming infection. We propose that had greater attention been paid to the initial drop in the neutrophil count, then an earlier follow-up FBC could have been performed, allowing for earlier cessation of the

clozapine therapy. This may require the introduction of a delta-neutrophil count by CPMS, a simple estimation akin to the standard practice of the estimation of delta-cardiac troponin in the detection of acute coronary syndrome.16

With the benefit of hindsight, the drop of the neutrophil count to 37% of its former value within days of starting clozapine is a significant result that should have alerted closer monitoring.

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Remote Working: The Experiences of Two Trainee Psychiatrists

Dr. B Harman-Jones, (Psychiatry Trainee) & Dr. C Harman-Jones (Psychiatry Trainee)

Introduction

Shortly after the World Health Organisation declared COVID-19 a pandemic, the UK Government published a list of individuals whom they considered to be extremely vulnerable to complications of the disease.1 For these individuals, who suffer from a wide range of pre-existing risk factors, stringent measures to protect against infection were advised, including remaining at home and limiting contact with others to an absolute minimum.
This advice had implications for a large and extremely heterogeneous group of people, ranging from very young children to the elderly, and affected a large number of working-age individuals. Many were able to make adjustments to their working arrangements very easily – e.g. those in office-based jobs already undertaking some home working prior to the pandemic. However, the situation for many others, including doctors, was more complex.

Medicine is one of the few professions that has, until now, remained largely untouched by the possibilities that improved connectivity provides in working effectively from home. This is in contrast to other economic sectors where home working for at least part of the week has largely become the norm, especially in the private sector where long commutes into central urban areas, especially London, are commonplace. Medicine has traditionally been considered a "hands-on" profession only, with a firm emphasis on bedside manner and the therapeutic benefits of close proximity between doctor and patient. However, COVID-19 has made this impossible in many cases due to social distancing requirements, and for those shielding the only possibility to continue clinical work has been through remote working.

Clearly, there are some areas of medicine where remote working is simply not possible, for example for those performing surgical procedures. Some areas, however, may be uniquely well-suited, with psychiatry being close to, if not top of the list. With a well-established doctrine of examination of the mental state based on the expression of thought through speech, with only a few modifications it is entirely possible for psychiatrists to conduct a very high quality consultation remotely. Additionally, the utilisation of information technology in psychiatry is high in comparison to other areas of medicine, with widespread use of portable laptop computers and electronic patient record systems.

In this article, we examine the experience of two trainee psychiatrists (one in an inpatient post, the other in a community post) working entirely remotely during the pandemic due to shielding advice. We explore how adjustments were made to their working patterns, the results of these interventions, and the potential future implications of this experience on psychiatric practice, and on medical practice as a whole.

Inpatient Trainee Experience

Working arrangements

The inpatient trainee was to continue to attend daily ward meetings and ward rounds over videoconference, to scribe notes based on the discussion, and to follow up on any jobs identified as part of the ward round. They were also responsible for completing any tasks delegated from medical staff physically present on the ward, for example the completion of reports, and communication with other healthcare agencies involved in care of patients on the ward.

Effects on patient care

In the early stages of remote working, it was noted that it was important for the trainee to introduce themselves formally with any new patient due to the unfamiliarity of having a doctor present via videoconference. Once this had been done, all patients were comfortable to continue the meeting with the trainee present virtually. A benefit of the trainee's attendance at these meetings being virtual was that the number of staff who could be physically present while social distancing rules were in place was effectively increased, possibly improving the patient experience. For particularly aggressive patients, this also allowed the presence of an extra staff member who could assist in the eventuality of physical aggression, which likely contributed to staff safety while social distancing was in place.

As our Trust has not yet moved to electronic prescribing, it was not possible for the inpatient trainee to prescribe for inpatients remotely. These responsibilities were accordingly taken up by more senior members of the ward medical team, who would usually delegate this to the junior doctor. For prescriptions for psychiatric medications, this was not an issue, as were prescriptions for straightforward physical health complaints such as paracetamol for headache. Where a more significant physical health concern was identified, involvement of the on-call SHO for the site was required, because a physical examination was likely to be required in order to prescribe appropriately or advise on management. This measure did not present any major issues to the running of the hospital.

