

**DEPRESSIVE STATES
AND DRUGS—III.
USE OF METHYLPHENIDATE
(RITALIN) IN OPEN PSYCHIATRIC
SETTINGS AND IN
OFFICE PRACTICE***

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THIS PAPER is another in a series²³⁻²⁵ on depressive states and drugs. While our previous papers dealt with the new agents, imipramine (Tofranil)²³ and phenazine (Nardil)²⁴ and made some comments on depressive states²⁵ respectively, the present paper is an attempt to shed new light on the action of a relatively older and well-established stimulant.

In all of this, as in the work with tranquilizers, the concept of the psychodynamic action,²⁶⁻³⁰ and of the specific pharmacological, and non-specific therapeutic,^{26, 28-30} action of psychopharmacological agents, as pioneered by Sarwer-Foner and some of his co-workers, was invoked. In addition, some of the clarifications on the placebo effects,^{1, 14, 15, 22, 36, 37} and the importance attached to transference phenomena^{23, 26-31, 33} induced by the administration of drugs, helped give impetus to a sophisticated approach to the study of drug effects in psychiatry, and is reflected in this work as well.

Methylphenidate (Ritalin§), a piperidine derivative, is a cephalotropic amine, a central nervous system stimulant, and has been used as a stimulator of motor and psychomotor activity, as an elevator of mood and as an "antidepressant".^{2-8, 17, 19} Biochemical properties have been described elsewhere.^{2, 13} It has been noted by several authors^{2, 11, 19} that the effects of methylphenidate lie somewhere between those of caffeine and those of the amphetamines. It seems to have the particular advantage of being relatively free from unpleasant side effects. Its physiological effects seem to offer few contraindications to its use. In respect of psychopharmacological effects, severe agitation and anxiety can be considered as relative contraindications to the use of methylphenidate.¹⁰ Since 1954, methylphenidate has been used as a central nervous stimulant, and was found by several investigators^{3, 11, 13, 20, 35} to be an effective drug in the treatment of depressive states.

The purpose of this study was to re-evaluate the stimulant or antidepressant properties of methylphenidate and to attempt to differentiate clearly between pharmacological effects as they appeared (that is to say, the pharmacological profile of the drug) and its effect on target symptoms (that is,

those symptoms which might be modifiable through the physiological action of the drug). The assessment of these factors was separated from the evaluation of the drug effects on the general therapeutic situation, and from those effects, non-specific as to drug, that can be produced by transference.^{26, 28-31, 33}

Agitated depressions were not included in this study to obviate the possibility of an exacerbation of agitation and anxiety in some patients.

PATIENTS, MATERIALS AND METHODS

In a two-year study, 159 patients were treated by methylphenidate. Of these, 121 are the subject of this communication, while 38 patients were dropped from the study. Sixteen of these were dropped because they had received electroconvulsive therapy (E.C.T.) in combination with methylphenidate. Twenty-two other patients, who received other antidepressants in combination with or before receiving methylphenidate, were also excluded from this series, because our research design precluded combining the drug with other organic treatment modalities. The 121 patients included in the study received no other medication but methylphenidate, with the exception of those patients who needed night-time sedation. This consisted of 3 grains of a combination of equal parts of secobarbital and amobarbital or 1½ grains of secobarbital according to the degree and pattern of their insomnia.

Treatment Setting

Twenty-five patients were treated in the in-patient service of the psychiatric department of the Jewish General Hospital. This is an open psychiatric unit of psychoanalytic orientation. The treatment philosophy is based on the use of psychotherapy along with whatever organic adjuvants may be necessary.³⁴

This setting offered good facilities for individual psychotherapy by residents, under the direct supervision of senior psychiatrists, all of whom are university teachers and qualified psychoanalysts, or undergoing psychoanalytic training. It offers good observation of the patient by the residents and nursing staff. A ratio of one nurse to two patients permits intensive nursing care and very good observation of the daily behaviour of the patients. Good psychological services, with testing of all patients as required and the use of two social service workers on the wards, exists. This milieu permits good levels of observation and intensive psychodynamic study.

