Negative Symptoms in Schizophrenia: Comments From a Clinical Psychology Perspective

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2The NIMH-MATRICS Consensus Statement on Negative Symptoms is covered from the perspective of Clinical Psychology. The neurobiological model implicit in the Statement can be criticized on the basis that it is scientifically restrictive and narrow and poorly serves clinical practice and service development. Aspects of the Statement relating to psychological treatments are discussed.

Key words: schizophrenia/negative symptoms/clinical psychology

In commenting on the NIMH-MATRICS Consensus Statement on Negative Symptoms, I do so as a clinical psychologist who has been involved in the investigation of psychological and psychosocial factors in schizophrenia and in the design and evaluation of psychological and psychosocial treatments for over 3 decades. My research and clinical work have been carried out within the UK National Health Service, a system of universal health care, and it is from this perspective that I write. This is probably a somewhat different perspective from the participants in the Consensus Development Conference. There is much within the Consensus Statement that I would agree with, but I am not sure I would arrive at the same conclusions as to the most productive way forward. That the array of symptoms that are categorized as negative symptoms represents a distinct clinical problem that is often considered subsidiary to positive symptoms, at least in terms of outcome in clinical trials, is no doubt true. That these various symptoms need better investigation and understanding in their definition, course, and interaction through experimental and longitudinal studies would be difficult to dispute. What I do not see in the statement is an indication of how comprehensive, theory-driven research might advance our understanding of these phenomena, or any recognition that nondrug approaches are necessary or important. It will no doubt be argued that these topics were not within the terms of reference of the working group; however, the publication of the statement clearly sets an agenda with conceptual and practical implications. There appears to be an underlying assumption that neurobiological mechanisms will be the sole explanatory medium, and there is an explicitly stated objective of a search for pharmacological agents as the principal, if not only, therapeutic objective. I think this reductionist approach does not serve us well. There are a number of problems with taking this route.

First, it does not encourage the development and test of theories other than those which refer or relate to putative neurobiological processes. Second, treatment options will be severely restricted. If such an approach had been adopted with positive symptoms, the range of psychological and psychosocial treatments with demonstrated efficacy would not now be available. A focus solely on neurobiological mechanisms strongly favors pharmacological solutions. There must also be concerns, which have often been expressed, about the strong influence the pharmaceutical industry has on psychiatric practice and the publication of research. Many sections of the statement refer to improvements in the methodology of drug trials, which would aid the evaluation of therapeutic agents. This is all well and good, but similar advances in trial methodology for evaluation of nondrug treatments are, in my view, as important.

Third, there is no attempt to address the issue of transition from applied research into clinical practice and health services development. Presumably this will be left to drug company marketing departments! Psychosocial researchers are acutely aware of issues of dissemination and “roll out” of empirically supported treatments into clinical practice, and these issues are significant and need consideration. Biomedical and health science research are essentially two sides of the same coin. To define one in isolation from the other is not productive, not the least when there is a pragmatic question to be answered of how patients suffering this disorder can best be treated. Last, I note there appears to have been no consideration of service-user (consumer) opinion.

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It is worth commenting on each of the 11 points that were agreed upon by the conference participants:

1. Similar to drug trials, psychosocial intervention trials have focused on positive symptoms as the primary focus of treatment and outcome measure. However, while data are not exhaustive, there are indications that medium-term improvements in negative symptoms are evident in patients who are receiving cognitive-behavioral treatments for positive symptoms in addition to treatment as usual (TAU), when compared with TAU alone.7,8

2. The difference between primary and secondary symptoms, essentially cause and consequence, is a commonly held distinction that is not exclusive to negative symptoms or schizophrenia. The idea that some negative symptoms are enduring manifestations of a disease process while others are secondary effects is, of course, attractive, although not without its problems.9 There is, however, a potential confusion between origin, primary and secondary, and course, enduring or transient and stable or variable. Secondary symptoms may arise from a range of factors that belie any homogeneity. For example, secondary symptoms may be a reaction to the psychotic process, a result from treatment, or a result of the environment in its many forms. From a psychosocial treatment perspective, an intervention will be very different if secondary negative symptoms result from depression or social anxiety or drug effects.

3. That the presence of negative symptoms represents a reduction in quality of life seems reasonable but does rather depend on the definition and measurement of quality of life. Quality of life could be viewed as an objective universal or an idiosyncratic subjective appraisal with different results. Selten et al. investigated the experience of negative symptoms in schizophrenic and depressed patients and concluded that “a large number of schizophrenic patients are somewhat aware of negative symptoms but that they are less aware of these impairments and less concerned about them than are patients with a depressive disorder.”10

4. Longitudinal studies are clearly a priority, although the difficulty in clearly defining primary and secondary symptoms and their measurement has yet to be satisfactorily resolved (see point 11 and unresolved issues of the statement). Indication of the prevalence and course of negative symptoms is essential if the designs suggested in point 7 of the statement are to be viable. Many of the published studies that investigate primary and secondary symptoms are cross-sectional, and thus omit any interaction with time and course, and have relatively small sample sizes (less than 100).

5. The primary and secondary distinction has been commented on above (point 2). The suggestion that treatment trials will include patients with both primary and secondary negative symptoms most probably reflects reality but does seem to confuse the earlier points made in the statement. Investigation of the origins of negative symptoms requires studies of sufficient size and statistical power to be able to arrive at conclusions with confidence. Reliance on drug response for definition of primary and secondary further runs the risk of tautology.

6. Unambiguous conclusions regarding specificity of effect and underlying mechanisms are difficult to make in psychosocial trials, many of which are now designed as large pragmatic trials. Theory-driven studies of experimental psychopathology are used to further refine psychological and psychosocial treatments. However, the potential for direct and indirect effects cautions against premature conclusions on specific mechanisms.

7. Such paradigmatic designs as suggested for drug treatments are difficult in psychosocial treatments due to potential confounding factors, lack of understanding of the underlying mechanism, and the difficulty of recruiting representative samples of sufficient size to test specificity hypotheses.

8. An agreed upon, clinically meaningful effect size would be applicable to all types of intervention.

9. Conventional practice in drug trials differs from trials of psychosocial interventions, and results may be open to different interpretation. In trials of psychosocial interventions, a medium-term follow-up (1 to 2 years) over a period after the termination of the experimental treatment is usual to test maintenance of treatment effects. Absence of a maintenance effect is usually interpreted as a significant shortcoming of the treatment. Similar results in a drug trial, however, could be interpreted as evidence for a therapeutic effect and argument for continued medication.

10. How the different domains of negative symptoms are associated and what factors affect them will be the basis of empirical investigation. The statement that they “may have separate neurobiological substrates and may represent separate therapeutic targets” may indicate assumptions about causality that ignore other important factors. Furthermore,
analyses of individual domains or interactions in a drug trial would require the trial to have sufficient statistical power to detect such changes.

11. Advances in scales and measurement would benefit all types of intervention.

In summary, I find the Consensus Statement disappointing. It is heavily biased toward neurobiology as the only legitimate level of explanation and the development and testing of pharmacological agents as the only considered therapeutic strategy. By placing the ball centrally in the court of pharmacological interventions and licensing arrangements, the agenda is set and nondrug treatments initially excluded. One has to ask, who is the likely beneficiary of endorsing such an approach? I would advocate the development of testable models from a range of domains, including cognitive models, to explain different negative symptoms, and I use the term “cognitive” broadly and not just to signify deficits in information-processing capacity. Furthermore, I would advocate the development of different nondrug treatment approaches and evaluative methodologies and due consideration of health service practice on how any advances of treatment will penetrate into clinical delivery.

References


