2015

Negative symptoms of schizophrenia: a historical, contemporary, and futuristic view

Shae-Leigh C. Vella
University of Wollongong, vella@uow.edu.au

Nagesh B. Pai
University of Wollongong, nagesh@uow.edu.au

Publication Details

Vella, S. Cynthia. & Pai, N. B. (2015). Negative symptoms of schizophrenia: a historical, contemporary, and futuristic view. Archives of Medicine and Health Sciences, 3 (2), 329-334.

Negative symptoms of schizophrenia: a historical, contemporary, and futuristic view

Abstract
This paper explores the evolution of the conceptualization of schizophrenia. Specifically, the paper focuses upon negative symptomology and the emphasis that such symptoms have garnered over time. Negative symptoms are associated with higher levels of impairment and poorer outcomes in schizophrenia. Historically, negative symptoms were the core feature of schizophrenia in the early conceptualizations of Kraepelin and Bleuler, holding precedence until the emergence of Schneiderian theory in the 1970's. The focus on negative symptoms then changed to positive symptoms; which is still the key focus today. This shift in emphasis has resulted in a dearth of knowledge and treatment for such symptoms and as such an area requiring further research. The paper also addresses the conceptual changes in the nosology of Schizophrenia and other psychosis with respect to the Diagnostic and Statistical Manual of Mental Disorders-5. Further the potential for the clinical assessment interview for negative symptoms to facilitate understanding and treatments for negative symptomology in schizophrenia is also discussed.

Disciplines
Medicine and Health Sciences | Social and Behavioral Sciences

Publication Details
Vella, S. Cynthia. & Pai, N. B. (2015). Negative symptoms of schizophrenia: a historical, contemporary, and futuristic view. Archives of Medicine and Health Sciences, 3 (2), 329-334.

Wolters Kluwer

Medknow

Volume 3 | Issue 2 | July-December 2015

ISSN: 2321-4848

ARCHIVES OF MEDICINE & HEALTH SCIENCES

A M&H S

www.amhsjournal.org

The Official Journal of Yenepoya University

Special Article

Negative symptoms of schizophrenia: A historical, contemporary, and futuristic view

Shae-Leigh Cynthia Vella, Nagesh B. Pai

Graduate School of Medicine, University of Wollongong, New South Wales, Australia

ABSTRACT

This paper explores the evolution of the conceptualization of schizophrenia. Specifically, the paper focuses upon negative symptomology and the emphasis that such symptoms have garnered over time. Negative symptoms are associated with higher levels of impairment and poorer outcomes in schizophrenia. Historically, negative symptoms were the core feature of schizophrenia in the early conceptualizations of Kraepelin and Bleuler, holding precedence until the emergence of Schneiderian theory in the 1970's. The focus on negative symptoms then changed to positive symptoms; which is still the key focus today. This shift in emphasis has resulted in a dearth of knowledge and treatment for such symptoms and as such an area requiring further research. The paper also addresses the conceptual changes in the nosology of Schizophrenia and other psychosis with respect to the Diagnostic and Statistical Manual of Mental Disorders-5. Further the potential for the clinical assessment interview for negative symptoms to facilitate understanding and treatments for negative symptomology in schizophrenia is also discussed.

Key Words: Diagnostic and Statistical Manual of Mental Disorders-5, Diagnostic and Statistical Manual of Mental Disorders-IV-Text Revision, history, negative symptoms, schizophrenia

Introduction

Schizophrenia is a chronic and debilitating condition with the frequently reported prevalence rate of 1% or 1 in 100 individuals being affected, internationally.[1-3] Schizophrenia is a devastating condition for those that are afflicted as well as their families and friends. Further schizophrenia, also exacts a tremendous toll upon society, economically through service utilization, and lost productivity.[4] As well as impacting upon societal outcomes such as violence, substance misuse, homelessness, and suicide within the community.[5]

Access this article online	
Quick Response Code:	Website: www.amhsjournal.org
	DOI: 10.4103/2321-4848.171943

Schizophrenia is a complex condition having a multiplicity of symptoms that impact upon the core of an individual's being; affecting their cognition, emotions, and behaviors.[6,7] That is, individuals with schizophrenia may have problems perceiving what is real from what is not real (delusions and hallucinations). They may behave in a bizarre manner ranging from childlike behavior to unprovoked agitation (disorganized behavior). They could completely lack any motivation for pursing any goal-directed activities (avolition). Further, they

How to cite this article: Vella SLC, Pai NB. Negative symptoms of schizophrenia: A historical, contemporary, and futuristic view. Arch Med Health Sci 2015;3:329-34.

