Endogenous Substances, Brain Dysfunction and Perceptual Changes in Schizophrenic Patients

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Abstract

Schizophrenic patients with certain endogenous chemicals were found to have a different brain response and perceptual experiences than schizophrenic patients without these substances.

Introduction

Thirty years ago researchers began to report that substances found in the urine of some individuals may be metabolites of toxic chemicals in the body, that could cause brain dysfunctions associated with stability of perception (Hoffer, 1966a; Hoffer & Mahon, 1961; Hoffer & Osmond, 1961b, 1962; Irvine, 1961). These urinary substances were given various names, such as unidentified substances (Hoffer & Mahon, 1961), mauve factor (Hoffer & Osmond, 1963), kryptopyrrole (Irvine, et al., 1969), and most recently, 2-hydroxyl hemopyrrolene-5-one or HHPO (Irvine, 1981). (Throughout this paper the term HHPO shall be used.) It was found that psychiatric patients with HHPO had elevated scores on a psychological test (Hoffer-Osmond Diagnostic Test or HOD) which, among other things, purports to measure perceptual instability (Hoffer, 1965, 1966a & b; Hoffer, Kelm & Osmond, 1975; Hoffer & Osmond, 1961a & b, 1962, 1963).

The purpose of the present study is an attempt to shed more light on possible brain dysfunctions associated with HHPO, using a laboratory measure of perceptual instability called the visual figural aftereffect or VFA.

Figural aftereffect phenomena, of which the VFA is one type, purports to measure two kinds of brain responses: augmenting and reducing (Petrie, 1978; Barnes, 1976; Kelm, 1981). An augmenting response is one in which an individual increases his/her sensory environment (perceives an expansion in the distance between two figures, called inspection— and test-figures, used in the VFA); a reducing brain response attenuates sensory input (phenomenal contraction of the inspection— test-figure distance). Augmenting and reducing have also been measured with a procedure using cerebral evoked potentials which have been found to correlate significantly with the figural aftereffect (Barnes, 1976).

In VFA-'HOD studies of both schizophrenic patients and normal individuals, it was found that those with elevated HOD scores showed relatively large augmenting responses (phenomenal expansion of the inspection— test-figure distance) with relatively mild visual stimulation, but as this stimulation was intensified by repeated exposures of the test-figure (called test-time), the brains of these individuals greatly reduced this stimulation, as manifested by a perceived shrinkage of the inspection—test-figure distance (Kelm, 1981, 1989). Thus, high HOD scores (unstable perceptions) were associated with a relatively wide range of augmenting — reducing, which experientially manifests itself in terms of perceptual instability. Schizophrenic and normal individuals with lower HOD scores showed a significantly narrower range of augmenting — reducing, and thus more stable perceptions.

Since schizophrenic patients with HHPO have been found to have higher HOD scores than schizophrenics without HHPO (Hoffer & Osmond, 1962; Hoffer, 1966b), and since high HOD-scorers were found to have VFAs of different magnitudes than those with lower HOD scores (Kelm, 1981, 1989), it can be predicted that HHPO and HHPO-free schizophrenic patients will have different VFA magnitudes. Also, since high HOD-scorers were found to have a wider range of cerebral augmenting — reducing than low scorers, it can be predicted that HHPO schizophrenic patients will show greater perceptual instability than HHPO-free patients. The present study

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will test these predictions.

Method

The VFA is measured by asking an individual to fixate on a figure (inspection-figure) for a period of time, it is removed and replaced by another figure (test-figure). The person is then asked to make a number of judgements of this figure over a period of time (called test-time). Phenomenally, the test-figure appears displaced, and the magnitude of this displacement or distortion may be measured as a function of test-time.

Subjects

Schizophrenic patients between the ages of 22 and 55 years who had not received any medication for at least 48 hours, were tested within two days of admission to a psychiatric hospital. Ten patients were tested: five with HHPO and five without HHPO. The former group consisted of four males and one female with a median age of 34 years; the latter group included three males and two females with a median age of 35 years

Apparatus and Procedure

The apparatus and procedure used to measure the VFA were the same as in earlier studies (Kelm, 1968, 1981; Kelm and Hall, 1967), which involved the measurement of the magnitude of three phenomenal displacements: immediately, 30 and 60 seconds (called test-time), following 30 seconds visual fixation of the inspection-figure.

The chemical analyses followed the same procedure as used by Hoffer and Mahon (1961). Both the VFA and chemical tests were carried out on the same day by two technicians, neither of whom knew the purpose of the study, nor did they collaborate with each other.

