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Appendix A

Evidence for the Neurotoxicity of Antipsychotic Drugs

The History of Neuroleptics

The modern history of psychiatric drugs dates back to the early 1950s, when derivatives of the synthetic dye and rocket fuel industries were found to have medicinal properties. Following World War II, a wide variety of compounds came to be tested in humans. The antihistamine known as chlorpromazine (Thorazine) is generally regarded as the first “anti-psychotic” drug, responsible for igniting the psychopharmacology revolution. As Thorazine grew in popularity, medications replaced neurosurgery and shock therapies as the favored treatments for the institutionalized mentally ill. (For three excellent reviews on this subject, see Cohen, Healy, and Valenstein).¹⁻³

When, in 1955, Drs. Jean Delay and Pierre Deniker coined the term “neuroleptic” to describe Thorazine, they identified five defining properties of this prototype: the gradual reduction of psychotic symptoms, the induction of psychic indifference, sedation, movement abnormalities (parkinsonism), and predominant subcortical effects.⁴ At its inception, Thorazine was celebrated as a *chemical lobotomizer* due to behavioral effects which paralleled those associated with the removal of brain tissue.⁵ As the concept of lobotomy fell into disfavor, the alleged antipsychotic features of the neuroleptics came to be emphasized. Ultimately, the two terms became synonymous.

Ignorant of the historical definition of neuroleptics as *chemical lobotomizers*, members of the psychiatric profession have only rarely acknowledged the fact that these dopamine blocking compounds have been, and continue to be, a major cause of brain injury and dementia. Nevertheless, the emergence of improved technologies and epidemiological investigations have made it possible to demonstrate why these medications should be characterized as neurotoxins, rather than neurotherapies.

Evidence for Neuroleptic (Antipsychotic) Induced Brain Injury

Proof of neuroleptic toxicity can be drawn from five major lines of evidence:

- 1) postmortem studies of human brain tissue
- 2) neuroimaging studies of living humans
- 3) postmortem studies of lab animal brain tissue
- 4) biological markers of cell damage in living humans
- 5) lab studies of cell cultures/chemical systems following drug exposure

Line of Evidence #1: Postmortem Studies in Humans

In 1977, Jellinger published his findings of neuropathological changes in the brain tissue of twenty-eight patients who had been exposed to neuroleptics for an average of four to five years.⁶ In most cases, the periods of drug treatment had been intermittent. At autopsy, 46% of the subjects were found to have significant tissue damage in the movement centers (basal ganglia) of the brain, including swelling of the large neurons in the caudate nucleus, proliferation of astrocytes and other glial cells, and occasional degeneration of neurons. Three patients exposed to chronic neuroleptic therapy also demonstrated inflammation of the cerebral veins (phlebitis). An example of the abnormalities is shown below:



This photo demonstrates reactive gliosis (black dots represent scar tissue) in the caudate of a patient who had received neuroleptic therapy. Patients in this study had received the following drug treatments: chlorpromazine (Thorazine), reserpine, haloperidol (Haldol), trifluoperazine (Stelazine), chlorprothixen (Taractan), thioridazine (Mellaril), tricyclic antidepressants, and/or minor tranquilizers.