Effects on training experience

As attendance at ward rounds and follow-up on relevant tasks forms the majority of work for any trainee psychiatrist working on an inpatient ward, the training experience was relatively preserved. In the vast majority of cases, tasks identified as part of the ward round were possible remotely, as in large part these involve completion of forms and liaison over the telephone with other medical teams and specialities. The trainee maintained regular contact with the ward's nursing and medical teams both over the telephone and using e-mail which was adequate to facilitate most tasks requiring action on the ward. It was also straightforward for the trainee to discuss directly with patients by staff bringing them to the ward's telephone.

Contingency measures for regular face-to-face supervision were put in place, using telephone calls or videoconferences. These measures were adequate to provide the same level of support to the trainee as face-to-face meetings, with no periods where the trainee felt unsupported in relation to clinical decision-making. Teaching sessions were accessed via videoconference, which allowed the trainee to maintain learning requirements in line with their colleagues.

How the trainee found the experience

Subjectively, the inpatient trainee found joining ward meetings and ward rounds over videoconference to be a positive experience. High quality audiovisual equipment on the ward facilitated ease of notetaking and observation of body language important for the mental state

examination. All members of the team were visible and audible, making it easy to participate fully in the meetings as if physically present. Patients and staff alike were found to be accepting of the modifications to the trainee's working situation, and there were no major interface issues noted in this regard.

Working remotely was of course more isolating than being physically present in work, and it was more difficult for the trainee to feel actively involved in the running of day-to-day proceedings than if they had been physically present. However, this feeling was addressed appropriately in supervision through discussion, and was not excessive when compared to the psychological impact of shielding generally.

Community Trainee Experience

Working arrangements

The outpatient trainee was to continue to conduct their daily clinic remotely, in line with the rest of the community team who had also switched to remote consultation during the pandemic. Other duties would continue to include liaison with other teams and agencies involved in the care of patients as required based on individual patient requirements.

Effects on patient care

Telephone consultations formed the mainstay of remote consultations. The trainee felt that the quality of consultation over the telephone was not significantly impaired compared to face-to-face communication, particularly because those patients in the community are more likely to be stable and less agitated than in an inpatient setting, where patient visibility would be more important. It was felt by the trainee that it was perfectly possible to conduct even an initial psychiatric assessment over the telephone and formulate an appropriate management plan safely. Provision of patient telephone numbers required no extra work as these were available as standard in electronic patient records. Patients were contacted at the time of appointment booking to obtain consent for a telephone call, and no patients raised any concerns or issues with having a consultation over the telephone.

While telephone consultations seemed fit for purpose, the trainee felt that if videoconferencing were promoted more widely this would have slightly improved the quality and scope of consultation possible. There were significant barriers to achieving this. Early in the pandemic, the Trust had advised that video calls to patients were only acceptable if conducted using a particular proprietary software solution, requiring inputting a meeting code and password. This extra step presented a significant logistical barrier to engagement with this solution, and indeed, several patients declined to use this service when offered, opting for a telephone consultation instead. We discuss what alternatives may improve access below.

Effects on training experience

The trainee felt fully able to conduct quality assessments and reviews of patients over the telephone, and gain appropriate experience of managing community patients as if attending in person. There was no perceived negative impact on the quality of training opportunity provided.

Prescribing was not an issue, as this is routinely done via the GP in a community setting. An electronic signature was set up for requests for changes to medication, and these were sent electronically to GP practices to be enacted. More detailed communication with patients and GPs is also routinely conducted using postal letters, and as postal services continued to run at near-normal capacity during the pandemic, this method of communication was not disrupted.

How the trainee found the experience

Experience with supervision was equivalent to that of the inpatient trainee, with similar contingency measures employed to good effect, with the trainee feeling supported at all times in terms of clinical decision-making.

Similarly to the inpatient trainee, there was an inevitable impact on the trainee's sense of inclusion in the team when compared to being physically present. Again, this was appropriately addressed through supervision and was not out of keeping with the psychological impact of shielding in general.