Corresponding Author:
Shae-Leigh Cynthia Vella, Graduate School of Medicine, University of Wollongong, New South Wales, Australia. E-mail: vella@uow.edu.au

may have problems with emotional expression, with an inability to express emotion (affective flattening or blunted affect) or the expression of contextually inappropriate emotions (inappropriate affect).

Although schizophrenia has been a focus of scientific investigation for more than a century,[8,9] a dearth of knowledge regarding the structure, nosology, and treatment of the disorder pervades.[10] This scarcity of knowledge is especially prevalent in regards to the symptoms that reflect a diminution of normal functioning termed negative symptoms.[11,12] Approximately, 28-36% of individuals with schizophrenia comprise a latent group of individuals who experience severe and enduring negative symptoms.[13]

Arango and Carpenter[14] ascertain that the most common negative symptoms are alogia, affective flattening (blunted affect), anhedonia, asociality, avolition, and apathy. Alogia is defined as a poverty of speech either in frequency or content. Affective flattening or blunted affect refers to a diminution of emotional expression. Anhedonia pertains to the inability to experience pleasure while asociality refers to a general lack of interest in social relationships. Avolition is defined as a general lack of motivation, and apathy pertains to a lack of interest in general.[14]

The presence of negative symptoms in schizophrenia has consistently been found to result in greater functional impairment and poorer illness outcomes for those that are afflicted.[15-17] Further, there are no psychopharmaceutical agents despite the multitude of them or psychosocial interventions that effectively treat negative symptomology.[6,18]

Even though the dearth of knowledge and the impact of negative symptoms are clear; the focus on negative symptoms in schizophrenia has varied significantly over time. This article aims to trace the theorizing pertaining to negative symptoms in schizophrenia over time. Specifically, this article will review historical and contemporary conceptualizations of schizophrenia with a focus on the inherent importance of negative symptoms in the nomenclature of schizophrenia. The recent nomenclature of negative symptomology in schizophrenia specifically in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 and the clinical assessment interview for negative symptoms (CAINS) will be discussed with a focus on the potential impact on the understanding and treatment of negative symptomology in schizophrenia.

The Past Nosology of Schizophrenia

Accounts of psychotic conditions akin to schizophrenia spectrum disorders are evident in literature as far back as pharaonic Egypt; predating the birth of Christ.[6] The first conceptual framework of a schizophrenia-like condition was described by Kraepelin in 1887.[6,9] Kraepelin[9] termed this condition *dementia praecox* and postulated that the condition was marked by reduced cognitive activity, diminished interest, and lethargy. Further, Kraepelin[9] viewed schizophrenia (*dementia praecox*) as a distinct singular disease entity.

Following Kraepelin, Bleuler[8] further theorized about the condition known as *dementia praecox*, which he renamed as schizophrenia in 1911. Bleuler[8] conceptualized schizophrenia as a group of disorders as oppose to a singular disease entity due to the heterogeneity of symptoms evident in different individuals. Bleuler[8] further outlined the nosology of schizophrenia, delineating the core of the disorder; the fundamental symptoms that he believed were pathognomonic to schizophrenia. In addition, Bleuler[8] also described a secondary set of symptoms, that is, symptoms that he believed were not unique to schizophrenia but were also apparent in other disorders. That is, Bleuler[8] ascertained that schizophrenia was a disturbance of association, affectivity, attention, and volition.

