Letters to the Editor

Haloperidol and Insulin Release

Dear Sir,

Samols and Stagner [1] were unable to confirm the reports of haloperidol-induced insulin release from the isolated canine pancreas [2]. They concluded that the inhibition was caused by ethanol, previously used as the solvent for haloperidol. However, Table 1 of Samols' paper shows that at high calcium concentration the infusion of ethanol plus haloperidol, but not ethanol alone, did inhibit insulin secretion ($-59\% \pm 3$). Moreover, Samols' and Hermansen's findings are in part conflicting and therefore provide few profitable data to elucidate the physiological role that the dopaminergic system (peripheral and/or central) plays in insulin secretion. It has been shown that haloperidol, at the doses employed in both Samols' and Hermansen's experiments, can block not only pre-

and postsynaptic dopamine receptors but also noradrenergic [3] and serotonergic [4] receptors. On the other hand, the fact that pretreatment with low doses of dopaminergic blocking agents, haloperidol and sulpiride can modify glucose tolerance and insulin secretion in humans and dogs (Fig. 1) [5], together with the fact that dopamine fluorescence has been found over the insulin granules [6], are consistent with the postulate that dopamine plays a physiological role in insulin release.

References

1. Samols E, Stagner JI (1980) Reinterpretation of the effect of haloperidol and ethanol on insulin secretion. *Diabetologia* 19: 81-83
2. Hermansen K (1978) Haloperidol, a dopaminergic antagonist: Somatostatin-like inhibition of glucagon and insulin release from the isolated, perfused canine pancreas. *Diabetologia* 15: 343-347
3. Monti JM (1979) The effects of neuroleptics with central dopamine and noradrenaline receptor blocking properties in the l-dopa and amphetamine-induced waking EEG in the rat. *Br J Pharmacol* 67: 87-91
4. Whitaker PM, Seeman P (1977) Hallucinogen binding to dopamine/neuroleptica receptors. *J Pharm Pharmacol* 29: 506-507
5. Lechin F, Coll-García E, van der Dijs B, Bentolila A, Peña F, Rivas C (1979) The effects of dopaminergic blocking agents on the glucose tolerance test in 6 humans and 6 dogs. *Experientia* 35: 886-887
6. Lundquist I, Ekholm R, Ericson LE (1971) Monoamine in the pancreatic islets of the mouse. 5-hydroxytryptamine as an intracellular modifier of insulin secretion, and the hypoglycemic action of monoamine oxidase inhibitors. *Diabetologia* 7: 414-418

Fig. 1. Eight days of sulpiride, but not of haloperidol, pre-treatment impaired oral glucose tolerance test and raised blood serotonin (5HT) levels in 6 normal humans and 6 normal dogs. No drugs were administered before control I test. Placebo was administered before control II test. Means $\pm$ SEM. Serotonin was assayed at 0 and 60 min, only. Changes in 5HT are expressed in percentage. $P < 0.001$. Statistical significance against zero-mean values at control I test (100%). Reproduced with permission from *Experientia* [5]

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