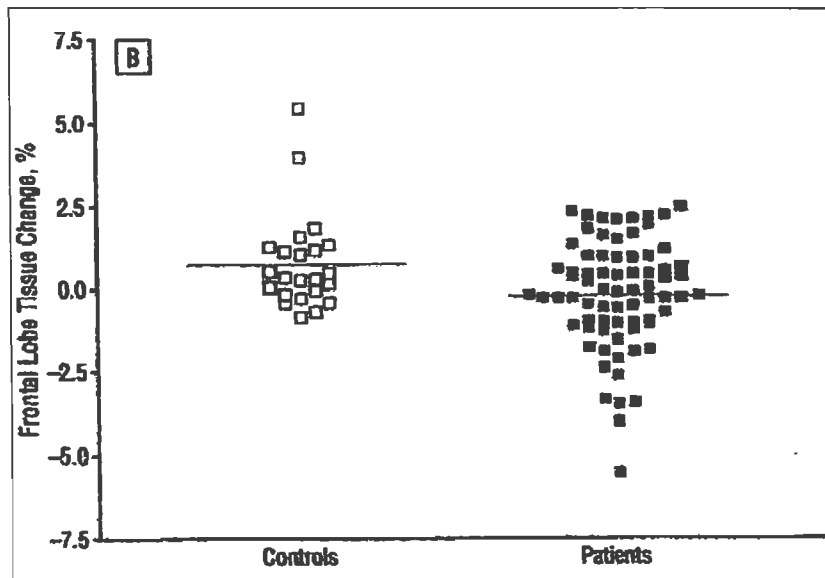
The Jellinger study is historically important because it included two comparison or control groups, allowing for the determination of treatment-related vs. illness-related changes. Damage to the basal ganglia was seen in only 4% of an age-matched group of psychotic patients who had *avoided* long-term therapy with neuroleptics; and in only 2% of a group of patients with routine neurological disease. Based upon the anatomic evidence, Jellinger referred to the abnormal findings as ***human neuroleptic encephalopathy*** (meaning: a drug-induced, degenerative brain process).

Line of Evidence #2: Neuroimaging Studies of Living Human Subjects

Several groups of researchers have documented a progressive reduction of frontal lobe tissue in patients treated with neuroleptics. Madsen et al. performed serial C.T. scans on thirty-one previously unmedicated psychotic patients and nine healthy controls. Imaging was performed at baseline and again after five years.⁷⁻⁸ During this time, the patients received neuroleptic therapy in the form of traditional antipsychotics (such as Thorazine) and/or clozapine. Findings were remarkable for a significant progression of frontal lobe atrophy in all of the patients, relative to the controls. ***The researchers detected a dose-dependent link to brain shrinkage, estimating the risk of frontal degeneration to be 6% for every 10 grams of cumulative Thorazine (or equivalent) exposure.***

Similar findings have been documented with newer technologies, such as magnetic resonance imaging (MRI). In 1998, Gur et al. published the results of a study which followed forty psychotic patients prospectively for 2 ½ years.⁹ At entry, half of these individuals had received previous treatment with neuroleptics, and half were neuroleptic naïve. All patients subsequently received treatment with antipsychotic medications. ***At the end of thirty months, the patients displayed a significant loss of brain volume (4 to 9%) in the frontal and temporal lobes.*** For both patient groups, this volume loss was associated with unimpressive changes in target symptoms (e.g., the inability to experience pleasure, restricted affect, and limited speech) and ***with significant deteriorations in cognitive functioning*** (such as attention, verbal memory, and abstract thought).

Researchers at the University of Iowa began a longitudinal investigation of psychotic patients between 1991 and 2001.¹⁰ Enrolling 23 healthy controls, and 73 patients recently diagnosed with schizophrenia, the study design called for a series of MRI exams to be conducted at various intervals (planned for 2, 5, 9, and 12 years). In 2003, the research team published the results from the first interval. Head scans and neuropsychological testing were repeated on all patients after a period of three years of neuroleptic treatment. Several findings were remarkable. ***First, patients demonstrated statistically significant reductions in frontal lobe volume (0.2% decrease per year) compared to the healthy controls:***



These changes were associated with more severe negative symptoms of schizophrenia (alogia, anhedonia, avolition, affective flattening), and with impairments in executive functioning (e.g., planning, organizing, switching). ***Second, almost 40% of the patients failed to experience a remission***, defined by the investigators as eight consecutive weeks with nothing more than mild positive symptoms (delusions, hallucinations, bizarre behavior, inappropriate affect, formal thought disorder). In other words, ***almost half of the patients remained floridly psychotic***. ***Third, these poor outcomes occurred despite the fact that the patients had been maintained on neuroleptics*** for 84% of the inter-MRI duration, and ***despite the fact that the newest therapies had been favored***: atypical antipsychotics had been given for 62% of the treatment period. Reflecting upon these disappointing results, the research team conceded:

“...the medications currently used cannot modify an injurious process occurring in the brain, which is the underlying basis of symptoms... We found that progressive volumetric brain changes were occurring despite ongoing antipsychotic drug treatment.”¹¹