Kraepelin[9] and Bleuler's[8] conception of schizophrenia differed through their preferred mode of defining the disorder with; Kraepelin's[9] definition being based on an epidemiological stance and Bleuler[8] favoring a nosological account of schizophrenia.[10,19] Conceptually, their definitions of the disorder were highly congruent.[8,9] Both Kraepelin[9] and Bleuler's[8] notion of schizophrenia emphasized the loss or diminution of cognitive, affective, and volitional capacities. Hence, both eminent theorists of schizophrenia conceptualized the core of schizophrenia to be negative symptomology.

This view of schizophrenia remained the prominent view until the 1960's when the emphasis shifted toward symptoms reflective of a disturbance of reality such as delusions and hallucinations.[6,20] Hence, the conceptualization of schizophrenia changed to focus on positive symptomology. This shift in focus occurred for a number of related reasons namely one primary reason pertained to improving the reliability of the diagnosis of the disorder.[6] As positive symptoms reflective of a reality disturbance are much more easily identifiable being either present or absent, as oppose to the diminution of functioning apparent in the negative symptomology described by Kraepelin[9] and Bleuler.[8]

Further stimulating this change in the conceptualization of the core of schizophrenia was the development and

utilization of the first antipsychotic, chlorpromazine[21] coupled with the emergence of Schneiderian theory.[22] Specifically, chlorpromazine, akin to most antipsychotics (especially the first generation antipsychotics), was effective in the treatment of positive symptoms associated with reality disturbances or an excess of functioning as oppose to symptoms reflective of a diminution of "normal" functional capacities or negative symptoms.

Schneider[22] proposed 11 first-rank symptoms of schizophrenia; however, Schneider's[22] view differed significantly from that of Kraepelin[9] and Bleuler's[8] conception. Although akin to Bleuler,[8] Schneider[22] believed the symptoms he described were pathognomonic to schizophrenia. The 11 first-rank symptoms described by Schneider[22] pertained to disturbances of reality and perception being much more easily identifiable than symptoms pertaining to a diminution of functioning. This significantly changed the symptomology that were viewed as pathognomonic to schizophrenia. This shift was accepted with alacrity and quickly became the favored nomenclature of schizophrenia.[6,19,23,24]

A few theorists continued to recognize the importance of negative symptomology.[25,26] With Andreasen[27] recognizing that although positive symptomology is readily identifiable, it is not the most fundamental characteristic of schizophrenia; hence, she developed the first scale for measuring negative symptomology in schizophrenia in 1983; the scale for the assessment of negative symptoms (SANS). This instrument offered the first operational definition of the negative symptomology construct.[27] The SANS measures the following negative symptoms: Alogia, affective blunting, avolition — apathy, anhedonia — asociality, and attentional impairment.[27] Attentional impairment is no longer viewed as a negative symptom of schizophrenia rather it is recognized as a cognitive symptom of schizophrenia, although negative symptoms and cognitive symptoms have been demonstrated to be related.[28]

Crow[25] defined two types of schizophrenia; Type I being associated with positive symptoms and Type II being associated with negative symptoms. Although the aforementioned types are not intended to be synonymous with positive and negative symptoms as they are based on a series of characteristics and not solely the predominance of positive and negative symptoms.[25,26] Crow[25] proposed the two dimensions of pathology in schizophrenia, one dimension being potentially amenable to treatment and the other associated with a deficit state, the latter being unchangeable by treatment and associated with poor long-term outcomes.

Furthermore within this period, Carpenter *et al.* delineated the distinction between primary (or enduring) and secondary (nonenduring) negative symptoms. That is, enduring or deficit negative symptoms were postulated to result from the clinical core of schizophrenia.[26] Whereas secondary or nonenduring negative symptoms result from other influences such as positive symptoms, antipsychotic treatment, depression, and social deprivation and are generally more amenable to treatment.[26] Furthermore during this period, Kay *et al.*[29] developed the positive and negative syndrome scale to assess both positive and negative symptomology along with general psychopathology.

