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Forum

Psychiatry beyond labels: introducing *contextual precision diagnosis* across stages of psychopathology

Introduction

George & Klijn (2013) provide cogent arguments for a change in terminology regarding the syndrome that currently goes under the name of schizophrenia. A name change at this stage would introduce significant improvement, but can only be regarded as the first intermediate step towards the much more incisive final goal of a complete redesign of psychiatric diagnosis, guided by two important parameters. First, given that an alternative system of mechanism-based system of diagnosis, based on specific 'biosignatures', is still a long time away – if ever (Kapur *et al.* 2012), a symptom-based approach will remain necessary for the foreseeable future. Second, given that diagnosis in medicine essentially refers to classification with (treatment and prognostic) utility, this should be the guiding principle for any diagnostic system, with a focus on reduction of suffering and incapacity of those who seek our care (Pies, 2012). In the following, we will describe, within these parameters, three requirements for a novel system of diagnosis in psychiatry based on (i) the need for a more individualized approach, based on causal influences in symptom circuits (precision diagnosis), (ii) the need to take into account the fact that symptoms reflect responses to context (context diagnosis), and (iii) the need to take into account that syndromes develop over time and have recognizable stages of expression (staging diagnosis) (Fusar-Poli *et al.* 2013).

The principle of contextual precision diagnosis

The main problem with psychiatric diagnosis is that groups identified by a common label, for example schizophrenia, in fact have little in common. The level of heterogeneity in terms of psychopathology, need for care, treatment response, illness course, cognitive vulnerabilities, environmental exposures and biological correlates is so great that it becomes implausible that these labels can provide much clinical utility. In spite of this, disorders continue to be stereotypically depicted as homogeneous. A case in point is the diagnosis of schizophrenia, which in prestigious scientific journals typically is described homogeneously in line with its early twentieth century asylum origins as a 'devastating brain disease' or similar stereotype (Sawa & Snyder, 2002; Corfas *et al.* 2004; Walsh *et al.* 2008; Esslinger *et al.* 2009; McDannald *et al.* 2011; Rico, 2012). Patients receiving the diagnosis of schizophrenia are thus exposed to pressure to conform to an identity that is compatible with this stereotype, resulting in a strong desire to 'recover' from this experience.

Although a name change likely would provide some relief in the short term, it does not address the underlying problem of low utility associated with extensive heterogeneity within the label. In other areas of medicine, unexplained heterogeneity is being addressed by the introduction of precision (or personalized) diagnosis. For example, blood pressure, plasma glucose, cardiac rhythm, EEG, muscle tone and other somatic outcomes can now be monitored in daily life, allowing for a diagnosis that yields individualized information about the pattern of *variation* of the parameter in question in response to daily life circumstances. This diagnostic information is *precise*, as it reflects highly personal patterns of variation, and it is *contextual*, as it traces variation to daily life circumstances of, for example, stress, sleep, medication and life style. This not only enables precise indexing of treatment needs (diagnosis), but also precise monitoring of treatment response (prognosis). A similar system of contextual precision diagnosis may be useful in psychiatry.

Precision: diagnosing mental causation in symptom circuits

How can diagnosis based on psychopathology be individualized? To date, the most commonly used attempt at individualization is based on assigning individuals to diagnostic categories, in combination with personalised ratings of psychopathology across different dimensions. In theory, this system of 'dimensionalized categories' ought to yield acceptable precision, given that two individuals within the same diagnostic category will nearly always have different psychopathological profiles. While attractive, recent research nevertheless indicates that it is based on the false premise that symptoms always vary together as a function of a latent underling dimension or category – which does not appear to be the case (Kendler *et al.* 2010; Borsboom *et al.* 2011). Instead, it has been argued that mental 'disorders' in fact may represent sets of symptoms that are connected through a system of causal relations that may explain individualized co-occurrence of different symptoms (Cramer *et al.* 2010; Kendler *et al.* 2010). For example, the negative and positive symptoms of schizophrenia have largely independent courses (Eaton *et al.* 1995) and aetiological factors appear to operate at the symptom level rather than the diagnostic disorder level (Bentall *et al.* 2012; Cramer *et al.* 2012; Linscott & van Os, 2012).

