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Precision psychiatry: promise for the future or rehash of a fossilised foundation?

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Abstract

Precision psychiatry is currently described as an approach that would bring significant advance to psychiatric clinical practice. Theaim of this article is to investigate Precision Psychiatry's promise for the future; should we substantially invest in this new approach? Thearticle is based on a review of the literature and reports a conceptual analysis. A critical examination of Precision Psychiatry's foundationsshows us that its fundaments are obsolete and flawed: we cannot reduce mental suffering to essences in biology. It is problematic to statethat biological processes hold and capture qualia and meaning, and in themselves and without context would hold and capture somethinglike abnormality. Despite its good efforts, precision psychiatry does not represent a sufficiently promising alternative to the phenotyping thatcomes with the current classification systems.

Introduction

In newspapers and journals, precision psychiatry is often described as an approach that would bring significant advance to psychiatric clinical practice. However, the question is whether it is legitimate to invest substantially in this new approach (Joyner & Paneth, 2015). It seems prudent to critically assess this new idea before embarking on a different course. The foundation of precision psychiatry must be sound, and therefore this concept must be critically examined. In this commentary, we will describe what precision psychiatry is purported to entail, discuss its foundation and finally evaluate its promise for the future.

What is precision psychiatry?

Precision Psychiatry has its roots in the 'Precision Medicine Initiative', launched by President Obama in 2015. The endeavour is to personalise medical treatments on the basis of (neuro) biological differentiation. Vieta coined the term precision psychiatry (Vieta, 2015) and Fernandez et al. defined it as: '*technologies and treatments are not developed for each individual patient, as the term personalised suggests, but rather* […] *a high level of exactness in measurement will be achieved such that, eventually, it will be personalised*' (Fernandes et al., 2017). Multi-omics, neuroimaging, big data and high-density data approaches, exposome and molecular epidemiology and physiology should converge towards specific biomarkers that can lead to biological stratification and ultimately to 'precise', person-specific treatments. The approach builds on the objectives of the Research Domain Criteria (RDOC) of the NIMH (Fernandes et al., 2017) and is based on the implicit hypothesis that mental experience and social context are represented in our body/brain (circuits, molecular/cellular processes). The idea is that this approach should make it possible to investigate, predict and/or treat groups that are biologically (in structure and function) rather than phenotypically (in symptomatic appearance) homogeneous. Precision psychiatry thus tries to deal with two unresolved dilemmas that currently are widely acknowledged to cloud the scientific validity of 'evidence-based' psychiatric practice: (i) how to conduct treatment research based on fuzzy phenotypes that do not represent valid stratification, (ii) how to work with patients at the required idiographic level on the basis of data at the nomothetic level.

Conceptual problems with 'precision' and 'personalisation'

Precision psychiatry relies on progress in biological research but confuses undeniable progress in neuroscience with progress in its applicability to mental health care. Decades of research in the field of markers, brain regions, genes and developmental precursors have not produced any latent disease entity, biological subgroup or aetiological essence for the main psychiatric syndromes (Zachar & Kendler, 2007). The main outcome of much research, described by Kapur,

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Phillips and Insel is therefore the *absence* of valid, replicable and useful associations between biology and mental suffering, despite significant progress in brain research *per se* (Kapur, Phillips, & Insel, 2012).

For example, one of the most important replicable biological findings in psychiatry is that every human being has thousands of genetic risk variants for transdiagnostic mental suffering (Brainstorm et al., 2018). This means, in other words, that it is part of the human condition to have a broad, elusive biological vulnerability to develop mental suffering (Kendler, 2015). Members of the DSM workgroups have therefore not been able to include biological evidence in the criteria for the most important mental disorders (American Psychiatric Association, 2013). Given this state of affairs, without clear hypotheses or directions to guide us towards future findings that would be able to yield discrete clinical distinctions, it remains debatable whether precision psychiatry, using the same translational approaches, will ever be able to provide any diagnostic, prognostic or therapeutic benefit to clinical practice (Marsman et al., 2020; van Os, 2018).

Such a position can only be considered 'pessimistic' or 'nihilistic' (McGorry & Mei, 2020) if there are strong *a priori* reasons to suppose that mental suffering is associated with discrete causes occasioning differentiation of treatment responses, and that there is an ethical prerogative for it to be so – i.e. the position that only translational science yielding novel medical approaches can provide valid therapeutic options. However, this does not seem to be what decades of intense psychiatric research has revealed. On the contrary, scientific findings provide a powerful case for mental suffering as broad, poorly delineated syndromes that show high levels of transdiagnostic within- and between-person variability and low levels of determinedness and predictability (Brainstorm et al., 2018). In addition, evidence suggests that the most powerful – and perhaps most neglected – factor driving change over time appears to be the human capacity to adapt over time and to respond to expectation-rich therapeutic rituals, particularly if they offer meaningful connections with a significant other (van Os, Guloksuz, Vijn, Hafkenscheid, & Delespaul, 2019).

The problem of representation and relevance: a thought experiment

Apart from the fact that the biological evidence to date is not convincing, hampering translation to clinical practice and the individual patient, there are problems of a more fundamental nature. The implicit premise of precision psychiatry is that phenomena of the mind are physically represented and that these representations are relevant to our understanding of mental suffering. The question, however, is whether phenomena of the mind are physically represented and whether finding biomarkers is of relevance in understanding mental processes. We turn to a thought experiment to clarify these fundamental problems.