In 2005, Lieberman et al. published the results of their international study involving serial MRI scans of 58 healthy controls and 161 patients experiencing a first episode of psychosis.¹² Most patients (67-77%) had received prior treatment with antipsychotics for a cumulative duration of at least four months. Throughout the two-year period of follow-up, patients were randomized to double-blind treatment with olanzapine (5 to 20 mg per day) or haloperidol (2 to 20 mg per day). The study protocol permitted the use of concomitant medications, such as minor tranquilizers (up to 21 days of cumulative therapy). Mood stabilizers and antidepressants other than Prozac (which could be used at any time) were allowed only after the first three months of the study. The primary outcome analysis involved a comparison of MRI changes from baseline, focusing upon seven regions of interest: whole brain, whole brain gray matter, whole brain white matter, lateral ventricles, 3rd ventricle, and caudate. ***Haloperidol recipients experienced persistent gray matter reductions throughout the brain.*** These abnormalities emerged as early as twelve weeks. ***For olanzapine recipients, significant brain atrophy (loss of gray matter) was detected in the frontal, parietal, and occipital lobes following one year of drug exposure:***

Average change in tissue volume (cubic centimeter) by week 52			
	olanzapine	haloperidol	controls
frontal gray	- 3.16	- 7.56	+ 0.54
parietal gray	- 0.86	- 1.71	+ 0.70
occipital gray	- 1.49	- 1.50	+ 0.99
whole brain gray	- 3.70	- 11.69	+ 4.12

In addition to these changes, both groups of patients experienced enlargements in whole brain fluid and lateral ventricle volumes. These disturbances in brain morphology (structure) were associated with retarded improvement in symptoms and neurocognitive functioning.

Line of Evidence #3: Postmortem Animal Studies

Acknowledging the longstanding problem in medicine of distinguishing the effects of treatment from underlying disease processes, scientists at the University of Pittsburgh have advocated the use of animal research involving monkeys (non-human primates). In one such study, the researchers attempted to identify the effects of lab procedures upon brain samples prepared for biochemical and microscopic analyses.¹³ Eighteen adult male macaques (aged 4.5 to 5.3 years) were divided into three groups and were trained to self-administer drug treatments. *Monkeys received oral doses of haloperidol, placebo (sham pellets), or olanzapine for a period of 17 to 27 months.* During this time, blood samples were taken periodically and drug doses were adjusted in order to achieve plasma levels identical to those which occur in clinical practice (1 to 1.5 ng/mL for haloperidol; 10-25 ng/mL for olanzapine). At the end of the treatment period, the animals were euthanized. Brains were removed, and brain size was quantified using two different experimental procedures.

A variety of behavioral and anatomical effects were noted. ***First, all animals appeared to develop an aversion to the taste and/or subjective effects of the medications.*** This required creative changes in the methods which were used to administer the drug treatments. ***Second, a significant number of monkeys became aggressive during the period of study*** (four of the six monkeys exposed to olanzapine; two of the six monkeys exposed to haloperidol). One monkey, originally placed in the sham treatment group, engaged in self-mutilatory behaviors. A switch to olanzapine resulted in no improvement. However, when the animal was provided with increasing human contact, a doubling of cage space, a decrease in environmental stimuli, and enhanced enrichment, his behavior stabilized. ***Third, the chronic exposure to neuroleptics resulted in significant reductions in total brain weight compared to controls (8% lower weight for haloperidol, 10% lower weight for olanzapine).*** Regional changes in weight and volume were also significant, with the largest changes identified in the frontal and parietal lobes:

volume reduction in brain weight (relative to sham controls)		
	olanzapine	haloperidol
frontal lobe	10.4%	10.1%
parietal lobe	13.6%	11.2%

Based upon these results, the researchers concluded that the progressive reductions in brain volume which have been reported in many studies on schizophrenia may reflect the effects of drug treatment. They proposed that further studies be undertaken to characterize the mechanisms responsible for these changes and to identify the precise targets (neurons, glia) of these effects.

