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Conference proceedings of the 4th Masterclass Psychiatry: Transcultural Psychiatry – Diagnostics and Treatment, Luleå, Sweden, 22–23 February 2018 (Region Norrbotten in collaboration with the Maudsley Hospital and Tavistock Clinic London)

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ABSTRACT

Background: According to estimates from the European Commission, Europe has experienced the greatest mass movement of people since the Second World War. More than one million refugees and migrants have arrived in the European Union in the past few years. Mental health and primary care professionals are more likely than ever to meet patients from different cultures and backgrounds.

Aims: To equip mental health and primary care professionals with transcultural skills to deal with patients from unfamiliar backgrounds.

Method: Lectures and case discussions to explore the latest advances in the diagnosis and treatment of serious mental health problems in a transcultural context.

Results: Lectures covered transcultural aspects of mental health problems, treatment in different cultural and ethnic contexts, and assessment of risk factors for self-harm and harm in migrant populations.

Conclusions: Clinicians require a sound grounding in transcultural skills to confidently and empathically deal with patients from unfamiliar backgrounds.

Acknowledgement

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Disclosure statement

At this event, the following exhibitors were present: Janssen, Otsuka/Lundbeck, Sunovion, and Shire.

Funding

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Editorial: Culture makes a person

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We are not born with cultures but into cultures, which shape our cognitive schema and also our world views. Within each culture, we carry micro-identities and micro subcultures that shape us. As clinicians, we manage patients who come to us with similar or dissimilar micro cultures, thereby affecting therapeutic interactions and therapeutic alliances.

Never before, have so many people been on the move. Irrespective of whether they flee from war and terror, try to propel themselves and their families out of poverty, educational reasons or simply want a new life, most are united in the desire to find peace and safety. According to estimates from the European Commission, Europe has experienced the greatest mass movement of people since the World War II. More than one million refugees and migrants have arrived in Europe, never before has so many people been on the move. The events of the past decade have contributed to improving our understanding and care for patients, we feel we have accomplished our mission.

At the same time, it is important to call mental disorders for what they are. Using terms such as “mental health issues” or “mental health concerns” instead of “mental disorder” or “mental illness” can seem to imply experiences are less severe or less chronic or less worthy [4]. Such terms aim to avert stigma by removing from policy and practice what is perceived as pejorative, but they tend to under-rate both the seriousness and the severity of the patient’s distress and experience. There is no evidence suggesting that abandoning the term mental illness has eliminated any stigma. Changing the label may not affect stigmatizing attitudes. Discrimination can be reduced using legal means. Using terms such as mental health issues is far too ambiguous and vague to take on any legal slant. Recognition and public acknowledgement of illness experiences can enable policy makers and planners to plan services and public mental health services accordingly. Terms such as “mental health issues”, however, may not be seen as models for public mental health education or intervention.

Rethinking psychiatry in cultural terms is an incentive for rethinking psychiatry in general. Exploring mental disorders in a cultural context promotes the understanding of individual experiences and their significance for social functioning. Every patient tells a story. That narrative or story is more than just medical facts [5]. Even in physical terms, reality is not cast in stone, but ultimately probabilistic and observer-dependent. Accepting the uncertain nature of reality can improve the clinician’s preparedness to listen and integrate the patient’s experience into diagnosis and treatment [6]. Better communication about diagnosis and treatment and increased patient participation may significantly increase adherence to treatment [7]. The eminent North American physician Sir Willian Osler already understood the importance of the personal experience of illness and patient participation at the turn of the twentieth century: “It is much more important to know what sort of patient has a disease than what of disease a patient has” [8].

This Masterclass has been about rethinking psychiatry in cultural terms. In this masterclass, many different stories have been told. Stories about delusion, possession and religion, guilt and shame, pain and depression, eating disorders and sexual stigma and suicide in the face of utter hopelessness, radicalization, and risk. We have explored the connection between culture and neuroscience and looked at innovative approaches to psychotherapy and psychopharmacology. The Masterclass Psychiatry programme originates in the Region Norrbotten, right beneath the Arctic Circle. Its mission is to provide medical education with high clinical relevance by world leading experts in mental health for the greater benefit of our patients. This masterclass “Transcultural Psychiatry – Diagnosis and Treatment” has been the forth event bringing together clinicians from Scandinavia, Europe and the rest of the world [9]. And if this event has contributed to improving our understanding and care for patients, we feel we have accomplished our mission.

Disclosure statement

Dinesh Bhugra has no interest to declare.
Funding

Ursula Werneke has received funding for educational activities on behalf of Norrbotten Region (Masterclass Psychiatry Programme 2014–2018, EAPM 2016 Luleå, Sweden): Astra Zeneca, Janssen, Eli Lilly, Novartis, Otsuka/Lundbeck, Servier, Sunovion and Shire.

References


Trainee Editorial: Psychiatry should be taught from day one in medical school

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“Help me doctor, I have nothing to return to. My family is dead. I will be tortured if I return to my home country. I do not want to commit suicide, but it will at least be a peaceful and dignified death.”

We had just finished our medical studies. Our training in psychiatry was sufficient for taking a proper psychiatric history, perform a mental state examination and diagnose the most common conditions. It is our first workplace as newly graduated physicians. The woman who’s looking at us is at least 30 years older than us. She is on her bare knees as she quivers and cries. She is stretching her arms towards the sky while asking God and us for help desperately. We are not prepared and feel completely inadequate.

“To cure sometimes, to relieve often, to comfort always” might strike a recognizable chord as a modernized simplified version of the two thousand year old Hippocratic Oath. A more recent interpretation of doctoral duty is the World Medical Association’s declaration of Geneva “physicians’ pledge”, wherein the health and well-being of our patients will be our first consideration [1]. But then again what does health and well-being mean to our patients?

During early training, we learn that our primary medical role is to diagnose and treat a patient’s disease by prescribing medication to relieve certain bodily symptoms. We rarely think about the person who is experiencing the illness and how her/his condition affects mental state and functioning in daily life. We are trained to separate panic disorder from unstable angina, functional spasm from epilepsy, sending patients home with a blatant message that their condition is not as harmful as any strict somatic disease. Separating body and mind this way, we pull apart what belongs together. Our risk to miss potentially severe mental illnesses also increases.

In Sweden, psychiatric diagnoses account for the highest burden of illness in both men and women with high incidence and long duration. In 2016, 45% of women and 32% of men working were on sick-leave due to psychiatric disorders. For unemployed, these figures rose to more than 50% for both men and women [2]. In face of this reality, it is concerning that medical schools only allocate a few weeks of psychiatric training during undergraduate medical training.

During this masterclass in transcultural psychiatry, Professor Dinesh Bhugra argued that “Psychiatric training should already start from day one of medical school” [3]. We salute this idea and contend that psychiatry integrated early during medical training is essential to learn to treat an illness in a way that includes the whole person. That way, the medical practitioners’ responsibility would not be defined by and limited to organ dysfunction, specific symptoms or test results, but to the wellbeing of the whole individual. Considering body and mind as one, would honor the increasing evidence that physical health affects mental health and vice versa [4–6]. Depression for example is a common secondary outcome after a myocardial infarction. But depression is also an important independent risk factor for the progression of cardiovascular disease [6].

Another important issue raised by Professor Bhugra concerned the terms of ‘disease’ and ‘illness’. Whereas physicians diagnose and treat diseases, patients suffer from illness in the context of loss of social functioning [3]. As our agendas may differ, we need strategies to understand patients’ interpretation of their illness.

In addition, we learned that understanding mental disorders is not possible without understanding cultural differences. In our daily practice, we should be attentive that prominent features of common psychiatric disorders will vary in different ethno-cultural settings [7]. Ethnic differences might have a great impact on received diagnoses [8]. Considering culture and adapting intervention accordingly improves response [9].

During the masterclass, several strategies were presented that might help us medical interns and prospective psychiatrists to improve our consultation skills in transcultural
settings. **Shared decision-making**, based on the principle that patients share the responsibility for healthcare decisions in agreement with their doctors, fosters autonomy and self-determination of the patients entrusted in our care [10]. **An interpretation of an interpretation**, relates to Kleinman’s vigorous statement that patients interpret their symptoms based upon their own cultural settings. In clinical consultations, physicians should convey how they perceive the patient’s own interpretation [11]. Finally, the “**Cultural Formulation Interview**”, is a person-centred DSM-5 based interview tool that can help us systematically to assess cultural factors during consultation [12,13].

The woman with deportation order will forever be stuck in our memories. She is a reminder of that there will be many situations during our work life where skilled communication, knowledge in pathophysiology and drugs cannot “fix” a human. We must accept that “there is art to medicine as well as science, and that warmth, sympathy, and understanding may outweigh the surgeon’s knife or the chemist’s drug” [14]. Values concerning the well-being of the patient as an individual and as an entity are important in medical training as well as in everyday clinic practice. Transcultural psychiatry is one way to ensure that such values keep gaining ground, improving psychiatry as a whole.

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No interest to declare.

**References**


**Cultural neuroscience: ideas worth knowing**

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**ABSTRACT**

**Background:** Neuroscience is now promising significant advances in medical practice, such that it can improve the art and science of personalized medicine. A new discipline of cultural neuroscience is now forming, and few clinicians, researchers or educators are aware of it.

**Aim:** To set out a brief synopsis of cultural neuroscience.

**Methods:** A narrative, non-systematic, review of experts on cultural psychiatry and cultural neuroscience.

**Results:** Cultural neuroscience proposes that culture and biology have co-evolved with mutually beneficial affordances in human abilities that promote positive selection that help people to flourish. Neuroscience can support and improve cultural interventions when applied in a pan-diagnostic manner to culturally specific groups, ethnic minorities, and migrants.

**Conclusions:** Cultural neuroscience is an exciting new discipline with the potential for clinical benefit. Cultural psychiatry can advance in this direction, and, at the same time, offer a critique of the culture of neuroscience.

**KEYWORDS** Culture; psychiatry; neuroscience; innovations

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**Introduction and context**

The Masterclass held in Lulea in February of 2018 was themed on learning about cultural psychiatry practice, teaching, and research. The introduction of neuroscience may seem like an uncomfortable distraction, and far removed
from the interests or domains in which cultural psychiatry has traditionally operated.

Cultural psychiatry methods involve clinical ethnography, participant observation, and research methods originally from sociological and anthropological sciences. More recently, cultural psychiatry methods, variables, and practices inform qualitative research on other areas of health, epidemiological studies, health services research and improved design and reporting of randomized trials. Yet, this trend been accompanied by less emphasis on culture, and more on other social processes, and simplified designs that do not always permit more in-depth case studies, or knowledge to emerge from participant stories. Rather, emerging research now relies on cultural psychiatry to assess acceptability and feasibility of putative interventions, learn about the cultural adaptation of outcome, and include some qualitative or ethnographic work within mixed methods studies. Culture is a complex process often conveniently treated as a variable, operationalized into race, ethnic group, identity measures, or some measure of health belief at the individual level. We are less often seeing analyses of culture as a group phenomenon, recognizing the importance of kinship systems, and shared supports, and affordances that culture enables.

Mental health research can still benefit from a critical engagement with the methods of cultural psychiatry, assessing their relevance and appropriateness for culturally and linguistically diverse populations, but not just minorities or dislocated populations. Defining the population of study, in cultural rather than racial and ethnic group terms, is also a common contribution of cultural psychiatry to research [1]. The interaction of cultural variables with other social processes needs more thought and refinement but is an important contribution. For example, cultural influences and processes, especially in migrant populations to high-income countries, contribute to inequalities, poverty, acculturation, and then multiple forms of disadvantage that cluster in deprived areas, or multiple adverse or traumatic effects at an individual level [2–4]. Revealing hidden stories or narratives that better represent the lives of people perceived to be culturally isolated or unique remains an important element of cultural psychiatry methods, although this opening up of cultural world views is an important asset for all research, not captured in the promotion of public and patient involvement, now mandated by many funding bodies and research councils, as well as in the formulation of new practices, policies, and service organization. One might argue that cultural psychiatry has been powerful and successful as an enabling discipline, but its own identity is then less discrete, visible, or valued. Not least, many of the topics of cultural psychiatry are perhaps not easy for politicians, funding councils, or society to grasp: racism, structural violence towards women and minorities, asylum and refugee processes; advocacy and protest against injustice is an important component value inherent in studies of culture and mental health more recently [5,6]. There is now less emphasis on discovery of exotic culturally defined, influenced or embedded expression of distress; and at the same time a drive to improve the practice of psychotherapy and therapeutics in general in diverse cultural groups, taking account of the culturally defined, embedded, influenced therapies, and whether ethnic matching is helpful [7,8].

In the context of these emerging trends in cultural psychiatry, a new field of study seems to be emerging. This new approach makes use of cultural variables, applied to brain function and structure. ‘Cultural neuroscience’ asserts a particular set of ideas about the relationship between culture and biology, and the potential impact on mental health research and practice [9].

