

Peter Lehmann

**Coming off “atypical” neuroleptics (like Clozaril,
Risperdal, Seroquel, Zyprexa):
Challenges and Experiences**

Workshop at the Third Annual Recovery Conference
“Medicating Human Distress: Concerns, Critiques and Solutions”

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“Atypical” neuroleptics

On the market

clozapine **Clozaril** ♦ amisulpride **Solian** ♦ sulpiride **Dolmatil**
tiapride **Delpral** ♦ remoxipride **Roxiam** ♦ risperidone **Risperdal**
sertindole **Serdolect** ♦ quetiapine **Seroquel** ♦ zotepine **Zoleptil**
paliperidone **Invega** ♦ ziprasidone **Geodon** ♦ olanzapine **Zyprexa**
perospirone **Lullan** ♦ aripiprazole **Abilify** ♦ iloperidone **Fanapt**
lurasidone **Latuda** ♦ blonanserin **Lonasen** ♦ asenapine **Sycrest**

In the pipeline

cariprazine ♦ ocaperidone ♦ etc.?

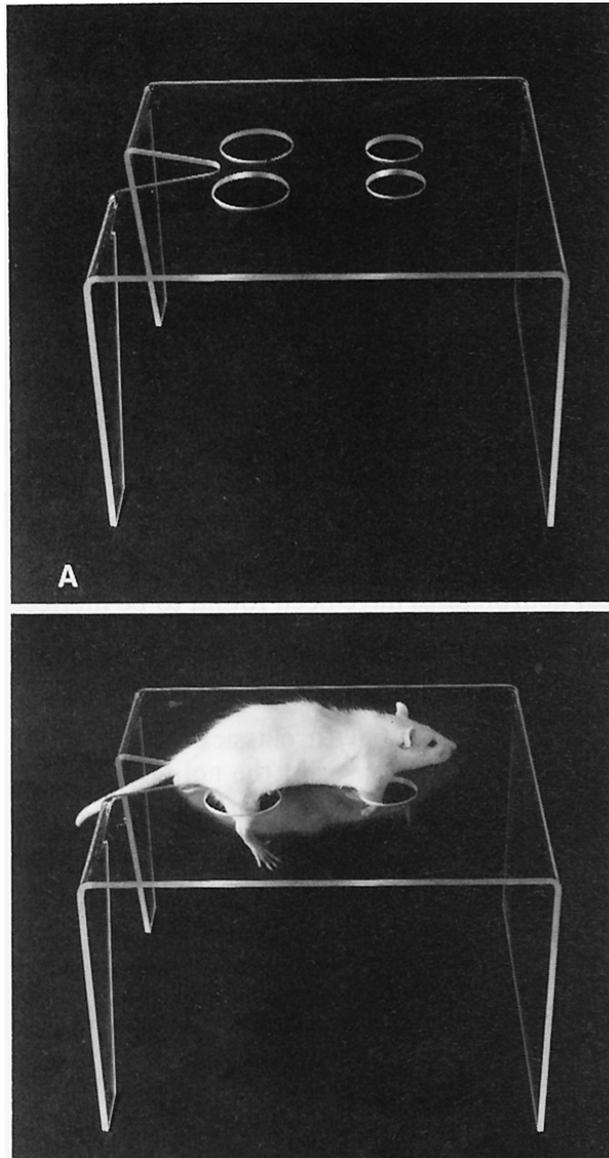
Difference between typical and “atypical” neuroleptics



A. Traditional impact test

In J. Delay & P. Deniker (1961).
*Méthodes chimiothérapeutiques en
psychiatrie – Les nouveaux
médicaments psychotropes.*

Paris: Masson et Cie, p. 224



Difference between typical and “atypical” neuroleptics

B. Paw test for scientific differentiating of typical and atypical neuroleptics

Ellenbroek, B. A., Peeters, B. W., Honig, W. M., & Cools, A. R. (1987). The paw test: A behavioural paradigm for differentiating between classical and atypical neuroleptic drugs. *Psychopharmacology*, 93, 343-348

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We went “... in principle, one step back again and have recently developed substances (...) that, beside the mechanism primarily relevant for the [*antipsychotic*] effect, also influence additional mechanisms. But in contrast to the old substances, here the intent was to implement only such mechanisms into the molecular structure that dampen specific qualities of side effects (especially EPS [*extrapyramidal symptoms*]). Though, in the pharmacological sense, the newest generation of neuroleptics are ‘dirty drugs’, that is, substances with more than one mechanism of action” (p. 54).