Line of Evidence #4: Biological Markers of Cell Damage

Researchers in Austria have been interested in identifying a biological marker which can be used to diagnose Alzheimer's dementia or other forms of degenerative disease prior to death. In 2005, Bonelli et al. published the results of an investigation which involved the retrospective analysis of the cerebrospinal fluid (CSF) from 84 patients who had been hospitalized for the treatment of neurological conditions.¹⁴ Hospital diagnoses included two forms of dementia (33 cases of Alzheimer's dementia, 18 cases of vascular dementia), low back pain (9 patients), headache (5 patients), and neuropathy (4 patients). Researchers evaluated the fluid samples for tTG (tissue transglutaminase), an enzyme which is activated during the process of apoptosis or programmed cell death. Medical histories were also reviewed in order to identify pharmaceuticals consumed within 24 hours of the fluid collection via lumbar puncture.

Findings were remarkable for significant relationships between treatment with neuroleptics and elevations in tTG, particularly for females and patients with Alzheimer's dementia. When specific medications were reviewed, five antipsychotics (***including three of the so-called atypicals: melperone, olanzapine and zotepine***) were associated with above average levels of tTG:

tTG levels for patients receiving antipsychotic medications	
melperone	14.95 ng/dL
zotepine	8.78 ng/dL
olanzapine	8.50 ng/dL
flupentixol	7.86 ng/dL
haloperidol	7.30 ng/dL
average tTG for entire patient group:	4.78 ng/dL

Based upon these results, the research team drew the following conclusions:

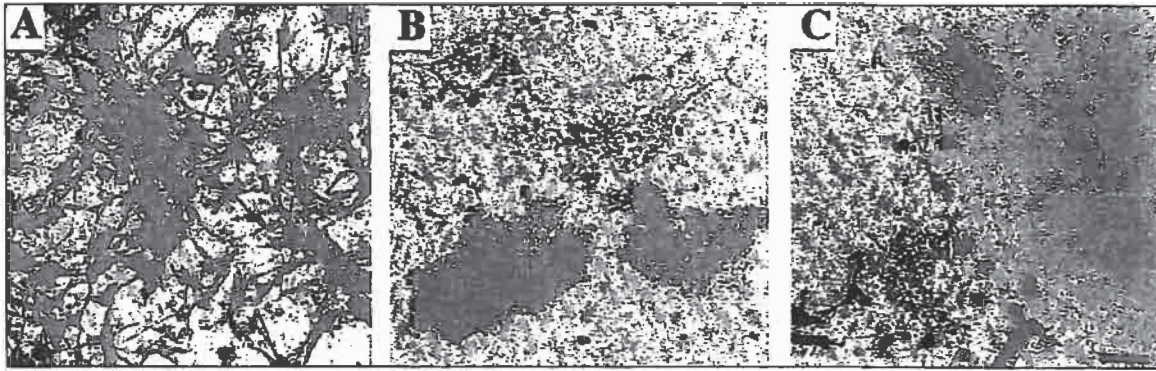
“...our study failed to show a difference in neurotoxicity between atypical and typical neuroleptics, and we should be careful when using neuroleptics as first-line drugs in Alzheimer's dementia patients...Because the level of cerebral apoptosis of non-demented patients on antipsychotics appears to be indistinguishable to [sic] Alzheimer's dementia patients without this medication, the question might arise as to whether neuroleptics actually induce some degenerative process...In conclusion, we suggest that typical and atypical neuroleptics should be strictly limited in all elderly patients, especially in females and all patients with Alzheimer's dementia.”¹⁵

While there were limitations to the Austrian study, it remains the only existing investigation of cell death in living subjects – none of whom received neuroleptics for mental illness. Furthermore, although the study failed to address possible relationships between apoptosis and antipsychotic exposure in terms of *dose* and *duration of treatment*, the implications extend far beyond the geriatric population. In fact, the finding that neuroleptic medications (and other psychiatric drugs) induce the process of apoptosis has inspired the oncology community to research these chemicals as adjuvant treatments for cancer. In other words, many psychiatric drugs are lethal to rapidly proliferating cells. To the extent that these chemotherapies are lethal to normal as well as cancerous tissues, there exists an urgent need for medical professionals and regulatory authorities to properly characterize the full effects of these toxins.