The Physiological Effects

The pharmacological profile of the drug, i.e. its clinically observed physiological effects, was sought. The amount of time needed for them to appear after medication was begun was observed. Changes in weight, appetite, blood pressure, sleep patterns, pulse and temperature were observed. Laboratory

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tests for toxicity (urine analysis, hemogram, blood cholesterol, alkaline phosphatase, fasting blood sugar) were periodically performed. The psychodynamic and mental status observations were made independently by residents, physicians, supervising psychiatrists and nursing staff.

*Psychiatric Drug Treatment Clinic*¹⁶

Forty-four patients were studied in the psychiatric drug treatment clinic of the Jewish General Hospital and in the general psychiatric outpatient department clinic by members of the drug treatment team. The clinic was organized to handle selected patients who might benefit from a supportive relationship and from the use of drugs to attack specific "target symptoms". Patients were selected for this facility on the basis of either a "magic typifying attitude" towards medicine and physicians, or an orientation towards a classic doctor-patient model. Patients are seen once weekly in a short (15-minute) supportive interview during which a drug designed to control target symptoms is administered. An internist follows their physical well-being. This setting offers a group of well-known and specially selected patients up to six months of drug and supportive psychotherapy.³⁴

Office Practice

Fifty-two were patients in the office practice of two of the investigators (A.B.K. and E.K.K.). In the latter more intensive psychodynamic observation, by fully qualified psychiatrists, was available. The physiological data obtained on each patient, however, were not as complete as those obtained from the hospital group.

With the exception of those cases suffering from agitated depressions or severe suicidal depressions, who were excluded from this series, patients were selected at random.

The doses of orally administered methylphenidate ranged from 10 to 60 mg. daily in divided doses of 10 mg. once a day to 20 mg. thrice daily, given after meals.

Before the use of the drug each inpatient underwent a thorough physical examination, special laboratory tests, recording of weight, pulse, blood pressure and respiration, and one or more psychiatric interviews. Mental status, clinical diagnosis, psychodynamic evaluation, and interpretation of the psychopathology were recorded. Particular attention was paid to data pertaining to mood and affect, motor and psychomotor activity, work capacity, somatic complaints, feelings of fatigue, the psychodynamic assessment of the presence and depth of guilt feelings, of ideas of personal worthlessness, of suicidal thoughts, of the capacity to relate to external objects and to interpersonal relations, especially in terms of anger, hostility, and the ability to establish a working relationship with the psychotherapist. Changes in major symptomatology, and appearance of the psychopharma-

TABLE I.—ORIENTING DATA ON 121 PATIENTS
SEX, AGE, DOSE AND DURATION OF TREATMENT

Sex:	29 female, 92 male
Age:	Range 22 to 80 years
	Average 48 years
	Average for inpatients —58 years
	“ “ office patients—47 years
	“ “ drug clinic —44 years
Daily dose:	Range 10 to 60 mg.
	Average inpatients —32.8 mg.
	“ office patients—34.3 mg.
	“ drug clinic —34.1 mg.
Duration of treatment range:	—2 to 317 days.
	Average for inpatients —38 days*
	“ “ drug clinic patients —134 days
	“ “ office patients —115 days

*Some were continued on an outpatient department basis, but were not included in this study.

cological profile of the drug, in terms of the above-mentioned systems, were recorded. Assessment of the therapeutic results was arrived at by combining data from the changes of the major symptoms, of how the patient felt ("helped"; "not helped"; "made worse") and the psychiatric staff assessment. Grades of improvement were rated as "much improved", "improved" ("helped"), "no change" ("not helped"), or "made worse".

OBSERVATIONS AND RESULTS

Table I summarizes the data as to sex, age, dose, and duration of treatment. All patients treated in the above settings presented some depressive symptomatology, regardless of the diagnostic categories. They were given the drug in the hope that it would ameliorate various aspects of the depressive symptomatology.

TABLE II.—PATIENT STATUS AND IMPROVEMENT RATES

Patient status	Number of patients	Much improved	Improved ("helped")	No therapeutic change	Made worse
Inpatients	25	16	3	5	1
Outpatients	44	22	9	9	4
Office patients	52	33	10	7	2
Total	121	71	22	21	7

"Much improved" and "improved": 93 patients = 77%.