Cultural neuroscience: a new paradigm?

The central premise of cultural neuroscience is that culture and biology co-evolve, both being adaptive, and that just as genetics, and biological vulnerabilities and affordance give rise to specific abilities within which culture emerges, so cultures that give permits populations to flourish, are not only selected for survival value but also shape biological affordances [10]. Advances in molecular genetics, neuroscience and cultural psychology and cultural psychiatry, make possible empirical testing of hypotheses that will better inform the links between culture and biology.

Research in neuroscience has shown differences between different cultural or national groups on a number of neurophysiological or imaging markers, or on tests of performance. For example, three is allelic variation of the serotonin transporter gene (5-HTLPR) and this is correlated with cultural collectivism across nations [11]. The counter argument is that cultural practices of sustained inter-dependence may lead to culturally encoded neural responses in the brain that represent culture [12]. Thus, cultural neuroscience tries to define and construct better research variables for culture, whilst also using advances in neuroimaging, molecular genetics, psychophysiology, and behavior variables together, to better understand a transdiagnostic underlying mechanism that explains cultural variations with translational potential for discoveries of new interventions [13]. It necessarily needs some integration of diverse research fields and epistemologies. Chiao et al. show that cultural neuroscience brings together different constructs of emotion including the notion of basic modular or innate emotions, social constructed emotional experiences, cognitive, and psychological [14]. Chiao goes on to assert that basic and socially constructed notions represent genetic and cultural processes, and that these reflect the same underlying processes but at different levels of analysis, and that co-evolution is the norm rather than the exception [14]. There is also a strong possibility that experiments in cultural neuroscience will help us better understand brain–body processes, and the way physical complaints and bodily signatures emerge for emotional and psychiatric problems and vice versa. Might neuroscience explain cultural variations in pain perception and somatic symptoms prominence that provides potential mechanisms for intervention [15–18]?

The appeal of neuroscience-based clinical interventions is that they may be more effective if they can be developed to modify specific neurophysiological and neuroanatomical
targets, coming closer to the aspiration of personalized medicine. Personalized medicine seeks to provide treatments for specific patients, tailored to their symptoms and illness characteristics and health beliefs, with a minimum of adverse and untoward or unexpected effects, for example, improving the precision of prescribing practice in psychoses [19–20].

This is a hopeful but potentially realizable expectation and reflects how psychiatric treatment today is still mostly focused on identifying pathologies, symptoms, and then taking action to minimize these as if invariant culturally diverse groups of people and that these are somehow specific to diagnostic groups. Pilot studies examining the cultural salience of emerging DSM5 classifications hold important lessons and methods to better elicit information to make a more culturally authentic diagnosis taking account of all information that the patient has to offer, rather than only that which permits a speedy checklist of symptom identification, as if this is unproblematic [10].

Yet, perhaps less celebrated is a role of cultural psychiatry, drawing on the disciplines of sociology and anthropology, to critically engage with evidence noting the ideologies, and power relationships that may be at play when one discipline or another asserts superior benefits and gains. The age of the brain and neuroscience hopes must, therefore, be closely interrogated for the robustness of the evidence that supports the claims made in neuroscience research.

**From cultural psychiatry to cultural neuroscience**

A further attraction, which may be illusory, is that neuroscience-based interventions, may bypass the complexities of cultural psychiatry, of requiring cultural adaptation of interventions, ensuring recruitment of ethnic minorities and linguistically diverse groups into trials, and the significant resource implications. If a neuroscientifically based diagnosis can be made, and then intervention targets the mechanism, might this obviate the need for cultural assessments and accommodations? It is likely that patients from diverse cultural background will still have relevant concerns and explanatory models of their distress, and reactions to proposed neuroscientific formulations of mind and mental distress. There may be just as great a need to assess acceptability and feasibility of applying such interventions, and willingness to use these interventions. Taking the example of trauma leading to PTSD or borderline personality disorder with depression, emotional dysregulation makes both harder to treat. When cultural factors are invoked, there is a need for better understanding of cultural meanings and contexts of trauma; asylum seekers fleeing war-torn countries will need perhaps a different level of awareness and sensitivity to bullying in childhood, and in both emotional dysregulation and depression could undermine a psychotherapy treatment, or engagement, or ability to function in employment. What is more likely is that neuroscientific interventions could be a complementary rather than an alternative treatment.

Neuroscience promises solutions for the cultural conundrum, that care of culturally diverse communities requires more resources, more skills and competencies, and cultural adaptations of interventions; and that despite these efforts outcomes might not be measurable or comparable across cultures. This arises as different cultural, religious, and spiritual heritages determine that people cope with distress in many ways that take account of variations in identity and self, health beliefs and explanatory models, local assets and resources, and that the value of relevance of these is influenced by both past experiences and cultural beliefs. These, I call intensive and high-level optimal interventions.

Aspects of neuroscience, which are pervading aspirations for psychiatric intervention include connectomics [10,21], better recognition of networks of white matter between brain regions, which may explain the presentation of psychiatric symptoms and locations for intervention. Dimensional constructs of mental illness have been proposed by DSM5, assuming these represent underlying brain structure and function. Yet in reality it has been difficult to prove such correlations or that a practical classification can be built on dimensional nosologies, especially to serve culturally diverse populations [10].

Relying in part on better imaging techniques and connectomic science, neuromodulation techniques offer hope to those with treatment resistant depression, with personality disorders, and where emotional regulation undermines therapeutic interventions. As a case study, if a person has emotionally unstable personality difficulties or PTSD due to violence, indeed the clinician cannot tell; her experience is of conflict or extreme trauma; and she speaks in a different language from the service provider, and she expresses fractured moral framework as lying at the heart of her distress; how can her home be restored and her former sense of self and justice and trust in the world be reconciled by what she has witnessed and how she feels? One might try interpreters to deliver CBT, or psychoanalytic work. Yet we know that even if therapies are minimally or mechanistically culturally adapted, the philosophical or moral aspects of engagement in therapies may not be addressed [22,23]. If unsuccessful, what would happen? The patient would be considered untreatable [24], or worse, the persistent explained as a personality difficulty, or that they were unable to do more than work towards stabilization in a framework of trauma therapies [25].

An alternative is to better understand the underlying neuroscience, and perhaps she needs help primarily with emotional regulation, and controlling impulsivity.

In a series of case studies, we showed that repetitive transcranial magnetic stimulation (rTMS) is helpful, stimulating descending inhibition from pre-frontal cortex [26]; and this seems to improve impulsivity and symptoms of emotionally unstable personality difficulties. There are specific targets that seem to explain this benefit on impulsivity in personality difficulties as well as in depression and even where there are suicidal risks [27]. Thus neuromodulation may enable better use of psychological therapies, reduce suicidal risk, treat co-morbid depression and provide greater opportunity.
Conclusions

Cultural neuroscience offers hope and optimism, and opportunity to better understand how culture is encoded in the body and brain, and how cultural biology might transform the way culture is understood and how cultural psychiatry evolves, especially in medical practice. Cultural psychiatry and psychology are also necessary as observers of the culture of neuroscience as a new paradigm, to explore and critique the future analytic power of the discipline and support translational applications.

Disclosure statement

No interest to declare.

References


Clinical challenges in cultural psychiatry – searching for meaning, searching for methods

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\textbf{ABSTRACT}

\textbf{Background:} Mental health services in Sweden are confronted with globalization and refugee migration from conflict- and war-torn countries.

\textbf{Aim:} To discuss how clinicians in Sweden can deal with a series of challenges in a changing globalized society, ranging from difficulties of overcoming barriers to help seeking to difficulties of identifying trauma and finding culturally adapted clinical tools.

\textbf{Method:} Case vignettes are presented to exemplify challenges. Different approaches developed to support clinicians are presented.

\textbf{Results:} The concepts of patient centered care and shared decision-making, as well as the Cultural Formulation Interview, are recommended to explore the significance of culture and context in psychiatric assessments. Acknowledging relational aspects of care and of paying attention to the patients’ social worlds in clinical work is also essential.

\textbf{Conclusions:} The article includes recommendations for training as well as an appeal for the involvement of the wider society in the work to guarantee equitable and
high-quality mental health services for some of the most vulnerable patient groups in society.

KEYWORDS Cultural psychiatry; refugees; trauma; cultural formulation interview; patient centered care

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Introduction

Mental health services in Sweden are confronted with globalization and refugee migration from conflict- and war-torn countries. In this article, we will discuss some current clinical challenges and dilemmas in Swedish mental health care and argue for the significance of developing clinical methods addressing cultural variety and including an interest in patients’ meanings, but also paying attention to the patients’ social contexts and social determinants of mental health. We will also point to some current clinical arenas of importance for further discussions and orientations concerning human rights and ethical issues.

Clinical challenges in transcultural psychiatry

Clinicians encountering new groups of patients in a changing social context are confronted with a series of challenges, for example:

- Problems of grasping unfamiliar life circumstances and their impact on the health state of the person [1]. This includes taking account of the vulnerable social position of many newly arrived migrants, with poor housing conditions, lack of financial resources, disruption of social networks, and experiences of discrimination and, sometimes, racism.
- Providing equal care to persons living in deprived conditions, among them undocumented migrants, a group that is likely to increase in Sweden in the years to come.
- Addressing language difficulties that constitute barriers to access of health care, even though the use of interpreters is prescribed and publicly financed in Sweden. However, due to a lack of qualified interpreters the right of good interpretation is often not secured.
- Acknowledging cultural aspects of the encounter in mental health care, including variety in cultural idioms of distress, illness explanations, stigma, and lack of knowledge of mental health services that constitute barriers to help seeking.
- Assessing and managing suicide risk in asylum seekers, where the clinician and the patient, though not always explicitly, share powerlessness confronted with a threatening and insecure life situation [2].
- Identifying and having knowledge about consequences of trauma, including torture and its effects on physical and mental health.
- Overcoming the focus on the individual patient in the encounter with families, accustomed to and demanding a role in the care of their close ones. Such an approach is often important in care with immigrant families.
- Being alert to and assessing mental health problems in vulnerable persons with a risk of being attracted by violent ideologies. Mass violence, radicalization and terrorism constitute complex challenges for mental health professionals affecting different areas such as impact on victims; stigmatization effect of the association between violence and mental illness; the need for research on motives; and professional confidentiality [3].

In the following, we will describe some of the approaches developed to address these challenges and exemplify with short case vignettes.

Case: Razia

Razia, a young asylum-seeking woman from Pakistan, is in compulsory care after a suicide attempt. It is well known and documented in the medical records that she has a story of having been subjected to sexual torture in prison in her home country, after which she was rejected by her entire family and had to flee the country. Now her appeal of the rejection of her asylum application has been turned down, inhibition of the deportation has been denied, and deportation is impending. One doctor notes in the records: “Nothing to do. This is not psychiatry.” Razia tells the physiotherapist: “The asylum situation does not matter; the rapes are still there.”

Implementing patient centered care and shared decision-making in multicultural milieus

Models of care that imply patients’ involvement, such as patient centered care [4] have increasingly been evaluated as the golden standard for good quality of care. For mental health care, the importance of shared decision-making is emphasized [5]. Patient-centered and person-centered care are concepts used with different definitions but with shared meanings of actively involving the patient in order to make him or her an active partner in care and treatment [4]. One important element is to listen to the patients’ stories and use them when framing treatment plans.

Patient centered care has been shown to be important irrespective of migration background but may have a special importance increasing awareness of areas of more specific concerns to immigrants and refugees [6]. However, patient centered care may be hampered by communication barriers, especially languages barriers, between clinicians and patients [7]. This, in turn, reduces the possibility for shared decision-making, as this requires a shared understanding of the meanings for the other. The human value of shared decision-making in care for refugees is emphasized in a UNHCR report about Syrian refugees [8]. Syrian refugees have often lost power and control over most aspects of their lives, including work, home, friends, and family members. Displaced Syrian refugees may gain a sense of empowerment only if they are actively involved in decision-making on the intervention plans [8]. Both patient centered care and shared decision-
making require that clinicians work actively on overcoming communication barriers. Additionally, these approaches require that mental health care is based on culturally sensitive methods to gain insights into patients’ meanings related to symptoms, distress, situations and treatment expectations.

Case Naimah

Naimah, a 28-year-old asylum-seeking Syrian women, lives in a refugee center outside a small city in the central part of Sweden. After Naimah’s younger brother died in a bomb attack at the Syrian-Turkish border, a woman living in the same room as Naima noticed that she looked increasingly more tired and did not eat much. The room-friend encourages Naimah to seek help from the primary care center. With the support of an Arabic-speaking interpreter, Naimah tells the general practitioner about being tired, having pain, headache, sleeping problems, and feeling hopeless due to her brother’s death. The clinician thinks this could be signs of a crisis reaction or a depression and asks Naimah if she experiences a depressed mood. Naimah denies this but says that her psyche is suffocating. Asked about suicidal thoughts, Naimah denies all suicidal ideas but says she wishes she could sleep and not wake up (itmana nam ma fik, أنا أتمنى أن أتبيع). She says she thinks about returning to her village despite ongoing bombings there. The clinician finds it difficult to decode Naimah’s expressions of distress and to assess whether she suffers from a depressed mood or not. Additionally, the clinician finds it hard to evaluate the suicide risk, and what meanings Naimah tries to convey about her life situation.

