

Salivary and Blood Pressure Responses to Methacholine in Depressive Illness

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Many attempts have been made to measure some of the changes in various bodily functions that occur during the course of a depressive illness. These changes (and their responses to drugs) have been used in investigations that try to correlate such changes with the clinical syndromes of "endogenous" and "reactive" depressions (10). No reliable and valid correlations have, however, yet been found (4, 5).

It has been shown in several investigations (9, 3) that depressed patients secrete significantly less saliva than normal controls, though no correlation has been established between severity of the depression and the amount of saliva secreted (1).

The blood pressure response to a parasympathomimetic compound—acetyl β -methyl choline—was part of a test of autonomic functioning first described by Funkenstein *et al.* (1949). This test has been widely used in a variety of psychiatric conditions and several conclusions drawn about its application to clinical psychiatry (6). One such claim, that a significant alteration in a patient's mental state is invariably accompanied by a change in the physiological response to methacholine, has been shown not to be the case in depressive states (2).

An injection of methacholine causes not only a drop in blood pressure but also a marked increase in salivary secretion. This last effect has not been studied objectively in psychiatric illness.

The aim of the present investigation was to measure the salivary and blood pressure responses of a group of depressive patients to a standard dose of methacholine, and to compare the results with those obtained from a normal control group. Patients were also re-tested before discharge, when they were free from depressive symptoms.

MATERIALS AND METHODS

Patients tested were 22 consecutive female admissions to the Bethlem Royal Hospital with a primary depressive illness. The severity of the symptoms was rated on a simple 4-point scale (0=none, 1=mild, 2=moderate, 3=severe). This scale was found to be reliable for several observers.

Normal controls were members of the female nursing staff, matched for age and weight with the patients. The age range was 21-60 (mean 42.3) and the weight range 102-168 pounds (mean 133 pounds).

The test was first performed two days after admission, and because of the diurnal variation in salivary secretion (9), between 7 p.m. and 8 p.m., at least one hour after the last meal. Smoking was not allowed at this time. The procedure was explained to the patient and the test was then performed with the patient lying down in a quiet room. Patients were not receiving any anti-depressive treatment, though sodium amytal 3-6 gr. was allowed as a hypnotic on the night before the test. Systolic blood pressure was recorded by auscultation at two-minute intervals until three consecutive similar readings were obtained. This was considered to be the resting level. The resting salivary secretion was determined at the same time by the method described in detail by Davies and Gurland (1961). Dental cotton rolls 4×2 cm. in size were placed in a waxed cardboard sputum cup and weighed. A roll was then placed on each side of the mouth against Stensen's duct, and another under the tongue. They were left in place for 2 minutes, then replaced, with forceps, back into the sputum mug, which was re-weighed within 4 hours. Three such readings were taken at two-minute intervals and the mean of these was taken as

the basal reading. Ten mg. of methacholine was then given intramuscularly, and the systolic blood pressure followed every minute for 15 minutes, while salivary secretion was measured every two minutes for 20 minutes. Clinical tests had shown that the maximum amount of saliva was secreted in this time; and laboratory tests had shown that the three swabs would completely absorb more fluid than in fact was secreted.

Tests were repeated on the depressed patients before their discharge, and the controls were tested on two occasions with a similar interval of time between the tests. The control group showed no significant differences in salivary and blood pressure responses to methacholine between these two tests.

Various methods have been used to score the blood pressure responses to methacholine. Hamilton (1959) found that the basal blood pressure and the drop in blood pressure are highly reliable measures, with a reliability coefficient of 0.80 and 0.75 respectively. Other measures, e.g. slopes of the blood pressure readings, have been shown to be unreliable. Basal blood pressure and maximal drop in blood pressure, along with basal salivary output and maximal increase in salivary output, have been used to calculate the results, which were analysed using Student's "t" test.

DISCUSSION

It will be seen from Table II that significant differences were found between the depressed patients and the controls, and also between the different grades of depression, in the resting salivary secretion. No such differences were found when the resting systolic blood pressures were compared.

The differences found between the resting salivary secretion of the depressed patients as a group and the controls are similar to those previously reported (1, 8, 3). When the depressed patients recover, their salivary secretion increases by about 100 per cent. and is then similar to the control group. These changes presumably reflect alterations in autonomic function which occur during the course of a depressive illness.

Significant differences were also found between the resting salivary flow of patients classified by one observer, after a short clinical interview, as either mild, moderate or severe depression. Such a finding has not been found by other workers (1, 3). This aspect of the investigation should be studied further in a larger group of patients by several observers, as its confirmation would indicate that the level of salivary secretion could be used as an objective index of the severity of a depressive illness.

It will be seen from Table III that when methacholine is given, the differences in salivary secretion described above persist. The diminished salivary secretion of the severely depressed patient (mean 0.16 g.) is increased on stimulation about 10 times (mean 1.7 g.). The salivary secretion of the controls (mean 0.86 g.) is also increased about tenfold after methacholine.

Significant differences were found in the systolic blood pressure responses to methacholine within the depressed group, the more severely depressed patients tending to have a larger drop in systolic pressure. The figures however only just reach significance, and because of the observer errors present in estimating systolic blood pressure by auscultation, need to be interpreted cautiously. They did not appear to correlate with anxiety level, which was clinically more prominent in the mild and moderately depressed patients.

