Integrative psychiatry
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Summary

Integrative medicine (IM) is a new concept of health care that was launched by a consortium of eight academic health centers in the USA in the late nineties of the past century. It has been defined as (1) the practice of medicine that reaffirms the importance of the relationship between practitioner and patient, (2) focuses on the whole person, is (3) informed by evidence, and makes use of all appropriate therapeutic approaches, healthcare professionals and disciplines to (4) achieve optimal health and healing (The Consortium, 2004). Since its start there has been great interest from the medical and scientific community and a steady growth. Today fifty-five academic health centers in North America are active members of this consortium. Also in Europe (United Kingdom and Germany) Asia and Australia, IM initiatives regarding clinics and research have been undertaken.

Many research groups, health centers, educational, advocacy and policy activities related to IM exist, but the part of psychiatry / mental health care seems undervalued, especially as regards research. Because of that, we collaborated with researchers and clinicians from Australia and the United States of America to assess the need for IM in mental health care and to propose solutions to current challenges (Saris et al., 2013).

Mental illness now accounts for about one-third of adult disability globally, reflecting marked societal and personal suffering, and enormous social and economic costs. However, the most common treatments in psychiatry (medication and psychotherapy) have turned out to be not as effective as previously thought (Kirsch et al., 2008; Turner et al., 2008; Cuijpers et al., 2010; Cuijpers et al., 2011). So, it seems there is a need for change in the paradigm and practices of mental healthcare (Bracken et al., 2012). Integrative medicine in mental health care (Integrative Mental Health; IMH) may offer some answers to these challenges. It adoption of the biopsychosociospiritual model, utilizing evidence-based treatments from different medical traditions. Besides mainstream interventions (e.g. psychopharmacology, psychosocial therapies) IMH incorporates the judicious use of evidence-based complementary and alternative (CAM) medicines and therapies in addition to health-promoting lifestyle changes (Sarris et al., 2013).

Part I: Conceptual foundation

As the use of complementary and alternative medicine (CAM) in conventional health care (implicit in part 3 of the definition) is the most controversial part of IM and because this subject led to heated debates in the Netherlands, we decided to focus our research on this part of IM. The heated debates seem to indicate that CAM provokes strong emotions. This can be explained by strong adherence to (opposing) paradigms: those in favor of CAM (the vitalism / holism paradigm) and those against (the mechanism / reductionism paradigm; Hoenders et al., 2008).

IM provides a bridge between these paradigms, because it accommodates both conventional treatments and CAM, emphasizing wellness and healing of the entire person (biopsychosociospiritual dimensions) in the context of a supportive and effective physician-patient relationship (Bell et al., 2002). Its success seems related to the fact that integration is not only a current tendency in medicine, but also a trend fitting the contemporary spirit of the age in which integration seems to be the most
common focus. It can be observed in religion, philosophy, spirituality and psychotherapy as well. It follows a period in which differentiation took central stage but did not lead to absolute, unquestionable truths (Hoenders et al., 2012).

Part II: Implementation

We did an inquiry into the use of CAM by psychiatric outpatients and found that 42% of nearly 600 participants had used CAM in the previous year, most of them with perceived good results, but mostly without telling their conventional doctor about this use. This may explain why we found, when asking their doctors, that they underestimated this use (Hoenders et al., 2006). Others have reported similar findings: 43% of patients with anxiety disorder (Bystritsky et al., 2012), and 53% of patients with depression (Wu et al., 2007) use complementary or alternative medicine (CAM). These patients perceived such treatments as improving their physical, emotional, cognitive, social, and spiritual functioning, reducing symptom severity and promoting recovery and wellness (Russinova et al., 2009).

Most patients in our study also reported that they want their conventional doctors to inform them about CAM and assist them in making health care choices (Hoenders et al., 2006). This is also what the European Parliament (1997) and World Health Organization (2003) have advised their membership states to do. Because of that, we felt there was a need to formulate a protocol to assist patients and doctors in using CAM in a judicious way. We felt it should answer patients’ needs and wishes; respect their freedom of choice; offer western medicine and CAM that are safe and effective; protect against quackery and abuse; be based on Dutch law, the jurisprudence of the Medical Disciplinary Tribunal and the rules of the Dutch Association of Medical Practitioners (KNMG); and be based on scientific evidence. This resulted in the CAM protocol (Hoenders et al., 2011).

Part III: Effectiveness

The CAM protocol emphasizes the need for an evidence-based approach. To assess the evidence base for CAM we did reviews on complementary medicines for severe mental illness.