Remote working in this setting did, however, present an interface issue with other teams which was not observed in the inpatient setting. In a community setting, the trainee often acts independently during assessments and if, for instance, a need for crisis intervention is identified, it is their responsibility to arrange this. Some teams require face-to-face patient contact to be made before referral can happen, which was obviously not possible, and introduced an extra layer of complexity into the process. However, this was easily overcome by the increased role which the community team took on during the pandemic, with extended opening hours and an enhanced remit to take on crisis intervention work which would usually not form part of their role.

Discussion

Many clinicians have been surprised at how well remote consultations can work, with even the use of this approach for psychotherapy being well-received.2 While it is a valuable technique, there are several procedural barriers to its implementation, most importantly gaining consent and ensuring patients are comfortable with its use, as the Royal College of Psychiatrists identifies.3 Despite this, for some adults with certain conditions such as PTSD or panic disorder, it may actually be preferable to face-to-face contact.2 Telepsychiatry, referring to the use of video in consultations, has been wholeheartedly supported as a validated and effective practice by the American Psychiatric Association.2 The UK's Royal College of Psychiatrists has taken a more reserved approach, suggesting it is used only as an adjunct to face-to-face consultation, but do acknowledge the necessity to explore any options to continue patient care during the unprecedented situation.3

From this experience, both trainees felt the experience of working remotely in their roles to be overwhelmingly positive. Existing workflows were relatively preserved, with any disruption to service delivery from the patient's perspective being consistent with that seen in other areas during the pandemic. Patients were accepting of the alterations to consultations, with no objections to contact via telephone in the community setting, or via videoconference in the inpatient. The quality of patient care and training experience was relatively unaffected once appropriate contingency measures were in place.

In the community setting, wider use of videoconferencing may have improved consultation quality, but this was hindered by procedural barriers. Despite the NHS advising it was appropriate to use existing and widely available videoconferencing technologies including WhatsApp and Facetime,4 the Trust issued guidance that it was only acceptable to use the proprietary solution in which it had invested, which is less accessible to patients at home as it requires inputting a specific URL and password. As noted above, this was less attractive to some patients than a telephone call, and did in our opinion result in a lost opportunity to engage these patients using telepsychiatry. We feel that if more accessible technologies were permitted for use, the quality of remote consultations could be increased.

The only marked negative aspect of working remotely for both trainees was a feeling of isolation from the work environment and the psychological wellbeing associated with seeing colleagues and patients in person. However, adequate contingency plans were made for holding regular supervision meetings remotely, which were sufficient to support the psychological wellbeing of the trainees. Overall, both trainees felt that the benefits of maintenance of their sense of professional identity facilitated by continuing to work through the pandemic greatly outweighed any such negative effects.

Conclusion

We already know that theoretically psychiatry is uniquely suited towards remote working, but this experience provides new evidence to support this novel method of working in psychiatry. Remote engagement in clinical work was relatively seamless and allowed both clinicians to continue their roles within their existing teams with relative ease. There are of course tasks which are not possible remotely, but these are few in number, and in this example alternative arrangements were made relatively easily and with little disruption to existing services.

We would therefore suggest that remote working is an entirely appropriate alternative to face-to-face working where it is required. Telepsychiatry via videoconferencing is the ideal, and because most people now own a smartphone, there are numerous existing services which put this capability in the hands of almost every patient. We would encourage widespread adoption and support of use of such services as the COVID-19 pandemic continues.

Additionally, this model of working has several potential implications for future psychiatric practice. Accessibility to more specialist psychiatric services could be increased, as reaching patients who cannot travel to specialist centres is now possible. This may be particularly relevant for child and adolescent services where geographical restrictions have been historically very significant in limitations in service provision. However, the implications also extend to other areas, for example those working in neurodevelopmental conditions, genetic syndromes with psychiatric features, and treatment-refractory mental disorders.