Therefore, there is increasing interest in how multiple symptoms in individuals arise not as a function of a latent construct, but as a function of symptoms impacting on each other, for example insomnia impacting on depressive symptoms (Sivertsen *et al.* 2012) or on paranoia (Freeman *et al.* 2009), depressive symptoms clustering with anxiety symptoms (Kendler & Gardner, 2011), affective disturbance impacting on psychosis (Garety *et al.* 2001; Myin-Germeys & van Os, 2007), and hallucinations impacting on delusions (Maher, 2006; Smeets *et al.* 2012). Not only between-symptom dynamic relationships have been described, intra-symptom temporal dynamics resulting in *persistence* are also important. For example, intra-symptom dynamics over time, in the form of intra-symptom feedback loops, have been described in the area of psychosis, in the form of psychotic experiences impacting on persistence of such experience over time, both at the momentary 'micro-level' over the course of a single day in daily life (Wigman *et al.* 2013*a*), or over the course of months or years (Dominguez *et al.* 2011; Wigman *et al.* 2011), under the influence of genetic and non-genetic risk factors (Mackie *et al.* 2011; Kuepper *et al.* 2011; Wigman *et al.* 2013*a*).

The notion that traditional diagnostic categories and dimensions need to be transformed to represent the dynamics of symptoms impacting on each other over time in a model of 'mental causation' is tantalizing. It implies that special methodology is required to collect repeated measures of symptoms over time in the flow of daily life, both at the momentary level and over more extended periods (Myin-Germeys *et al.* 2009). This type of information allows for a detailed analysis and systematic presentation (Epskamp *et al.* 2012) of how symptoms impact each other (Cramer *et al.* 2010; Kendler *et al.* 2010; Wigman *et al.* 2013*b*).

Context: diagnosing environmental reactivity

Although it is widely believed that mental disorders have their origin in altered cerebral function, disease categories as defined in DSM and ICD do not map on to what the brain actually does: mediating the continuous flow of meaningful perceptions of the social environment that guide adaptive behaviour. The use of *ex-cathedra* static diagnostic categories appears distal from the neural circuits that mediate dynamic adaptation to social context.

Therefore, reformulation of the basic psychopathological unit towards capturing dynamic reactivity, modelled on the role of neural circuits in mediating adaptive functioning to social context, may be productive in the context of diagnosis. Momentary assessment technology phenotypes capturing dimensional variation in mental states [typically assessed as continuous variables, using Likert scales, in the Experience Sampling Method (ESM)] in response to other mental states in the symptom circuit on the one hand, and environmental variation on the other, are well placed to fill these requirements (Fig. 1), resulting in a diagnosis that is both contextual and precise. It is proposed that momentary assessments of contextual symptom circuits, using the ESM, will provide a fertile phenotype for investigation of psychopathology, encompassing phenotypes at multiple levels of neurofunctional organization (Yordanova *et al.* 2010). For example, momentary assessment technology studies of exposure to early trauma in humans have yielded replicated evidence that early environmental exposures predict altered momentary response to stress in adulthood that increase the risk of mental disorder (Glaser *et al.* 2006; Wichers *et al.* 2009; Lardinois *et al.* 2011). There is a suggestion that these ESM phenotypes of behavioural sensitization (Myin-Germeys *et al.* 2005*a*) can be linked to biological models of sensitization (Myin-Germeys *et al.* 2005*b*; Collip *et al.* 2008), thus suggesting that the momentary environmental reactivity may represent a key variable in linking mental and neurobiological phenotypes (van Os *et al.* 2010). Also, several ESM mental state measures have shown that connections between momentary mental states and environments are sensitive to genetic effects, not just

