SHIFT IN DOSE-RESPONSE CURVE OF PRAUSNITZ-KÜSTNER REACTION BY DIRECT SUGGESTION UNDER HYPNOSIS*

BY

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It has been shown that inhibition of the immediate-type hypersensitivity (I.T.H.) response can be produced in varying degrees in suitable subjects by direct suggestion under hypnosis (D.S.U.H.) and that such inhibition appears to be related to the depth of trance into which a subject can be hypnotized (Black, 1963). An objection to drawing such conclusions from these experiments is based on the possibility of desensitization of the subject by the experimental inoculations required before D.S.U.H. is given not to react. Although there was no evidence for this, confirmation by a technique which eliminated this objection was obviously desirable.

Prausnitz and Küstner (1921) demonstrated that transfer of skin-sensitizing antibodies from the serum of an allergic subject giving an I.T.H. reaction to the appropriate allergen can be carried out by intradermal injection of the allergic donor's serum into a non-allergic recipient. After 24 hours an I.T.H. response can then be elicited in the recipient by pricking in the appropriate allergen at the site of intradermal injection. If serial dilutions of the donor's serum are made and injected separately at different sites on the recipient, subsequent pricking in of the allergen at each injection site will produce a series of decreasing responses as measured in terms of weal area. It can be shown in this way that the size of the weal is a function of the dilution of the donor's serum, and by plotting weal area against serum dilution a dose-response curve for any two subjects in this experiment can be obtained.

The aim of the present work was to determine whether inhibition of the Prausnitz–Küstner reaction by D.S.U.H. could be produced and to measure the degree of any such inhibition in terms of a shift in the dose-response curve.

Methods and Materials

Subjects.—Thirty-eight hypnotic subjects were screened in the selection of 14 subjects thought suitable for the experiment. Of these 14 subjects seven were deep-trance subjects, spontaneously amnesic of the period of the hypnotic trance and psychologically regressable to childhood states, and seven were medium-trance subjects, easily hypnotizable but not amnesic or regressable. All 14 subjects had been skin-tested by the single-prick-through-drop technique for the sensitivity to horse serum, and had been found to be insensitive.

Design of Experiment.—The experiment was divided into two parts: an initial estimation of the subject's Prausnitz–Küstner reaction dose response on the flexor surface of one arm to horse serum at sites previously inoculated with serial dilutions of a human serum containing skin-sensitizing antibodies against a component of horse serum. A subsequent estimation of the response to the same dilutions on the flexor surface of the other arm was then made, following D.S.U.H. not to react to the horse serum.

Materials.—The skin-sensitizing human serum which had been used by Humphrey and Porter (1957) in their studies on reaginic antibodies, and was known not to carry any danger of producing hepatitis, and the horse serum, were both obtained from Dr. J. H. Humphrey, the National Institute for Medical Research, Mill Hill, and were kept in a refrigerator at 4° C. Fresh dilutions at 1/10, 1/50, 1/250, 1/500, and 1/1000 were made up with normal saline immediately before each experiment and were then injected intradermally in 0.1-ml. volumes using a clean 1-ml. syringe and a 26 needle for each injection.

Technique and Procedure.—All injections were given at points 4 cm. apart on the flexor surface of the subject's arm, starting at a point 8 cm. distal to the medial epicondyle of the humerus. Each injection was given with the needle entering the skin from the lateral aspect of the arm and the area of the bleb so produced was marked out with a ball-point pen. At 24 hours the subject attended again and drops of horse serum in approximate volumes of 0.1 ml. were then placed on each injection site. With a 22 hypodermic needle, the horse serum at each site was then pricked in with a single prick which was aimed to produce a small drop of blood within the horse serum at the centre of the area to which the anti-horse/human serum had been delivered. A stopwatch was then started. At one minute the serum on all sites was wiped off with absorbent cotton-wool.

Records of the Response.—At 15 minutes records of the weal areas were taken. To make these records a strip of "sellotape" 2½ in. (6.3 cm.) wide was applied to the arm, and the shape of the underlying weal at each site was outlined on the sellotape with a ball-point pen. The sellotape was then stripped off the arm and stuck on a single sheet of paper in the notes. In some cases two records of this initial response were made at the same time on the same subject, the dilutions of serum having been injected as decreasing dilutions down the arm on the medial aspect of the flexor surface and as decreasing dilutions up the arm on the lateral aspect of the flexor surface. In other cases the subjects attended two or more times for the assay of their responses in this way, but all initial injections of serum were always given in the same arm and at fresh sites.