Müller, W. E. (2003). Wirkungsmechanismen älterer und neuerer Neuroleptika. In F. König & W. Kaschka (Eds.), *Interaktionen und Wirkmechanismen ausgewählter Psychopharmaka* (pp. 37-54). 2nd edition. Stuttgart / New York: Thieme Verlag

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“Clozapine behaves similar to other neuroleptics, to which you add an increasing dose of anti-parkinsonian drugs” (p. 143).

Haase, H.-J. (1988). Neuroleptika: Fakten und Erlebnisse. In O. K. Linde (Ed.), *Pharmakopsychiatrie im Wandel der Zeit* (pp. 137-154). Klingenmünster: Tilia Verlag Mensch und Medizin 1988

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“It is not a case of fewer side-effects, but of different ones which can be just as debilitating even if the patient isn’t immediately aware of them. Therefore, patients can be more easily motivated to take these drugs because they no longer suffer instantly and as much from the excruciating dyskinesias/extrapyrarnidal side-effects” (p. 30).

Ebner, G. (2003). Aktuelles aus der Psychopharmakologie – Das Wichtigste vom ECNP-Kongress. *Psychiatrie* (Switzerland), online-edition, (1), 29-32

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Neuroleptics turn “... the psychiatric patients (...) essentially into neurologic patients, with the appearance and disability of Parkinson's cases” (1980, p. 367).

“We temporarily turn the mentally suffering patient into a person with an organic brain disease, with ECT it happens in a more global way, but for a substantially shorter period of time than with pharmacological therapy” (1992, p. 545).

Dörner, K., & Plog, U. (1980). *Irren ist menschlich*.
Bonn: Psychiatrie-Verlag

Dörner, K., & Plog, U. (1992). *Irren ist menschlich*. 7th edition.
Bonn: Psychiatrie-Verlag

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Chemical structure groups of “atypical” neuroleptics

azabiphenyles

benzamides

benzisothiazolylpiperazines benzisoxazoles

chinolines

dibenzapines

dibenzothiepinines

dibenzoxapines

iminodibenzyles

phenylindoles

thiazepines

thienobenzodiazepines

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“Long-term administration of antipsychotic drugs to animals induces supersensitive mesolimbic [*referring to nerve tracts from the mid-brain to the cerebral cortex*] postsynaptic dopamine receptors. It is possible that a similar process can occur in man. Following a reduction in the dose of antipsychotic medications, or their complete discontinuation, mesolimbic dopamine receptor supersensitivity could be reflected in rapid relapse of schizophrenic patients, the development of schizophrenic symptoms in patients with no prior history of schizophrenia, or in the necessity for ever-increasing doses of long-acting depot fluphenazine to maintain a remission” (p. 699).

Davis, K. L. & Rosenberg, G. S. (1979). Is there a limbic system equivalent of tardive dyskinesia? *Biological Psychiatry*, 14, 699-703

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“The authors suggest that dopaminergic supersensitivity also occurs in the mesolimbic [*referring to nerve tracts from the mid-brain to the cerebral cortex*] region after chronic neuroleptic exposure, resulting in the development of a supersensitivity psychosis. (...) An implication of neuroleptic-induced mesolimbic supersensitivity is that the tendency toward psychotic relapse in such patients is determined by more than just the normal course of the illness” (p. 16).

Chouinard, G. & Jones, B. D. (1980). Neuroleptic-induced supersensitivity psychosis. *American Journal of Psychiatry*, 137, 16-21

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“We suggest that the rapid deterioration observed in our cases was due to a clozapine-induced supersensitivity of the mesolimbic [*referring to nerve tracts from the mid-brain to the cerebral cortex*] DA [*Dopamin*] receptors parallel to the striatal [*referring to the subcortical striatum*] DA supersensitivity, which at least in part is thought to be involved in the development of tardive dyskinesia. (...) The rapid appearance of the symptoms after withdrawal, and the fact that new symptoms were apparent, support the suggestion of a clozapine-induced supersensitivity psychosis” (pp. 293-294).

Ekblom, B., Eriksson, K., & Lindström, L. H. (1984). Supersensitivity psychosis in schizophrenic patients after sudden clozapine withdrawal. *Psychopharmacology (Berlin)*, 83, 293-294

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“These receptors may thus be most liable to develop supersensitivity after chronic clozapine treatment. The counterpart of tardive dyskinesias after chronic haloperidol may thus be potentiation of psychotic behavior after chronic clozapine!