There is also a great history of attracting doctors internationally to experience how healthcare, particularly psychiatry, is delivered in the UK. The use of remote working technologies could open up these opportunities to trainees from all over the world who are not able to travel, and also to allow UK doctors to access learning opportunities internationally. The opportunities for international medical congress are also self-evident, and the traditional model of thousands of delegates travelling at great expense to meet in-person at a conference centre may rapidly become obsolete given the opportunities afforded.

Finally, the implications for widening the diversity of those involved in psychiatric practice are particularly exciting. Those suffering from disabilities that prevent them from engaging in traditional clinical practices may be able to overcome these barriers by using the model of working described here, helping to both widen the diversity of psychiatrists working, and address the staffing crisis which our speciality currently faces.

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Mitigating the Impact of the Closure of Religious Centres due to the COVID-19 Pandemic on Patients with Mental Illness

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Abstract

Religious and spiritual centres namely churches, temples, mosques, synagogues, and others, provide immense resources to patients living with mental illness. Studies have established that patients use spirituality and religion for coping, while attaining a sense of purpose and meaning. Many spiritual and religious activities are communal and occur on the premises of these centres, providing social outlets to patients. The COVID-19 pandemic has led to an unprecedented widespread disruption of services including closure of religious centres. This paper reviews the likely impact of social isolation and other effects due to the closure of religious centres on patients with mental illness, and how this can be mitigated.

Introduction

The World Health Organization (WHO) defines Mental Health as a state of well-being in which every individual realizes his or her own potential, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to her or his community [1]. Many studies have shown the link between well-being and spirituality and religion, and have demonstrated how religious groups provide support towards recovery and rehabilitation of patients with mental illness, to aid mental health systems [2, 3]. Whilst some researchers say it is difficult to distinguish between spirituality and religion [4], Cook [5] has defined spirituality as a distinctive, potentially creative, and universal dimension of human experience arising both within the inner subjective awareness of individuals and within communities, social groups, and traditions. It may be experienced as a relationship with that which is intimately “inner”, immanent and personal, within the self and others, and/or as a relationship with that which is wholly “other”, transcendent and beyond the self. It is experienced as being of fundamental or ultimate

importance and is thus concerned with matters of meaning and purpose in life, truth, and values.

Social (physical) distancing measures introduced to curtail the spread of the COVID-19 pandemic, ranging from mandatory quarantine to voluntary self-isolation and including restrictions on many activities outwith our immediate household, have the potential to put the mental health of many people in general, and vulnerable patients with mental illness in particular, at risk [6]. In particular, the curtailment of meetings and acts of worship for many religious groups (at least where these involve meeting in person) mean that patients with mental illness may be unable to participate in these. In this paper, the mechanisms through which spirituality and religion influence mental health, and the possible impact of the COVID-19 pandemic on these are briefly discussed, before steps that have been taken to mitigate these are reviewed.

Mechanisms through which spirituality and religion influence mental health

Research has identified five main mechanisms through which spirituality and religion influence mental health, namely: a) coping styles, b) locus of control and attribution, c) social support and social networks, d) physiological mechanisms, and e) architecture and the built environment [7]. A brief description of each of these mechanisms is provided in Table 1. Whilst some of these mechanisms are largely either individual or concern the relationship between the individual and God (coping style, locus of control and attribution, physiological mechanisms), others depend on the community aspect of spiritual and religious networks (social support and social networks) or physical location (architecture and the built environment).

Table 1. Mechanisms through which spirituality and religion influence mental health

Mechanism	Description
Coping styles	A collaborative coping style where an individual collaborates with God in problem solving was associated in studies with greater involvement in recovery-enhancing activities [8].
Locus of control and attribution	Spiritual or religious beliefs such as belief in an all-powerful and all-controlling God may help individuals to reframe or reinterpret uncontrollable events, thus making them more meaningful and less stressful [4]. This optimistic attributional style [9] and internal locus of control (through relating to God) are usually associated with better health outcomes [10].
Social support and social networks	Spiritual and religious networks can provide stability over time and a valuable source of support in terms of self-esteem, information, companionship, and practical help in coping with stress [11]. Hospital chaplains [12], local religious leaders and clergy have a role in promoting the mental health of those in their localities [13], and this, in addition to the support from other members of religious congregations, is considered to be a key mediator between spirituality and mental health [14].
Physiological	Encouragement of positive emotions such as hope, contentment, love and