Table II shows the rates of improvement in the clinical conditions of the various groups, and Table III the rates of improvement in terms of the different diagnostic categories.

Physiological Changes

These were systematically recorded only in the inpatient group. Blood pressure, pulse, temperature, respiration, and biochemical laboratory findings were not significantly changed in the majority of patients when they were recorded.

Appetite and Weight

Methylphenidate taken in the doses mentioned, after meals, seemed to have no unfavourable effect on the appetite. A weight increase of more than 5 lb. was recorded in the first five weeks in 74% of

TABLE III.—DIAGNOSES AND IMPROVEMENT RATES

<i>Diagnosis</i>	<i>Number of patients</i>	<i>Much improved</i>	<i>Improved ("helped")</i>	<i>No therapeutic change</i>	<i>Made worse</i>
Manic-depressive reaction, depressed	23	15	4	1	3
Depressive reactions	29	18	5	5	1
Depressive reactions of the aged without organic brain syndromes	17	11	3	3	0
Depressive reactions of the aged with organic brain syndromes	14	6	2	4	2
Depressive reaction in the involuntional period	12	7	3	2	0
Schizophrenia, schizoaffective type with depressive affect	12	6	2	3	1
Psychoneuroses (anxiety). Phobic, obsessive-compulsive, with depressive features	8	4	2	2	0
Character disorders with depressive affect	6	4	1	1	0
Total	121	71	22	21	7

"Much improved" + "improved": 93 patients = 77%.

the patients. A weight increase of less than 5 lb. was seen in 18% of the patients (this is not significantly different from that seen with hospitalization as milieu care, in this setting). A weight loss of up to 5 lb. in 8% of the cases was recorded. The gain in weight correlated closely with improvement in other aspects of depressive psychopathology and represented a renewed ability to seek new object relationships. An interest in food, hunger and appetite are therefore again seen in the patient. Exceptions, however, were noted in those patients in whom mild exacerbations of depressive mood were accompanied by compulsive overeating with resultant gain in weight.

When taken not later than 4 p.m., methylphenidate seemed to have no adverse effect in terms of increasing insomnia.

Change in Mental Status

(a) *Motor activity.*—The most constant significant change observed, once the pharmacological profile of methylphenidate was established, was in motor activity, i.e. mobility and bodily movements. Eighty-six per cent of patients with motor retardation showed a marked increase in motor activity. These cases represented patients with neurotic depressions without true motor retardation but with considerably decreased activity patterns, as well as manic-depressive patients in the depressed phase with diminished motor activity. Schizophrenic patients with apathy showed the least improvement in their motor activity. Many of these patients, nevertheless, both reported and showed some improvement in drive, interest and ambition. This was seen from the character of their speech and mental content and in their ability to relate to their therapist and to the significant people in their milieu. The other groups including the geriatric cases, involuntional depressions, neuroses and character disorders responded with moderate degrees of improvement (between the first group and the apathetic schizophrenic patients).

(b) *Mood.*—Methylphenidate seemed a very potent mood stimulant. Improvement in mood was seen in 81% of the cases. Patients were less depressed, less apathetic and better able to relate to others and to their own visualizations of their lives,

and were more outgoing. One patient compared it with a glass of whisky, and stated that it produced a state of definite euphoria. The majority of patients responded with a sense of relative well-being and with increased satisfaction with themselves and the world. One patient, a 52-year-old woman with a long history of manic-depressive psychosis, with several manic-depressive episodes, developed a manic attack after taking 10 mg. twice daily for three days. The same patient had previously developed manic episodes after one E.C.T., and, on another occasion, after one tablet of Premarin® 0.3 mg.

(c) *Psychomotor activity.*—If all groups of patients were considered, an increase in psychomotor activity, particularly marked as to speech, was seen in 62% of the cases. This increase in verbal communicativeness helped the patient relate to the therapist and to the people in his environment. Facilitation of the expression of anger,¹² and a resultant relief of depression, with all the concomitants of guilt and self-depreciation, were seen in most cases as psychotherapy progressed.