The cultural formulation interview

In the field of cultural psychiatry, a Cultural Formulation Interview has been developed and introduced into the DSM-5 as a tool to explore the significance of culture and context in psychiatric assessments in an individualized and non-stereotyping way. The CFI approaches culture and context in relation to the current illness and pays attention to patients’ meanings related to illness and care. The interview has a semi-structured character with 16 open questions addressing the patient’s own problem formulation, the patient’s illness explanation; communication with the patient’s network about illness; stressors and coping strategies; identity and background as well as earlier experiences of help seeking and barriers to help seeking; current expectations of care, as well as the experience of the relation with the clinician [9].

The Cultural Formulation Interview is recommended for use with all patients, not only those whose cultural background differs from the clinician’s background. The CFI is described as the most patient centered portion of DSM-5 [10]. There are twelve supplementary modules to the Cultural Formulation Interview, some of them allowing in-depth exploration of some of the initial questions, others for use with certain groups of patients, like children and adolescents, older persons, migrants and refugees, and caregivers. The Cultural Formulation Interview stimulates clinicians to become aware of the role of families, relatives and other close persons in the social network. Not only is there a special interview for informants, a supplementary module on the social network and a supplementary module for caregivers – there are also questions in the Cultural Formulation Interview on how the patient talks with his family, friends, or others in his community about his problem and its causes and questions about who and how other persons provide support or cause stress that affect his or her problem.

Relational aspects of culture and care

Encountering patients with a different cultural background, especially if the person lives in harsh and insecure situations, and has experienced violence, war and torture may have profound emotional effects on professionals. Clinicians’ reactions of countertransference may for example include feelings of hopelessness, anger, and lack of trust and may lead to professionals distancing themselves from patients but also to over-involvement or loss of capacity for using professional skills. Consultation and supervision can help professionals to be aware of their emotional reactions and culturally affected countertransference. For good quality of care, it is important that clinicians are supported by supervision, counseling, and consultations, and given time to reflect on ethical issues. Different models of cultural consultations have been developed internationally [11].

There is a link between emotional reactions and empathy. Empathy may be an essential component of the professionals’ ability to approach the vulnerable situation of newly-arrived refugees and asylum seekers. Empathy is an important human capacity to empathize and identify with others and is essential to all social relationships and to helping behavior. Rasoal [12] argues that relationships in health care with clients from different ethno-cultural groups can be understood in terms of the presence or absence of ethnocultural empathy, referring to empathy directed towards people from cultural groups different from one’s own.

Kirmayer [13] discusses the clinical limits of empathy in situations of radical cultural difference and suggests that when empathy reaches its limits the other may be experienced as alien and unknown. He argues that empathy depends on detailed knowledge of the other’s world. Methods supporting clinicians getting knowledge about the local world of the patient can support empathy for the patient and in turn facilitate clinicians’ capacity of using their knowledge without getting stuck in feelings of hopelessness or lack of understanding. Professionals’ feeling of empathy may contribute to the capacity for approaching the vulnerable situation of refugees and asylum seekers [14].

Attention to the patient’s social world

Against the background of knowledge about increased risk of mental illness for immigrants, and particularly refugees, in Sweden [15,16], and with knowledge about the importance of postmigration factors [17,18], clinicians need to acknowledge and address the social realities of their patients.
Collaboration with social services and other social actors is essential, but there is also a need for clinicians to address the social determinants of mental health in their clinical interventions. Concrete suggestions for the use of stress-reducing strategies and improving positive coping, as well as using the Cultural Formulation Interview for the exploration of discrimination and social exclusion have been made [19,20].

Education and training

Training with interdisciplinary perspectives is needed to support clinicians facing dilemmas in cultural psychiatry. Social determinants of health, human rights issues globally and locally, migration processes and their impact on health, intersectionality and discrimination are some of the necessary themes. Education and training have to convey knowledge about international conventions guiding rights to health and care ratified by Sweden, and the rights for victims of torture to rehabilitation [21].

Training in cultural aspects of the care encounter, and in the Cultural Formulation Interview, is essential. Other necessary themes include knowledge about effects of trauma, collaboration between different social actors, family and network approaches, and approaches emphasizing the importance of exploring the patient’s subjectivity in suicide assessment and management [22].

Training must encompass not only knowledge, but also attitudes and skills. Training sessions involving reflecting on the participants’ own experiences, case discussions, and role play aim at developing the clinician’s awareness of how his or her own identity, stereotypes and prejudices affect the clinical encounter. The European Psychiatric Association has published comprehensive guidelines on cultural competence training [23]. The guidelines stress the importance of both individual and organizational competence and list a series of recommendations for policy makers, service providers, and clinicians. The Swedish Psychiatric Association [24] has recently published guidelines in transcultural psychiatry to support clinical assessment and treatment. The guidelines include practical information about training resources and courses for mental health professionals [25].

Conclusions

There is a widening spectrum of both needs and developments of knowledge and tools to support clinicians facing dilemmas in cultural psychiatry. However, there are concerns about clinicians not being fully empowered to use available tools intended to grasp the meanings patients give to illness and life situations and their expectations of care. In global psychiatry, there is a concern about mechanization and de-contextualization of psychiatric services. In everyday practice, time is often considered too short for a proper assessment, especially an assessment involving the patient’s perspectives. Psychiatry needs to involve not only patients and their networks, but also opinion builders, policy makers, and other scientists in the work to guarantee equitable and good mental health services for all patients, including some of the most vulnerable groups in society and argue for mental health promoting strategies targeted towards these groups.

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Delusion, possession, and religion

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\textbf{ABSTRACT}

\textbf{Background:} Religion and psychiatry may be both considered to be two different ways of explaining the unknown, of responding to questions about the meaning of life, and of bringing healing.

\textbf{Aims:} To discuss the border between religion and psychiatry.

\textbf{Method:} This lecture explores the interface between religion and psychiatry and discusses the border between soul and mind.

\textbf{Results:} Religious beliefs may affect behaviors and may be seen on a psychopathological continuum with overvalued ideas and delusions. There is overlap between psychiatric and religious categories, in possession states described in research literature and by many cultural groups. Several studies suggest possible factors for differentiating schizophrenia from demonic influence and report on the efficacy of exorcism among possessed/psychotic subjects. Diagnostic criteria have been proposed for dissociative trance disorder or possession disorder.

\textbf{Conclusions:} Both mental health professionals and religious believers may require criteria to distinguish adaptive and maladaptive expressions of religious experience.

\textbf{KEYWORDS} Psychiatry; religion; delusion; possession; psychosis

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\textbf{Introduction}

Religion and psychiatry may be both considered two ways of explaining the unknown, of responding to some questions about the meaning of life, and of bringing healing. Thus, it is important to integrate religion into daily clinical practice where relevant and consider a patient’s cultural and religious beliefs in order to select tailored clinical treatments \cite{hollander2016}. However, there are no universally accepted criteria or guidelines to distinguish between adaptive and maladaptive expressions of religious experience, and religious beliefs may be seen in a psychopathological continuum with overvalued ideas and delusions.

Freud argued that religious beliefs are delusional, identifying the devil with the incarnation of psychological repression \cite{freud1926}. Sargent attributed so-called ‘spiritual phenomena’ to a pure suggestion of mind \cite{envall2018}, whereas recent diagnostic criteria for mental disorders reflect attempts to exempt religious doctrine from operational definitions of delusional beliefs \cite{sundvall2018}. Recent literature recommends that psychiatrists include assessment of religious and spiritual beliefs of patients, given that religious beliefs may be clinically relevant, are related to worse global functioning in research studies, and associated with need for higher doses of antipsychotic drugs \cite{schouler2015}.

\textbf{Religion and psychiatry}

Psychiatry and religion have always been connected. In the Middle Ages, mental disorders were generally considered the action of the Devil, or witchcraft \cite{laban2015}. Religious beliefs have been handed down for generations, and people exhibiting psychotic symptoms have tried to find explanations within their existing systems of knowledge \cite{laban2015}. In some settings, supernatural forces are frequently conjectured as a causal explanation of mental illness, and consequently the practices of magic-religious healers are often considered as a first-step treatment of mental disorders \cite{laban2015}. Several studies have reported greater occurrence of religious delusions and hallucinations among subjects with higher religiosity \cite{laban2015}, while experiencing a psychotic episode may increase religiosity in around a quarter of patients \cite{laban2015}.
Possession and religious delusions

Possessions by an evil spirit have early origins within Paganism, Wicca, Haitian voodoo, African traditionalism, Buddhism, Hinduism, Judaism, and Christianity. These phenomena have been most commonly described in rural populations with low level of education, above all among women [11,12]. They also can be found in cases of hysteria or psychosis, where mystical hallucinations and delusions are common [11,12].

Muslims believe that mental illness can occur as a result of divine punishment, or personal weakness. In most cases, possession of a person’s body is attributed to possession by jinn, invisible spirits capable of entering a person’s body, controlling and influencing it. Patients afflicted by jinns are typically subjected to medical and spiritual treatments such as exorcism ceremonies called “Zar” [11,12].

In the Qur’an, insanity is linked to sin, and people with mental illness are considered to be jinn-possessed as a result of a sin. A cross-sectional study of 4129 people in Baluchistan found that the prevalence of the Djininati Syndrome, a culture-related state of possession by jinn with symptoms such as changes in consciousness, hallucinations, emotional liability, was 0.5% in the general population and around 1% in women [13]. Lim et al. analyzed 47 case reports of jinn-possession and found that 66% of patients were suffering from a psychiatric disorder and 45.2% were affected by schizophrenia spectrum disorders [14]. Patients practicing Christian religions report more delusions of grandeur, guilt and sin, than patients belonging to other religions including Islam. Cross-cultural studies show that in case of paranoid delusions, Christians report persecutors to be supernatural beings more frequently than Muslim and Buddhist patients [15].

Neurobiological hypotheses

Based on assessment of religious phenomena in epilepsy, near-death experiences, hallucinogenic effects, psychotic disorders, and dementias, it has been postulated that the limbic system may produce states of divergent affects and cognitions, such as perceptions of overheard importance or self-reference, deep joy and noetic feelings, typically found in religious and mystical experiences. Other evidence supports temporolimbic overactivity as an underlying process in religious/psychotic phenomena. Dysfunctional mesolimbic activity can generate altered perceptions of reality, including distorted sense of time, autoscopy, depersonalization, derealization, de jà vu and jamais vu, and the direct stimulation of these areas, may result in similar events [16,17].

Diagnostic criteria

The experience of pathological possession is included in the DSM-5 (Diagnostic and Statistical Manual of Mental Disorders-5th edition) under the description of identity destruction. A recent study of Afro-Brazilian religious practice examined whether the diagnostic criteria of DSM-5 were able to differentiate between non-pathological religious possession and dissociative identity disorder (DID). DID is defined as a disruption in identity characterized by a discontinuity in one’s sense of self with alterations in affect, behavior, memory, consciousness, cognition, perception and sensorimotor functioning. This study suggested that DSM-5 criteria failed to address the ambiguity of affect surrounding possession experiences [18].

Trauma

However, dissociative phenomena are not necessarily pathological and may be a part of cultural expressions associated with different systems of religious meaning. They also may represent dissociative reactions as a response to stress or trauma [19,20]. There is a current evidence for the relationship between traumatic experiences and spirit possession. It is a considerable phenomenon occurring worldwide. A recent review showed a strong association between trauma exposure and spirit possession with high prevalence rates found in post-war areas in Africa [21].

Agency

A new psychopathological approach relates trance states and possession states to the concept of agency, or the ‘ability of an individual to act.’ Agency refers to feeling a sense of being able to do something in the world that is your own. The term possession can indicate a process, in which a person experiences a displacement of his/her ‘own agency’ by that of another. This is normally an unpleasant/unwanted phenomenon and often manifests itself in stark changes in behavior, impairment in functioning, and distress [22].