mechanisms	forgiveness by spiritual traditions while discouraging negative emotions like anger or fear, help to modulate the neural pathways that connect to the endocrine and immune systems [9]. Mindfulness meditation training was shown to alter brain network functional connectivity patterns and reduce Interleukin-6, an inflammatory marker, compared to relaxation training, thus explaining the improvements in inflammation [15].
Architecture and the built environment	The artistic grandeur of many historical [16, 17] and modern religious buildings are considered to have therapeutic power as many people find solace in the significance of churches, temples, and mosques [18, 19]. The sense of connectedness within these spaces, to other people, to oneself (immanence) or to God or other (transcendence), is a key factor that underpins many expressions of spirituality [7].

Impact of the COVID-19 pandemic

Following guidance by the UK government in 16th March 2020 to limit non-essential contact with others, many acts of worship and other meetings by religious groups were suspended. The Muslim Council of Britain called for 'the suspension of all congregational activities at UK mosques and Islamic centres' on that day [20] whilst the Church of England suspended all services [21] and the Chief Rabbi ordered the closure of all synagogues affiliated with the United Synagogue [22] the following day. This unprecedented widespread disruption of services, closure of religious centres [23] and limitation of access to chaplaincy services will invariably impact the mechanisms by which spirituality and religion impact mental health, with a potential to have a negative effect on patients. These changes likely impact some mechanisms (social support and social network, architecture and the built environment) more directly than others; however, it is likely that loss of these mechanisms may also impact other mechanisms (for example through patients finding it harder to 'collaborate with God in problem solving' without the support of others in their faith community).

Psychological impact of social isolation

The psychological impact of social isolation has been studied and documented previously. Trauma-related mental health disorders, including PTSD, were found to be at least four times higher in children and parents quarantined for the 2009 influenza A (H1N1) pandemic in the US [24]. Restriction of movement, loss of social connections and employment, loss of financial income, fear of contagion, or concern about lack of access to basic needs such as medicines, food, or water can potentially lead to anxiety, low mood, stress, fear, frustration, and boredom, and reduced psycho-social functioning [6]. Loneliness is a psychological manifestation of social isolation which studies have found to be associated with premature death at rates comparable to obesity and smoking[25, 26]. The elderly, people with pre-existing mental illness and people with learning difficulties have been identified as being at increased risk of psychological harm due to social isolation [27]. It is therefore very important to consider ways in

which the impact of the closure of religious centres can be mitigated.

Mitigating the impact of closure of religious centres

Identification of needs

Many studies advocate asking service users about their spiritual and religious needs upon entry to the service and throughout their care and treatment [7]. Identification of those at increased risk from the COVID-19 lockdown amongst patients with mental illness by primary and secondary-care doctors, other health workers, carers and chaplains is important in order to provide prompt psychological support to improve patient outcomes [28, 29]. Increased alertness is necessary when the risk of mental illness is further complicated by other risks including older people living alone or in care homes, learning and communication disabilities, recent bereavement, illness or hospitalisation, domestic abuse, unemployment or loss of income, alcohol and substance misuse, those in quarantine or self- isolation (shielding) due to serious physical health conditions, those with caring responsibilities, young people (due to closure of schools and sports facilities) and refugees/migrants [27].

As some patients may not openly report psychological symptoms or needs, using our clinical judgment, prior knowledge of the patient, and individual risk factors will help in identifying those who require intervention [6]. Starting with open-ended questions, clinicians are encouraged to use validated screening questions such as Patient Health Questionnaire-4 (PHQ-4) screening questions for anxiety and depression [30], UCLA Loneliness Scale [31] for severe loneliness and HOPE questions (See Table 2 and 3) to identify spiritual needs [32].