Patient's Level of Depression as a Guide to Treatment

Methylphenidate is a stimulating drug. It was most useful with those patients who had reached the following clinical level in their depression. They had formed a positive transference and therefore considered the physician as a helpful, beneficial person, and they showed regression to a level of increased sleep, fatigue, lack of "pep", some apathy, and complained of a dearth of energy. Within this context these patients were now beginning to seek gratifying ("good") object relationships. Methylphenidate, given at this point, enabled the patients who were ready to form new object relationships, as demonstrated in the transference, to perceive an increase of necessary "pep". This offered an impetus to overcome their regressions. Such patients felt the physiological effects of the drug as direct evidence of the physician's power to help them have the renewed energy to live again and to form new object relationships.

On theoretical grounds a relative contraindication may exist to stimulating in this manner suicidal

patients who are apathetic and psychomotorally retarded, without consideration of the transference situation. Giving a stimulating drug to such patients could well increase their already barely tolerable aggressive impulses and could result in an increase in the available energy and drive, sufficient to facilitate discharge of their aggression. Patients who are agitated, who show that they can barely control the threatened outburst of the great quantity of their aggressive energies (either directed externally or against themselves), should not be given a stimulating agent. Such patients perceive the pharmacological profile as increasing the strength of their inner impulsivity, which they feel they can barely control as it is. These patients are best managed by either electric shock or by energy-reducing neuroleptic agents.

E.C.T. and Methylphenidate

Observations were also made on the combined use of electroconvulsive therapy (E.C.T.) and methylphenidate. Although not part of this project because of our research design, some comments are offered on the observations of the 16 patients who receive E.C.T. combined with the adjuvant use of methylphenidate. Favourable changes were noted, especially during that period of time before the therapeutic effects of the series of E.C.T. had time to accumulate. This was usually before the third or fourth E.C.T. (E.C.T. given three times weekly). A favourable response was seen on E.C.T.-free days, in the sense that the patients felt more energetic and less apathetic.

Other Antidepressants and Methylphenidate

When other antidepressant drugs had failed, or before they had started to take effect (in the other 22 patients dropped from this series), methylphenidate was sometimes useful in bridging the first one to three weeks in terms of giving the patient more energy or more "pep". The patients were then offered a physiological agent, the pharmacological effects of which they could perceive as increasing their energy and outgoingness. It is our impression that patients who take imipramine, in particular, showed a shorter lag than usual in response to that drug when a combination of imipramine and methylphenidate was given. In the case of an acute exacerbation of depression, one of the authors (A.B.K.) found that 20 mg. of methylphenidate, intravenously, helped the patient verbalize with greater facility the current problem related to the depressive affect. This in essence was an abreactive technique used within the transference situation.¹²

Patients with deep-seated dependency needs, however, sometimes attempt to manipulate the therapist into the role of the giver of the "magic goodness" for rather minor difficulties that could easily be handled in the ordinary psychotherapeutic context. The authors, therefore, do not feel that the

parenteral use of methylphenidate as a "quick relief" is indicated except in special cases. Similarly, when a patient is very severely depressed, the giving of the drug intravenously, or with expectation of quick relief, may merely make the patient feel that his inability to justify fully the physician's expectations is just another expression of his own worthlessness. If the doctor expects him to do well on this drug, and he does not, it is because he just "isn't any good", and it is "all his fault for not trying hard enough." Here the lack of an immediate therapeutic response is integrated by the patient into his own self-critical, self-punitive, depressive illness.^{23, 28, 29}

Side Effects

Patients were free of side effects in 72% of the cases. Twenty-one per cent had mild side effects but they were not incapacitating or too disturbing. These consisted of increased tremor of the extremities, cardiac palpitations, a feeling of "butterflies in the stomach", and mild elevations of blood pressure of 5 to 10 mm. Hg.

Seven per cent showed an increase in their levels of anxiety or an increase in their psychomotor activity, even to the level of increased agitation. Only these latter categories of side effects were particularly disturbing to the patients. Most of these patients had latently agitated depressions, or were schizophrenic patients with a great deal of barely controlled aggressiveness and irritability.