Schizophrenia and religion

Evidence suggests that religious belief can act as both a risk and protective factor for psychosis, since there is interplay with symptoms of schizophrenia, such as hallucinations and delusions. For the individuals affected by schizophrenia, there may exist many connections between their religiosity and mental health, including the decision to access help, severity of symptoms, coping strategies, engagement, and adherence to treatment [15]. Patients from communities characterized by higher tolerance for religious delusions may be less stigmatized, but this tolerance may prolong the duration of untreated psychosis (DUP). Furthermore, religious coping is clinically important and can have negative or positive impact on mental health of these patients [23]. In South Africa, for example, traditional healers play an important role in the delivery of mental health care [24]. Since adherence to treatment may be influenced by religious beliefs, it may be helpful to educate spiritual leaders about mental illness in order to involve them in community services for optimizing care and treatment adherence [23]. Wen (1998) found that 75.6% of first-episode schizophrenia cases in Taiwan sought help from shamans, Taoist priests, and 25% of them described experiences of spirit possession [25].
Psychopathological aspects of schizophrenia, such as delusions and hallucinations, can be influenced by patients’ cultural and religious experiences. In fact, religious delusions and hallucinations commonly take on religious themes (prayer, sin, possession) or religious figures (e.g., God, Jesus, devil, Prophets) [15]. For instance, in a recent observational study on a Hindu population of schizophrenia patients it was found that premorbid private religious practices like private praying, watching religious programs, reading religious books and praying before/after meals, were significantly more common among those patients reporting religious delusions compared to those without, and that the presence of mystic delusions increased the duration of untreated psychosis [7].

Conclusion

Religion and psychiatry have been connected for centuries and they share functions, values and some explanatory models. Both of them can be considered different ways of explaining the unknown, of responding to questions about the meaning of life, and two different ways of bringing healing. Religious beliefs may affect behaviors and may be seen in psychopathological continuum with overvalued ideas and delusions. Also, there is an overlapping between psychiatry and religion in all possession states described in the literature and in many cultures. Mental health professionals and religious believers require criteria to work out what counts as adaptive, and maladaptive, expressions of religious experience.

Disclosure statement

The authors certify that they have no interests in the subject matter or materials discussed in this manuscript.

References


Radicalization and mental health

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ABSTRACT

Background: Although radicalization is invoked to explain how people become terrorists, there is little empirical evidence.
Aims: To set out the approaches to understanding radicalization, ethical and definitional issues, and how public health approaches may help.
Methods: A non-systematic narrative review.
Results: Radicalization is proposed to explain how people become terrorists. Factors such as social connections, political engagement, group belonging, mental illnesses, and other social and cultural influence show a complex interplay that we are still trying to understand. Common
mental illnesses appear to be a risk factor at a population level for developing extremist beliefs, and psychoses and autism are reported as more common amongst some terrorist offenders. The activation of stereotypical and reactive fears and fantasies may distort our understanding of how to prevent radicalization and terrorism.

**Conclusions:** A public health framework offers a societal, inclusive, and positive approach to preventing radicalization, alongside criminal justice actions.

**KEYWORDS** Radicalization; mental illness; public health; risk and protective factors

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**Definitions and context**

Radicalization is a process by which ordinary citizens in high-income countries, usually of ethnic minority status (first, second or subsequent generations) seem to transform and commit themselves to terrorism [1,2]. The way the term radicalization is being used applies mostly to Islamist extremist groups, rather than all extremists. This has attracted criticism for overlooking violence more generally, and for stigmatizing Muslim people leading to Islamophobia, and for excluding Muslim people from the solution as citizens who also want to protect their homes and defend their faith against distorting messaging and political rhetoric of terrorists [3]. There is more attention to extremist violence from all ethnic groups now, and the far right are, it appears, on the rise in the EU not least as austerity seems to trigger concerns about resources and perceived threats from the ‘other’. The troubling aspect of radicalization processes is that people are living in relative wealth, at least not poverty, in relatively safe countries and have had education and exposure to the countries that they then decide to attack. This sense of the enemy within promotes anxiety and worry, and perhaps even collective paranoia; it certainly provokes a need to be thoughtful about how inter-cultural, inter-faith, and international groups are mediated and who these are regulated and toned within social, immigration, foreign and terrorist policies that governments evolve. Existing counter-terrorism intelligence and activities are largely centered on criminal justice systems analysis of convicted terrorists, and scientists that try to predict terrorist actions. Much energy is devoted to close supervision or observation of people linked to formal terrorist groups or known to be associated through networks, or indeed those espousing hatred and expressing terrorist views more publicly. Although threatening violence is an offence in British law, expressions of religious beliefs, which assert superiority or inferiority of other religious, cultural or ethnic groups, even if obviously prejudicial these can fall short of a criminal offence. So much radicalizing may be taking place through legal but provocative communications, and some through more obvious attempts to incite violence and hatred. There is little moderation of social media sites and persuasive technologies are actively curated by radicalizing influences [4,5]. Hateful extremist materials are available on the internet and in digital and social media. These can vicariously influence wider networks, but more likely these sites attract those searching for a cause or identity and are already thinking or feeling aggrieved by their position in the world. There is less moderation, suggestive that people are already forming these extremist beliefs as a precursor to more formal contact with organized terrorist cells, or before commitment to actually commit a terrorist offence.

**Radicalizing influences and public health**

How people move from indifference to a position of preliminary interest in extremist attitudes and then adoption of them is critical to understand the process of radicalization. Several studies have attempted to conceptualize the stages of radicalization [1,2,6-11]. Bhui et al. have previously proposed a public health framework for understanding radicalization, from early indicators to later signals, and that shifting population risk factors may be a better way of reduced the pool of people from whom recruits might emerge [12]. The expectation of health service staff to play a role in preventing radicalization [13] is also alarming some, yet calls for better empirical research into how mental health might affect people to make them more or less vulnerable to terrorism [14].

Silber and Bhatt [https://sethgodin.typepad.com/seths_blog/files/NYPD_Report-Radicalization_in_the_West.pdf] studied the 9/11 atrocity and suggest a typology for the process of radicalization; they propose phases of pre-radicalization, indoctrination, commitment, and then Jihadization. If a public health model is applied, then it is the pre-radicalization phase that becomes important for preventive actions. Mental health, along with other social and cultural influences, then are understood as potential risk and protective influences, or influences that moderate and modify chains of events, and loops that interact to take some down a pathway of terrorism, and others down other pathways, perhaps criminal offending, or perhaps gang membership or even legitimate political protest along with campaigning through democratic means.

**Mental illness**

So is mental illness relevant? Some argue even mentioning it stigmatizes people with mental illness and risks more prejudice towards them; others fear that this seems to propose some mitigation or understanding of terrorism which is not justifiable and may perhaps make terrorism seem like an illness less worthy of the full force of the criminal justice system. We established an early link with depressive symptoms, and have since progressed this research to identify how social and political processes may operate [15-17]. Depressive symptoms, criminal histories, low levels of social contact, a lack of political engagement all seem like risk factors, as was being born in the UK. Yet positive social support and political engagement including giving money to charity appears protective, although these data are from cross sectional study, so reverse causality is a possible explanation. Nonetheless, since our early work, others have shown that for some, lone actors in particular [18],
mental illnesses may indeed be relevant as being a susceptibility factor for the actions of persuasive radicalizing influences. Psychoses and autism were implicated, although the lone actors were not that isolated and were not showing signs of being secretive or avoiding detection, indeed they leaked information a long way ahead of the terrorist acts [19]. There is much debate about the relationship between mental illness and violence in general and mental illnesses in soldiers returning from war [20–22] and that mental illnesses are found in a third of convicted murderers, but only 10% in one study were ill at the time of the offence [23]. It is possible, that mental illnesses emerge after committing violent offences. Depressive symptoms were less common in those lone actors, so better fit our model of public health [18]. Depression is heightened by psychosocial stressors and by experiences of discrimination [24–26]. Yet, in our study, we found discrimination was not a relevant correlate of extremist beliefs, and nor was religious practice [15–16], emphasizing the need for empirical verification of the underlying basis of policies and practices. Our findings of low social contact and political engagement in those holding more extreme attitudes also speaks to better social policy of cohesion and cultural integration and citizenship models that are inclusive and do not create suspect communities.

Emotion, fantasy, and strategy: emotionally intelligent leadership

Studying or researching a radicalization as a process includes a number of outcomes: no violence, or a range of other behaviors including criminal offending, or active political protest that is legitimate, or violent offending. Studies of these processes in a cohort study or experimental design are clearly untenable, and even unethical, given the potential adverse consequences and the rarity of extremist terrorist actions. Studies of terrorism in general, and studies of early phases of radicalization, generate much moral panic. A fear that the activity of research may worsen inter-group relations, stigmatize individuals and groups, make matters worse and lead to conflict and argument, and that it may even encourage radicalization by giving it the legitimacy of an academic debate as if we were debating other health outcomes like smoking cessation or teenage pregnancy [3]. Emotional reactions include fears about ones in-group being under threat, and fears about not being able to reconcile feisty disagreements. Such discussions can escalate to the activation of latent identities of historical past events by which the identity group defines itself, often of overcoming persecution and threat, so activating more paranoid, persecutory and survival responses. Inter-group (racial, religious, national, sexual) discrimination and prejudice and persecution has a long history, and many have tried to understand why. David Marriott’s On Black Men [27] gives a classical and historical account of black men being lynched, sexually mutilated, and feminized in the deep American South, raising the role of fantasies of black men’s bodies in White European and American cultural discourses as an influence on black identity [28]. The role of the imagined other in violence inflicting on the imagined other, through fantasy rather than reality, is evidenced using film and cultural analyses. This process may be relevant not only to terrorist group formulation and representation of the enemy, but also how counter-terrorism responses risk misalignment to attack an imagined enemy, invoking identities and intentions that are not empirically informed. How can this be possible? Elizabeth Young-Bruehl [29] has asserted that psychoanalytic concepts can be applied to better understand prejudice, within the context of destinies of desire, a belief and ideology that is powerful and erotic even. She argues these ideologies link or bridge an imagined and idealized past with a desire for an imagined restoration of power and authority and protections in the future. She invokes, dissociative or hysterical mechanisms, suggesting these operate in the unconscious and as a consequence can result in deep violence to the ‘other’ who is perceived to be a persecutor.

Thus, our political leaders, and policy makers, must be able to dispel myth and fantasy, seek empirical evidence, and distinguish between qualities of evidence and the failures of predictive science when applied to terrorism [18,30] not least as broader understanding of mental illnesses are poor, with conflation of diagnostic categories and implications. A more nuanced, thoughtful, and refined research approach is needed. This should improve better assess specific diagnostic groups or symptoms of mental illnesses using validated questionnaires. The stage of the process, from ordinary citizen, exposure to or adoption of extremist thinking, and then subjugation to radicalization forces (digital or personal), or engagement with terrorist organizations and or a commitment to a violent act alone. Furthermore, the type of outcome being considered, violent or non-violent progression along the pathway to terrorism, need to be linked to both types of mental illness (or its absence) and the stage of the process. Social and cultural influences also need to be considered as these are likely to vary from country to country. Mental illnesses can be relevant, and psychological distress can be a risk factor for early or late stages of radicalization processes; yet the majority of terrorist acts are committed in the absence of mental illness and might be better understood as political violence. Given the nature of emotional distress early in the life course, and the need to reduce risk factors for radicalization early in the life course, public health and life course approaches may be helpful as universal interventions. These would have the advantage of also having positive outcomes on a number of other non-radicalizing or terrorism related domains.

Conclusion

Radicalization is complex societal problem and needs research and policy at all stages of the process, including public health and criminal justice emphases. Any research must better understand the cultural variables that are being proposed and ensure careful research methods include public perspectives and deeper insights across a range of socio-cultural contexts and ethnic and cultural groups. Leadership is essential to research and deliver evidence-based policy, to...
ensure empirical evidence is pursued, and that policy is not based on fear or socially powerful fantasies provoked by the sense of threat and moral panic induced by terrorist atrocities. The role of health services, and public agencies, need careful and thoughtful reappraisal as one element of a resilient systems response.

Disclosure statement

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Shame, culture and mental health

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ABSTRACT

Background: Shame is a powerful negative emotion, associated with many mental disorders, both as an etiological factor and as a consequence affecting symptoms, psychological defences, and therapeutic outcomes.

Aim: To summarize some of the findings to date regarding cultural influences on the role of shame within mental disorders.

Method: This lecture explores the concept of shame and its impact on mental disorders from a transcultural perspective.

Results: Whilst there has been growing interest in recent years in the role of shame in mental disorders, there has been little research examining the links between shame, mental health and culture. Guilt and shame are often used interchangeably, but there are differences in their respective meanings in different cultures.

Conclusions: Addressing patients’ experiences of shame is an important part of culturally competent treatment of mental disorders.

KEYWORDS Culture; shame; guilt; mental disorders

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Culture and emotions

The relationship of emotions and culture is much debated. However, there is general consensus amongst researchers from many fields that there exist primary emotions that are biologically driven and emerge within the first year of life [1]. Although the list of basic emotions varies somewhat in the literature, they usually include anger, fear, happiness, sadness, surprise, lust, and disgust. By definition, these emotions should occur across cultures, and are similar in their subjective experience, expression and function, serving the evolutionary demands of physical survival and reproduction. Secondary, or ‘self-conscious’, emotions develop later in childhood, usually towards the end of the second year, and require a greater cognitive capacity and an awareness of self in relation to other. Secondary emotions show substantial differences across cultures in their antecedents, internal experience and expression according to the values and morals of the particular culture and what is deemed acceptable behavior. Self-conscious emotions include pride, shame, guilt and embarrassment.