Results

The magnitudes of the VFAs for the HHPO and HHPO-free patients at the immediate, 30 and 60 seconds test-times are shown in Figure 1 (p. 44). A negative VFA indicates that the phenomenal inspection and test-distance was less than in the control condition (control judgements have no prior fixation of the inspection-figure); a positive value, greater than the control. A summary of an analysis of variance is given in Table 1 (p. 44). This analysis shows that these two groups of patients have significantly different magnitudes of figural distortion ($F = 12.250$, 1 and 8 df, $p<.01$). It also shows that the VFA changes as a function of test-time, which is the usual expected phenomenon ($F = 27.233$, 2 and 16 df, $p<.001$). The statistically significant interaction ($F = 6.927$, 2 and 16 df, $p<.01$), indicates that the two groups differ in their magnitudes of distortion as a function of test-time.

Discussion

The first prediction that schizophrenic patients with HHPO would have different VFA magnitudes than schizophrenics without HHPO was confirmed. The second prediction that HHPO patients would manifest greater figural instability than the HHPO-free group was not confirmed. Instead, it was HHPO-free patients who showed a wider range of cerebral augmenting — reducing, and thus greater perceptual instability than schizophrenics with HHPO.

How may these data be explained? One approach which may be helpful would be to compare the HHPO and HHPO-free VFAs with those of normal individuals. The VFA curve of five normal subjects is shown in Figure 1.

Analyses of variance show that both HHPO and HHPO-free patients have significantly different magnitudes of figural distortion than normals ($p<.01$ and$<.05$, respectively). These results are in agreement with earlier HOD and VFA studies which report that schizophrenic patients generally (without regard to HHPO status), have significantly different HOD scores and VFAs than normal subjects (Barnes, 1976; Kelm, 1962; Kelm, Hoffer & Osmond, 1981).

Analysis of variance of the HHPO-free group and normal individuals shows that their VFAs differ as a function of test-time ($p<.05$). Using t test analyses reveals that these groups do not have significantly different VFAs at the immediate and 30-second test-times, but differ at the 60-second interval ($p<.01$). In other words, during the earlier stages of sensory input the HHPO-free patient's brain shows a similar level of augmenting as the normal brain, but as this stimulation continues, unlike the normal response, this patient switches to extreme neurological reducing. According to

Petrie, this patient would be experiencing a "... turbulent... unpredictably expanding and contracting sensory environment" (1978, p. 78). This kind of perceptual instability would not just be confined to figural displacement as measured in the present study, but also would include changes in depth, brightness, size and shape perception, and could as well involve instabilities in other sense modalities (Koehler & Wallach, 1944; McEwen, 1958).

Since these patients manifest perceptual instabilities within less than two minutes of rather intense sensory stimulation as the present study indicates, it would be reasonable to expect that they would also experience changing perceptions over much longer periods of time, especially in stimulating and stressful environments. Consequently, it should not be surprising that when they take the HOD, they will admit to many changing experiences described by the Test, and thus have relatively high scores. A quick reading of the HOD will reveal that most of the statements deal with changing visual experiences, changes in hearing, touch, taste, etc., and include words such as "sometimes, often, now and then, much more, at times, before, lately", which describe changing states.

By way of contrast, analysis of variance of the HHPO patients and normal group shows that they do not differ in the rate of change of the VFA as a function of test-time (similar cerebral augmenting - reducing range). That is, as sensory input is intensified, these patients maintain the same degree of perceptual stability as the normal group. When Dr. Osmond (personal communication) first saw the three VFA curves in Figure 1, his immediate response was that, in one sense, substances associated with HHPO may actually be beneficial in that they appear to combat perceptual instability. These data suggest that when an HHPO patient is bombarded with sensory input, his/her chemical state produces neurological reducing, and thus narrows the range of augmenting - reducing, thereby stabilizing the patient's perceptual world.

Dr. Osmond's observation becomes more significant when one considers that substances associated with HHPO may be CNS depressants. According to Dr. Irvine (personal communication), based upon the known CNS depressant effects of kryptopyrrole, HHPO may be classified as a CNS depressant. The effects of CNS depressants on both figural aftereffect phenomena and cerebral evoked potentials have shown a tendency toward reducing (Barnes, 1976). Thus, if the substances associated with HHPO have a depressant effect on the CNS, then they would be expected to produce the differences in the VFRA found between HHPO and HHPO-free patients in the present study, namely, a tendency toward neurological reducing in HHPO patients, thereby narrowing the augmenting - reducing range, and thus stabilizing their perceptual experiences.

