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The Significance of Brain Damage in Persistent Oral Dyskinesia

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In the last ten years there have been a number of studies reporting an association between certain persistent oral dyskinesias in elderly people (particularly women) and prolonged medication with phenothiazines. Many of the cases described in these studies also showed some evidence of brain damage and because of this it has often been suggested that brain damage is an important contributory cause of oral dyskinesia. Buccal factors such as the edentulous state have also been incriminated (Joyston-Bechal, 1965; Evans, 1965). However, very few controlled studies have been carried out. The literature on this subject has been well reviewed by Crane (1968) and Kline (1968).

In a previous paper (Pryce and Edwards, 1966) the total phenothiazine intake and the incidence of brain damage were estimated in twenty-one elderly chronic psychiatric female patients with persistent oral dyskinesia and in a control group of twenty-one patients matched for sex, age, type and length of illness. The total phenothiazine intake was significantly greater in the dyskinetic group. The incidence of brain damage was very high and there was no difference between the two groups. Possible reasons for this were discussed, and it was stated that a rigid test would require a separate study in which cases with oral dyskinesia were compared with a control group matched for phenothiazine intake.

This was the purpose of the present study, in which the incidence of brain damage and buccal abnormalities was estimated in a group of women who showed oral dyskinesia and in a control group matched for age, sex, and total phenothiazine intake. It was postulated that the dyskinetic group would show a significant excess of brain damage.

Method and Subjects

Initially a survey was made of 131 patients in three long-stay female wards in a mental hospital, and then, in order to obtain an adequate number of matched controls, a further fifty-three patients from other wards were seen. Thus 184 patients were reviewed in all. The presence or absence of abnormal movements in any part of the body was noted on a check-list for each patient. As was noted in the previous study (Pryce and Edwards, 1966), abnormal movements of lips, tongue and jaws varied considerably both in severity and persistence. In view of this, each case which showed such movements was classified as severe, moderate, mild or doubtful. The numbers placed in each category were: severe, sixteen; moderate, eighteen; mild, fifteen; doubtful, twenty-two; absent, 113. The severe and moderate categories were combined to give an experimental group of thirty-four cases.

The total phenothiazine intake was then measured for all the cases in the experimental group and in those who showed no abnormal movements. Each patient in the experimental group was then matched for age and total phenothiazine intake with one who showed no dyskinesia. Matching for age was within a five-year range and phenothiazine intake to plus or minus 25 per cent. The only two exceptions were one patient in the experimental group who was matched with a patient six years older, and another who was matched with a patient eight years younger. Data on the two groups are given in Table I. It will be seen that the groups are well matched for age and phenothiazine intake. Any medication with phenothiazines was discontinued in the experimental group shortly after they were first seen. Phenc-

thiazines were not discontinued in the control group.

TABLE I

Data on experimental (E) and control (C) group

(i)

Age range (years)	Number of subjects E	C
45–49	2	2
50–59	3	3
60–69	11	11
70–79	15	15
80–84	3	3

(ii) *Total phenothiazine intake (weeks on the standard dose)*

	Number of subjects E	C
OU.	1	1
1– 49 U	3	3
50–149 U	9	9
150–249 U	7	7
250–499 U	10	10
500–749 U	2	3
750–950 U	2	1

Measurement of phenothiazine intake

A detailed description of the way in which drug intake was measured is given in the previous paper (Pryce and Edwards, 1966). The principle was to reduce the dosages of the various phenothiazines to a common unit, defined as the standard dose for each drug given for one week. The total number of units of drugs prescribed was calculated for each patient in the experimental group and for all the patients who showed no abnormal movements.

Assessment of brain damage

As described in the previous paper (Pryce and Edwards, 1966), brain damage was judged to be present when there was firm evidence of any one of the following: organic psychiatric syndrome, leucotomy, any of the signs of "organicity" listed by Shapiro *et al.* (1956) (i.e. focal cerebral attacks, confusional episodes, incontinence, character change, neurological signs, perplexity, atypical psychiatric syndromes, grossly abnormal EEG), or inability to learn the meaning of six out of ten new words in six trials in the Modified Word-Learning Test of Walton *et al.* (1959).

Local factors

The presence or absence of teeth or dentures was noted.