Shame versus guilt

Although the terms shame and guilt are often used interchangeably, they are distinct emotional states with different evolutionary, biological and psycho-developmental origins and functions. Guilt is the awareness of having done something bad, a feeling of responsibility or remorse for an offense, crime or wrong that the person has committed, whether real or imagined. Shame is a sense of falling short of the standards and ideals of oneself or others, making the person feel small, inferior, or worthless. In guilt, the focus of negative evaluation is on the behavior, whereas shame is focused on the self and is experienced as painful and pervasive, affecting how the individual feels about the core of his identity, which needs to be hidden. Shame is a more primitive and narcissistic emotion, whereas guilt requires a capacity for empathy and concern for others.

Shame and guilt cultures

Cross-cultural research studies on shame and guilt have shown that there are differences in their respective meanings, experiences and behaviors in different cultures. Cultures which prioritize the collective over the individual, such as those in more traditional Eastern countries, including India, China and Japan, have been described as ‘shame societies’, where shame is a collective phenomenon and the shameful behavior of an individual risks shaming the whole community. In contrast, more Westernized countries characterized by more individualistic cultures have been described as ‘guilt societies’. In a shame society, the primary device for maintaining social order is the inculcation of shame and threat of ostracism of the individual from the group. A guilt society is one in which social control is maintained by creating and reinforcing feelings of guilt and fears of punishment for unacceptable behaviors.

Feelings of shame are reinforced in countries such as Japan and China, where it is viewed as a pro-social device promoting group cohesion and preventing social disintegration. In India, shame may be considered a healthy emotion and protects against rage [2]. In China, shame is regarded as an important moral aspect and having a sense of shame is advocated [3,4]. Shame cultures may be characterized by specific “honor codes”, often associated with strict gender roles and behaviors, which, if transgressed, result in shame and violence. These cultural differences have been demonstrated between different ethnic groups within the same country. For example, Ratanasiripong (1997) [5] found that US Asian-Americans’ experiences of shame were both more frequent and prevalent than those of European-Americans.

Shame, mental disorder, and culture

In mental health, shame is a transdiagnostic phenomenon [6] and is linked to many forms of psychopathology, including depression, anxiety, social phobia, post-traumatic stress disorder, eating disorders, substance misuse, certain personality disorders such as borderline and narcissistic, eating disorders, and body dysmorphic disorder. Differences in how shame is viewed and manifests in different cultures have been shown to impact on how individuals suffering from these mental disorders within a particular culture experience their illness, its symptomatology, and sense of stigma [7].

Depression is one of the most important mental disorders where shame is a prominent feature of symptoms. A meta-analytic review in 2011 of 108 studies examining shame, guilt and depressive symptoms showing that shame had significantly stronger associations with depressive symptoms than guilt [1]. It has been well documented that although core symptoms of depression such as low mood, biological symptoms of changes in sleep and appetite are similar across cultures, the presence or absence of symptoms of feelings of shame and guilt in depression varies across cultures [8]. Feelings of guilt in depression are more common in Western countries, a finding that has been linked to the influence of Christianity, whereas shame in depression has been found to be more prevalent in socio-centric societies, such as North India [9].

Cultural differences in experiences of shame related to the stigma of having depression, which is a barrier to recovery, have also been demonstrated. In one recent study of a sample of Canadian university students, those of Asian origin reported greater levels of stigma related to familial shame compared to students of European origin [10]. Another study examining beliefs about depression as a function of ethnic background and age in a sample of British Bangladeshis versus British Whites showed that older British Bangladeshis were more likely to believe depression was an illness that brought a sense of shame and loss of dignity to the individual and his or her family [11].

Other psychiatric disorders in which there are powerful feelings of shame include social anxiety and social phobia, which are characterized by a fear of exposure to others linked to feelings of shame and resulting in social isolation,
which may become shameful in itself. Zhong et al. (2008) [12], in a study examining the relationship between experiences of shame, personality structure and social anxiety in Chinese and American college students, found that shame was a mediator between personality traits and social anxiety in the Chinese sample, a finding not seen in the American students, supporting the hypothesis that shame has a more important effect on social anxiety in Chinese culture compared to its effect on Americans.

Shame may also be a prominent feature of certain etiological factors associated with mental disorders. Of these, sexual abuse in childhood has been the most researched and has been linked with the later onset of many mental disorders including eating disorders, personality disorders, posttraumatic stress disorder, depression and substance abuse [13]. Experiences of sexual abuse are minimized or denied in some cultures, leaving victims isolated with feelings of shame and confusion, or in more extreme cases vulnerable to ostracism by society or the target of retributive violence culminating in honor killings.

Culturally competent psychotherapeutic treatment of shame

In the treatment of mental disorders and psychological difficulties where shame is prominent, clinicians and therapists need to recognize such feelings and be sensitive as to how to address them in treatment. To talk about shameful feelings within a therapeutic relationship can in itself be experienced as shameful. For the therapist to work with the patient it is crucial to have some knowledge and understanding of the cultural factors that have precipitated, shaped and perpetuate the patient's shame. Cultural differences are not only relevant to macro-cultures such as individualist or collectivist societies, but also to micro-cultures, such as minority ethnic groups, or membership of a criminal gang.

It is important to recognize how the strategies and behaviors that patients employ to defend against feelings of shame, may be influenced by culture. In societies which stigmatize mental illness as weakness, to avoid bringing shame and loss of dignity on their family and community, individuals may become secretive or untruthful about their mental distress, or socially withdrawn and isolated. Persons with personality difficulties or disorders who find it difficult to modulate their impulses and affects may react to feelings of shame by self-harm, or anger and aggression towards others, which is sometimes referred to as 'humiliated fury'. A recent study indicated that humiliated fury is not universal, but influenced by culture, by demonstrating that American students were more likely to report shame related anger in response to shame situations, than Japanese participants [14].

Finally, it is important to acknowledge one's own feelings of shame which may become evident when working with patients, and to be aware of our own cultural biases in the generation of such feelings and how these may impact on working with patients from different cultural backgrounds.

Disclosure statement

No interest to declare.

References


Transcultural aspects of eating disorders and body image disturbance

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Abstract

Aim: To describe some key areas in the transcultural aspects of eating disorders (ED) and body image disturbance (BID).

Method: This lecture describes a different and complementary manner of understanding eating disorders,
specifically anorexia nervosa (AN), from a cultural, social and psychoanalytic perspective.

**Results:** Social norms vary massively within cultures, social strata, ethnicity and gender. Social norms also vary over time leading to substantial changes in body shape preferences and the epidemiology of eating disorders.

**Conclusions:** Understanding eating disorders, requires integration of psychological factors into a cultural and epidemiological context.

**KEYWORDS** Feeding and eating disorders; anorexia nervosa; bulimia nervosa; culture; body image

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Eating disorders and culture bound syndromes

Anorexia Nervosa (AN), along with the other eating disorders, has excited intellectual discourse in academic psychiatry for decades. Unlike the majority of “culture bound syndromes”, it is one of the few initially conceptualised as “culture bound” to North America/Europe. Diagnoses have proliferated. First AN emerged, then Bulimia Nervosa (BN), described by Gerald Russell as recently as 1979 [1], then Binge Eating Disorder (BED), and Eating Disorder not Otherwise Specified (EDNOS)/Atypical, defined and redefined, including Other Specified Feeding or Eating Disorder (OSFED). This proliferation is seen as an “exemplar of the cultural mediation of illness presentation, experience and pathogenesis” [2].

The cultural mediation of eating disorders

Evidence exists in many spheres for the cultural mediation of body image and risk of eating disorder. Social norms vary massively within cultures-class, ethnicity and gender. Over time there have been substantial changes in body shape preferences (e.g. in USA), with fluctuating preferences for “curvaceous and tubular” body shapes [3]. Research in Fiji has shown the cultural mediation of body size ideals and their plasticity over time, specifically following the introduction of TV and the concomitant emergence of disordered eating attitudes and behaviors [4]. This has been replicated in Bhutan, the last country in the world to be exposed to TV, with evidence of subsequent pressure to get thinner, look thinner, and regulate one’s appearance from media, more so than from one’s own peer group. As a result, there are “comparable levels of body dissatisfaction to the USA” [5].

What links are there between this cultural premium on thinness and disordered eating? Much research points to a link between “the internalization of a thin ideal, body dissatisfaction and disordered eating”.

Two influential models

There are two important theoretical models, both of which relate socio-culturally mediated body weight ideals to the pathogenesis of EDs, via body dissatisfaction.

The first concerns the dual-pathway model" (Figure 1) [6]. This model attempts to synthesize three prominent etiological theories that have been advanced to explain the emergence of bulimic spectrum eating disorders, the socio-cultural model, the dietary restraint model, and the affect regulation model. In the dual-pathway model, internalization of an unrealistic thin ideal promotes the development of body dissatisfaction, which increases the risk for bulimic symptoms via the dual mechanisms of dietary restraint and negative affect. These mechanisms increase the risk of bulimic symptoms because eating may provide comfort and distraction from negative, unwanted emotions. Binge eating can counteract the discomfort of dietary restraint [6,7].

The second model is the tripartite influence model (Figure 2) This proposes that three primary sources of influence – parents, peers and media – all combine to contribute to the development of body image and eating disturbances. Additionally, the model suggests that at least two factors mediate the relationship between influences and disturbance – “appearance comparison” and “internalization of media information” [8]. Regional data from several countries and continents support the linkages from the tripartite model. The model also fits with evidence supporting the increased prevalence of EDs with increased exposure to global commerce and media via access to communications technology.

An example from South Africa

A good example of the way in which culture change is linked with the development and increased recognition of EDs comes from South Africa. Szabo and Allwood (2004) described how prior to 1993, no Black South Africans had been described in the eating disorder literature [9]. Intuitively, this was unexpected given the high rates of malnutrition. The first description in South Africa of ED in a black female was in 1993. By 2004, a decade after the change of regime, increasing prevalence was hypothesized, and studied. Szabo and Allwood conducted a study of teenage girls in a secondary school in Johannesburg, using the EAT-26 instrument. They found nearly identical prevalence figures in black and white students of 18.6% in black students and 18.7% in white students. The investigators concluded, “…with a seductive emphasis on consumerism, Western culture is indeed a powerful culture. …Assimilation of the associated Western value system, where physical appearance and self-worth are seemingly synonymous, seems inevitable” [9].

Heterogeneity of expression

Not all EDs are expressed in the same manner. In Hong Kong, a high proportion of “non-fat phobic AN” (NFP-AN) has been described [10], which is decreasing in importance as conventional AN, in line with ongoing cultural change in Hong Kong, becomes more prevalent. And in a UK gastrointestinal clinic population, there was a high prevalence of “atypical” AN, patients with all the features of “typical” AN, other than a denial of any wish to be thin. This group was found to have a worse prognosis than the comparison group of typical AN patients at
the Maudsley Hospital. In this study, “atypical” AN patients had very high rates of medical consultations, investigations, and usage of complementary/alternative practitioners [11].

**Cultural and political factors in the generation of scientific knowledge**

Our knowledge of the cultural factors in the epidemiology, prevalence and management of eating disorders is not reflected in the coverage of cultural factors in the generation of scientific knowledge. High impact journals under-represent 90% of the world’s population in published papers [12]. Mental Health is already marginalized and under-represented in the global Health agenda, and within that, EDs are themselves often marginal [13]. But there is substantial heterogeneity regarding attitudes towards food and body image, and the expression of ED’s within and between countries and ethnic groups. There have been, and continue to be, changes in the prevalence of EDs and within EDs. It is also clear that most research in EDs relates to women, mostly to women of fertile age and less to older women. Much less research relates to men and even less to trans populations [14].

**Where is the “Psycho” in biopsychosocial?**

But where is the psychological understanding of what goes on in the mind of a patient with AN or BN? As Culbert et al. have written: “The etiology of EDs likely involves a complex interplay of biopsychosocial effects “… “Most studies have exclusively focussed on… risk factors in young adult females, without … adopting a developmental perspective” [15].
A rich psychoanalytic and psychiatric literature on anorexia describes a multitude of psychic processes, defenses, and states of mind [16–19]. Anxieties about sexuality, greed, orality, genitalia, and oral impregnation; the role of the mother, the father, and the couple have all been hypothesized to be implicated in the development and maintenance of AN. In addition, external events—specifically actual or fantasied sexual intrusion—have also been invoked as important causal factors.

Family therapists have described a trans-generational conflict of loyalties and the families’ need to have a perfect child or family characteristics of enmeshment, overprotectiveness, rigidity, and lack of conflict resolution with a psychologically vulnerable child in a “psychosomatic family” [20].