Line of Evidence #5: Lab Studies of Isolated Cells or Tissues

In vitro studies refer to research conducted upon tissue samples or isolated chemical systems obtained from lab animals or humans. In one such project, researchers in Germany exposed cell cultures to varying concentrations of haloperidol (Haldol).¹⁶ The experiment involved the removal of hippocampal neurons from embryonic rats. Some of these neurons were then incubated with the neuroleptic and or its active metabolite (reduced haloperidol), while a control group of neurons remained drug free. Following a twenty-four hour period of incubation, neurons exhibited a dose-related reduction in viability, relative to the control:

drug concentration	Haldol	Reduced Haldol (drug metabolite)
1 uM	27% cell death	13% cell death
10 uM	35% cell death	29% cell death
100 uM	96% cell death	95% cell death



Examples of neuronal cell loss (death) following incubation with Haldol

- A: normal neurons (dark) from unmedicated hippocampal brain tissue
- B: 100 uM of Haldol: severe loss of cell bodies and neuron extensions.
Note: Dark patches at bottom of slide represent abnormal cells which have rounded up and detached from the culture dish.
- C: 10 uM of Haldol: moderate loss of neurons and neuronal extensions.

Although this particular investigation involved a non-human species (rats), its results were medically concerning. First, the study employed Haldol concentrations which are clinically relevant to humans. In common medical practice, psychiatric patients are exposed to doses of Haldol which produce blood levels of 4 to 26 ng/mL. Brain levels are five to forty times higher. This means that psychiatric patients are indeed exposed to Haldol concentrations (1.4 to 2.8 uM) identical to the low levels that were tested in the German study. Second, the potential toxicity of Haldol in humans may be far greater than that revealed here, based upon the fact that this experiment was time limited (24 hour incubation only). Third, the neurons sampled in this experiment were taken from the key brain structure (hippocampus) associated with learning and memory. The possibility that Haldol kills neurons in this area (even if limited to 30%) provides a mechanism of action which accounts for the cognitive deterioration that is frequently observed in patients who receive this neuroleptic.

Dementia

Several teams of investigators have documented the problems associated with the use of neuroleptics in patients with pre-existing dementia. In a study which enrolled 179 individuals diagnosed with probable Alzheimer's disease, subjects were followed prospectively for an average of four years (range: 0.2 to 14 years).¹⁷ Symptoms were evaluated on an annual basis, and changes in medication were carefully observed. Over the course of the investigation, 41% of the subjected progressed to severe dementia, and 56% of the patients died. Using a statistical procedure called proportional hazards modeling, the **researchers documented a statistically significant relationship between exposure to neuroleptics and a two-fold higher likelihood of severe neurobehavioral decline.**

In England, a longitudinal investigation followed 71 demented patients (mean age: 72.6 years) over the course of two years.¹⁸ Interviews were conducted at four-month intervals, and autopsy analyses of brain tissue were performed on 42 patients who expired. Main outcomes in this study were changes in cognitive functioning, behavioral difficulties, and (where applicable) postmortem neuropathology. **The research team discovered that the initiation of neuroleptic therapy was associated with a doubling of the speed of cognitive decline.** This relationship was independent of the degree of dementia or the severity of behavioral symptoms for which the medications may have been prescribed.

While the methodology could not definitively prove that the drugs were the cause of mental deterioration, the study clearly demonstrated their inability to prevent it. The researchers concluded that:

“an appropriate response at present would be to undertake regular review of the need for patients to continue taking neuroleptic drugs, pursuing trials without medication where possible. This study highlights the importance of understanding the neurological basis of behavioural changes in dementia so that less toxic drugs can be developed for their treatment.”¹⁹

In 2005, an United Kingdom team of investigators performed autopsies on forty patients who had suffered from dementia (mean duration: four years) and Parkinsonian symptoms (mean duration: three years) prior to death.²⁰ Based upon a postmortem tissue analysis of the brain, exposure to neuroleptics (**old and new**) was associated with a four-fold increase in neurofibrillary tangles, and a 30% increase in amyloid plaques in the cortex of the frontal lobes. Due to the fact that the prevalence of symptoms did not vary between patients who received neuroleptics and those who remained neuroleptic free, the abnormalities detected appeared to be a result of the pharmaceutical agents, rather than a pre-existing disease. Most importantly, the findings suggest that all of the antipsychotics (**old and new**) are capable of inducing or accelerating the pathological changes (plaques and tangles) which are the defining features of Alzheimer's disease.