Technique of Hypnosis and D.S.U.H.—The initial responses having been estimated, the subjects attended again after periods which varied from two weeks in some cases to several months in others—and the second half of the experiment was then carried out. With the other arm the procedure was identical, except that before testing the subject's response with horse serum on the second day D.S.U.H. not to react to the horse serum was given. To do this the subject lay supine on a couch and was hypnotized as deeply as possible by use of a code word established by previous post-hypnotic suggestion, and the depth of trance was then reinforced by count-down repetition of the code or by Mason and Black's modification of the Erichson–Wolberg hand-levitation technique (Black, 1963). Suggestions were then made as forcibly as possible over a period of five minutes with the specific statement that "there will be no reaction to the horse serum, your skin is nowhere allergic to horse serum, there will be no redness, no heat, no swelling, no itching, and no pain—your arm is different, it will not react to the horse serum now." With

*A paper by Dr. Black on inhibition of the immediate-type hypersensitivity response was published last week (p. 925).

the subject still hypnotized, the horse serum was then pricked in as before, wiped off after one minute and a record made of the response at 15 minutes. In the course of these 15 minutes, reinforcement of the suggestion was made regularly at one-minute intervals. In a number of cases follow-up of the effects of the D.S.U.H. were also carried out at varying intervals, when the process of injection and pricking in at 24 hours was repeated but without further hypnosis or suggestion.

Measurement of Weal Area.—To measure the weal area the paper to which the sellotape record had been stuck was placed in an epidiascope and an enlarged image was reflected from a silver-surfaced mirror on to a horizontal ground-glass screen. The size of the enlarged area was then measured by planimetry, and from the degree of enlargement involved the true area was calculated in square millimetres.

TABLE I.—*Shift in Dose Response of Prausnitz-Küstner Reaction after D.S.U.H. not to React to Horse Serum. Site Response at 15 Minutes to Horse Serum at 24 Hours After Intradermal Injection of Anti-Horse/Human Serum*

Subject and Depth of Trance	History of Psychosomatic Response: None/Expt./Clinical	State in Test	Area of Weal from Horse Serum in sq. mm. at Dilutions of Skin-sensitizing Serum				
			1/10	1/50	1/250	1/500	1/1000
1 Deep	Expt. immediate inhibition by D.S.U.H.	A	119·20	8·98	3·06	1·63	0·0
		H+D	28·56	7·35	10·81	19·38	2·45
2 Deep	" "	A	23·04	8·16	1·02	0·0	0·0
		A	19·38	4·49	4·29	3·06	0·0
		H+D	1·23	1·23	0·0	0·0	0·0
3 Deep	" "	A	13·56	4·02	2·35	1·80	0·42
		H+D	0·0	0·0	0·0	0·0	0·0
4 Deep	Control of psoriasis by repeated D.S.U.H.	A	7·76	9·39	5·72	0·0	0·0
		A	17·35	41·84	12·25	0·0	0·0
		H+D	0·0	0·0	0·0	0·0	0·0
5 Deep	None	A	33·88	20·19	9·80	1·84	2·25
		H+D	8·37	1·63	0·0	0·0	0·0
6 Deep	Control of psoriasis by repeated D.S.U.H.	A	38·90	15·77	17·22	4·72	2·22
		A	41·67	31·87	26·11	15·77	1·95
		A	49·17	33·34	22·22	21·11	2·22
		A	58·05	40·56	20·28	10·55	2·22
		H+D	0·0	0·0	0·0	0·0	0·0
7 Deep	None	A	28·23	8·86	35·01	2·22	0·0
		A	34·46	20·90	12·04	4·98	0·0
		A	41·11	10·93	11·08	1·80	0·0
		A	38·77	21·17	9·00	2·77	0·0
		H+D	25·33	4·57	0·97	0·0	0·0
		A day 6	0·0	0·0	0·0	0·0	0·0
		A day 7	0·0	0·0	0·0	0·0	0·0
8 Medium	None	A	15·71	7·55	19·38	8·37	7·04
		H+D	21·22	5·31	2·45	2·25	0·0
9 Medium	Expt. inhibition by repeated D.S.U.H. Backache relieved by D.S.U.H.	A	34·46	16·47	2·77	0·55	0·10
		H+D	3·60	1·25	0·0	0·0	0·0
10 Medium	Expt. immediate inhibition by D.S.U.H.	A	27·41	15·09	4·57	1·66	0·69
		A	38·62	17·58	20·07	8·17	0·83
		A	57·03	28·09	3·32	1·25	0·42
		H+D	10·39	3·46	4·85	0·55	0·0
11 Medium	None	A	43·00	20·55	1·84	4·25	0·60
		H+D	19·37	30·95	4·02	2·60	1·77
12 Medium	None	A	63·10	24·30	4·65	3·81	3·00
		A	75·51	28·12	2·01	2·75	2·75
		H+D	42·70	25·90	7·00	5·20	0·0
13 Medium	Expt. immediate inhibition by D.S.U.H.	A	81·21	15·20	12·50	6·39	5·28
		H+D	13·05	6·39	0·0	0·0	0·0
14 Medium	Expt. immediate inhibition by D.S.U.H. Asthma controlled by repeated D.S.U.H.	A	67·51	53·33	21·48	12·23	4·44
		H+D	46·67	0·0	0·0	0·0	0·0