Alternative approaches

There is strong evidence that remote telephone or video consultations are acceptable, safe, and effective [33] and in addition to social prescribing [34], they form the strategies recommended to reduce psychological harm during the pandemic [6]. The Church of England validates the challenges of providing remote pastoral care particularly in the context of supporting the bereaved (many of who have been socially and physically distanced from their relatives who died from COVID-19) or isolated church members. They also encouraged the holding of services electronically with many churches implementing regular online services with community aspects maintained through the use of comments sections and Zoom meetings. Many other church activities have also gone ahead using digital means while churches continue to provide previously established services such as running local volunteering schemes, foodbanks, and care of the homeless. The Church of England recommends maintaining wellbeing by 'rootedness in God, relationship with oneself and other creatures of the world, and maintaining rhythms (routine)' [35].

Studies show that the impact of quarantine can be mitigated by making the quarantine or lockdown 'as short as possible', providing adequate and clear communication, ensuring basic supplies (such as food, water, and medical supplies) and reinforcing the sense of altruism [27], which spirituality or religiosity supports. Acknowledging the benefits of places of worship on spirituality and mental health, the UK Government agreed to ease the lockdown from the 15th of June 2020, to allow individual prayers in places of worship, however communal worship remained prohibited until 4th July 2020 [36, 37]. Putting safety first, particularly with many of its adherents belonging to the Black and Ethnic Minority (BAME) communities who are disproportionately impacted by the coronavirus

infection, the Muslim Council of Britain (MCB) has taken a very cautious and gradual approach to re-opening the mosques for congregational prayers [38]. They have arranged a weekend 'Visit My Mosque Day Digital', with mosques across Britain offering live virtual tours to members of the public to showcase the support Imams and mosque leaders are providing to their local communities during lockdown, in terms of 'opening up as foodbanks, delivering hot meals to those in need and supporting their local hospitals with food donations' [39].

The Westminster Synagogue website provides information on offering Shabbat Services and educational classes over Zoom and how adherents of the faith can get involved during the COVID-19 lockdown while making their festivals meaningful [40]. BAPS Swaminarayan Sanstha (BAPS) in the UK, with their headquarters at the Neasden Temple in London, have highlighted their relief work in providing health awareness videos and presentations in English and Gujarati, telephone support, delivery of food and basic amenities, using over 1000 volunteers across the UK [41].

Discussion

The impact of the closure of spiritual and religious centres or spaces, and restricted access to chaplains and clergy due to the COVID-19 pandemic have a potential to worsen the mental health of patients significantly by interfering with the mechanisms through which spirituality influences mental health. Meeting the spiritual or religious needs of patients in these times is challenging, however individuals and religious leaders have been resourceful and creative in facing the challenges, using evidence-based approaches to mitigate the impact of social isolation. Identifying those at risk promptly is important so that they can be linked to resources to meet their spiritual needs.

The past few months have been a period of substantial innovation across religious groups with many novel ways of worshipping and meeting together having been explored and developed. Approaches such as online services make it easier for some to try a religious gathering for the first time; however, others may struggle to join (for example due to a poor internet connection or poor technological literacy) and it is not clear how the move online affects how people are welcomed into the community (it is easier to remain anonymous on the internet than in a church building).

Further research is needed on the impact that the current restrictions have had on patients' mental health. In addition, research should consider ways in which the limitations of the current approaches can be addressed, for example how new members can be better welcomed to a community in an online setting. Finally, it should be investigated whether these new approaches to congregational meetings could be used to help engage patients who have previously been unable to do so (e.g. inpatients, those who are housebound) with the benefits of religion and spirituality.

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Clinical Manifestations of BPAN in a patient with moderate learning disability

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Abstract

This is a case report of a patient with complex psychiatric presentations with polymorphic symptoms that cut across mental health as well as neuropsychological specialties. We present the case history and diagnosis to highlight the neuropsychiatric manifestations of BPAN in a 26 year old female with moderate learning disability.

We highlight the importance of and need for early genetic testing in all patients presenting with challenging behaviour on a background of early developmental problems and learning disability. We also stress the requirement for mental health professionals to be conversant with neuropsychiatric conditions where diagnoses may be challenging to make while mainly focused on psychiatric presentations.

