

THE CHANGE OF BLOOD PROLACTIN LEVEL DUE TO THE WITHDRAWAL OF MAINTENANCE NEUROLEPTICS

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ABSTRACT

Thirteen chronically institutionalized male psychiatric patients were studied. Blood samples were taken before and after the two-day withdrawal of maintenance neuroleptic treatment. The blood levels of prolactin, luteinizing hormone, follicle stimulating hormone, growth hormone, thyrotropin, serotonin, immunoreactive insulin, glucose, free fatty acids, triglyceride were estimated and a 50 gramme glucose tolerance test was done before and after the drug holiday.

No changes were found before and after the drug withdrawal except prolactin and growth hormone. Prolactin was in the normal range before the drug withdrawal and fell to the lower limit of the normal range after. More growth hormone was released in the glucose tolerance test after than before the drug withdrawal.

The concept of hypersensitivity of the central nervous system (particularly tubero-infundibular dopaminergic system) is consistent with the present findings.

MATERIAL

The patients studied were chronically institutionalized (3 - 28 years) male psychiatric in-patients from 33 to 62 years of age. Twelve were chronic schizophrenics and one had general paralysis. Their medications had not been changed for at least 6 months prior to the experiment. All medications were "maintenance" dosage of either phenothiazines, butyrophenones or iminodibenzyls with or without other medications (e.g. antiparkinson drugs and hypnotics). No antidiabetic treatment was given.

Five of the sample patients were obese (above +10% of the standard weight derived from Matsuki's table (ref. 1)). Three were found diabetic. The criterion of diabetes is that of the Japanese Committee on the Criteria of the Oral Glucose Tolerance Test (ref. 2).

METHOD⁺

The medications were stopped for two days in every week. This was called the "drug holiday" by Ayd (ref. 3). All examinations were done on the first day of the "drug holiday" (the "on" drug sample) and the first day of re-starting medication (the "off" drug sample), so that the interval of two examinations would be 48 hours.

The assays done were the blood level of PRL, LH, FSH, GH, TSH, serotonin, IRI, glucose, FFA, TG, and GTT. In GTT, blood samples were taken 0, 30, 60 and 120 minutes after 50 gramme of oral glucose load, and the blood levels of glucose, FFA, TG, IRI, and GH were assayed.

RESULTS

The blood PRL level of the "on" sample was 7.08 ± 8.12 ng/ml and the "off" sample level was 2.20 ng/ml (Fig. 1). Since the normal range of PRL is 2-20 ng/ml, the "on" sample level was in the normal range, but the "off" sample level fell to the lower limit of the normal range ($p = .01$ by the two-tailed Walsh test).

No change between the "on" and "off" samples was found in the LH, FSH, TSH, serotonin, serotonin/platelet ratio, glucose, FFA, TG, IRI, and GH values.

The fluctuations of items during GTT were compared between the "on" and "off" drug samples. It was defined that the "rise" means the difference between the maximum level and the initial level during GTT, and the "fall" means the difference between the initial and the minimum level during GTT. Only GH "rise" was higher "off" drug than "on" drug ($p = .031$ by the one-tailed Walsh test) but no other items showed any difference between the "on" and "off" samples (Fig. 2).

DISCUSSION

PRL is usually in the normal range among the schizophrenics and is increased by neuroleptic treatment and decreased to the normal range immediately after the discontinuation of the medication (ref. 4, 5, 6). In this study, however, PRL showed a quite unique change. If the mechanism here were the same as that in the withdrawal of the acute medication, then the "on" drug PRL level should be higher than the normal range. If the normal value of the "on" drug PRL level were caused by the small and insufficient dosage of neuroleptics, then no change of both PRL and GH should happen after the discontinuation of neuroleptics. Hence the concept of hypersensitivity is consistent with the present findings.

⁺Abbreviations used: GTT = glucose tolerance test, PRL = prolactin, GH = growth hormone, LH = luteinizing hormone, FSH = follicle stimulating hormone, TSH = thyrotropin, IRI = immunoreactive insulin, FFA = free fatty acids, TG = triglycerid

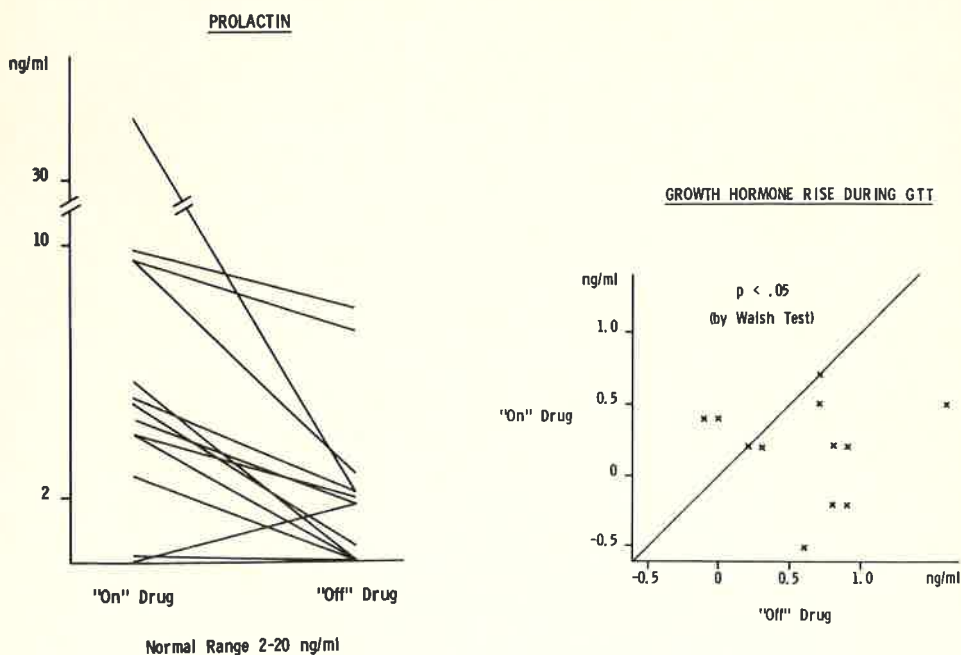


Fig. 1. Blood prolactin level before ("on" drug) and after ("off" drug) two-day withdrawal of maintenance neuroleptics. Each line represents one patient.

Fig. 2. Growth hormone "rise" during GTT before ("on" drug) and after ("off" drug) two-day withdrawal of maintenance neuroleptics. The dividing line separates "rises" that were higher after the drug withdrawal (below the line) from those which were higher before the drug withdrawal. Each cross represents one patient.

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