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Lack of Use in the Literature From the Last 20 Years Supports Dropping Traditional Schizophrenia Subtypes From DSM-5 and ICD-11

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The diagnoses of paranoia, catatonia, and hebephrenia preceded the use of dementia praecox and Bleuler's subsequent recognition of a heterogenous "Group of Schizophrenias." With some modification, traditional schizophrenia subtypes have been formalized for many years in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) and International Classification of Diseases (ICD) classification systems. While widely used in the past, it is not clear that the schizophrenia subtypes remain in wide use or are influential in 21st-century research and clinical practice, and especially in the scientific literature. A review of published articles reveals over the last 20 years (1990, 2000, 2010) the use of traditional subtypes in the literature has fallen from 27.7% to 9.8% to 6.5%. Thus, by 2010, the use of subtypes in the leading literature venues declined to <10%. These facts strongly support DSM-5 and ICD-11 proposed elimination of traditional schizophrenia subtypes from a research and evolving knowledge perspective because traditional subtypes are simply no longer being used much in the scientific literature.

Key words: schizophrenia/subtypes/classification

Introduction

During the past century, psychiatric nosology has relied heavily on "subtypes" as a scientific, clinical, and conceptual framework for understanding "the Group of Schizophrenias."[1] Bleuler understood the wide heterogeneity in secondary symptom manifestations of schizophrenia while positing dissociative pathology as primary and fundamental in schizophrenia patients. The concept of heterogeneity has been greatly expanded today as several features are considered to be core to schizophrenia pathology (eg, reality distortion, disorganization, psychomotor and negative symptoms, and cognitive deficits, neurophysiological, neural circuit, and genomic dysfunctions). This has led to the recognition that individual patients vary widely across these crucial and highly explored domains while, in contrast, *Diagnostic and Statistical Manual of Mental Disorders*, DSM-ICD subtypes have fallen into disuse. The heuristic value of traditional subtypes has been challenged along several dimensions.

Traditional (DSM-ICD) subtypes are no longer symptomatically distinguishable as was expected from original descriptions.[2,3]

- The catatonic subtype may be misleading in the direct link with schizophrenia because catatonia is manifest in a number of disorders and more often in mood disorders than in schizophrenia. A catatonia specifier seems more informative than a subtype.[4] But it is noteworthy that only 1% of Medicaid schizophrenia patients were diagnosed with the catatonia subtype in the United States. In China, 19 000 patients with schizophrenia were categorized. Only 0.2% received a catatonia subtype vs 91% for undifferentiated.[5]
- Subtypes have sometimes been considered to have prognostic significance, but this has principally related to differences in baseline pathology and prognostic value and was based on a tautology rather than independent factors. For example, the paranoid subtype is partly defined by a lower level of negative symptoms and greater cognitive impairment. These two pathology domains are robust predictors of future functioning

and these attributes, rather than the subtype designation, are the focus of clinical and research attention.
- Evidence-based treatment guidelines, such as the Schizophrenia Patient Outcomes Research Team (PORT) project,[6,7] do not rely on subtype designations.
- Traditional subtypes of patients are not responsive to unique therapeutic pathways of care. Pharmacotherapy and a variety of cognitive, psychosocial and family education, and supportive therapies are relevant but have no subtype-specific indication. The use of subtypes has not advanced individualized treatments, and with schizophrenia's trenchant heterogeneity, comprehensive personalized therapies for schizophrenia are still a distant goal.[8]
- Subtypes often are not stable over time.[9] The suggestion that subtypes capture state rather than trait pathology limits the usefulness of traditional subtypes.
- More recently, traditional DSM-ICD schizophrenia subtypes have not proven robust in advancing our understanding of the genomics of schizophrenia despite its high heritability. With the advent of characterization of gene networks for understanding both schizophrenia and endophenotypes,[10,11] as well as the emergence of the importance of de novo mutations, methylation events, transcription factors, the connectome and other "omes" as well as dark matter, "gene desert" regulatory processes,[12] the genomic basis of schizophrenia as well as other common but complex disorders is dauntingly difficult to subtype or characterize. It appears likely that both common and rare genetic variants make highly variable contributions to the schizophrenia clinical phenotype.[13] Schizophrenia genomics does not appear to "line up" in any meaningful way with traditional subtypes. Still, there is an evolving literature on genotype-guided treatments for some aspects of schizophrenia pathology such as negative symptoms, where genotype predicts negative symptom reduction with folate plus vitamin B12 treatment.[14]
- Latent class/genetic studies tend to reinforce the newer deficit subtype (DS) rather than traditional subtypes.[15–17] However, DSM-5 would not be enhanced by adding one subtype such as the DS without a valid definition of other nondeficit subtypes.
- Heterogeneity reduction may be more informative if it is based on psychopathology domains[18] or behavioral constructs with known neural circuit substrates.[19] Endo- or intermediate cognitive and neurophysiological phenotypes may be more promising than traditional subtypes for discovering the genetic and cognitive architecture of the schizophrenia syndrome,[20] but intermediate phenotypes have not yet produced a comprehensive alternative for meaningfully parsing schizophrenia into subgroups.