A = Awake. H+D = Hypnotized plus D.S.U.H.

Results

The results of 14 experiments are shown in Table I, where each subject is listed with trance depth, history of any previous psychosomatic response either experimental or clinical, the state during the test, whether awake, hypnotized, or hypnotized and given D.S.U.H. not to react to the horse serum.

Statistical analysis shows a significant shift in the dose-response curve when comparing the first normal response with the experimental response at all dilutions except 1/500. At 1/10, $P<0.01$; at 1/50, $P<0.05$; at 1/250, $P<0.05$; and at 1/1000, $P<0.05$. The non-significant result at 1/500 ($P>0.05$) is probably due to the recorded response after D.S.U.H. of Subject 1 at this dilution, and may be attributed to a failure in technique. Analysis of the significance of the results for the seven medium-trance subjects shows no significant change for any dilution below 1/10 at the 5% level. If we ignore this anomalous result for Subject 1 the results for the deep-trance subjects show a significant shift at 1/10 and 1/50, where $P<0.02$.

On those subjects where more than one initial assay of the dose-response curve was carried out there is considerable variation in the experimental results, and this must again be attributed to failures in technique. No significant trend was observable in these successive uninhibited responses and certainly no tendency to a decrease in the response. Instant and complete inhibition of the response was obtained in two deep-trance subjects, and in one subject followed for six days complete inhibition was obtained eventually. A comparison of these results for deep-trance subjects and medium-trance subjects is shown in Table II, where the

TABLE II

	State in Test	Mean Weal Area in mm.²: 7 Deep-trance and 7 Medium-trance Subjects at Dilutions of Skin-sensitizing Serum				
		1/10	1/50	1/250	1/500	1/1000
7 deep-trance subjects	Awake ..	37·64	18·70	12·76	4·81	0·75
	Hypnosis + D.S.U.H.	9·07	2·11	1·68	2·77	0·35
	Difference	28·57	16·59	11·08	2·04	0·40
7 medium-trance subjects	Awake ..	50·36	22·63	9·26	4·94	2·52
	Hypnosis + D.S.U.H.	22·41	10·46	2·62	1·52	0·25
	Difference	27·95	12·17	6·64	3·42	2·27

difference between the mean response following D.S.U.H. is also given. The shift in the dose-response curve for the main results for the seven deep-trance subjects is shown in Fig. 1, where the dilution of skin-sensitizing serum is plotted on semilog paper against the log of the weal area × 10. Fig. 2 shows a similar plot of the mean results for the seven medium-trance subjects.

Discussion

A shift in the dose-response curve following D.S.U.H. not to react to horse serum is indicated by the mean results for all 14 subjects, but the extent to which the Prausnitz–Küstner reaction was inhibited appears to be a function of the depth of trance into which the subject can be hypnotized.

As was shown with regard to the I.T.H. response in actively sensitized subjects (Black, 1963), the ability to inhibit an allergic response in this way appears to be related to the extent of the psychological reaction or

emotional tone which can be created with regard to the suggestions of inhibition by the hypnotist, if it can be assumed that such emotional tone is related to the trance depth of the subject. This is once again in keeping

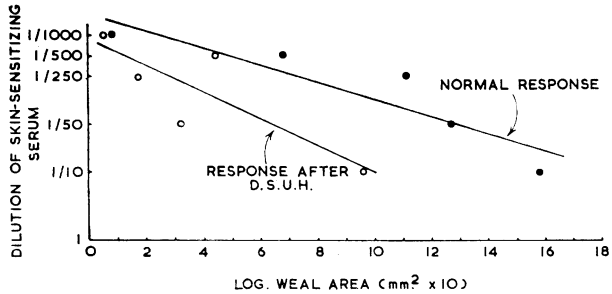

FIG. 1.—Mean of the results in seven deep-trance subjects.