**The “No entry” hypothesis**

The central defining features of AN all point to a problem with allowing things in, to what Gianna Williams has described as a “No Entry” system of defenses [21,22]. Williams, working at the Tavistock clinic in London, mainly with adolescents coined the term “No Entry”. By this she refers to the signs and behaviors that many patients with anorexia may manifest. Her proposal is that as infants, young people who develop an eating disorder have been the recipients of the powerful projections of their parents, particularly their mothers [21]. Such patients have not only lacked containment, but also perceived themselves as receptacles of un-metabolized phantasies and experiences projected into them by their parents.

This line of thinking derives from Bion’s notion of containment, according to which one of the functions of the mother is to receive and modify the projections of the infant [23]. Such maternal containment may fail under certain circumstances and the child is then left to re-introject its own anxieties, unmodified and not understood. In addition, the mother may well project her own disturbed feelings into the child. The refusal to take in food is viewed as a misguided defense against taking in the unbearable feelings projected by the parent.

This theory makes sense clinically; it not only describes the anxieties in the anorexic about allowing anything in to the mouth/mind/other orifices, and the intense need for control and blocking of outside intrusions. It also helps explain the sort of countertransference frustrations felt, and sometimes acted on, by those in the presence of an anorexic patient—the wish to force something in, to breach the “no entry system of defenses”, or to give up in a state of impotence.

**Conclusions**

In conclusion, there are two complementary challenges. For those working in transcultural psychiatry, the challenge is to not forget about or ignore the internal reasons why certain people may be more and others less prone to developing and maintaining ED’s. Which psychological and psychodynamic factors might help to explain why some Fijians/Americans/Swedes develop AN or BN, and others not? The other challenge, for psychologists and psychotherapists, is to remain constantly alert to cultural factors in their patients. Such include the role of culture, ethnicity, social class, religion, and other belief systems both in the patient, his/her family and network, and in the therapist. It is this complementary approach—respect for the societal and the internal factors, conscious and unconscious—that makes both academic and clinical work with this patient group so fascinating and potentially rewarding.

**Disclosure statement**

No interest to declare.

**References**

Sexual variation and mental health

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ABSTRACT
Background: Cultures play a significant role not only in the causation and management of emotional distress and psychiatric disorders but also in sexual variation and attitudes towards sexual minority groups.

Aim: To discuss the potential impact of culture on sexual minorities.

Method: This lecture reviews the relation between sexuality, culture and mental health.

Results: Cultures define what is deviant and unacceptable or even illegal. Attitudes to sex, perceived role of and actual sexual activity are very strongly influenced by cultural values. Cultures may see sexual activity as largely procreative (sex-negative) or as a pleasurable (sex-positive) activity. Furthermore, gender roles and gender role expectations influence relationships between different-sex partners. Although epidemiological data on prevalence of sexual minorities across cultures are scanty, it may reflect underlying attitudes to minority groups.

Conclusions: It is crucial that clinicians are aware of the role that culture plays in acceptance or rejection of sexual minorities.

KEYWORDS Culture; sexual variation; sexual minorities; homosexuality

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Introduction

Nature of sexual variation is related to what has been seen as deviant or variant desires. These include various conditions, some of which are simple variations whereas others are pathological extremes. There is no doubt, cultures influence definitions of normality and deviation, which then becomes a legal matter. Once the culture has decided what is abnormal, then legal templates are often used to make the behavior illegal so that the behavior gets managed in legal rather than medical system. Legal status of a behavior will also determine whether individual seeks help from medical sources or not or whether treatment is given compulsorily. Sexual orientation and behavior are affected by sexual feelings, gender identity, bodily differences, reproductive capacities and interest as well as sexual needs, fantasies, and desires.

Background

Cultures have also been divided into sex positive and sex negative cultures [1]. In sex-positive societies, main purpose of sexual activity is seen as receiving and giving pleasure whereas in sex-negative societies, sexual activity is largely for procreative purposes. Of course, cultures are not static and many sex positive cultures over centuries have become sex negative and vice versa. These attitudes will be affected by a number of factors. Therefore, it is inevitable that cultures will determine attitudes to sexuality, sexual minorities and sexual dysfunction and variation.

Definitions

Sexual variation or sexual minorities are defined in relationship to gender identity or sexual attraction. Various terms illustrate sexual minorities or sexual variations. Lesbian, gay, bisexual, transgender and queer/GSM (gender and sexual minorities/DSG: diverse gender and sexualities). Another broad term used is Quiltbag: queer (questioning), undecided, intersex, lesbian, bisexual, asexual (allied) and gay. Sexual and gender fluidity indicate a fluctuating mix of options available. Of particular interest are those who question and explore their own sexual orientations. A pansexual person is someone who experiences sexual, romantic, physical or spiritual attractions for members of all gender identities and expressions. A person whose gender identity, gender expression and biological sex all align is cisgender whereas transgender is a blanket term for all those who are not cisgender. Homophobia – though technically not a clinical phobia – consists of irrational fear and hatred heterosexual people may feel towards homosexual individuals. It may be internal or external. Similar negative attitudes towards bisexual and trans people can produce discriminatory actions.

Attitudes towards sexual orientation and identity as well as sexual variation are strongly influenced by social attitudes to masculinity. It can be hypothesized that feminine cultures [2] such as Scandinavian cultures may well be more tolerant of sexual variations. Other factors such as social expectations of gender roles may well contribute to negative attitudes or homophobia/bi-phobia or transphobia. In many cultures such as the Sambia [3] and hijras in India, such attitudes are culturally accepted [4]. It is also likely that people in sex positive cultures may well have higher rates of paraphilias in comparison with sex negative cultures although robust data are not available [5].

Prevalence

In any given population, it can be difficult to determine accurate numbers of non-heterosexual individuals, since these depend upon the methods used for identification and other factors including self-identification and objective
assessment across various domains. Prevalence rates are said to vary between 1% and 16% [6]. These authors suggest that by age 28, 2% men and 4% women identify their sexual orientation as gay, lesbian or bisexual, whereas 6% of men and 20% women claimed that they were not exclusively heterosexual.

Mental ill health

Minority stress experienced by minorities, whether they are sexual or ethnic or religious, can contribute to a sense of bewilderment, frustration, alienation and possibly anger. While growing up, individuals with a minority status may realize that they are not being accepted. This will hit their self-worth and self-esteem, which may contribute to higher levels of depression. As a result, they may feel less valued. By internalizing negative experiences, they may experience depression and anxiety, thereby increasing their vulnerabilities and risks.

Those individuals with alternate sexuality or belonging to sexual minority tend to navigate their lives differently. The associated stresses increase their likelihood of developing mental ill-health. Higher rates of anxiety and depression have been shown in sexual minorities in Australia [7]. Sexually variant women also showed higher rates of suicidal ideation, self-harm, and attempted suicide [7,8].

In an interesting series of studies, Hatzenbuehler et al. (2009) investigated the modifying effect of state-level policies on the association between mental health and sexuality [9]. In a survey of 34,653 participants of whom 577 were identified as LGBT individuals, psychiatric co-morbidity among LGBT individuals was 3.5 times higher in comparison with self-identified heterosexual individuals. Not surprisingly, those states with no policies of protection to LGBT individuals, i.e. which did not have policies of equality, showed higher rates. Rates of any mood disorder were twice (20.4%) in comparison with heterosexual sample (10.2%), as were anxiety disorder (30.1% versus 16.1%) and substance abuse (40.8% versus 20.9% heterosexuals). But alcohol use was even higher at 2.5 times. In a subsequent study [10], the same group noted that once the state had approved and legalized same-sex marriage, there was a clear and significant decrease in mental health care and hospital visits related to physical ill-health in sexual minority men, when compared with data 12 months prior to legalization. This confirms a clear role of social factors. In a further study in the USA, these authors [11] reported that higher levels of local approval of same-sex marriage lowered the probability that LGBT (and non-LGBT) individuals reported smoking and fair/poor self-rated health. Interestingly, LGBT disparities in smoking were lower in communities where residents were most likely to support same-sex marriage. This indicates that social factors contribute in a significant way to rates of smoking and psychiatric disorders.

Around the globe, 72 countries are using laws which make same-sex behavior illegal. Attitudes to alternate sexuality among doctors are related to age, ethnicity, experience and speciality [12]. A study of 428 medical students (50% male) showed that although the majority of the sample held positive views, a significant proportion (10-15%) held very negative views. It appeared that religious views molded negative views [13]. It is important to explore and understand the attitudes of medical students, because these future doctors need to manage their own negative attitudes while dealing with patients from sexual minorities. A recent study from India has shown that of 270 students who responded, 22% felt that homosexuals were neurotic, 28% thought homosexuals were promiscuous; 8% thought homosexuals posed danger to children and surprisingly 16% saw homosexuality as an illness [14]. From Paraguay, Torres et al. (2018) studied 77 medical students using a questionnaire [15]. Over a quarter (28.6%) showed negative score in their attitudes to homosexuality. More positive scores were reported if they had at least one gay friend. The question, therefore, arises for this sample whether the positive attitudes came first or whether friendship with gay individuals came first, which may well show positive and open-minded attitudes.

Whether an individual is gay, bisexual or trans, at some stage they all have to acknowledge their sexual variation in a public way. This process of coming out is critical in development of the self and functioning suitably. Coming out means acknowledging own sexuality to others. The process can be stressful and may well last a long time. There are several stages. The first stage concerns acknowledging to oneself. Generally, the next stage concerns acknowledging to significant others, most likely first a friend and then family or colleagues. Most people find it easier to come out to their siblings first before coming out to their parents. Again, there are clear cultural differences. People may use strategies in hiding their sexual orientation and pretend to be heterosexual using a number of means and methods. Within a gay or lesbian couple, the two individuals may well be at different stages of coming out. This can create tensions between both partners.

Clinicians need to be aware of these broad areas of sexual variation from theoretical and clinical perspectives and should be willing to explore these with their patients when necessary. Patients and clinicians may well feel transference and counter-transference related to sexual orientation. It is difficult to know whether under these circumstances, clinicians should disclose their own orientation. There are both advantages and disadvantages in doing that. The decision will depend upon individual circumstances.

Conclusions

The rapid movement of people, resources, and acculturation as a result of exposure to social media raises important issues for assessment and management of individuals who may belong to sexual minority. Attitudes towards sexual activity and procreation will also influence acknowledgement and help-seeking. Clinicians need to be open-minded during their assessments and develop therapeutic strategies adjusted to the problems patients from sexual minorities may face.
Discourse statement

No interest to declare.

References


Ethnopharmacology

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ABSTRACT

Background: Ethnopharmacology relates to the study of substances used medicinally by different ethnic of cultural groups or handling of, drugs-based ethnicity or pharmacogenetics.

Aims: To review key aspects of ethnopharmacology.

Method: This lecture gives an overview over the relationship between geography, culture, pharmacogenomics and prescribing.

Results: Although the majority of antipsychotics, antidepressants and mood-stabilisers are widely and cheaply available in generic forms, prescription rates can vary. Clozapine is one such example with prescribing-rates ranging from less than 10 patients per 100,000 population to nearly 190 patients/100,000 population. Pharmacogenetic studies of antipsychotics and antidepressants concern gene polymorphisms that may affect both, pharmacodynamic or pharmacokinetic properties. Considerable genetic and ethnic variability has been shown for the P450 microsomal enzymes CYP 2D6 and 1A2.

Conclusions: With accelerated global mobility and increased understanding of medicinal substances at molecular level, understanding of ethnopharmacology will become increasingly important in routine clinical practice.

KEYWORDS Ethnopharmacology; pharmacogenomics; CYP; antipsychotics; antidepressants

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Introduction

The subject of ethnopharmacology encompasses two distinct areas of study: substances used medicinally by different ethnic of cultural groups (e.g. folk remedies); and differences in response to, or handing of, drugs-based ethnicity or pharmacogenetics. Both aspects share the same promise of step-change advances in pharmacotherapy but neither has yet delivered on this expectation.

Ethnopharmacology – geography, culture, and prescribing

The treatment of psychiatric disorders is perhaps somewhat uniform around the world. The majority of antipsychotics, antidepressants and mood-stabilizers have long since lost any patent protection and are widely and cheaply available in generic forms. Uniform availability does not, however, always assure uniform prescription rates. A good example here is the use of clozapine. Christian Bachmann and colleagues collected data on clozapine prescribing in 17 countries [1]. The rate of prescribing ranged from less than 10 patients per 100,000 population to nearly 190/100,000. More striking than this variation was the varied pattern of clozapine prescribing in each country. Lithuania, the highest user of clozapine, showed perhaps the expected pattern: minimal use in those aged under 19 and over 80 years and peak use in those in middle age. The United States and Sweden showed usage if a similar pattern of Lithuania but with something of a right-shift because of higher rates of prescribing in the 50+ group.