Statistical analysis was by the chi-square test using Yates' correction for small numbers.

TABLE II

Comparison of experimental (E) and control (C) groups

(i)

Diagnosis	Number of subjects E	C
Schizophrenia	13	21
Depression	8	8
Dementia	12	3
Other	1	2

(ii)

Length of current admission (years)	Number of subjects E	C
0– 3	8	9
4–10	15	9
11–20	6	2
over 20	5	14

(iii)

	Number of subjects E	C
Any previous admissions	22	25

RESULTS

Comparison of experimental and control groups

Table II (i) and (ii) gives data on diagnosis and length of current admission in experimental and control groups. It will be seen that there is a marked preponderance of dementia in the experimental group. There is a preponderance of schizophrenics in the control group, and this accounts for the relatively large number of

patients who had been in hospital over twenty years.

Incidence of brain damage

Table III (i) and (ii) gives the evidence provided by the case-notes and Modified Word Learning Test. It may be seen from Table III (iii) that twenty-eight of the thirty-four cases in the experimental group had evidence of brain damage on at least one of the criteria described above as compared with fourteen out of the thirty-four controls. This difference in frequency is significant ($\chi^2 = 10 \cdot 5$, d.f. $= 1$, $p < 0 \cdot 005$). Moreover, twenty-two of the cases in the experimental group had evidence of brain damage on more than one of the criteria as compared with eight of the cases in the control group. This difference in frequency is also significant ($\chi^2 = 12 \cdot 1$, d.f. $= 1$, $p < 0 \cdot 001$).

As can be seen from Table III (i) and (ii), when each of the criteria (signs of "organicity", diagnosis of organic psychiatric syndrome, failure with Word Learning Test) are studied separately there is again a significant difference between the two groups.

TABLE III

Evidence of brain damage in experimental (E) and control (C) groups

(i) *From case-notes*

	Number of subjects		
	E	C	p
Leucotomy	3	2	
"Organicity" in all cases	22	10	$p < 0 \cdot 02$
Diagnosis of organic syndrome (dementia)	12	3	$p < 0 \cdot 01$
ECT	11	8	

(ii) *Modified Word-Learning test (Walton, White and Black, 1959)*

	Number of subjects		
	E	C	p
Untestable (too deaf or withdrawn)	5	9	
Died or discharged	3	3	
Success in 1–6 tries	7	15	
No success in 6 tries	19	7	$p < 0 \cdot 02$

(iii)

	Number of subjects		
	E	C	p
Evidence of brain damage on at least one of the criteria (leucotomy, "organicity", diagnosis of organic psychiatric syndrome or failure with word learning test)	28	14	$p < 0 \cdot 005$
Evidence of brain damage on more than one criterion	22	8	$p < 0 \cdot 001$
No evidence of brain damage	6	20	

(iv) *Functional cases with and without any evidence of brain damage*

(a) *With evidence of brain damage*

	Number of subjects	
	E	C
Schizophrenia	9	6
Depression	6	3
Other	1	2

(b) *Without evidence of brain damage*

	Number of subjects	
	E	C
Schizophrenia	4	15
Depression	2	5

Table III (iv) gives details of those patients with functional psychiatric illnesses, and shows that sixteen of the twenty-two functional cases in the experimental group showed evidence of brain damage as compared with eleven of the thirty-one controls. This difference is significant ($\chi^2 = 5{\cdot}7$, d.f. $= 1$, $p < 0{\cdot}02$).

Electroconvulsive therapy

Eleven patients in the experimental group had had ECT (mean number of treatments was twenty-six), and eight of the control group (mean number of treatments was thirty-six). It is unlikely that this number of treatments would have caused brain damage.

Local factors

Seventeen subjects in the experimental group were without teeth or dentures as compared with only ten in the control group, but this difference is not statistically significant ($\chi^2 = 2{\cdot}5$, d.f. $= 1$, $p > 0{\cdot}05$).

Effect of discontinuing phenothiazines

In eleven cases in the experimental group it became necessary to recommence phenothiazines after intervals ranging from two weeks to four months. Usually this was because the patient had become restless, agitated and confused or aggressive. Three patients became hallucinated and one became hypomanic.