These findings obviously pose serious questions concerning the strategy we should adopt in trying to find new, effective antipsychotic drugs. Will a ‘specific’ receptor blocking drug cause ‘specific’ receptor supersensibility and thus ‘specific’ side effects, i. e., *potentiate the disease itself?*” (p. 199)

Ungerstedt, U. / Ljungberg, T. (1977). Behavioral patterns related to dopamine neurotransmission. *Advances in Biochemical Pharmacology*, 16, 193-199

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“There is a worsening of the psychosis (delusions, hallucinations, suspiciousness) induced by long-term use of neuroleptic drugs. Typically, those who develop supersensitivity psychosis respond well initially to low or moderate doses of antipsychotics, but with time seem to require larger doses after each relapse and ultimately megadoses to control symptoms” (p. 44).

Tornatore, F., Sramek, J. J., Okeya, B. L., & Pi, E. H. (1987). *Reactions to psychotropic medication*. New York / London: Plenum Medical Book Company

“Thus, a tolerance to the antipsychotic effect seems to develop” (p. 53).

Tornatore, F., Sramek, J. J., Okeya, B. L., & Pi, E. H. (1991). *Unerwünschte Wirkungen von Psychopharmaka*. Stuttgart / New York: Thieme Verlag

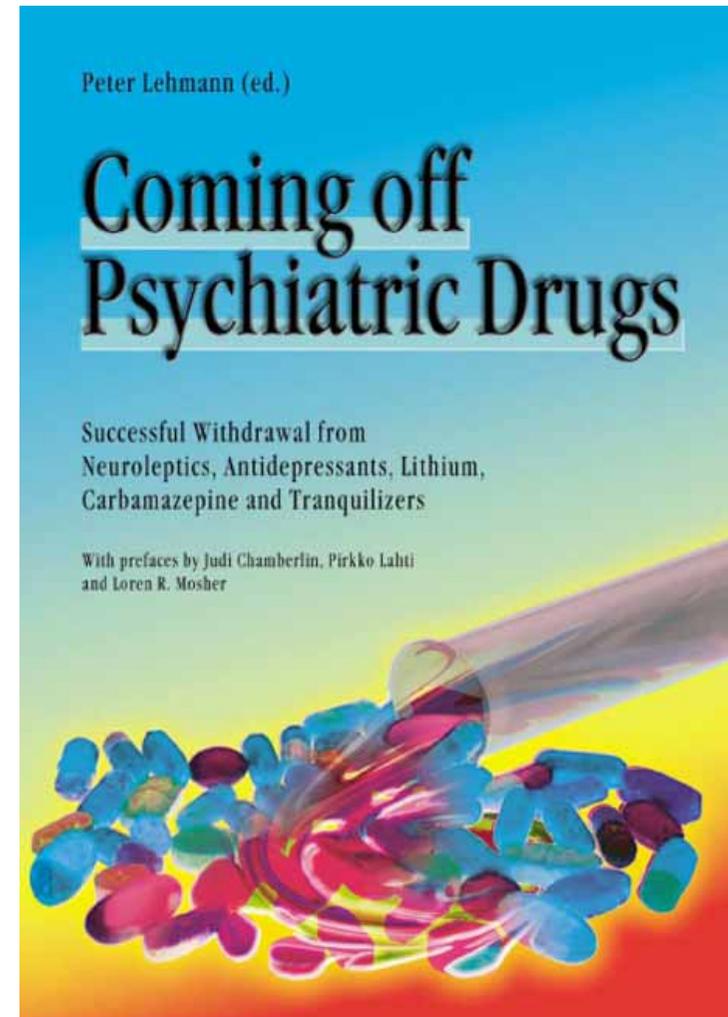
Peter Lehmann (Ed.):

Coming off Psychiatric Drugs

**Successful withdrawal from
neuroleptics, antidepressants,
lithium, carbamazepine
and tranquilizers**

Prefaces by Judi Chamberlin,
Loren R. Mosher & Pirkko Lahti

Berlin / Eugene / Shrewsbury:
Peter Lehmann Publishing 2004



www.peter-lehmann-publishing.com/books/withdraw.htm

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Ideal preconditions for withdrawal:

- adequate speed of reduction, gradual dosage reduction
- responsible attitude
- supportive surroundings
- proper help
- supportive self-help group
- competent professionals

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