None of the cases seen in this series developed a dependency on or addiction to methylphenidate.²¹ Some patients showed the type of somatic complaint, concern over body image, and concern over "what are you doing to my body" that is a transference response, described in an earlier work of Sarwer-Foner.^{26, 28-31, 33}

DISCUSSION

Our therapeutic results were strikingly similar to those found by several other investigators.^{3, 11, 13, 20, 35} The particular composition of our group of patients revealed some interesting differences and are suggestive of certain important conclusions. Table I shows that the drug was slightly more effective in office practice and in the inpatient group and least effective in the outpatient group. This was particularly noted in so far as the "much improved" category is concerned. The other suggested difference was seen in the length and duration of treatment, which was longest in the outpatient group — 134 days; shorter in office practice — 115 days; and shortest in the inpatient group — 38 days. The majority of the latter group, of course, continued to receive medication after discharge from hospital; the 38 days therefore is an artifact. It represents only that period of hospitalization necessary to reintegrate the patient's ego-defences sufficiently to permit his return to the community.³⁴

The differences in improvement rates and duration of treatment shown above were not due to

differences in the specific drug effects but rather to different amounts and intensities of psychotherapeutic interaction in the various groups of patients, and also to differences in the approaches used to attempt to master the problem in the patient — ego-supportive and integrative psychotherapy in a hospital setting for the in-patient group; mainly supportive psychotherapy with drug therapy for selected groups of largely oral, passive, dependent and magically typifying patients in the psychiatric drug clinic and outpatient group; more intensive psychotherapy with the hope of attaining some level of insight in a group composed largely of neurotic depressions, in office practice. The relative amount of attention offered to patients and what the patients felt they were receiving in terms of "oral givingness" to replace their lost love objects were important in this regard.

We noticed that outpatients were especially sensitive to any attempts on the part of the therapist to replace a sympathetic and meaningful relationship by perfunctory dispensation of drugs.²³ This was true even if the sessions were of relatively short duration (20 minutes per week). If the patient did not feel the basic interest of the therapist, feelings of rejection and abandonment occurred. This was clinically expressed either by verbal statements of unhappiness, but more often by somatization, demands for more treatment, or simply more symptoms (a worsening of the condition). It is as though these patients were saying, "Doctor, you are not giving me enough, give me more."^{23, 33} Many patients came to identify the personality of the "good giving doctor" with the capacity of dispensing a "good giving drug". It is as though they feel that the doctor because of his benevolence is giving them the "goodness" that drives out the "badness".³² In this study, the drug was used as an adjuvant to reduce the patient's suffering, particularly in terms of energy dearth, and the feeling that he could not control his symptoms. By preference, it was used in the early phases of his illness (particularly with the office patients), while accenting the need for the patient to attempt to handle his illness through an increased understanding of those feelings producing his mourning and depression. This approach, it was felt, offered a better solution to his fundamental problem than drug therapy alone.

Although Table II does not lend itself to statistical analysis because of the relatively small number of patients in the various categories, the following conclusions are nevertheless delineated. Patients with depressions responded better to the medication and a supportive psychotherapeutic approach than patients suffering from schizophrenic or from organic illnesses with depressive symptomatology. Although the physiological effects of the methylphenidate medication are largely the same in all the patients (i.e. all the patients show the same pharmacological profile in response to the drug),

it was therapeutically not nearly as beneficial in the last-mentioned groups. Many factors involved in relationship therapy and the meaning, in the transference,²⁹⁻³¹ of what is done, especially in response to energy shifts and the stimulatory effects of the drug, are probably of great importance here.

Our findings confirmed many of the findings of authors^{8, 11, 13, 29, 35} who earlier had demonstrated the effectiveness of methylphenidate in various depressive states. Our evidence, however, in contradistinction to the conclusions of some of these authors, suggests that the mode of action of drugs in depressive states is far more complicated than suggested by them. In the case of methylphenidate its effects are not just the sum total of its actions on mood and motor and psychomotor activity. By facilitating the greater availability of energy for speech, it can promote desirable communication between patient and doctor.¹² It thus becomes a valuable adjuvant, both in the psychotherapy of depression and as a motor and mood and psychomotor stimulator. When used with minimal or no psychotherapeutic interaction, the effectiveness of the drug in helping patients overcome depressive mourning, feelings of personal worthlessness or anger turned against the self, is less convincing, although its pharmacological profile was always present if the drug was given in adequate dosage. On the other hand, if the type of patient already referred to is treated only with psychotherapy of short periods (once a week), many of them become frustrated by their energy dearth, by their inability to express themselves and by inhibition in their interpersonal relations. They come to equate these with lack of progress, thus increasing their feeling of hopelessness. This helps confirm their already established pattern of internalized anger, guilt, and depression. We feel that methylphenidate is an effective agent in breaking this cycle if given to the properly selected patient, especially at the right time and cycle of his illness. Its action in helping to channel energy into motor patterns is helpful in suggesting to the patient that he now has the necessary energy to form more meaningful human contacts. When the above occurs in terms of a good transference relationship, the facilitation of verbalization helps the patient exteriorize himself and gives meaning to his capacity for other externalizations, both of motor energy and of externalized interest. The use of this drug in such situations helps give the patient a sense of therapeutic movement and increases his sense of optimism and hope.

