Title: Crossing boundaries in schizotypy research: An introduction to the special supplement.

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Abstract:

For nearly six decades, the schizotypy construct has served as a conceptual guide for understanding the phenotypic and clinical variability associated with schizophrenia-spectrum vulnerability. Despite the impact of schizotypy on academic research, the public burden of schizophrenia-spectrum pathology has not diminished over time, and it remains poorly understood with no cures, few treatments and heavy stigma from the lay public. Following on the success of the 2013 Lemanic Workshop on Schizotypy, the International Consortium on Schizotypy Research (ICSR) was formed to address these needs by accelerating scientific discovery of schizophrenia-spectrum pathology. The ICSR convened its 2017 meeting in Beijing China with the theme of "Crossing Borders". This included a focus on expanding schizotypy research across five domains across: academic disciplinary borders (promoting brain and genetics/genomics research), clinical borders (promoting clinical and non-clinical applications), geographic borders (promoting cross-cultural research), laboratory borders (promoting "big" and "small" data collaborations), and methodology borders (promoting emotion, cognition and behavior research using novel methods). This special supplement provides the highlights from this meeting and related work, including three theoretical and position articles, seven research articles and one invited commentary.

For nearly six decades, schizotypy has served as a "grand unifying" conceptual model explaining the phenotypic variability and complex causes of schizophrenia-spectrum pathology. Few other psychiatric disorders benefit from a comprehensive, integrative and specific model of this kind. Among the academic community, there is remarkable consensus on most definitional aspects of schizotypy: that it reflects a multidimensional personality trait determined by genetic and epigenetic/psychosocial factors and is expressed neuro-developmentally across key dimensions which specify a phenotype that varies considerably in functional and clinical consequence.[1–3] In large part, this consensus and broad acceptance reflects organizational efforts by Paul Meehl (in his 1962 address to the American Psychological Association[1]), the 1993 NATO scientific workshop on schizotypy, the International Lemanic workshop on schizotypy,[4] countless organizational symposia, academic journal articles, special issues, and government-sponsored projects around the world. It is difficult to quantify the impact that schizotypy has had on the academic community, in part, because it is the conceptual lynchpin connecting research on clinically disparate populations – comprising individuals with schizophrenia, first episode psychosis, schizophrenia-spectrum personality disorders, clinical high risk and prodromal symptoms, and relatively atypical personality traits.

Despite the impact of schizotypy on academic research, the public burden of schizophrenia-spectrum pathology has not diminished over the last six decades.[5–7] At present, there are no cures for schizophrenia-spectrum disorders, and treatments are palliative at best, and at worst carry severe health and psychological consequences.[7] Managing them is a public burden that many communities are unable or unwilling to shoulder,[8] and the disorders continue to carry a massive stigma that is poorly appreciated by the public and is often dangerously portrayed in the media.[9] While the schizotypy construct has certainly improved our understanding of schizophrenia-spectrum vulnerability, there are, as yet, no genetic, neurobiological, behavioral, clinical or functional markers that can serve case identification functions at the individual level for predicting outcome with acceptable sensitivity/specificity.[10] In short, we still have much work to do.

To advance scientific discovery and clinical translation of psychiatric disorders more generally, there have been repeated calls to reconceptualize psychopathology from relatively ambiguous clinically syndromes to more precise transdiagnostic phenotypes. The benefits of these approaches are that they allow for more organized and efficient evaluation of the phenotype across levels of complexity within various "systems". One of the more important systems under investigation involves the central nervous system as popularized by the National Institute of Mental Health's Research Domain Criteria Initiative [11] and by translational sciences more generally.[12] However, understanding phenotypic complexity across other systems has also been highlighted, such as across hierarchically-organized psychological functions (e.g., HiTop),[13] illness stage/outcome,[14] clinical needs,[15] neurodevelopment,[16] and culture.[17] Understanding phenotypic complexity across these various functions requires consensus in operational definition; a task largely achieved by the schizotypy research community. However, data should accurately reflect the full spectrum of the system in question. Often, this necessitates large data sets of individuals drawn from diverse demographic, cultural and racial backgrounds, and from a broad range of functional outcomes. Long has schizotypy research focused on translational, neurodevelopmental and cultural issues, but it is only recently that technology, analytic and assessment techniques, informatics, geopolitical and legal advances allow scalability to meaningfully and comprehensively model and understand it across various neurobiological, psychological and functional systems. Leveraging these advances to understand schizotypy across a broad range of systems, outcomes, phenotypes, cultures and contexts is a primary goal of the International Consortium on Schizotypy Research (ICSR).

To this end, the ICSR held its 2017 meeting in Beijing China with a focus on expanding schizotypy research across five domains, crossing: academic disciplinary borders (i.e., promoting brain and genetics/genomics research), clinical borders (i.e., promoting clinical and non-clinical applications), geographic borders (i.e., promoting cross-cultural research), laboratory borders (i.e., promoting "big" and "small" data collaborations), and methodology borders (i.e., promoting emotion, cognition and behavior

research using novel methods). This special supplement highlights some of the work that was presented at this consortium meeting, and from related work from researchers not in attendance.

In total, there are 10 articles in this special supplement. The first article, by Docherty and colleagues, [18] is an introduction and proposal for an international data-sharing collective meant to leverage open-source platform technology, big data informatics and analytics, and genetic, deep phenotypic, self-report and clinical data for understanding schizotypy. The second article, by Fonseca-Pedrero and colleagues, [19] builds on international collaboration of data sharing and employs graph theory and network analysis to understand the relationships between various schizotypy traits. This, and the next set of articles showcase relatively advanced analytic techniques for understanding schizotypy. The third article, by Kristoffer Madsen and colleagues, [20] provides an engineering and computational perspective on the use of machine learning for classifying schizotypy based on neurobiological data. The fourth article, by Wang and colleagues, [21] employs functional connectivity analysis of critical neural regions of interest during a visual facial processing task to understand anomalies in individuals with high schizotypy. Building on this, the fifth article, by Derome and colleagues [22], focuses on resting state networks in adolescents experiencing depersonalization. These networks are examined both cross-sectionally and longitudinally.

The next set of articles focuses on key phenotypes of schizotypy. The sixth article, by Ettinger and colleagues [23], conducted a comprehensive meta-analysis of cognitive control, and its relationship to various facets of schizotypal traits. The seventh article, by and Armando colleagues [24], examines the role of coping strategies in individuals with 22a11.2 deletion syndrome, and their relationship to clinical symptoms and schizotypal traits. The eighth article, by Lui and colleagues [25], examines the structure and organization of schizotypal features in biological relatives of schizophrenia patients. The ninth article, by Chan and colleagues [26], evaluates an interview-based clinical assessment tool for understanding negative symptoms across various clinical outcomes of the schizotypy-spectrum, with a particular focus on cross cultural validation. The final article, by Grant and colleagues, [27] examines the evolution of the schizotypy construct since its inception, and highlights various points of contention, unresolved issues and ways forward for better delineating the construct.

This supplemental section concludes with a commentary by Lenzenweger [28] discussing the ten articles included here within the context of schizotypy's conceptual roots and its potential future. Together, this rich set of papers and invited commentary, reunited into the special issue, reflect the contemporary richness of schizotypy, and ambitiously calls for a crossing of borders to reach beyond a specialized understanding of unique facets or methodology in schizotypy research, towards the development of a common empirically grounded understanding that may be applicable to real-life and clinical realities.

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