All available cases were re-examined some months after discontinuing phenothiazines (ten to twelve months in most cases). During the interval three experimental subjects had died, and of the control subjects one had died and two had been discharged. For the purposes of re-assessment the patients in the two groups were combined and seen in alphabetical order without the original findings in relation to dyskinesia at hand. In only three of the experimental subjects was the dyskinesia found clearly to have improved (originally rated as of "moderate" severity, reassessed as of "mild" severity), although two of these had restarted phenothiazines less than two months after stopping. These were all patients with a functional diagnosis, one of them showing no evidence of brain damage. However, in five experimental group cases the movements were rated as being more severe on re-assessment, although they had all then been off phenothiazines for at least thirty weeks. All but one of these showed evidence of brain damage.

Two control group cases had developed dyskinesia by the time of re-examination. One was seen to be constantly chewing or pursing her lips and this dyskinesia was so marked as to have warranted her inclusion in the experimental group had it been present initially. This patient had taken 269 units, i.e. five years on standard doses of phenothiazines. Another was noted to be intermittently pursing her lips or pushing her tongue against her lower lip. These movements were, however, only rated as "mild" in severity. This patient had taken eighty-three units, i.e. over eighteen months on standard doses of phenothiazines. Both of these patients showed evidence of brain damage.

Nineteen cases in the experimental group had not re-started phenothiazine treatment at the time of re-examination. In only one case did the movements appear to be definitely less severe, while in five, as noted above, they were thought to have become more severe. Only four of these nineteen cases showed no evidence of brain damage. The dyskinesia persisted after drug withdrawal for the following intervals: fifteen weeks, one subject; thirty-two weeks, one subject; forty-four to forty-nine weeks, three subjects; fifty-four to fifty-six weeks, eleven subjects; 250–500 weeks, three subjects. In the majority, therefore, it had lasted for approximately twelve months after phenothiazines were discontinued.

Discussion

The data support the postulate that the persistent oral dyskinesias observed in elderly women in mental hospitals are associated with a high incidence of brain damage, and substantiate the widely held opinion that brain damage may predispose to dyskinesia.

The difference in the incidence of cases showing evidence of brain damage on more than one criterion in the experimental and control groups (Table III (iii)) is particularly striking. It is also worth noting that among patients with functional psychiatric illnesses (Table III (iv)) the incidence of cases with

evidence of brain damage remains significantly greater among the dyskinetic group than the non-dyskinetic group, i.e. it is not only the unequal distribution between Groups E and C of patients diagnosed as organic dementia which accounts for the differences shown in Table III (iii).

In the previous paper (Pryce and Edwards, 1966) it was shown that a group of patients with oral dyskinesia had a significantly greater total phenothiazine intake than a control group. It is generally held that phenothiazine derivatives may induce fits in patients with brain damage and increase the frequency of fits in epileptics (Hollister, 1961). If phenothiazine derivatives can cause permanent neurological damage, then, as was pointed out by Hunter *et al.* (1964), it seems likely that this should occur earlier and be more marked in patients with pre-existing disease of the brain who are known to be more prone to develop toxic reactions to these drugs.

One author (Kline, 1968) has questioned the "irreversible" nature of oral dyskinesias following phenothiazine medication, pointing out that in many of the studies the duration of follow-up was only one or two months. Because traces of most phenothiazines are still to be found after three to four months he insists that a minimum of six months should be required to label the condition, even tentatively, as irreversible. In this study, however, all but two of the nineteen subjects who had not recommenced phenothiazines at the time of re-examination had been off these drugs for at least forty-four weeks. In only one of these cases had the dyskinesia clearly improved, and in five it was thought to be more severe.

There was a predominance of subjects without teeth or dentures in the experimental group, although this difference was not statistically significant. Similar findings were obtained in the previous study (Pryce and Edwards, 1966) and were discussed there.

Summary

The incidence of brain damage and buccal abnormalities was estimated in thirty-four elderly chronic female patients with persistent oral dyskinesia and in a control group of thirty-four patients matched for sex, age and phenothiazine intake. The incidence of brain damage was significantly greater in the dyskinetic group, but there was no significant difference in the incidence of buccal abnormalities. The significance of these results is discussed.

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