Although some theorists remained interested in negative symptomology, the primary focus upon a disturbance of reality and perception as the fundamental basis of schizophrenia has largely continued until today.[14] With the pervasiveness of this view, further reflected by the omission of negative symptoms associated with a diminution of "normal" functional capacities' from classificatory systems until the DSM-IV.[14,30] Such a focus significantly impeded the development of knowledge pertaining to negative symptoms and, consequentially, has impacted on the development of treatments for the aforementioned symptomology.

The Present and Future Nosology of Schizophrenia

The DSM-IV-Text Revision (TR)[31] defines schizophrenia as a "disorder that lasts for at least 6 months and includes at least 1-month of active-phase symptoms (i.e., two or more of the following: Delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, negative symptoms)." Further, the DSM-IV-TR[31] also stipulates that these symptoms cause discernible social and occupational dysfunction.

The DSM-IV-TR[31] does incorporate the existence of negative symptoms into the classification of schizophrenia spectrum disorders with the DSM-IV-TR[31] including affective flattening, alogia, and avolition as negative symptoms. Anhedonia commonly recognized as a negative symptom is merely classified as an associated feature of schizophrenia in the DSM-IV-TR.[14,31] Further others[14] ascertain that in addition to the negative symptoms outlined in the DSM-IV-TR[31] asociality and apathy are also generally accepted as negative symptoms of schizophrenia and thus should be included as such.

The DSM-IV-TR[31] and the ICD-10[32] are comparable in the diagnosis of schizophrenia with; both making reference to negative symptomology and requiring the presence of

delusions and hallucinations for a diagnosis of schizophrenia. However, although both systems require 1-month of active-phase symptoms the ICD-10[32] only requires 1-month of symptoms in total for the diagnosis of schizophrenia in comparison to the DSM-IV-TR[31] that requires a 6 months duration of symptoms. Differentially, the ICD-10[32] places greater emphasis on Schneiderian first-rank symptoms and has a more detailed complex list of the symptoms of schizophrenia than the DSM-IV-TR.[31] However, the ICD-10[32] also places a greater emphasis upon negative symptomology as well; including a subtype of simple schizophrenia a purely negative variant of schizophrenia.[20]

Therefore, it is apparent that even though the study of negative symptoms has come back into favor in recent times[33,34] the study of the construct remains constrained by the most widely utilized classificatory system; the DSM-IV-TR.[35] With symptoms that were historically conceptualized as the core of schizophrenia; negative symptoms set aside in favor of a Schneiderian view of the schizophrenia spectrum.[36,37] Further, the nomenclature delineated in the DSM-IV-TR only captures a small subset of the clinical core of schizophrenia due to the stipulated severity (high) required of both primary negative and disorganized symptoms.[37] Parnas[37] asserts that this delineation impacts upon the diagnosis of nonparanoid schizophrenia cases.

In addition to the aforementioned issues with the nosology of schizophrenia as operationalized in the DSM-IV-TR, there are many who advocate that schizophrenia as characterized by enduring primarily negative symptoms is a distinct separate syndrome.[34,36] Being clinically distinguishable through several features including; distinct neuroanatomical features, asocial developmental pattern, reduced substance use, reduced depression and suicide.[36] Further, the dimensionality of psychopathology and negative symptoms, in particular, has also been highlighted.[34]

The DSM-IV-TR has now been superseded by the completion of the DSM-5.[38] Tandon and Carpenter[39] ascertain that there were only to be minor changes to the schizophrenia and other psychotic disorders nomenclature between the DSM-IV-TR and the DSM-5 however, the changes outlined may assist with overcoming some of the shortcomings of the predecessor classificatory system. Further Tandon *et al.*[40] ascertain that the DSM-IV definition of schizophrenia is retained in the DSM-5, however, there is further clarification of negative symptomology included in the DSM-5.

