Schizophrenia: inorganic no more

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Schizophrenia is a mental illness affecting millions of people worldwide and is characterised by “fundamental and characteristic distortions of thinking and perception” (ICD)[1]. The international diagnostic criteria classify schizophrenia as a non-organic disorder, at the same clinicians continue to use "organic" in day-to-day practice to refer to non-“functional” causes of psychosis and *vice versa*. This is despite mounting evidence to the contrary and has important implications for our treatment of patients with schizophrenia and resource allocation.

In the medical context, the term organic is generally taken to mean an illness in which there is change in the structure or function of an organ. In addition, the ICD-10 describes several criteria to differentiate between non-organic and organic disorders (table).

Table: Supporting criteria for making diagnosis of an organic mental disorder (ICD-10)	
ICD-10 Criteria supporting a diagnosis of organic disorder[1]	**Key findings in schizophrenia**
Evidence of cerebral disease, damage or dysfunction.	Increase in lateral ventricle size[2]. Reduced cross-sectional area of the corpus callosum[3]. Reduced volumes of the temporal structures[3]. Reduced fronto-temporal white matter connectivity[4] . Elevated microglial cell density *post mortem*[5] and microglial activation *in vivo*[6]. Neurochemical dysfunction including elevated striatal dopamine synthesis capacity[7].
A temporal relationship between the development of the underlying disease and the onset of the mental syndrome	There is a temporal relationship between the development of structural[8] and neurochemical abnormalities[7] and the onset of psychosis .
Recovery from the mental disorder following removal or improvement of the underlying presumed cause	Schizophrenia is associated with raised striatal dopamine synthesis and release capacity[7] and symptoms of schizophrenia improve when this is blocked with dopamine antagonists.
Absence of evidence to suggest an alternative cause of the mental syndrome such as a strong family history or precipitating stress.	This criterion is not appropriate. "Organic" illnesses can be hereditary or contributed to by stress (e.g. hypertension).

The organic nature of schizophrenia has long been hypothesised. A century ago Emile Kraepelin suggested that we would one day be able to elucidate the neuropathology of dementia praecox (what we would now call schizophrenia).[9] It took some time to develop the tools to investigate this in vivo, but many studies have now tested this.

In 1976 Johnstone *et al*.[2] were the first to demonstrate, using computed tomography (CT), that patients with schizophrenia have increased lateral cerebral ventricle size. These results have since been replicated multiple times and further evidence of additional structural brain changes have been consistently found[3]. Moreover, brain imaging shows promise in the differential diagnosis of schizophrenia and mood disorders[10]. Structural changes have also been shown to pre-exist the first episode of psychosis, leading to the hypothesis that schizophrenia is a neurodevelopmental disorder[8,11]. Additionally, a meta-analysis using diffusion tensor imaging (DTI) has shown reduction in connectivity of two separate networks of white matter tracts, hence disconnection between grey matter regions[4]. This provides an organic basis for the functional dysconnectivity, i.e. abnormal connections, observed clinically in terms of symptomatology and experimentally, across a range of measures, in schizophrenia.

Furthermore, a classically described marker of an organic disease process is the presence of inflammation. Post-mortem studies have shown evidence of elevated microglial cell density in the brains of patients with schizophrenia, particularly in the frontal and temporal lobes[5], and there is recent in vivo evidence supporting these findings in participants at ultra-high-risk of developing psychosis[6]. These findings pre-date the onset of

frank psychosis, suggesting causal association of the inflammatory activity and psychosis, and hence organic pathology.

In view of all this evidence, the fundamental criteria for organicity are either met in schizophrenia, or appear questionable (table). We can no longer divide illness into organic and inorganic based on the technological limitations of late 19th Century anatomy and histology. Moreover, the current classification implies that there is a non-organic aetiology to schizophrenia, and by extension that this should direct management. Whilst it is clear that psychological and social factors play a major role in the illness, no psychological or social mechanism has been established as solely underlying the disorder or present in all cases, just as is the case for biological factors[11]. Instead, in most patients, a combination of psychological, social and biological factors play a role in the illness and its treatment, just as is the case with other common medical conditions such as diabetes mellitus.

The current classification of schizophrenia as a non-organic illness influences service organisation and resource allocations. Mental health services continue to be mostly separate from the rest of medical services, with distinct hospitals, teams and management. Moreover, in many countries, per capita spending on healthcare for patients with psychiatric illnesses is below that for non-psychiatric disorders. Already within an under-resourced sector, in the English National Health Service mental illnesses are further categorised into "non-psychotic", "psychotic" and "organic" illnesses for the purposes of resource allocation. This out-dated and trichotomous categorisation continues to be used in clinical decision-making and the commissioning and payment of services whereby patients are "clustered" and receive a "package of care" with a set tariff based on which category they fall in rather than healthcare need (https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/300864/Guidance_to_mental_health_currencies_and_payment.pdf). A patient with an "organic" illness attracts a higher care cluster and different payment tariff irrespective of actual needs. Despite decades of research indicating that this categorisation is inappropriate it continues to dominate resource allocation, with negative consequences for patients.

The suggestion of a non-organic aetiology of mental illness also has an impact on its perception by the public and the rest of the medical profession. Despite psychiatry being a medical speciality, patients with schizophrenia are referred to psychiatrists from other specialists with comments in their clinical notes including that they are "medically fit" and have "no evidence of organic illness". This perpetuates a Cartesian dualistic fallacy that schizophrenia, and by extension other psychiatric illnesses, are quasi-illnesses that do not require the full range of healthcare available. Despite mental illnesses contributing a growing proportion of the disease burden, spending accounts for comparatively small proportions of clinical care, public health and medical research. For example, every year the UK Government invests approximately £61 per patient affected in research into psychotic illnesses, compared to £1,571 per patient for cancer[12].

Given the evidence for organic involvement in schizophrenia, and the implications of the non-organic distinction, it remains unclear why schizophrenia continues to be categorised as a non-organic illness despite evidence to the contrary. Perhaps refusal to accept the accumulated data might offer evidence for another clinical construction with its roots in the 19th century: the psychoanalytic concept of denial?

Contributors

MAPB and ODH conceptualised the paper. All authors contributed to the intellectual content, critically edited, and approved the final version of the manuscript.

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