Particularly important with methylphenidate is the fact that there is no appreciable time lag in the appearance of its pharmacological effect ("pharmacological profile") and its therapeutic effect. This is in contradistinction to what has been reported of some of the other antidepressants. With this agent a patient perceives biologically that things are "moving" and that energy is increased. This feeling is integrated by the patient in an ego-sup-

portive way if it is done in the context of a positive transference relationship. The patient associates it with the therapist's intervention, with the "goodness" given by the doctor to drive out the "badness". This often establishes or strengthens positive transference feelings.

The immediate increase in concentration and alertness facilitates recapture of lost fragments of memory and in some cases helps capacity for insight. As seen above, the drug's psychopharmacological profile and the psychotherapeutic effects emanating from it are integrated by the patient in a complex manner, understanding of which helps us to treat the depressed patient.

SUMMARY

Over a two-year period, 159 patients were treated by methylphenidate (Ritalin) and 121 of them are the subject of this report. These patients suffered from various depressive states and were treated by doses of 10 to 60 mg. of methylphenidate daily, in one to three divided doses, for an average length of approximately three months.

Twenty-five of these were inpatients, 44 were outpatients and 52 were patients in office practice. All patients were given psychotherapy concomitantly; office patients generally received more, inpatients less, and outpatients the least psychotherapy, in terms of amount of time offered and the intensity of the relationship.

On this regimen, 72% of the inpatients, 70% of the outpatients and 82% of the office patients showed improvement in the depressive symptomatology. This improvement occurred rapidly and in direct relationship to the pharmacological profile of the drug. It always occurred in terms of what the "pharmacological profile" meant to the patient in terms of his total situation. His transference relationship with the therapist at the time was particularly involved in the meaning given by the patient to the pharmacological profile of the drug.²⁹⁻³¹

As to changes in symptomatology, the greatest improvement was seen in motor activity (86%), mood (81%) and psychomotor activity (62%), in that order. In the latter case, facilitation in speech, through the increase of energy available for this, resulted in improved verbalization of anger and hostility with very evident relief of depressive and self-punitive feelings in the patient. Increased alertness and an improved ability to concentrate helped in some cases by facilitating memory recall. This made the patient feel that the medication was changing him and restoring his capabilities. The pharmacological profile of the drug is integrated by most patients as something representing the "goodness" offered by the doctor to drive out the "badness" that they felt to be in them. It was thus helpful in establishing or confirming a positive transference with the therapist.

Those patients most inhibited in their expression of anger and the depressed group of manic-depressive patients seemed to benefit most readily in the therapeutic sense. Next in order were patients suffering from neurotic depressions. Patients with latently agitated depressions and those with neurotic depressions associated with marked degrees of anxiety translated into somatic sources often tended to become more anxious in response to the physiological effects of the drug.

Methylphenidate was also a useful adjuvant in an additional 16 patients in whom it was combined with electroconvulsive therapy and in 22 other patients in whom its use was combined with other antidepressant drugs which have a time lag before their therapeutic action is noted.

Side effects of methylphenidate were seen in 21% of the patients and were negligible in the majority of them. Only 7% of cases had *markedly* increased anxiety, palpitations or increased agitation.

In conclusion, methylphenidate is a most useful adjuvant in treatment of various depressive states, provided that the concept of patient selection, the timing of its use, and the proper technique in using supportive psychotherapy are considered.

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