Significantly Schneiderian first-rank symptoms of schizophrenia are likely to receive less importance in the diagnosis of schizophrenia, although there was no mention of placing more emphasis on negative symptomology.[39] Further, there are no plans to expand the specific symptoms under the negative symptom construct to reflect all the symptoms that are commonly conceptualized as a negative symptom of schizophrenia.[14,39] Rather the terms diminished emotional expression, and avolition are utilized to capture the negative symptomology construct, along with alogia, anhedonia, and asociality.[38]

Further the traditional subtypes of schizophrenia (disorganized, paranoid, and catatonic) have been abandoned to reflect the fact that most people with schizophrenia have the symptomology associated with multiple subtypes of schizophrenia and move through the different subtypes over the duration of their illness.[40] Rather the heterogeneity of schizophrenia will be characterized by the incorporation of dimensional ratings of the different psychopathological domains of schizophrenia and psychotic spectrum disorders.[38,39] Each of the psychopathological domains is rated on a scale from 0; not present through to 4; severe.[38] This abandonment of the traditional subtypes and the acceptance of a dimensional approach may increase the heuristic value and clinical utility of the nosology. As the adoption of a dimensional approach aligns to reflect the heterogeneity of schizophrenia; thus increasing the pragmatic value of the diagnosis for both research and clinical practice alike.[21] Such an approach will also reduce the heterogeneity that is apparent in the traditional subtypes of schizophrenia.[41] Further, this approach to the diagnosis of schizophrenia has particular significance in regards to functional assessment. However, others have contended that the key strength of the DSM-IV criteria is its clinical utility and as such the DSM-5 should be even more superior for clinical usage,[35] through time and use it should become apparent whether the DSM-5 has increased clinical utility. In contrast, they also ascertain that the DSM continues to limit understanding and research into the schizophrenia construct through the atheoretical diagnostic criteria espoused.[35]

It still remains that more emphasis needs to be placed upon negative symptomology with the conceptual domains and relationships between the specific symptoms clearly delineated. Recently, the National Institute of Mental Health (NIMH) - measurement and treatment research to improve cognition in schizophrenia (MATRICS) released a consensus statement highlighting recommendations to assist with the development of treatments for negative symptoms in schizophrenia.[42] It is only with a clearer conceptualization as well as placing more importance upon these symptoms that advances can be made. However, Tarrier[43] noted that the NIMH-MATRICS consensus statement was biased toward the neurobiological mechanisms that underpin

negative symptomology and thus the development of psychopharmaceutical agents to the exclusion of psychosocial interventions. In addition, Tarrier[43] ascertained that further delineation and focus on the conceptual basis of negative symptomology would be beneficial in the development of both psychopharmaceutical and psychosocial treatments for negative symptoms in schizophrenia.

Recently, the collaboration to advance negative symptom assessment of schizophrenia (CANSAS) was established to develop a clinical assessment scale for negative symptomology in schizophrenia.[33,44,45] This working group has developed and commenced validating a measure for the clinical assessment of schizophrenia namely; the CAINS.[33,44,45] The CAINS was specifically designed to overcome the limitations inherent in the existing instruments.[45] Further, the development of the CAINS aims to promote innovative research into treatments for negative symptoms both pharmacological and psychosocial.[45] Along with advancing understanding pertaining to the underlying causes of schizophrenia as well as assisting with endeavors to forge and unite neuroscience based accounts of schizophrenia with other clinical and theoretical descriptions of schizophrenia.[45]

The CAINS offers immense hope to the assessment and treatment of negative symptomology in the future. Through a unique development and validation process the CANSAS has conducted initial validation of the CAINS, with the CAINS incorporating five core negative symptoms, namely asociality, avolition, anhedonia (both consummatory and anticipatory), blunted affect and alogia.[45] Initial validation procedures have demonstrated a two-factor model pertaining to experiential and expressive negative symptoms.[45]

It is hoped that the changes evident in the DSM-5 schizophrenia criteria although only indirectly linked to negative symptomology, through less reliance upon Schneiderian first-rank symptoms of schizophrenia will increase awareness of negative symptomology. Similarly it is anticipated that the new instrument for the assessment of negative symptoms; the CAINS will promote the significance of the negative symptomology in schizophrenia and the necessity for a greater understanding of the construct, along with the development of effective treatments for such debilitating symptoms. Further, it is also hoped that the aforementioned changes that have the potential to facilitate a greater understanding of negative symptomology are also apparent in the forthcoming ICD-11.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