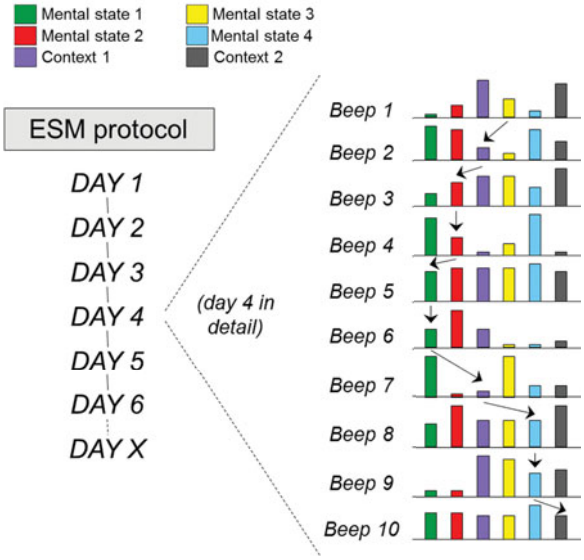

Fig. 1. Momentary assessment with the Experience Sampling Method (ESM). Experience sampling methodology showing the details of a single day in the ESM paradigm. At 10 random moments during the day, mental states (e.g. anxiety, low mood, paranoia, being happy) and contexts (stress, company, activity, drug use) are assessed. The arrows represent examples of prospectively analysing the impact of mental states and contexts on each other over time.

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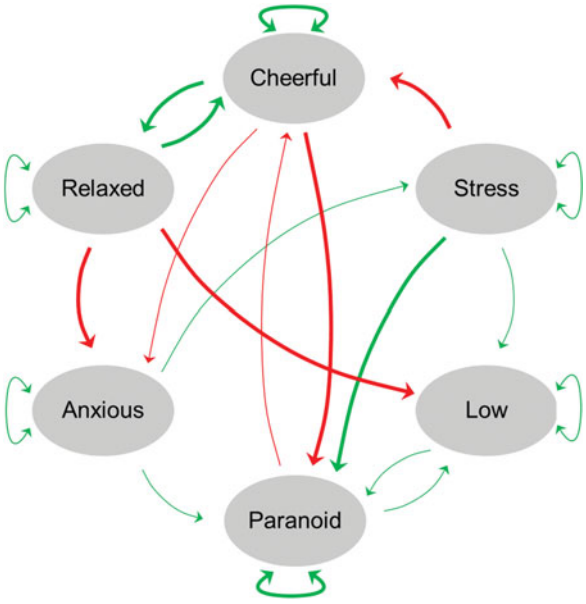

Fig. 2. Contextual precision diagnosis. Thicker lines indicate stronger associations. The (simulated) patient in this example did 6 days of experience sampling in order to determine circuit patterns of stress and mutually impacting mental states. The resulting causal circuit is depicted above. A strong positive feedback loop exists between positive states (relaxed and cheerful) and a negative feedback loop exists between the opposite mental states of being cheerful and being paranoid. Stress occasions paranoia and impacts negatively on cheerfulness. Being relaxed helps reducing low mood and anxiety. Both cheerfulness and paranoia have a strong tendency to persist over time, increasing the probability of stable symptoms (Wigman *et al.* 2013*a*,*b*).

in terms of heritability and familial resemblance (Jacobs *et al.* 2006; Menne-Lothmann *et al.* 2012), but particularly in terms of the genetics underlying environmental sensitivity (Myin-Germeys *et al.* 2001; van Winkel *et al.* 2008; Wichers *et al.* 2008*a*,*b*; Lataster *et al.* 2009; Simons *et al.* 2009; Collip *et al.* 2011; Peerbooms *et al.* 2012), a mechanism referred to as gene–environment interaction.

The nomenclature of contextual precision diagnosis in psychiatry

An example of contextual precision diagnosis is depicted in Fig. 2. 'Diagnosis' here refers to the visual display of causal relationships between symptoms and environment (in the example: stress) in the circuit. The circuit not only focuses on environment and symptoms, but also includes positive affective states, thus increasing therapeutic relevance. Previous work has shown that contextual precision diagnosis is highly sensitive to longitudinal development of phenotypes across definable stages, in that connection strength and connection variability between mental states differ in a predictable fashion across different stages of psychopathology (Wigman *et al.* 2013*b*).

Contextual precision diagnosis is idiographic and sensitive to stages of psychopathology, replacing the need for nomothetic approaches that lack validity and practical utility (McGorry & van Os, 2013). Perhaps it may be useful to retain some of the higher order syndromal groupings, such as common mental disorder and severe mental disorder. The focus of contextual precision diagnosis, however, is on the individual, neutralizing the forces of stereotyping that George & Klijn wish to attenuate.

Declaration of Interest

None.

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