Introduction

Neurodegeneration with brain iron accumulation (NBIA) is a genetically and clinically heterogeneous group of disorders with the common feature of iron accumulation in the basal ganglia and substantia nigra (1, 2). Beta-propeller protein-associated neurodegeneration (BPAN) is the most recently identified subtype of neurodegeneration with brain iron accumulation (NBIA), with X linked dominant inheritance (3, 4). It is an extremely rare disease typically characterized by early-onset seizures, infantile-onset global developmental delay, intellectual disability, absent to limited expressive language, disordered sleep, motor dysfunction (ataxia), and abnormal behaviours often similar to autism spectrum disorder in childhood, followed by a decline in adulthood with the development of parkinsonism, dystonia and dementia (5, 6). There are also characteristic MRI findings which are more specific in later childhood, adolescence or early adulthood (7).

The diagnosis of BPAN is established on molecular genetic testing by identifying de novo mutations in the WDR45 gene which plays a critical role in autophagy through a WD40 repeat protein with a beta-propeller platform structure (2, 3, 6, 8, 9). Molecular genetic testing approaches can include a combination of gene-targeted testing (multigene panel or single-gene testing) and genomic testing (comprehensive genome sequencing) depending on the phenotype. Gene-targeted testing requires the clinician to determine which gene(s) are likely involved based on the phenotype, whereas genomic testing may not. In some cases, the phenotype of BPAN may be distinctive enough to warrant single gene-targeted testing, whereas those with a phenotype that is indistinguishable from many other inherited disorders with intellectual disability and neurological findings (including seizures) are more likely to be diagnosed using genomic testing. In cases where a pathogenic variant of WDR45 has been identified in an affected family member, prenatal testing for a pregnancy at increased risk and preimplantation genetic diagnosis for BPAN is possible. (7)

Some individuals who have been diagnosed with intellectual disability or early-onset parkinsonism based on their signs and symptoms have later been found to have BPAN when genetic testing was done, suggesting a high frequency of BPAN among patients with intellectual disability and young onset parkinsonism (10).

Case History

The subject (Case X) is a 26 year old female with moderate learning disability who was referred to a Mental Health of Learning Disability Service at 20 years of age with worsening mood, unprovoked inconsolable crying for long periods with very few minutes of respite in between, and increasing challenging behaviour mainly consisting of shouting, screaming obscene and abusive words and throwing things or banging her head when distressed. The cause for this was unknown because the behaviour was mostly unprovoked and largely unpredictable.
Case X has one sibling, a sister who is four years older and without any learning disability. Neither parent has a learning disability however a paternal uncle has Down syndrome. There is no family history of psychiatric illness.

She had an extensive medical history. Antenatal and pregnancy history were unremarkable and she was born at term with polydactyly which was surgically corrected. She suffered significant developmental delay from six weeks. She sat at 16 months and did not walk until two years of age. She also started demonstrating challenging behaviour with temper tantrums at 33 months. She was diagnosed with sleep apnoea, epilepsy with focal seizures and hypokinetic disorder in childhood. Brain MRI was performed at the age of five years with non-specific findings, described in her records as a shadow on the left side of the brain. She attended special school and college for people with special needs and was studying living skills. Prior to her referral she was initially managed by Child and Adolescent Mental Health Services for depression and behavioural problems, and had been on high doses of antipsychotics and anxiolytics to manage challenging behaviour.

Following referral, she was initially diagnosed with a moderate depressive episode and subsequently recurrent depressive disorder with anxiety. She had various courses of treatment with antidepressants including Sertraline and Venlafaxine, mood stabilisers and low dose antipsychotics to manage arousal and challenging behaviour as described above. She was also supported with benzodiazepines for agitation with little effect.

Physical health issues that may be contributing to the presentation were investigated for, including urinary tract infections and ear infections. She also received hormonal treatments as early menopause was considered a possible cause. She had assessments for hearing and visual impairments and hearing aids were prescribed, as well as pain relief for dysmenorrhea as this was thought to be possibly contributing to her distress. However, there was little improvement despite these interventions. She had brief periods of stability in terms of mood and behaviour which seemed to be as a result of alterations to her medication but her behaviour and mental state continued to decline steadily. She had no acute admissions and was referred for psychological support but disengaged after a short while.