References

1. McGarth J, Saha S, Chant D, Welham J. Schizophrenia: A concise overview of the incidence, prevalence, and mortality. Epidemiol Rev 2008;30:67-76.
2. Saha S, Chant D, McGarth J. Meta-analyses of the incidence and prevalence of schizophrenia: Conceptual and methodological issues. Int J Methods Psychiatr Res 2008;17:55-61.
3. Wheeler A, Humberstone V, Robinson G. Outcomes for schizophrenia patients with clozapine treatment: How good does it get? J Psychopharmacol 2009;23:957-65.
4. Kooyman I, Walsh E. Societal outcomes in schizophrenia. In: Weinberger DR, Harrison PJ, editors. Schizophrenia. 3rd ed. Oxford, UK: Wiley-Blackwell; 2011.
5. Covell NH, Essock SM, Frisman LK. Economics of the treatment of schizophrenia. In: Weinberger DR, Harrison PJ, editors. Schizophrenia. 3rd ed. Oxford, UK: Wiley-Blackwell; 2011.
6. Andreasen NC. Concept of schizophrenia: Past, present, and future. In: Weinberger DR, Harrison PJ, editors. Schizophrenia. 3rd ed. Oxford, UK: Wiley-Blackwell; 2011.
7. Blider RM. Schizophrenia. In: Snyder PJ, Nussbaum PD, Robins DL, editors. Clinical Neuropsychology: A Pocket Handbook for Assessment. 2nd ed. Washington: American Psychological Association; 2006.
8. Bleuler E. Dementia Praecox or the Group of Schizophrenias. New York: International Universities Press; 1978.
9. Kraepelin E. Lectures on Clinical Psychiatry. Cornell: Cornell University Library; 2009.
10. Tandon R, Maj M. Nosological status and definition of schizophrenia: Some considerations for the DSM-5 and the ICD-11. Asian J Psychiatry 2008;1:22-7.
11. Blanchard JJ, Cohen AS. The structure of negative symptoms within schizophrenia: Implications for assessment. Schizophr Bull 2006;32:383-345.
12. Stahl SM, Buckley PF. Negative symptoms of schizophrenia: A problem that will not go away. Acta Psychiatr Scand 2007;115:4-11.
13. Blanchard JJ, Horan WP, Collins LM. Examining the latent structure of negative symptoms: Is there a distinct subtype of negative symptom schizophrenia? Schizophr Res 2005;77:151-65.
14. Arango C, Carpenter WT. The schizophrenia construct: Symptomatic presentation. In: Weinberger DR, Harrison PJ, editors. Schizophrenia. 3rd ed. Oxford, UK: Wiley-Blackwell; 2011.
15. Foussias G, Mann S, Zakzanis KK, van Reekum R, Remington G. Motivational deficits as the central link to functioning in schizophrenia: A pilot study. Schizophr Res 2009;115:333-7.
16. Leifker FR, Bowie CR, Harvey PD. Determinants of everyday outcomes in schizophrenia: The influences of cognitive impairment, functional capacity, and symptoms. Schizophr Res 2009;115:82-7.
17. Rabinowitz J, Levine SZ, Garibaldi G, Bugarski-Kirola D, Berado CG, Kapur S. Negative symptoms have a greater impact on functioning than positive symptoms in