In order to better characterize the usefulness of schizophrenia subtypes, we examined the 5 highest impact factor psychiatry journals (from 2012) in 1-year periods circa 1990, 2000, and 2010. The journals are *Molecular Psychiatry, American Journal of Psychiatry, Archives of General Psychiatry, Schizophrenia Bulletin, and Biological Psychiatry*. The frequency with which DSM-ICD subtypes are used in reports was determined. All articles from these journals with "schizophrenia" as a keyword were examined in 1-year epochs to determine the frequency with which subtypes were actually used. We hypothesized that we would find a declining use of subtypes over time resulting in minimal attention to subtypes in the current literature. The results are depicted in tables 1–3. In fact, subtype usage fell over time and is now being used in <10% of the articles surveyed.

The proportion of reports using subtype designations decreased from 28.9% in 1990 to <10% of studies utilizing subtypes in 2010. This result reinforces the view that the field does not use traditional subtypes when addressing the heterogeneity of schizophrenia. Categories generated from Scale for the Assessment of Negative Symptoms (SANS) and Scale for the Assessment of Positive Symptoms (SAPS) ratings, deficit vs nondeficit designation, or the use of genes and intermediate phenotypes for classifying schizophrenia subtypes are common but hardly definitive. Also common, and an issue of concern, is the fact that many studies are weakened by unspecified heterogeneity. Schizophrenia, as a complex clinical syndrome, is a less robust target for discovery if investigators do not address heterogeneity.

Alfred Adler said if you want to understand a person look at the tongue in his shoes (behavior), not the tongue in his mouth (pronouncements). Our field, especially in the scientific publication realm, has rendered its verdict a decade into the 21st century: DSM-IV subtypes are simply not being used. This finding strongly and empirically

Table 1. 1990 Subtype Usage 28.9%

Journal	Number of Articles/ Schizophrenia	Subtypes Used
Molecular Psychiatry	N/A	N/A
American Journal of Psychiatry	29	10
Archives of General Psychiatry	24	10
Schizophrenia Bulletin	48	8
Biological Psychiatry	36	10
Total	137	38

Note: N/A, not applicable.

Table 2. 2001 Subtype Usage 13.7%

Journal	Number of Articles/ Schizophrenia	Subtypes Used
Molecular Psychiatry	33	3
American Journal of Psychiatry	41	4
Archives of General Psychiatry	23	2
Schizophrenia Bulletin	56	6
Biological Psychiatry	54	13
Total	207	28

Table 3. 2010 Subtype Usage 6.8%

Journal	Number of Articles/ Schizophrenia	Subtypes Used
Molecular Psychiatry	22	0
American Journal of Psychiatry	43	3
Archives of General Psychiatry	30	2
Schizophrenia Bulletin	35	9
Biological Psychiatry	83	0
Total	213	14

supports plans by DSM-5 and ICD-11 to abandon the use of subtypes.

Conclusions

- There are a number of compelling reasons to believe that current DSM-ICD schizophrenia subtypes do not clarify the heterogeneity or etiopathophysiology of schizophrenia.
- Use of traditional schizophrenia subtypes is now uncommon in scientific reports. Genotype-guided subtype classification is promising, but still a distant goal.[21]
- Dropping subtypes in DSM-5 and ICD-11 schizophrenia classification is justified by the lack of stability, validity, heterogeneity reduction, and practical utility in the scientific literature.
- Hopefully, as new "cuts" through the complex data space of schizophrenia evolve, we will develop more useful and valid subtype nosologies in the future.[8,21]

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