In a comprehensive review on bipolar disorder we found several positive controlled studies of nutrients (such as folic acid) and Chinese herbs in combination with conventional mood stabilizers and antipsychotic medications in bipolar depression, while branched-chain amino acids and magnesium seem effective (in small studies) in attenuating mania. In the treatment of bipolar depression evidence was mixed regarding to omega-3 fatty acids, while isolated studies provide provisional support for a multi-nutrient formula, n-acetylcysteine (NAC), and for L-tryptophan. We concluded that current evidence supports the integrative treatment of BD using combinations of mood stabilizers and select nutrients or herbs (Sarris et al., 2011).

In a systematic review on schizophrenia we found that high-quality research on natural medicines for schizophrenia and other psychotic disorders is scarce. However, there is emerging evidence for glycine, sarcosine, NAC, some Chinese and Ayurvedic herbs, ginkgo biloba and vitamin B6 in improving symptoms of schizophrenia when added to antipsychotics (glycine not when added to clozapine).
Summary

There is inconclusive or absent evidence for omega-3, D-serine, D-alanine, D-cycloserine, B vitamins, vitamin C, dehydroepiandrosteron (DHEA), pregnenolone (PREG), estradiol, inositol, gamma-hydroxybutyrate (GHB) and des-tyr-gamma-endorphin when added to antipsychotics. Omega-3 without antipsychotics might be beneficial in the prevention of schizophrenia. Ayurvedic herbs seem effective without antipsychotics in one large study. Other agents without antipsychotics (vitamin B3, vitamin C, sarcosine, glycine, protilerin) do not seem effective or have only been tested in single or small trials. Ginkgo biloba and vitamin B6 seem effective for diminishing side effects of antipsychotics by omega-3, melatonin and DHEA is inconclusive. All identified agents produce only mild or no side effects. Most study samples are small, study and treatment duration is generally short, studies only cover a modest part of the globe's geography, and most results need replication (Hoenders et al., in preparation).

The next step was to assess the effectiveness of the integrative psychiatry approach in daily practice. Psychiatric research in the past 50 years has focused primarily on neurobiological mechanisms and psychotherapeutic techniques. More recent research has explored lifestyle moderators of mental health, mind-body therapies, and natural products (Sarris, 2011). At present there is a scarcity of real-practice research on integrative approaches in medicine and psychiatry (i.e. approaches that combine multiple interventions in a personalized manner), with most studies employing randomized control trial (RCT) designs to examine single interventions at a group level, thereby ignoring individual differences (Slade & Priebe, 2011; Molenaar & Campbell, 2009). Advances in research and clinical practice of psychiatry will take place when research methodologies permit the rigorous evaluation of complex interventions involving multiple therapeutic modalities (mirroring true clinical practice) to treat real-world clinical populations. So a truly integrative research focus is needed. While methodologically challenging, this approach may have the potential to elucidate the relative contributions of social, psychological, biological and spiritual factors in each unique patient's response to combined treatment modalities (Sarris et al., 2013).

Along these lines we did a single-subject study using time-series analysis to unravel the dynamic interplay between symptom and treatment variables in a multi-component treatment of anxiety disorder. We found that relaxation practice increased this patient’s energy levels, and - via these - reduced his anxiety levels. Physical activity appeared to have the opposite effect, worsening the symptoms. Further, a feedback effect from energy to relaxation was found; increases in energy increased the patient’s tendency to do his relaxation practices, indicating a positive spiral. Although the effects found in this paper were significant, they only applied to one patient, so the generalizability to the population was low. More studies are needed to confirm or refute our findings. The study did show the potential of high-intensity time-series designs to disentangle complex interactions in systems of multiple interconnected variables (Hoenders et al., 2012).

Also routinely assessed outcomes can be used to assess real-life effectiveness of treatments. We evaluated the outcome of treatment at the Center for Integrative Psychiatry, using routine outcome measurement (ROM). We discussed pitfalls associated with the assessment, analysis, and interpretation of ROM data, using data of 376 patients. The sample consisted of 115 men and 261 women. Mean age was 41.3 years (SD = 12.8). Fifty percent had a high educational level. Median illness duration was 11 years (IQR = 15). Median treatment duration was 288 days.
(IQR = 356). The sample was highly heterogeneous as regards diagnosis. Mood (36%) and anxiety disorders (15%) (axis I of DSM IV) and borderline (8%) and type C personality disorders (18%; axis II) were most prevalent. Patients’ satisfaction with the treatment center was good (median = 8; range 1 to 10). 206 patients (55%) completed one or more follow-up measurements. Mixed-model analysis showed significant improvement in symptomatology, quality of life, and autonomy, and differential improvement for different subgroups. Effect sizes were small to large, depending on the outcome measure and subgroup. Subtle variations in analytic strategies influenced effect sizes substantially. Because of many problems inherent to the design and analysis of ROM data we could not draw conclusions about (comparative) treatment effectiveness. Still, this paper yielded some insights into the characteristics of patients visiting centers for integrative mental health, their diagnoses and their satisfaction with integrative psychiatry (Hoenders et al., 2013).