schizophrenia: Analysis of CATIE data. Schizophr Res 2012;137:147-50.
18. Buckley PF, Stahl SM. Pharmacological treatment of negative symptoms in schizophrenia: Therapeutic opportunity or cul-de-sac? Acta Psychiatr Scand 2007;115:93-100.
19. Andreasen NC, Nopoulos P, Schultz S, Miller D, Gupta S, Swayze V, *et al*. Positive and negative symptoms of schizophrenia: Past, present, and future. Acta Psychiatr Scand Suppl 1994;384:51-9.
20. Andreasen NC, Flaum M. Schizophrenia: The characteristic symptoms. Schizophr Bull 1991;17:27-49.
21. Tandon R, Nasrallah HA, Keshavan MS. Schizophrenia, "Just the facts" 4. Clinical features and conceptualization. Schizophr Res 2009;110:1-23.
22. Schneider K. Clinical psychopathology. Grune and Stratton: New York. Translated by Hamilton MW. 1959.
23. Carpenter WT, Strauss JS, Muleh S. Are there pathognomonic symptoms in schizophrenia? An empirical investigation of Schneider's first-rank symptoms. Arch Gen Psychiatry 1972;28:847-52.
24. Strauss JS, Carpenter WT. The prediction of outcome in schizophrenia. Arch Gen Psychiatry 1972;27:739-46.
25. Crow TJ. Molecular pathology of schizophrenia: More than one disease process? Br Med J 1980;280:66-8.
26. Carpenter WT, Heinrichs W, Alphs LD. Treatment of negative symptoms. Schizophr Bull 1985;11:440-52.
27. Andreasen NC. Methods for assessing positive and negative symptoms. In: Andreasen NC, editor. Schizophrenia: Positive and Negative Symptoms and Syndromes. Modern Problems of Pharmacopsychiatry 1990. Karger: Basel Switzerland; 1990.
28. Foussias G, Remington G. Negative symptoms in schizophrenia: Avolition and Occam's Razor. Schizophr Bull 2010;36:359-69.
29. Kay SR, Fiszbein A, Opler LA. The positive and negaitive syndrome scale (PANSS) for schizophrenia. Schizophr Bull 1987;13:261-78.
30. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: DSM-IV. Washington, DC: The American Psychiatric Association; 1994.
31. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition: DSM-IV-TR. Washington, DC: The American Psychiatric Association; 2000.
32. World Health Organisation. ICD-10 Classifications of Mental and Behavioural Disorders: Clinical Descriptions and Diagnostic Guidelines. Geneva: World Health Organisation; 1992.
33. Blanchard JJ, Kring AM, Horan WP, Gur R. Toward the next generation of negative symptom assessments: The collaboration to advance negative symptom assessment in schizophrenia. Schizophr Bull 2011;37:291-9.
34. Kaiser S, Heekeren K, Simon JJ. The negative symptoms of schizophrenia: Category or continuum? Psychopathology 2011;44:345-53.
35. Linscott RJ, van Os J. Systematic reviews of categorical versus continuum models in psychosis: Evidence for discontinuous subpopulations underlying a psychometric continuum. Implications for the DSM-5, DSM-VI and DSM-VII. Ann Rev Clin Psychol 2010;6:391-419.
36. Carpenter WT. Schizophrenia: Disease, syndrome, or dimensions? Fam Process 2007;46:199-206.
37. Parnas J. A disappearing heritage: The clinical core of schizophrenia. Schizophr Bull 2011;37:1121-30.
38. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: The American Psychiatric Association; 2013.
39. Tandon R, Carpenter WT. DSM-5 status of psychotic disorders: 1 year prepublication. Schizophr Bull 2012;38:369-70.
40. Tandon R, Gaebel W, Barch DM, Bustillo J, Gur RE, Heckers S, *et al*. Definition and description of schizophrenia in the DSM-5. Schizophr Res 2013;150:3-10.
41. Buchanan RW, Carpenter WT. Domains of psychopathology: An approach to the reduction of heterogeneity in schizophrenia. J Nerv Ment Dis 1994;182:193-204.
42. Kirkpatrick B, Fenton WS, Carpenter WT, Marder SR. The NIMH-MATRICS consensus statement on negative symptoms. Schizophr Bull 2006;32:214-9.
43. Tarrier, N. Negative symptoms in schizophrenia: Comments from a clinical psychology perspective. Schizophr Bull 2006;32:231-3.
44. Forbes C, Blanchard JJ, Bennett M, Horan WP, Kring A, Gur R. Initial development and preliminary validation of a new negative symptom measure: The Clinical Assessment Interview for Negative Symptoms (CAINS). Schizophr Res 2010;124:36-42.
45. Horan WP, Kring AM, Gur RE, Reise SP, Blanchard JJ. Development and psychometric validation of the clinical assessment interview for negative symptoms (CAINS). Schizophr Res 2011;132:140-5.