The reasons for the wide differences in overall use and in patterns of use are far from clear. One obvious influence is...
the time of introduction of clozapine. For example, clozapine has been available in Japan for only a few years, so one would perhaps not expect widespread prescribing. Another factor is the differences in regulations relating to clozapine prescribing. A study conducted in 2016 [2] found significant variation in regulations for clozapine use across nine countries. Differences were found in licensed indications, frequency of blood monitoring, thresholds for stopping clozapine, definition of treatment resistance and even licensed dose range. Tacit recognition of the power of regulations to restrain clozapine use is provided by the introduction of the REMS (Risk Evaluation and Mitigation Strategy) in the USA – one of the lowest uses of clozapine in the Bachmann study. This scheme replaced all individual patient registries in an attempt to assure safe use and promote wider use of clozapine [3].

Aside from clozapine use, perhaps the best example of cultural variation in psychotropic use is that the St John’s Word [4,5] – a natural product of variable content used extensively in Germany and northern Europe but much less so elsewhere.

**Ethnopharmacology – pharmacogenetics**

The concept of prescribing according to pharmacogenetics characteristics offers the prospect of improved efficacy and tolerability as a result of targeted interventions. Efforts have been made to identify genetic factors associated with treatment response. This would allow specific drugs to be used in specific patients with a high likelihood of response. Where variation in response was found to be linked to receptor genotype, this would provide insight into the mode of action of the drug.

A review of studies examining clozapine response [6] identified numerous gene polymorphisms associated with good outcome. These included gene polymorphisms to D1, D2, D3, and D4 receptors as well as those for 5HT2A, 5HT2C, and 5HT6 receptors and numerous glutamine transporter genes. The high number of statistically significant associations may owe as much to the repeated application of statistical tests as to true associations. The same is true of clozapine and agranulocytosis where at least six gene polymorphisms were identified as being linked to this adverse effect. And likewise, olanzapine response where gene polymorphism associations were reported for six genes (COMT, D3 (2 polymorphisms), GRM3, 5HTT, and MDR1).

The associations discovered so far have not as yet led to any change in the way clozapine or olanzapine are prescribed. The most startling differences in outcome according to genotype have been identified for the antipsychotic iloperidone. In a controlled study versus ziprasidone [7], patients were grouped according to response to iloperidone and combinations of six marker genes. The group with the most favorable combination showed as response rate of 75%, those with the least favorable just over 10%. The same group [8] identified different genetic markets linked to iloperidone’s effect on the QT interval. Other studies have found 13 polymorphisms of a gene linked to antipsychotic-associated weight gain [9].

In the most recent study [10], 2413 patients were randomly assigned an individual antipsychotic treatment and genome-wide associations were investigated. Five new gene loci were found to be linked to response, most of these being related to synaptic function. Nonetheless, the authors of this study declared that their results had “scant clinical utility” at least at present.

Attempts to discover genetic predictors of response to antidepressants have also been somewhat unproductive. Combined results from three studies (GENDEP, MARS and STAR*D) were unable to show any predictive associations despite testing 1.2 million polymorphisms [11]. A further attempt to pull out something from these expensive and publically funded trials [12] found little of note. Other workers suggest that SHT2A receptor polymorphisms predict response to antidepressants [13].

A somewhat better developed aspect of pharmacogenetics is the study of the role of genetic variation in cytochrome function and its relationship to drug dosing and response [14]. Cytochromes and other phase I enzymes (alcohol dehydrogenase, aldehyde dehydrogenase, etc.) are usually found in the liver but also function in the gut wall and in the brain. The speed with which cytochrome enzymes catalyze reactions (and therefore rate of metabolism) is genetically determined. In poor metabolizers, drug metabolism is slowed. Thus, poor metabolizers are more prone to adverse effects. Slower conversion to active metabolites can potentially also lower efficacy. In rapid metabolizers, drug metabolism is accelerated. Thus, drug elimination rates are increases, and rapid metabolizers may need higher doses to achieve efficacy. The table below shows the relative frequency of poor and ultra-rapid metabolizers by CYP2D6 in different ethnic groups [14](Table 1). As most SSRIs and many anti-psychotics, including risperidone and aripiprazole are substrates of CYP 2D6, a higher proportion of patients from African or Middle Eastern background may experience lower drug efficacy and require dose increases.

Another example is CYP 1A2, implicated for instance in the metabolism of clozapine and olanzapine. Asian and African populations may experience lower CYP 1A2 activity than Caucasians [14,15]. For instance, one study showed that Swedes had 1.5 times higher CYP 1A2 activity than Koreans [15,16]. Thus, a higher proportion of patients from Asian and African background may have an increased risk of adverse effects and require dose decreases. The rate of CYP 1A2 reduction may also be influenced by other inducers, such as tobacco smoke. However, 35–85% of the CYP 1A2 response variability may be due to genetic factors [15,17].

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Poor metabolizer (%)</th>
<th>Ultra-rapid metabolizer (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caucasian</td>
<td>6–10</td>
<td>1–10</td>
</tr>
<tr>
<td>Asian</td>
<td>0–2</td>
<td>1</td>
</tr>
<tr>
<td>African</td>
<td>5</td>
<td>5–29</td>
</tr>
<tr>
<td>Middle Eastern</td>
<td>1–2</td>
<td>21</td>
</tr>
<tr>
<td>Amerindian</td>
<td>2.2–2.4</td>
<td>0</td>
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</tbody>
</table>

### Table 1. Ethnic variation of the cytochrome P450 CYP 2D6 [14].
Conclusions
With accelerated global mobility and increased understanding of medicinal substances at molecular level, understanding of ethnopharmacology will become increasingly important in routine clinical practice. Ethnic variability of pharmacogenetics factors should be considered as a potential cause for unexpected lack of effectiveness or increased experience of adverse effects. Testing for genotype or phenotype would inform drug choice and drug dose both for CYP2D6 and CYP1A substrates and other substances subject to genetic variability.

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Placebo and cultural responses
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ABSTRACT
Background: Features of placebo response in medicine have been forgotten and ignored over the last decade.
Aim: To explore why patients do get better with placebo in spite of its perceived inertness.
Method: This lecture reviews the relation between illness perception, psychopharmacology and culture.
Results: Placebo response must be considered in the context of how patients perceive their experience of disease (illness) and through their own cultures which determine cognitive schema and explanatory model of illness. Most of the placebo response relies on the classical conditioning and expectancy of patients. Also, the color, size, formulation, cost of medications can affect the psychological response to any pharmacological treatment.
Conclusions: Modern psychopharmacology should consider placebo and cultural variations as relevant factors of treatment response.

KEYWORDS Placebo; placebo response; culture; ethno-psycho-pharmacology

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Introduction
Placebo has been largely considered for its inert content and used as control in several clinical trials. However, features of placebo response in medicine have been forgotten and ignored over the last decade.
Shapiro in 1968 [1] argued that placebo, as a therapy or component of any therapy, is used for its nonspecific, psycho-physiological effect in spite of any specific activity for the medical condition being treated. Brody in 1999 [2] defined placebo as a form of medical therapy, or an intervention designed to simulate medical therapy, believed to be inefficacious and efficacious at the same time. A recent articulated definition by Price et al. [3] claims that placebo response is the change in a symptom or condition that an individual or a group of individuals may present as a direct effect of placebo or spontaneous remission.

The use of the word ‘placebo’ in medicine dates from the end of the eighteenth century. The interest in placebo effects started growing since the adoption of the randomized controlled trials (RCTs) after 1950, when it was noticed that people improved, sometimes dramatically, in placebo control groups. Henry Beecher in his famous meta-analysis [4] “The Powerful Placebo” stated that more than 35% of patients responded positively to placebo treatment, and placebo effect was a scientific event attributable to possible neurobiological and psychological factors.

**Explanatory models**

**Neurobiological factors**

Recent studies have demonstrated that different neurotransmitter systems are involved in the placebo response. The endogenous opioid anti-nociceptive system is undoubtedly involved in placebo analgesia. In 1978, Levine [5] administered placebo as an analgesic for postoperative pain, observing a significant reduction in painful symptoms and a reversal of this response by the opioid antagonist naloxone. Also, it was found that β-endorphin levels were higher in the cerebrospinal fluid of placebo responders than non-responders [6]. In addition, the endocannabinoid system has been recently identified as a new non-opioid component of placebo analgesia [7]. It has been observed that the administration of placebo, proposed as an anti-Parkinsonian drug, can lead to an improvement in motor performances among patients with Parkinson’s disease. This effect may be mediated by the endogenous release of dopamine in the dorsal striatum, a critical component of the motor systems [8]. In fact, the ventral striatum, and in particular the nucleus accumbens, are involved in the reward circuit, mediating reinforcement and motivational responses. Activation of the ventral striatum should be present in any response to placebo and the release of dopamine would be linked to the expectation of reward rather than the reward itself [8,9].

**Psychological factors**

According to the Pavlovian conditioning paradigm, the body responds therapeutically to a neutral conditioned stimulus, as the placebo, which had been previously paired with an unconditioned stimulus (conditioned response) [10].

However, Siegel acknowledges that all placebo responses cannot readily be attributable to Pavlovian conditioning. Pharmacological conditioned responses often do not meet the drug effect, and people can have placebo responses without previous drug experience [11].

Expectancy is a robust and comprehensive model for the explanation of placebo effect and its triggering. Expectancy may be defined as a patient’s level of expectation that he/she will be helped by the treatment. Verbal instructions or suggestions are important factors in triggering an expectancy-induced placebo response among patients [12]. For example, from a study of expectancy and placebo analgesia, Pollo et al. concluded that different verbal instructions produce different outcomes, which led to a significant change of behavior and a significant reduction of opioid intake [12].

‘Self-efficacy’ is a related factor defined as the belief that one can successfully perform actions required to achieve valued outcomes. This psychological mechanism leads to a positive feedback and patients feel their illness experience is manageable [13].

In fact, Bandura argues that placebos may play an important role in boosting patients’ perceived self-efficacy in their abilities [14]. While most of the attention to expectancy and self-efficacy has focused on the patient, Bootzin and Caspi explicitly connect these concepts to the therapeutic relationship, arguing that the clinician plays an important role in charging the intervention with positive expectation by providing information, teaching skills, and having confidence in the treatment [13].

In addition, Kaptchuk [15] argues that, unlike conventional medicine in general, a consultation in complementary and alternative medicine tends to produce an alternative diagnosis that closely corresponds with clients’ viewpoints. The process of getting this diagnosis combined with an elaborate ritual of patient–practitioner interaction can help to generate powerful non-specific effects.

**Cultural responses**

There is a plenty of evidences showing that culture determines cognitive schema and also how individuals express and deal with distress [6]. Placebo response must be seen in the context of how patients perceive their illness experiences and based on their explanatory models. Both factors are strongly affected by cultures [16]. Also, there are several factors connected to culture influencing placebo effects and responses as reported below [16].

**Cost of medications**

Placebo-cost studies found that placebo was more effective when its stated cost was higher. Perhaps greater expectations, generated by higher costs, mediate a greater placebo response. Patients might consider lower costs as the equivalent of lower treatment efficacy [16].

**Color of medications**

The size and color of the tablets are influencing factors [16]. Blue is usually seen as depressant-sedative, and yellow as...
stimulant-antidepressant. That is the reason why blue preparations are generically more soothing; and red, pink or yellow are more stimulating [16]. De Craen et al. [17] confirmed that ‘stimulation’ are often associated with drugs marketed in hot colors (red, orange, yellow), and antidepressants are marketed in cold colors (blue, green, purple).

In an Italian study, it has been demonstrated that blue sleeping tablets, or blue placebo represented as sleeping tablets, worked better than tablets of other colors among women [18]. In addition, Ou et al. [19] noted that color-related emotions can differ across nationalities; for example, Chinese subjects preferred colors which they saw as clean, fresh or modern. Madden et al. [20] found that blue is a preferred color through the countries, but there is a variation across cultures on the meanings given to different colors.

**Preparation form:** Preparation forms (capsule or tablet, drops, injection) and size are other factors that may affect a therapeutic outcome. Buckalew and Coffield [21] found that capsules and injections are perceived as stronger if compared with tablets. In fact, they concluded that the overall response to anxiety treatments is better when patients are treated with capsules [21].

**Therapeutic Regimen**

It is possible to show a small difference in the outcome depending on the number of times per day that individuals take their placebos [17]. Patients on a more intense regimen might have felt they were receiving more treatment. This might have induced a psycho-physiological response.

**Nationalities**

It is possible to show a number of substantial and significant variations in the outcome of placebo response among the countries. Several studies show that the rate of placebo response is very low in Brazil and in northern Europe (Denmark, Netherlands). Placebo response rate in Germany is extremely high. Moerman [22] argued that these results might be due to substantial differences in the doctor-patient relationship and cultures through the countries. Ninnemann [23] raises some interesting points about the role of ethno-psychopharmacology in the explanation of placebo effects. There is no doubt that discussion of ethnic, racial differences and identities are charged with irrational emotions. The emphasis on genomics and development of psycho-pharmacogenomics raises some significant issues, and cultural differences therefore deserve further exploration in the cultural, sociological and anthropological contexts.