**Integrative research focus**

Mental health research needs to span both the natural and social sciences (Van Os, 2012; De Jong, 2013). Evidence based on RCTs has an important place, but to adopt only concepts from one body of knowledge is to neglect contributions that other well-established methodologies can make (Slade & Priebe, 2001). In other words: besides an integrated treatment approach, a truly integrative research focus is also needed.

In this thesis we used different research methods in an effort to answer some of the research questions related to integrative medicine / psychiatry. Based on literature searches, we wrote essays on the conceptual foundation. Taking into account the Dutch law, scientific research, jurisprudence and rules of professional bodies, we wrote a treatment protocol for the judicious application of complementary medicine in conventional mental health care. We assessed the quality and results of RCTs on complementary medicine in two reviews. Then we used a single-subject study to unravel the interrelatedness of symptoms and treatment variables using time-series analysis. Finally, we provided some insights into the characteristics of patients visiting centers for integrative mental health, their diagnoses and their satisfaction with integrative psychiatry, using routine outcome monitoring.

**Future research**

Research into integrative (mental) health is still in its infancy. Far less than 1% of the research budget in the United Kingdom and the United States of America is spent on complementary / alternative medicine (Ernst, 2003). The rest is spent on conventional medicine. This thesis is a small step towards a more evidence-based integrative psychiatry.

Future research in integrative psychiatry should be integrative in methodology and include: 1) pragmatic trials comparing integrative treatment approaches to conventional treatments to examine (cost-)effectiveness and safety aspects; 2) clinical trials that study patient-tailored multiple-component interventions with both quantitative outcome measures (e.g. laboratory tests and validated psychometric scales) and qualitative experiences (e.g. subjective perceptions of improved functioning, placebo and nocebo effects), in RCTs as well as single-subject time-series designs; 3) use of pharmaco-genomic, epigenetic, and neuroimaging...
technologies to elucidate mechanisms of action; 4) exploration of the impact of lifestyle modification (e.g. diet, exercise, stress management) on mental health as both preventatives and treatments; 5) studies of the interactions between specific pharmaceuticals and complementary or alternative therapies and medicines (potentially beneficial synergistic and potentially dangerous adverse or toxic effects; Sarris et al., 2013); and last but not least 6) qualitative studies with epistemological consideration of the paradigms of widely used Eastern medicine such as TCM, Tibetan medicine and Ayurveda. This is an area where more of a systems approach is warranted than an approach that looks simply at the individual therapies of whole systems (e.g. acupuncture, herbal medicines, massage, etc). This kind of research holds the potential to yield important new insights for expanding the biomedical paradigm – with major implications for medical care and human health (Bodeker, 2012; Van der Greef, 2011).

Finally

In this thesis we differentiated integrative medicine, as a new concept of health care, from conventional medicine / psychiatry, arguing that it may provide some solutions to current challenges in health care. Looking closer one might argue that most aspects of integrative psychiatry should just be part of conventional psychiatry. Most conventional doctors agree that the therapeutic relationship is central, that we should not only look at diseases, but at the whole patient and that focusing on health is as important as trying to eradicate symptoms. Only the third principle, the use of non-conventional medicines, remains controversial. So, is integrative psychiatry really different from conventional psychiatry? Is it really necessary to distinguish them? The answer is yes and no.

Yes, because even though these three principles should be part of conventional medicine, they usually are not. Concepts like the biopsychosocial model are acknowledged in theory, but rarely practiced fully. Moreover the third principle often provokes strong emotional responses and prejudice, which are not evidence-based and hinder progress. That is why we discussed those responses extensively.

No, because most clinicians agree that these principles should be part of medicine. So, after differentiating at the start of this thesis we now arrive at integration once again, hoping that soon most aspects of integrative medicine are accepted and integrative psychiatry will just be ‘psychiatry’.
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Summary
