Methodological Issues in Tardive Dyskinesia Research*  

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Abstract
Research into tardive dyskinesia, an involuntary movement disorder secondary to chronic neuroleptic treatment, has so far produced conflicting results with no clear clinical applications. Heterogeneous diagnostic criteria, research designs, and rating scales, plus an emphasis on single-drug trials, are probably responsible. A strategy of developing pharmacological response profiles for patients participating in tardive dyskinesia research is suggested as one way to produce meaningful data, which may delineate pharmacological and clinical subtypes that would respond to different treatment approaches. Further suggestions are made about future trends in this area of research.

Despite the large and expanding literature on clinical investigations of tardive dyskinesia, the treatment and prevention of this serious neuroleptic-induced movement disorder remains nebulous and uncertain. A wide variety of drugs with many modes of action have been reported to improve tardive dyskinesia symptoms (Tarsy and Baldessarini 1976), but contradictory reports on the same drugs quickly follow, resulting in a continuous state of skepticism. For example, according to the current neuropharmacological hypothesis of tardive dyskinesia (dopaminergic-receptor hypersensitivity and dopaminergic-cholinergic imbalance), antipsychotic and cholinergic drugs should improve tardive dyskinesia, whereas dopaminergic and anticholinergic drugs should make it worse (Gerlach, Reisby, and Randrup 1974). There is mounting evidence suggesting that this hypothesized response is not found in all patients and the opposite response occurs in some (Carroll, Curtis, and Kokmen 1977; Casey and Denny 1977).

A Problem of Methodology
A review of the literature on drug trials in tardive dyskinesia suggests that methodological differences could account for many of the contrasting and confusing results. Briefly stated, it seems to be generally a problem of different investigators using different diagnostic criteria to study different patient populations, and employing different subjective or objective methods to measure the outcome of single drug trials of different research designs.

Such methodological heterogeneity is not likely to produce consistent results in a research area that is fraught with ambiguities. Consider the following sample of unanswered questions:

• What is the prevalence of tardive dyskinesia? A review of 22 reports shows a range of .5 to 41 percent (Crane 1973), which reflects diagnostic and epidemiological confusion.
• Are there differences between patients with orofacial symptoms versus extremity or trunk choreiform movements?
• Are there differences between patients with long-term treatment versus short-term treatment? Older versus younger patients?

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Do different neuroleptics produce different symptoms of tardive dyskinesia or a different incidence?

What is the relationship between acute neuroleptic-induced dyskinesia, akathesia, or parkinsonism to the late-onset dyskinesia (Crane 1972)?

Do acute extrapyramidal symptoms predict future vulnerability to tardive dyskinesia? Or is it the effect of anticholinergic drugs that patients with extrapyramidal side effects frequently (and often chronically) receive?

Do drug holidays decrease or increase (Jeste et al. 1978) the vulnerability to tardive dyskinesia?

How important is the role of dental status in the development of orofacial dyskinesia in certain patients (Brandon, McClelland, and Protheroe 1971)?

Finally, are there subtypes of tardive dyskinesia that would explain the mixed results obtained in most drug trials?

Possible Future Trends

Some of the other issues that need to be dealt with by researchers in this area include:

- Standardizing diagnostic inclusion and exclusion criteria for tardive dyskinesia.
- Use of standard, valid and reliable, clinical and laboratory measures of outcome—e.g., the NIMH-developed Abnormal Involuntary Movement Scale (AIMS) for clinical ratings, and polygraphic or intra-oral balloon (pressure transducer) measures of bucco-linguo-masticatory movements.
- Use of well-controlled, double-blind, crossover designs and a minimum drug trial duration.
- The strategy of using drugs (parenteral or oral) that affect various neurotransmitter systems in addition to dopamine and acetylcholine (e.g., gamma-amino-butyric acid, norepinephrine, serotonin, histamine, peptides) in order to develop more comprehensive pharmacological response profiles and gain further insights into the neuropharmacology of the movement disorder.
- The establishment of collaborative studies of tardive dyskinesia that would allow large numbers of patients to be studied under similarly controlled conditions.

Prospective studies of the development of tardive dyskinesia symptoms to trace the natural history of the disorder and to focus on methods of prevention.

References


Tarsy, D., and Baldessarini, R.J.
The tardive dyskinesia syndrome.

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Volume on Autism Published

Significant recent advances in understanding autism have promoted the development of better services for autistic children and their families. Autism: A Reappraisal of Concepts and Treatment (New York: Plenum Publishing Corporation, 1978), edited by Michael Rutter and Eric Schopler, presents the most up-to-date review of current knowledge, research, and clinical practice. The contributors, reporting on research conducted in a variety of environments, evaluate many new ideas and concepts in formulating fresh approaches to dealing with the problems associated with autism.

After a brief introduction to the diagnosis and definition of autism, the authors examine the social and familial characteristics of autistic children; psychological, genetic, and biological research findings; psychotherapy; biological and behavioral treatment approaches; the education of autistic children; and long-term followup studies.

Bringing together the major advances and developments in the field, this work will be of interest to psychologists, psychiatrists, mental health workers, and parents, as well as to others concerned with the research on, and the care of, autistic children.

The 552-page volume is based on papers presented at the International Symposium on Autism held in St. Gallen, Switzerland. Contributors are listed below:

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