To review:

Evidence from postmortem human analyses reveals that older neuroleptics create scarring and neuronal loss in the movement centers of the brain. These changes are an example of *subcortical* dementia, such as Parkinson's or Huntington's disease.

Evidence from neuroimaging studies reveals that ***old and new*** neuroleptics contribute to the progressive shrinkage and/or loss of brain tissue. Atrophy is especially prominent in the frontal lobes which control decision making, intention, and judgment. These changes are consistent with *cortical* dementia, such as Niemann-Pick's or Alzheimer's disease.

Evidence from postmortem analyses in lab animals reveals that ***old and new*** neuroleptics induce a significant reduction in total brain weight and volume, with prominent changes in the frontal and parietal lobes.

Evidence from biological measurements suggests that ***old and new*** neuroleptics increase the concentrations of tTG (a marker of programmed cell death) in the central nervous system of living humans.

Evidence from *in vitro* studies reveals that haloperidol reduces the viability of hippocampal neurons when cells are exposed to clinically relevant concentrations. (Other experiments have documented similar findings with the second-generation antipsychotics.)

Shortly after their introduction, neuroleptic drugs were identified as chemical lobotomizers. Although this terminology was originally metaphorical, subsequent technologies have demonstrated the scientific reality behind this designation. Neuroleptics are associated with the destruction of brain tissue in humans, in animals, and in tissue cultures. Not surprisingly, this damage has been found to contribute to the induction or worsening of psychiatric symptoms, and to the acceleration of cognitive and neurobehavioral decline.

Appendix B

Successful Alternatives to Antipsychotic Drug Therapy²¹⁻²²

In a paper entitled “The Tragedy of Schizophrenia,” psychologist and psychotherapist, Dr. Bert Karon, challenges the prevailing notion that psychosis remains a largely incurable brain disease which is best modified by pharmacotherapy. Mindful of the fact that “there has never been a lack of treatments which do more harm than good,” Karon explicitly contends that humane psychotherapy remains the treatment of choice for schizophrenia, and he understands why this has always been so.

Karon reminds his readers that history provides important lessons for contemporary practitioners. The Moral Treatment Movement in the late 18th century emphasized four essential elements in the care of the mentally ill:

- respect for the patient (no humiliation or cruelty)
- the encouragement of work and social relations
- the collection of accurate life histories
- the attempt to understand each person as an individual

When these imperatives were applied in the asylums of America and Europe, the rates of discharge reached 60-80%. This was far better than the 30% recovery rate which occurred about a century later, in the era of pharmacotherapy.

Although the Moral Treatment Movement was replaced by the tenets of biological psychiatry in the late 1800s, its elements were incorporated in the theory and practice of various psychosocial therapies. For reasons which were largely political and economic, however, the consensus in American psychiatry came to denigrate the use of these Moral Treatment offshoots – particularly, in the treatment of psychosis.

Academic opinion leaders in the field of psychiatry now contend that there is insufficient evidence to support the use of psychotherapy as a major or independent intervention for psychosis. This perspective is contradicted by a rich (but suppressed) history in the published literature, and by the success of many ongoing programs, some of which are summarized below.

The Bockoven Study

This study compared the prognoses of 100 patients who were treated at Boston Psychopathic Hospital between 1947 and 1952; and 100 patients who were treated at the Solomon Mental Health Center between 1967 and 1972. Patients were similar in the severity of their symptoms, but the earlier cohort received treatment that was limited to psychosocial therapies. In contrast, the 1967 cohort received medication, including neuroleptics. Five-year outcomes were superior for the earlier cohort: 76% return to community and a 44% relapse in terms of re-hospitalization. In comparison, the 1967 cohort experienced an 87% return to the community, but a 66% rate of rehospitalization. The investigators concluded that medications were associated with higher numbers of relapsing patients, and a higher number of relapses per patient.