**Conclusions**

Placebo response is a relevant factor of patients’ treatment. It is important to improve our current knowledge on the neurobiological and psychological aspects that determine the placebo response. In addition, future research should be focused on how cultural differences contribute to different responses. It is important that researchers, funders and regulators take into account the potential impact of placebo. It is imperative that clinical trials take into account the potential impact of non-pharmacological aspects of medications [24].

**Disclosure statement**

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Reducing the stigma of long acting injectable antipsychotics – current concepts and future developments

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\textbf{ABSTRACT}

\textbf{Background:} Long acting injectable antipsychotics (LAI-APs) are considered a major advance in psychiatric treatment concerning treatment adherence and outcomes. Yet, both, doctors and patients, remain sceptical.

\textbf{Aim:} To explain the rationale for using LAI-APs, review their effectiveness and explore barriers to use.

\textbf{Method:} Clinical overview of LAI-APs from the patient and doctor perspective.

\textbf{Results:} LAI-APs were developed to increase adherence to treatment, thereby improving treatment outcomes. LAI-APs may reduce risk of relapse and hospitalization. Yet, the evidence from the few meta-analyses available remains weak. Both patients and doctors may associate LAI-APs with stigma and coercion. Current means of improving adherence include more focus on the therapeutic relationship, better information, adverse effects minimization and halflife extension of LAI-APs. Future means of improving adherence include novel administration techniques that abolish the need for injection.

\textbf{Conclusions:} For both, clinicians and drug developers, drug adherence remains a major target for improving treatment outcomes.

\textbf{KEYWORDS} Antipsychotics; long-acting injections; adherence; relapse; blood–brain barrier

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The rationale for long acting injectable (LAI) antipsychotics

The introduction of antipsychotics (AP) in the early 1950s heralded a start of a new era for the treatment of schizophrenia. For the first time, drugs became available that could effectively treat positive symptoms of schizophrenia, including delusions, hallucinations and thought disorder. These first-generation antipsychotics (FGAs) significantly reduced or even eliminated harsh and ill-fated treatment attempts such as convulsive therapies or physical restraints \cite{1}. Yet, despite the initial therapeutic success, it soon emerged that many patients only poorly adhered to these novel oral formulations \cite{2}. This prompted the development of LAI-APs in the early 1960, first as fluphenazine and haloperidol decanoate. With the advent of second generation antipsychotics \cite{2}, LAI-FGAs use declined. But despite improved tolerability, adherence to oral SGAs did not prove any better than to oral FGAs. LAI-SGAs were developed once again to improve adherence rates \cite{2}. Thus, the goal of LAI treatment has remained the same, to improve adherence as a means to reducing the risk of symptom exacerbation, relapse, and hospitalization \cite{3,4}.

Non-adherence to oral APs

Non-adherence to oral APs (OPAs) remains high. Estimates vary between 40% and 90% \cite{3}. Non-adherence may explain treatment resistance in a significant number of patients. In a study of 99 patients, thought to be treatment resistant on OAPs, 35% had sub-therapeutic or undetectable plasma levels. Patients with sub-therapeutic or undetectable plasma levels were about three times more likely to be admitted to hospital \cite{4}.

Adherence to OAPs can be notoriously difficult to establish. Both patients and clinicians may over-report or overestimate adherence. A study conducted in 52 outpatients with schizophrenia or schizoaffective disorder compared four measures of adherence. These included patient self-reports, pill count and a medication event monitoring system (MEMS). Via a microprocessor in the cap, MEMS recorded when and how often a medication bottle was opened. Adherence estimated varied with measure; 95% for patient self-reports, 76% for clinician estimates, 74% for pill count, and 48% for MEMs \cite{5}.

Effectiveness of SGR LAIs

Several studies have shown that LAI-APs may reduce risk of relapse and hospitalization. There is also some preliminary evidence that LAIs may reduce comorbid violent behavior in patients with schizophrenia \cite{6,7}.

LAI risperidone

A randomized controlled trial (RCT) compared oral and LAI risperidone in 83 patients with recent onset of schizophrenia. The risk of exacerbation and/or relapse was significantly lower in patients treated with LAI-risperidone (7%) than with...
oral risperidone (50%) within 1 year. Mean time to relapse was significantly longer [8]. Another retrospective study showed that LAI-risperidone significantly reduced admissions and length of stay [9].

**LAI-paliperidone**

In a prospective study of 210 patients being consecutively prescribed paliperidone palmitate, 65% of patients were still receiving the LAI formulation after 1 year [10]. In a further prospective follow-up of 225 patients treated with paliperidone palmitate, 42% were still retained on the medication after 2 years. In this study, there was also a significant reduction of mean bed days. They decreased from 79.6 in the 2 years before to 46.2 in the two years after start of paliperidone palmitate [11]. Bressington et al. (2015) also found significant reduction of bed days after paliperidone palmitate initiation [12]. In a multicentre randomized controlled trial of paliperidone palmitate against oral APs, risk of relapse within 24 months was reduced by 29% with the LAI. Time to relapse was also significantly longer in the LAI than in the oral AP group [13].

**LAI aripiprazole**

In a prospective study of 160 patients consecutively treated with aripiprazole LAI, 51% still received the agent after one year. Mean number of admissions fell significantly from 0.71/patient/year in the three years before to 0.45/patient in the year after aripiprazole LAI initiation. Equally significantly decreased mean number of bed days from 30.4/patient in the 3 years before to 22.8/patient in the year after aripiprazole LAI initiation. Median bed days fell from 21.7 to zero in the same time frame [14].

**Meta-analyses**

There are few meta-analyses. These show conflicting results and are less optimistic. The most recent meta-analyses stem from 2016 and 2017 [15,16]. Kishi et al. compared LAI- SGAs with OAPs in patients with recent-onset psychotic disorder. This analysis, including five RCTs conducted between 2009 and 2015, concluded that LAI-APs were not superior preventing relapse but overperformed OAPs in terms of adherence and discontinuation due to ineffectiveness. LAI-APs had a higher incidence of at least one adverse effect and tremor [15]. Ostuzzi et al. compared LAI-FGAs and SGAs with OAPs from 18 RCTs conducted between 1964 and 2015. This study concluded that there was no robust evidence for better tolerability and efficacy of LAI-APs [16]. However, patients with better adherence may be more likely to participate in trials. Selection bias may then reduce any potential difference between OAPs and LAI-APs.

**Obstacles to LAIs use**

Both patients and clinicians may reject LAI-APs. Reasons partly overlap. In a survey of 317 psychiatrists, 69% regarded LAI-APs less acceptable to patients, 48% as stigmatizing, 40% as old fashioned and 38% more prone to adverse effects [17]. Patients may indeed associate LAIs with stigma and coercion [18, 19]. Fear of needles and injection pain may also shape negative attitudes towards LAI-APs [18].

In a study of 222 outpatients with schizophrenia or schizoaffective disorder, 43% currently treated with LAI-APs preferred this route of administration [20]. Conversely, only 6% currently treated with tablets would have preferred LAI-APs. Prior negative experience with AP and particularly LAI-AP treatment affected attitudes towards LAI-APs. Type of formulation may not drive attitudes towards AP. Need for treatment and symptom attribution to the underlying mental illness predicted appositive attitude towards antipsychotics. Extrapyramidal side effects shaped a negative attitude [20].

**Overcoming barriers to LAI use**

Information about LAI-APs and a good therapeutic relationship may promote LAI-APs use. In this context, it may be particularly important to rectify possible misconceptions about LAI-AP use. Patients may not know that LAI options exist, or they may associate injections with higher costs and even with addiction [18]. Doctors, on the other hand, may believe that LAI-APs cannot be used in first episode psychosis [21].

**Minimising adverse effects**

Choosing SGA LAI-APs over FGA LAI-APs and refraining from excessive doses may improve adherence. The use of FGA LAI-APs is particularly associated with tardive dyskinesia. Up to 11% of patients may be affected [22]. Using FGAs LAI-APs in escalating doses is therapeutically counter-productive. Optimizing haloperidol decanoate dosing illustrates this. At a dose of haloperidol decanoate 100 mg/4 weeks, corresponding to a daily total dose of 5 mg of oral haloperidol, about 90% of all patients remain well. At a dose of haloperidol decanoate 300 mg/4 weeks, corresponding to a daily total dose of 30 mg of oral haloperidol, about 92% of all patients remain well. There is only marginal improvement in relapse prevention. But there is a much higher risk dose-dependent of extrapyramidal side effects [23]. Changing the formulation of LAI-APs is a way of preventing adverse effects associated with the injection itself. Oil-based formulations used in LAI-FGAs are more likely to cause scar tissue, when used long-term. All later LAI-SGAs may minimize injection-related adverse effects by using aqueous solutions instead (Table 1).

**Extending half-life**

Extending the half-life of LAI-APs may be another effective way to improve adherence. Besides this, a longer half-life may extend the time to relapse once a LAI is discontinued [24]. Experience from the Maudsley Hospital in London shows that only few patients discontinue LAI paliperidone given at a 3-monthly interval. Advantages must be offset against disadvantage. On the one hand, longer half-life LAI-APs mean fewer injections overall, more autonomy, fewer
visits to mental health facilities and lower risk of admission. On the other hand, longer half-life LAIs may be perceived as high dose with an increased risk of adverse events. Further potential draw-backs include loss of regular contact with the community mental health team. Injection pain due to administration of a higher volume may be a further disadvantage [25].

New ways of delivering LAI-APs

The concept of using LAI-APs to improve adherence and reduce the risk of relapse remains appealing but meta-analytic evidence is inconclusive. Patients and doctors remain sceptical as well. LAI-FGAs were all oil-based. Developing formulations that are long-acting but not injectable (LANI-APs) may be another way to improve outcomes. Such novel formulations could do away with the unpleasantness of injection. If delivery to the brain could be optimized, they might also reduce the amount of drug to be administered. Finally, some formulations could make administration reversible, a significant advantage if faced with serious adverse event such as neuroleptic malignant syndrome. Here, we present and discuss some of the novel techniques of drug delivery that may become available in the future.

Drug administration via nasal cavity

Drug administration via nasal cavity provides rapid absorption into systemic circulation and avoidance of enzymatic degradation and first pass effect. Compared with oral delivery, intranasal delivery results in rapid onset of activity and enhanced bioavailability. Drugs can be targeted to the brain directly through olfactory and trigeminal nerve ending regions bypassing the blood–brain barrier (direct pathway). This is a way to increase drug delivery to the brain and hence efficacy. At the same time, drug delivery to the periphery is decreased. This can potentially alleviate the risk of systemic adverse effects such as cardiovascular or metabolic problems [26]. Reduced systemic concentrations may also benefit patients with severe renal or hepatic impairment. There is no antipsychotic substance approved or under examination in clinical trials based on intranasal drug delivery for brain targeting. However, there has been a great interest among the researchers in exploiting the benefits of intranasal brain targeting. This has resulted in the development of novel drug delivery approaches like solid lipid nanoparticles, polymeric nanoparticles or nanoemulsions [27]. For example, intranasal administration olanzapine-loaded PLGA microparticles to rats showed higher brain concentration (>10 times) of the drug as compared to the IV solution [28]. Specialized devices such as OptiNose and ViaNase electronic atomizer have also been developed to administer different drugs to middle and upper posterior regions of the nose for enhanced brain targeting. These studies showed a great potential for intranasal drug delivery of antipsychotics. But translating this research into successful clinical products depends on the local and systemic toxicity and safety of the drug loaded nanoparticulate systems. Long-term effects of higher concentrations of the drug in the brain should also studied.

Drug-loaded implants

While LAI-APs may enhance the compliance and decrease the morbidity and mortality as compared with OAPs, depot injections are irreversible and thus lack flexibility in clinical management. Besides, some LAI-APs can cause prolonged pain and scar tissue at the injection site. This coupled with a perceived stigma of injections can result in treatment discontinuation. Drug loaded implants for subcutaneous administration offer an alternative and novel drug delivery option for very long-term delivery of APs. Contrary to injectable drugs, implants could be removed after disposition. This reversibility of administration could be a significant advantage when managing risks of severe adverse drug reactions such as neuroleptic malignant syndrome. No product based on this technology is yet on the market, but clinical trials are underway. In a recent study on pharmacokinetics and safety of risperidone subcutaneous implants in patients with schizophrenia, therapeutic drug levels were quickly achieved and maintained near constant rates over six months [29]. This demonstrates the viability and potential of this new technology.

Conclusions

LAI-APs are an important clinical tool for improving adherence. Yet many patients and doctors perceive LAI-APs as coercive, old-fashioned, and stigmatizing. Means of overcoming barriers to LAI-AP use include a good therapeutic relationship, use of SGA-LAIs over FGA-LAIs and avoidance of excessive doses to minimize adverse effects. Novel intra-nasal and implant formulations may remove disadvantages of injectables such as irreversibility over several weeks, injection pain and scar tissue formation. Such novel formulations could also help to change the reputation of APs from old fashioned to high tech.
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