For many, falling in love is a 'boundary experience' which can bring the person close to the experience of intense mental suffering. To this end, the reader may think back to the time when he or she was seriously in love. How did that crush feel? Where did one feel that crush? What colour did the crush have? Some would be paralysed to the degree of no longer daring to talk with or eat in front of that coveted other, blush constantly, want the other – but at the same time avoid him or her. Some would feel themselves dissolve, no longer being able to separate their own wishes from those of the other, or end up in an 'ecstatic, pink wholeness experience'. Still others would experience a state akin to addiction or obsession in which their entire behaviour is focused at another 'shot' of the other. In short, being in love may represent a boundary experience with loss of ground and autonomy in the form of a mini-neurosis, a mini-psychosis or a behavioural pathology.

The hypothetical experiment for precision psychiatry is whether one can experience that same phenomenon of falling in love when it would be simulated by stimulation of its associated processes and metabolisms in the body/brain. The probable outcome is that at best some may experience a hint or whiff of their original crush, but not the real phenomenon. How likely is it exactly that the complex combination of someone's (sub)culture, genetic profile, the bacteria in mouth and intestines, the personalities of father and mother, the place one had in the family, the attachment to both parents, the first erotic image that settled, and so on, are physically represented by biomarkers? We simply do not know if or to what degree the determinants of falling in love have a physical representation, just as we do not know for the phenomenology of mental suffering. Even when consciousness and its qualia are understood as a physical state (known as the 'identity theory'), the question remains how we intuit that consciousness and its qualia arise and how and where they are represented (this is both a historical and topical debate in philosophy) (Crane, 2001). In the case of precision psychiatry, this question is settled with nothing more than a postulate.

When we wish to understand, decipher, capture and/or modify mental experiences such as falling in love or mental suffering, we can and should not reduce the experience to a linear, one-dimensional neurochemical chain in the brain (i.e. biomarkers). This is trying to understand and explain a three-dimensional phenomenon in two-dimensional terms losing the most important along the way (Frankl, 1958). Precisely that what escapes the objectifiable and quantifiable may be most relevant [see Köhne (2020) for an elaborate discussion on this topic]. Even more dynamic and complex descriptive biological knowledge that incorporates the multiple realizabilities of physical states to mental states (Putnam, 1967) does not provide an adequate accounting of subjective experiences and qualia in the understanding of mental processes [see e.g. Nagel (1974) on subjective experiences] and should therefore not be taken as the central resource of explanation in the field of psychiatry. The point here is that the 'representation' of mental processes in terms of biomarkers is not only reductionist, poor and insufficient but also not relevant enough for the understanding of mental processes. Thus, apart from the fact that this problematic starting point does not testify to a basic critical scientific attitude, it inevitably leads to shaky solutions.

A problem of practical nature is that we still know very little, and therefore are unable to determine which parameters should be chosen from the enormous amount of information. Which associations will be sought and how do we assume they will be mediated? The question is therefore whether there will be any diagnostic, prognostic or therapeutic usefulness of the efforts of precision psychiatry for clinical practice.

Low hanging fruit

Given that 'personal contact' and the 'therapeutic relationship' show a substantial impact on mental health outcomes, how rational is it to place our hopes on biomarkers? Research shows equivalence of psychotherapies but differences in the effectiveness of different psychotherapists (in naturalistic

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settings), independent of the specific type of treatment or the amount of experience of the practitioner (e.g. Goldberg et al., 2016). The same may be true for pharmacotherapy but this remains an under-researched topic. McKay, Imel and Wampold (2006) concluded that both psychiatrists (the person) and the specific psychopharmacological treatment (an antidepressant) contribute to the outcome of treatment of depression. However, psychiatrist effects appeared greater than psychotropic treatment effects. If research consistently shows that therapist effects are greater than the effects of the technical ingredients of treatment, would it not be productive to focus on this type of low hanging fruit (van Os et al., 2019)?

The future?

The definition of what we now call a 'mental disorder' (DSM/ICD classification) is in need of renewal. The current definition is rapidly eroding and should be broken open (e.g. Vanheule et al., 2019). Despite its good efforts, precision psychiatry may not represent a sufficiently promising alternative given that its axioms are obsolete and flawed. We cannot reduce mental suffering to essences in biology. It is problematic to state that biological processes hold and capture qualia and meaning, and in themselves and without context would hold and capture something like abnormality. In addition, the biological evidence to date not only has not been convincing, it seems to point to non-determinedness, non-predictability and non-stratification as inherent properties. Precision psychiatry seems to be the latest way of expressing the idea that mental disorders (mental states) can be traced back to – and are ultimately caused by – specific biological abnormalities (physical states), although this idea is convincingly challenged in the literature (see e.g. Bentall, 1999; Johnstone et al., 2018; Moncrieff & Middleton, 2015; Putnam, 1967).

Rather, let us become smarter in understanding and connecting the complexity of the interacting layers of the neurobiological, the psycho-experiential and the socio-cultural instead of focusing on isolated static biomarkers. Let us meaningfully separate our administrative model, our research model and our clinical model (reduction *v.* precision, group *v.* individual). The mind, the subject, the narrative and the therapeutic relationship will in any case have to be given more space in the medical specialty we call 'psychiatry'. After all, our field reaches beyond the natural sciences and into the realm of the mind.

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