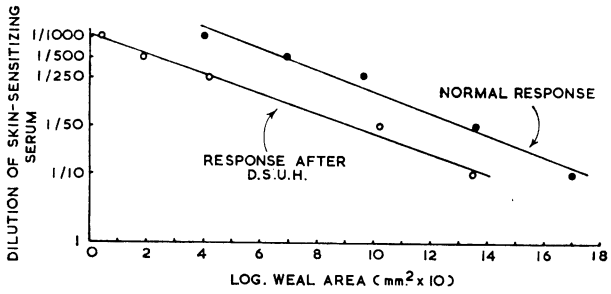

FIG. 2.—Mean of the results in seven medium-trance subjects.

with the background of clinical experience in the use of hypnosis for the treatment of psychosomatic disorders, whether allergic or otherwise, where the immediate and dramatic results are usually obtainable only with deep-trance subjects.

It was also shown earlier with regard to one case (Mason and Black, 1958) that after inhibition of the allergic response in the course of treatment for asthma and hay-fever it was still possible to produce a Prausnitz–Küstner reaction with the patient's serum in a non-allergic subject. Clearly one such case is an anecdote and not a series, and further experiments along these lines might help to clarify our understanding of the mechanisms involved. Of particular interest here, however, is the follow-up of Subject 7 (deep trance), where the first reaction to D.S.U.H. was incomplete inhibition, but complete inhibition was demonstrated six days and seven days later. This too is in keeping with the findings relating to the I.T.H. response and might favour the existence of a humoral mechanism in the psychic factor.

Of considerable interest, therefore, would be an investigation of these reactions and inhibitions in the presence of experimental nerve-block of the arm, or nerve-block due to neurological disease or trauma which might allow distinction between direct neurological central and indirect mediation by a humoral or hormonal factor.

It is concluded that a shift in the dose-response curve of the Prausnitz–Küstner reaction can be produced by direct suggestion under hypnosis and that the degree of shift is very probably a function of the depth of trance into which the subject can be hypnotized.

Summary

The effect of direct suggestion under hypnosis on the dose-response curve of the Prausnitz–Küstner reaction in seven deep-trance subjects and seven medium-trance subjects is reported. It is concluded that the degree of shift resulting is very probably a function of the depth of trance into which the subject can be hypnotized.

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EPIDEMIOLOGY OF SNAKE BITE IN NORTH MALAYA

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Fear of snakes and their bites is universal, affecting the reactions of both patient and doctor. The fear stems mainly from ignorance and a conditioned—contrary to popular belief, dread of snakes is not instinctive (Klauber, 1956)—exaggeration of the danger snake bite represents to man. Few doctors have studied patients in adequate numbers, because bites are mostly received in remote districts. Accurate statistics are rare, particularly in countries where snake bite is a serious medical problem. From 1958 onwards snake bite treated in Malayan Government hospitals was notified separately from bites or stings by other venomous creatures, and during the two years 1958–9 there were 2,114 admissions for snake bite. Of these bites, 68% were received in the two small north-west states of Perlis and Kedah (see Table I and Map), which contain only 12% of the total

TABLE I.—*Snake-bite Admissions to Government Hospitals in Malaya Notified During the Two Years* 1958–9

State	No. of Admissions	No. of Deaths	Population in 1,000's	Average Yearly Admissions per 100,000	Average Yearly Deaths per 100,000
Perlis* ..	415	3	107	194	1·40
Kedah	1,013	17	685	74	1·24
Penang ..	155	5	572	14	0·44
Perak	222	3	1,221	9	0·12
Selangor ..	32	—	1,013	1·6	—
Negri Sembilan	46	1	364	6·3	0·14
Malacca ..	6	—	291	1	—
Jonore ..	144	2	927	7·7	0·1
Pahang ..	60	2	313	9·6	0·32
Trengganu ..	5	—	278	0·9	—
Kelantan ..	16	1	306	1·6	0·1
Total ..	2,114	34	6,278	17	0·27

*Population of Langkawi Island is added to Perlis and subtracted from Kedah as victims from this island go to Perlis for treatment of snake bite.