

Advances in psychopharmacology – schizophrenia

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Every so often in the history of medicine, events occur which in retrospect seem to mark a defining moment. For psychiatry, the decade of the 1950s uses one such 'moment'. On 28 December 1951, J. Sigwald started solo chlorpromazine treatment of a 57-year-old psychotic lady and, thereby, it might be argued, began the modern era of psychopharmacology.

The impact of antipsychotic drugs on the management and also the conceptualization of schizophrenia has been enormous, but the unbridled enthusiasm with which their use was first greeted has had to be tempered. Most of the standard compounds are essentially derivative and none offers any clear advantage. As a group, they perform the tasks required of them inadequately in relation to the 'positive' features of the illness^{1,2} and marginally or not at all on 'negative' features^{3,4}, while a substantial cost may be exacted in adverse effects, especially those indicative of disruption to extrapyramidal motor function.

Despite an acknowledged need for new drugs, the field of antipsychotics has not until recently been productive. This does not relate to the number of compounds available, but to the breadth of vision applied to possible mechanisms of action. It is only in the past decade that developments have allowed us to break free from the strictures of the classical dopamine hypothesis into which antipsychotic pharmacology had to some extent become confined.

The highly selective approach

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The ready acceptance of the name by which antipsychotic drugs have become most widely known is revealing, for while alternatives were proposed that spoke more of their effects on mental state, 'neuroleptics' emphasised their neurological actions. This was in keeping with the widely held view at the time that extrapyramidal signs were a necessary herald of therapeutic efficacy, a view that by the mid-1960s had fallen into disrepute⁵. Nonetheless, the discovery by Carlsson and Lindquist

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