The correlation coefficient for maximal fall in blood pressure (X) to salivary ratio (Y)

$$\left(\frac{\text{maximal increase in salivary weight}}{\text{basal salivary weight}} \right) \text{ was}$$

found to be 0.884, and this was statistically significant at the 0.1 per cent. level. A regression equation relating maximum drop in blood pressure and the salivary ratio was calculated and found to be $Y = 0.397X - 0.784$.

Individual variations about the regression line are shown in Figure 1. It will be seen that values for patients and controls are evenly distributed about the regression line, showing that (a) for a given drop in blood pressure the salivary ratio can be estimated and (b) that the response of these two variables to the given

TABLE I
Means and Range of Salivary Secretion and Systolic Blood Pressure

Group	N	Salivary Secretion (G)				Blood Pressure (mm. Hg)			
		Resting Levels		Maximal Response to Methacholine		Resting Levels		Maximal Drop with Methacholine	
		Means	Range	Means	Range	Means	Range	Means	Range
1. All depressed patients on admission: ...	22	0.471	0.092-0.868	3.882	1.122-7.308	135.45	120-150	24.54	15-35
(a) Mild depression	6	0.771	0.644-0.868	5.654	4.165-7.308	135.80	125-140	20.83	15-30
(b) Moderate depression	10	0.477	0.358-0.589	4.085	2.763-5.912	132.00	120-140	23.50	20-30
(c) Severe depression	6	0.161	0.092-0.204	1.772	1.122-3.152	140.80	120-150	30.00	20-35
2. All depressed patients on discharge	22	0.885	0.408-1.286	7.047	4.232-9.063	132.95	125-145	23.70	10-30
3. Control group	22	0.864	0.620-1.216	8.206	6.399-9.525	130.70	120-140	26.36	20-35

TABLE II
Salivary Secretion and Systolic Blood Pressure

Groups	Resting Levels: Comparison of Means			
	Resting Salivary Secretion		Resting Blood Pressure	
	t	P	t	P
1. All depressed patients and controls	8.013	<0.001*	1.483	>0.1
2. All depressed patients on admission and on discharge	8.648	<0.001*	0.953	>0.1
3. Mild and moderate depression	7.105	<0.001*	1.201	>0.1
4. Moderate and severe depression	9.037	<0.001*	1.562	>0.1
5. Mild and severe depression	11.017	<0.001*	1.624	>0.1
6. Mild depression and controls	2.064	<0.05*	1.36	>0.1
7. Patients on discharge and controls	0.843	>0.1	0.782	>0.1

* Significant at more than 5 per cent. level.

TABLE III
Salivary Secretion and Systolic Blood Pressure. Maximal Responses to Methacholine: Comparison of Means

Groups	Maximum Salivary Secretion		Maximum Drop in Systolic Blood Pressure	
	t	P	t	P
	1. All depressed patients and controls	5.186	<0.001*	1.45
2. All depressed patients on admission and on discharge	3.648	<0.001*	0.87	>0.1
3. Mild and moderate depression	2.576	<0.05*	1.076	>0.1
4. Moderate and severe depression	4.423	<0.001*	2.508	<0.05*
5. Mild and severe depression	6.104	<0.001*	3.936	<0.05*
6. Mild depression and controls	3.816	<0.001*	1.82	>0.1
7. Patients on discharge and controls	0.819	>0.1	1.608	>0.1

* Significant at more than 5 per cent. level.

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REFERENCES

1. BUSFIELD, B. L., and WECHSLER, H. (1961). "Studies of salivation in depression." *A.M.A. Arch. Gen. Psychiat.*, **4**, 10-15.
2. DAVIES, B. M. (1960). "The methacholine test in depressive states." *Ibid.*, **3**, 14-16.
3. — and GURLAND, J. B. (1961). "Salivary secretion in depressive illness." *J. Psychosom. Res.*, **5**, 269-271.
4. — and MARTIN, I. (1962). "Sleep thresholds in depression." *J. Ment. Sci.*, **108**, 466-473.
5. — (1963). *Autonomic Functions in Depression*. In preparation.
6. FEINBERG, I. (1958). "Current status of Funkenstein test." *A.M.A. Arch. Neurol. Psychiat.*, **80**, 488.
7. FUNKENSTEIN, D. H., GREENBLATT, M., and SOLOMON, H. C. (1949). "Psychophysiological study of mentally ill patients." *Amer. J. Psychiat.*, **106**, 16.
8. HAMILTON, M. (1959). "Autonomic function and syndromes in depression." *Proc. Roy. Soc. Med.*, **52**, 584.
9. PECK, R. E. (1959). "The S.H.P. test. An aid in the detection and measurement of depression." *A.M.A. Arch. gen. Psychiat.*, **1**, 35.
10. SHAGASS, C., and MIHALIK, J. (1956). "An objective test which differentiates between neurotic and psychotic depression." *A.M.A. Arch. Neurol. Psychiat.*, **75**, 461-471.
11. WAWMAN, R. J., CLARIDGE, G. S., and DAVIES, M. H. (1963). "The Mecholyll test." *Brit. J. Psychiat.*, **109**, 553-557.

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