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Is Schizoaffective Disorder Still a Neglected Condition in the Scientific Literature?

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A recent editorial in *Psychotherapy and Psychosomatics* [1] discussed the boundaries between depression and psychosis. Indeed, the blurry boundaries that separate the classical Kraepelinian dichotomy of dementia praecox and manic-depressive illness were pointed out by the father of modern psychiatric nosology himself [2]. Despite the efforts for operational definitions of schizoaffective disorder (SAD) in the official nosology [3, 4], the endless debate is on and this disorder still struggles to generate consensus amongst experts and acceptance amongst clinicians [5].

The last 20 years have been characterized by major advances in scientific research concerning psychiatry, and, consequently, by an increase in publications regarding psychiatric disorders. Moreover, a general inflation of psychiatric diagnoses has happened, with a concrete risk for hyperinclusive diagnoses and medicalization of normal human behaviors [6]. Despite this, SAD shows only feeble trends to increase its number of studies. By performing a PubMed search for publications with 'schizoaffective disorder' in the title and using strict yearly time filters (i.e. from 1st of January 1990 to 31st of December 1990, and so on for every year), a numeric list of scientific publications on SAD in the last 20 years was obtained, further depicted in figure 1. SAD started with 5 publications in 1990, slowly growing up to 13 in 2000 and 56 in 2010. By performing the search only for the years 1990 and 2010, and using the key words 'bipolar disorder*' and 'schizophrenia', results were respectively 539 grown to 1,965 and 1,358 grown to 5,278. This means that, despite the low numbers, SAD-related papers have grown 11-fold as compared to 4-fold for bipolar disorder or schizophrenia within the past 20 years.

A number of reasons may justify this situation: (1) The clinical importance of this illness is not reflected by solid and reliable diagnostic criteria in DSM-IV and ICD-10, with some differences between the two. The McLean-Harvard International First-Episode Project [7] assessed that SAD, though least prevalent at baseline (0.20%), accounted for 12.2% of all 500 diagnoses at 2 years, and 53.6% of new diagnoses – a considerable 61-fold increase – mainly following the emersion of affective symptoms in patients psychotic at baseline. This low reliability is even worsened in SAD presenting with psychotic depression [8]. Thus, SAD is at least a pleomorphic clinical entity, and tailoring studies on this disorder

may present special problems in patient assessment. (2) Interest in targeting randomized controlled trials on treatments at schizoaffective patients is somewhat lower than in other psychoses, as most of the evidence is inferred from schizophrenia or bipolar disorder trials, and treatments deserve to be carefully tailored on patients [9]. The cause of this situation may be partly based on the clinical perception of the substantial overlap of the condition with schizophrenia and bipolar disorder and the low interest in studying novel treatments specifically addressed to SAD, because from the regulatory perspective an indication for 'psychoses' is already sufficient to justify the treatment in this condition. This situation is not unique for SAD as, for instance, a similar pattern is seen in the indication for major depression, irrespective of its unipolar versus bipolar nature, which has favored the use of antidepressants in bipolar illness. This has justified the lack of randomized controlled studies of bipolar depression therapies which does not slow down the massive use of antidepressants in bipolar depression, despite some critical issues highlighted thanks to new inputs in research [10]. Similarly, the extent to which the use of different classes of drugs in SAD is effective in pure samples has not been investigated. This lacks to give insight on specific treatments or combinations of treatments that could benefit schizoaffective patients and accounts for a consistent shortage in the increase of publications. (3) Most of the evidence until now produced points to quantitative rather than qualitative differences in genetic, clinical, neuroimaging and treatment features of SAD versus schizophrenia or bipolar disorder [11]. The implicit conceptual ascription of SAD to an extreme phenotype in bipolar disorder or schizophrenia, confirmed by clinical impressions as witnessed by naturalistic studies and by the scant evidence produced, may have lowered the general interest in the topic, partly justifying the low number of publications.

On a more theoretical level, it is hard to understand the respect that modern nosology still pays to the taboo of comorbidity between the two protagonists of the Kraepelinian dichotomy. This choice appears as one of the most long-lived contradictions in psychiatric nosology, considering that Kraepelin himself was perfectly aware of intermediate clinical presentations. The clinical introduction of new anticonvulsants and antipsychotics in different countries, especially since 1994, does not appear to have contributed substantially to the increase in scientific production in the field of SAD as, for instance, it happened to bipolar disorder [12]. However, despite the lack of a substantially improved knowledge of the clinical and diagnostic aspects of SAD, a slight input appears to have been given by improvements in therapeutic aspects in the last 5 years, with a growing attention for randomized controlled trials specifically aimed at schizoaffective populations [13], still far from being noteworthy.

Whatever cause or combination of causes may be ascertained, SAD still represents a neglected topic in psychiatric research when compared to its clinical severity, and urges specific research. Even

Fig. 1. Growth of publications concerning SAD from 1990 to 2010.

an extreme and still debated solution such as the removal of the diagnosis for the inconsistency of the clinical syndrome should come, at least, after extended research that as of today seems insufficient.

New inputs for research are not lacking. Research on diagnostic aspects should aim at stabilizing the diagnosis, as it suffers low reliability and seems the first premise to grant homogenous populations. The study of quantitative differences with the two extremes of the psychosis spectrum should be clearly assessed. Last, treatment response of this very population should be considered and researched, with special attention to combination treatment, an issue specifically common in SAD due to its intrinsic severity, which could help defining specific patterns of treatment. According to the increasing number of publications on the topic, SAD is likely to become an area of interest for researchers over the next decade.

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