Over the last two years, Case X suffered fluctuating deterioration developing new vision, speech and swallowing difficulties as well as tongue atrophy on the left side. Her mobility also worsened and she was diagnosed with arthritis, which was considered to be a cause for her limping and leaning to one side, and she was treated with two foot surgeries. Her mobility and speech progressively worsened alongside worsening tremors and she increasingly needed

to hold on to objects to walk. She now manifests with progressive cognitive decline, becoming increasingly dependent on her mother for activities of daily living and social functioning. Brain MRI showed evidence of mineral deposition in the basal ganglia, which is suggestive of beta-propeller protein associated neurodegeneration (BPAN). Results of confirmatory genetic testing are pending. The goals of treatment are to manage her symptoms by optimising her medication while offering psychological support to her and her family.

Discussion

Beta-propeller protein-associated neurodegeneration is an extremely rare disease with a variable phenotype. Neurodegeneration with brain iron accumulation disorders have a prevalence of 1/1,000,000 and, of these, BPAN constitutes only 7% (11). It is therefore essential that physicians of different specialties are familiar with this severe and debilitating condition. This report further expands the body of knowledge of the phenotype of BPAN highlighting potential neuropsychiatric manifestations (see Table).

The case demonstrates the classical presentation of BPAN as described in the literature (12). The typical two fold manifestation of symptoms was observed, with delayed psychomotor development and intellectual disability first manifesting in infancy, pronounced loss of expressive language skills and development of parkinsonism, dystonia and progressive cognitive decline in early adulthood. There were also comorbid features such as seizures and sleep disorder. This presentation is seen in the majority of cases, as described in several studies. There is, however, not a great deal of emphasis on the psychiatric symptoms of BPAN in previous reports. This report provides a more detailed picture of these especially in the context of learning disability.

The most common manifestation of psychiatric symptoms in learning disability is challenging behaviour and is often proportional to the severity of learning disability. It can be challenging to delineate and describe psychiatric symptoms in learning disability. This could be the reason why there are several incomplete and inconsistent reports of neuropsychiatric symptoms in BPAN. One case described yelling (8) while several others mention Rett-like stereotypic behaviours such as hand wringing and bruxism (11). This emphasises the need for early genetic testing in those presenting with such neuropsychiatric features in the context of learning disability. Accordingly, there is a growing consensus that genomic testing should be routinely performed for all people with a learning disability.

Table: Clinical features of Beta-propeller protein-associated neurodegeneration (BPAN) as seen in Case X

Neuropsychiatric features
Depression
Mood instability
Anxiety symptoms
Pathological crying or laughing
Disinhibition
Aggression
Self-harming behaviour
Neurological features
Neurological symptoms
Global developmental delay
Epilepsy
Limited speech
Dementia
Parkinsonism
Other features
Sleep disturbance
Swallowing difficulties with tongue atrophy
Deteriorating vision

Early genetic testing is vital because, as highlighted in Case X, early brain MRI may be normal in BPAN, with iron accumulation not producing changes detectable on neuroimaging until later in life and, as such, may not be helpful in diagnosing young patients (3, 8, 11, 12). Earlier diagnosis of BPAN will mean that affected families have earlier intervention and access to extra support to manage this severe condition which would likely foster better multidisciplinary management strategies as well as accurate assessment of recurrence risk and proper genetic counselling.

Conclusion

Management of BPAN is mainly symptomatic especially at the stage of decline in motor function. However, early diagnosis and regular clinical follow-up will enable appropriate therapeutic intervention for patients with subtle early symptoms of parkinsonism (12). For example, studies have reported substantial initial benefit with the use of oral levodopa in BPAN (13). Management of neuropsychiatric complications at a late stage is particularly challenging as antipsychotic medications can exacerbate movement problems as side effects as demonstrated in this case. This further emphasises the importance of early diagnosis, which also enables timely psychological support for patients and their families.

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