The Vermont Longitudinal Study of Persons With Severe Mental Illness

In 1955, a multidisciplinary team of mental health care professionals developed a program of comprehensive rehabilitation and community placement for 269 severely disabled, back wards patients at the Vermont State Hospital. When none of these patients improve sufficiently through two or more years of neuroleptic therapy, they were offered a revised plan of treatment. The intensive rehabilitation program was offered between 1955 and 1960. Subsequently, patients were released to the community as they became eligible for discharge, receiving a variety of services that emphasized continuity of care. At a long-term follow-up performed between 1980 and 1982, 68% of patients exhibited no signs of schizophrenia, and 45% displayed no psychiatric symptoms at all. Most patients had stopped using medication (16% not receiving, 34% not using, and 25% using only sporadically). A subsequent analysis revealed that all of the patients with full recoveries had stopped pharmacotherapy completely. (In other words, compliance with antipsychotic drug treatment was neither necessary, nor sufficient, for recovery.)

The Michigan State Psychotherapy Project

Between 1966 and 1981, Drs. Bert Karon and Gary VandenBos supervised the Michigan State Psychotherapy Project in Lansing, Michigan. Patients were randomly assigned to receive about 70 sessions of psychoanalytically informed psychotherapy, medication, or both over a period of 20 months. By the end of treatment, the psychotherapy group had experienced earlier hospital discharge, fewer readmissions (30-50% fewer days of hospitalization), and superior improvement in the quality of symptoms and overall functioning. The poorest outcomes occurred among the chronically medicated, even when drugs were combined with psychotherapy.

The Colorado Experiment

In 1970, Drs. Arthur Deikman and Leighton Whitaker presided over an innovative treatment ward at the University of Colorado. Occurring just 20 years after the advent of the neuroleptics, the Colorado experiment attached a priority to psychosocial interventions during the inpatient care of 51 patients diagnosed with severe mental illness. Individual and group psychotherapies were delivered in the spirit of the Moral Treatment Movement, motivated by a spirit of collaboration, respect, and a desire to understand behaviors as expressive of meaning. Furthermore, psychotherapies were used with the goal of restoring pre-psychotic abilities and independent functioning, rather than with the more limited goal of blunting symptoms in order to justify rapid discharge. *Medications were used as interventions of last resort.* After ten months of experimentation, the researchers made the following discovery: compared to “treatment as usual” (neuroleptics and supportive therapy), the recipients of intensive psychotherapy experienced lower recidivism (fewer readmissions after discharge) and lower mortality.

The Soteria Project

Between 1973 and 1981, Dr. Loren Mosher (then Director of Schizophrenia Research at the National Institute of Mental Health) presided over an investigational program in Northern California. Over the course of nine years, the Soteria project involved the treatment of 179 young psychotic subjects, newly diagnosed with schizophrenia or schizophrenia-like conditions. A control group consisted of consecutive patients arriving at a conventional medical facility, who were assigned to receive care at a nearby psychiatric hospital. Soteria was distinguished by an attitude of hopefulness; a treatment philosophy which de-emphasized biology and medicalization; a care setting marked by involvement and spontaneity; and a therapeutic component which placed a priority upon human relationship. Most significantly, Soteria involved the minimal use of neuroleptics or other drug therapies. Two-year outcomes demonstrated superior efficacy for the Soteria approach. Although 76% of the Soteria patients remained free of antipsychotics in the early stages of treatment; and although 42% remained free of antipsychotics throughout the entire two-year period, the Soteria cohort outperformed the hospital control group (94% of whom received continuous neuroleptic therapy) by achieving superior outcomes in terms of residual symptoms, the need for rehospitalization, and the ability to return to work.

