ture to obtain analgesia in three other patients. By observing the reaction of the patient during needling, I may speculate that the anesthesia effect may be in part due to the physical stimulation on the small nerve endings. Through a certain pathway, the stimuli may jam or sidetrack the higher center to modify or eliminate the pain. In acupuncture, the needling, as a rule, does not aim at any major peripheral nerves. The interest in acupuncture does point to a new field of investigation and application of physical means to obtain analgesia, anesthesia, and other therapeutic effects.

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Melatonin and Parkinsonism

To the Editor.—Lerner discovered melatonin (*N*-Acetyl-5-methoxytryptamine)[1] and showed that this pineal hormone can induce sedation in man.[2] This agent antagonizes the darkening of the skin and, therefore, perhaps also some other action of melanophore-stimulating hormone (βMSH).[3] Since injections of βMSH had aggravated the tremor of parkinsonism,[4] we had administered this antagonist of βMSH to a patient but induced only a diminution of tremor.[3] Others, however, reported impressive improvement of several symptoms of parkinsonism[5] at a time when we had reversed the adventitious movements caused by levodopa [3-(3, 4-dihydroxyphenyl)-L-alanine] with melatonin in experimental animals.[6] We conducted therefore a single-blind study in patients with parkinsonism who received either melatonin alone or melatonin plus levodopa, which had caused intermittent adventitious movements.[7]

The inpatients listed in the Table and all of the outpatients had idiopathic parkinsonism except patient 11 who had postencephalitic disease. Among them there were represented several stages and almost all symptoms of parkinsonism. On admission, medications were first tapered off in patients 1 to 4 over at least two weeks, while placebo was being administered. Patients 5 to 11 and all outpatients were given melatonin or placebo while also receiving levodopa. Inpatients 5 to 11 had levodopa-dependent, intermittent, involuntary movements involving one or more of the following: the head, jaw, face, mouth, tongue, trunk, or an extremity.

The signs of parkinsonism and the involuntary movements were scored at least weekly with systems referred to earlier,[8,9] and the data were evaluated after plotting them against time. The laboratory tests detailed earlier[7,10] failed to show changes, and so did stool cultures and determinations of prothrombin times.

Melatonin was dispensed in capsules containing 50 mg, 100 mg, or lactose to serve as placebo. The drug was started among the inpatients at 50 mg three times a day and was increased daily by 300 mg given in six portions while placebo was being decreased. Our petition to the Food and Drug Administration stipulated that the increments of melatonin were to be stopped when the first of the following occurred: (1) change of the parkinsonian signs; (2) change of the levodopa-dependent adventitious movements; (3) toxicity; (4) a maximal dose of 8.0 gm/day.

The doses of melatonin shown in the Table were tolerated remarkably well. Indeed, the patients reacted placidly even to the unpleasant among the episodes listed. Patients 1, 2, 3, 6, 9, and 11 became tranquil, whereas they had been frequently anxious, nervous, or depressed prior to the administration of melatonin.

Melatonin induced few isolated but definite episodes of cutaneous flushing, abdominal cramps, diarrhea, scotoma lucidum, and headaches typical of migraine (Table). Since some of these episodes were similar to those accompanying serotonin-producing tumors, measurements of 24-hour urinary 5-hydroxyindole acetic acid (5-HIAA) were made in patients 2, 5, 9, and 10 under appropriate precautions.[11] Patient 10, who showed no recognizable reactions to melatonin, excreted the same amount of 5-HIAA during the drug's administration as he did a week after its substitution by placebo (1.9 vs 1.9 mg/24 hr). While taking melatonin, the others excreted 5.8, 4.2, and 3.2 mg of HIAA/24 hr, compared to 1.2, 2.0, and 1.6 mg/24 hr a week after stopping the drug.

Melatonin did not affect the signs of parkinsonism, the antiparkinson effects of levodopa, or the levodopa-dependent adventitious movements. The nightly administration of melatonin to 5 outpatients (300 to 1,000 mg for one to four weeks) did not change their clinical status while it facilitated sleep in some.

Tranquilization and even somnolence emerged together with findings characteristic of the action of serotonin in our patients. Experimental animals receiving melatonin showed elevations of cerebral serotonin[7] whereas evidence for low-brain serotonin has been found in depressed and manic patients.[12] Because of its metabolic effects, melatonin should be tried in the therapy of manic and depressed patients, particularly since it contrasts to major tranquilizers by not posing the risk of pharmacological parkinsonism.

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Effects of Melatonin on Parkinsonism

Case No./Sex	Melatonin, gm/day	Duration, days	Levodopa, gm/day	MK-486*	Effects†
1/M	3.3	15	...	...	H,S,F
2/F	4.5	31	...	...	H,S,F,C,D,Sc.L
3/M	6.6	35	...	...	S
4/M	5.4	34	...	...	H,S
5/M	3.0	16	5.00	...	C,D
6/M	3.6	27	1.20	+	H,S,F,C,D
7/F	3.9	21	1.02	+	C,D
8/F	4.1	28	1.68	+	...
9/M	4.2	26	1.38	+	S
10/M	4.2	25	1.80	+	...
11/F	4.5	23	.36	+	F

*MK-486 is a peripheral inhibitor of dopa decarboxylase which potentiates the central actions of levodopa.[3,10]
†Effects of melatonin: H=headache; S=somnolent during the day; F=appearing unusually relaxed and contented; C=abdominal cramps; D=diarrhea; Sc.L=Scotoma lucidum. The maximal daily doses of melatonin are listed.

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