The Agnews State Hospital Experiment

In 1978, Rappoport et al. summarized the clinical outcomes of 80 young males (aged 16-40) who had been hospitalized in San Jose at Agnews State Hospital for the treatment of early schizophrenia. Following acceptance into a double-blind, randomized controlled study, subjects were assigned to receive placebo or neuroleptic therapy (chlorpromazine). Treatment effectiveness was evaluated using various rating scales for as long as 36 months after hospital discharge. The best outcomes, in terms of severity of illness, were found among the patients who avoided neuroleptic therapy both during and after hospitalization. Patients who received placebo during hospitalization, with little or no antipsychotic exposure afterward, experienced the greatest symptomatic improvement; the lowest number of hospital readmissions (8% vs. 16-53% for the other treatment groups); and the fewest overall functional disturbances.

Finland – Acute Psychosis Integrated Treatment (Needs Adapted Approach)

In 1992, clinicians in Finland launched a multi-center research project using Acute Psychosis Integrated (API) Treatment. Keenly aware of the problems associated with antipsychotic drug therapy, the research team adopted a model of care which emphasized four features: family collaboration, teamwork, a basic therapeutic attitude, and adaptation to the specific needs of each patient. The initial phase of the project enrolled 135 subjects (aged 25-34) experiencing a first episode of psychosis. All were neuroleptic naïve, and all had limited or no previous exposure to psychotherapy. Three of the six participating treatment facilities agreed to use antipsychotic medications sparingly. The experimental protocol assigned patients to two groups with 84 receiving the Needs Adapted Approach, and 51 receiving treatment as usual. Two-year outcomes favored the experimental treatment group: fewer days of hospitalization, more patients without psychosis, and more patients with higher functioning. These outcomes occurred despite the fact that the Needs Adapted group consisted of more patients with severe illness (diagnosed schizophrenia) and longer durations of untreated psychosis, and despite the fact that 43% of the Needs Adapted subjects avoided antipsychotics altogether (vs. 6% of the controls).

Subsequent refinements to the Needs Adapted Approach have expanded upon these initial successes.²³⁻²⁵ In a series of papers describing outcomes for what has evolved to be known as the Open Dialogue Approach, the Finnish clinicians have achieved the following five-year outcomes for first-episode, non-affective psychosis:

- 82% rate of full remission of psychotic symptoms
- 86% rate of return to studies of full-time employment
- 14% rate of disability (based upon need for disability allowance)

The results of the Finnish experiment stand in stark contrast to the results of the prevailing American standard of care, which currently features a 33% rate of lasting symptom reduction or remission; and, at most, a 40% rate of social or vocational recovery.²⁶

Pre-Therapy: A Client-Centered Approach²⁷

It has been suggested by many professionals that it is not possible to conduct meaningful psychotherapy with any individual who is deep in the throes of a psychotic process. Pre-Therapy refers to a client-centered form of psychotherapy which reaches through psychosis and/or other difficulties (such as cognitive limitations, autism, and dementia) in order to make contact with the pre-verbal or pre-expressive Self. Drawing upon the principles of the late Carl Rogers and developed by American psychologist, Dr. Garry Prouty, Pre-Therapy emphasizes the following treatment philosophy and techniques:

unconditional positive regard for the client:
“the warm acceptance of each aspect of the client’s world”

empathy: “sensing the client’s private world as if it were your own”

congruence: “within the relationship, the therapist is freely and deeply himself or herself”

non-directiveness: “a surrendering of the therapist to the client’s own intent, directionality, and process”

psychological contact: exemplified by the therapist’s use of contact reflections, an understanding of the client’s psychological or contact functions, and the interpretation of the client’s contact behaviors

Although Pre-Therapy has not been promoted or publicized within the United States, it has been used successfully around the world to assist regressed or language-impaired individuals in regaining or improving their capacity for verbal expression. (It has even been used to resolve catatonia successfully, without the use of drug therapy.)²⁸

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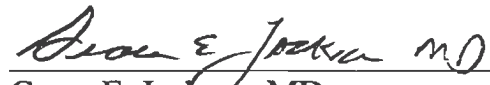
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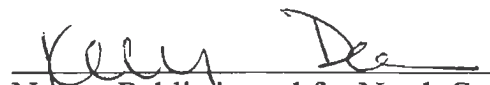
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SUBSCRIBED AND SWORN TO before me this 16th day of May, 2008.


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