It must be emphasized that although the stability of perception with increasing sensory stimulation in HHPO patients is not significantly different than the stability of normal perceptions, these patients are manifesting extreme neurological reducing ($F = 28.043$, 1 and 8 df, $p<.01$). Indeed, t test analyses show significantly greater reducing at each of the three test-times (p values all $<.01$) between the HHPO and normal groups. Thus, it would appear that the substances associated with HHPO may not only reduce the augmenting -reducing *range* of the brain, but also depress cerebral activity to such a low *level* that the individual is now confronted with a dearth of sensory input. Petrie has suggested that extreme reducing may confront such individuals with a perceptual world that "... may become unbearable — not because of what it contains, but because of what it does not contain ... having to cope with a new problem — the problem of being confronted with nothingness" (1978, p. 66). This patient's extreme neurological reducing may not only produce a dearth of sensory stimulation, but may also adversely alter affective experiences and cognitive processes as well.

The HHPO patient may indeed be more severely ill than the HHPO-free individual, as Hoffer and Osmond (1963; Hoffer, 1966b) have suggested. They have reported that individuals with these endogenous substances required longer periods of treatment in hospital, had more re-admissions, and received more drastic treatment than patients without these chemicals. It may also be noted that when neurologically reducing schizophrenic patients were started on phenothiazine therapy, within one day there was a statistically significant increase in cerebral augmenting under conditions of relatively mild sensory stimulation

(Kelm, 1985), not unlike the HHPO-free VFA in the present study.

As suggested earlier, most HOD test items deal with changing experiences, however, a number of statements also seek information about what appear to be relatively unchanging states. Examples of the latter may include: "Foods taste flat and lifeless" (item 49), "The world has become timeless for me" (127), "I feel as if I am dead" (131) and "I am not sure who I am" (145). In clinical diagnosis and in evaluating the results of treatment, it may be important to separate these two types of psychological experiences reflecting two very different neurological states. It may also be useful to analyze all of the 145 statements of the HOD in terms of these two states: 1) those that describe changing experiences and, 2) those that involve distortions, but are relatively unchanging.

Although the present study supports Hoffer's and Osmond's contention that HHPO patients have a more severe disease state than HHPO-free patients, it does not confirm their results that HHPO schizophrenic patients manifest greater perceptual instability than HHPO-free patients (Hoffer & Osmond, 1962; Hoffer, 1966b). Rather, it was HHPO-free schizophrenic patients who showed greater perceptual instability, as measured by the VFA.

Unfortunately, not all patients in the present study were given the HOD, but of those who did take the test (three HHPO and four HHPO-free patients), the direction of all but one of the scores shows that HHPO-free schizophrenic patients had higher HOD scores than those with HHPO. The median scores of the HHPO group were 42, 6, 4, 4, 1 and 7.2 compared with 78, 18, 4, 11, 5.5 and 11.1 in the HHPO-free group for TS, PerS, PS, DS, SF and RS, respectively. The mauvuria score (Hoffer & Osmond, 1961b, 1962) was 22 and 48 for HHPO and HHPO-free patients, respectively. The number of patients in these two groups was too small to do any very meaningful statistical analyses.

It is tempting to speculate about possible reasons for the different results of the present study and those obtained by Hoffer and Osmond, but in the end this discrepancy may best be resolved by additional research. However, one possibly important variable which future studies may attempt to control, is a hypothesized "longitudinal effect" of HHPO. That is, for possibly genetic causes, some patients may begin to produce depressant substances associated with HHPO as a defense against a growing range of cerebral augmenting - reducing condition, which displays itself in the form of perceptual instabilities. As the quantity of these depressant substances is increasing in the brain, it may gradually decrease the augmenting - reducing range of the brain, which experientially manifests itself in the form of *further* changing perceptual experiences. Since the HOD is sensitive to changing experiences, the patient's HOD scores would be expected to be rising temporarily. Indeed, Hoffer (1966a) found that increasing quantities of HHPO were associated with rising HOD scores.

As the quantity of these depressant chemicals increases until it has greatly narrowed the range of neurological augmenting - reducing, and then maintains an assumed steady or relatively unchanging level for an extended period of time, the resulting perceptual experiences would also be expected to be relatively unchanging. Without treatment to remove or counteract these endogenous substances for years, the patient's experiential world will, other things being constant, be relatively stable (lower HOD scores).

As stated earlier, this relatively stable perceptual state in HHPO patients is greatly distorted compared with normal perceptions, but it is not as variable or changing as in HHPO-free patients. When through appropriate treatment these depressant substances are gradually removed, or counteracted, HOD scores would be expected to increase temporarily, but if continued treatment is able to return the brain to the state of the normal augmenting -reducing *range and level*, then, with time, HOD scores would be expected to decrease and gradually reach levels found in normal individuals.

Unfortunately, in all HHPO-HOD-VFA studies to date, the effects of a hypothesized "longitudinal effect" of HHPO have not been controlled or investigated.

It should be noted that in terms of the above hypothesized "longitudinal effect", Hoffer's and Osmond's data were obtained from patients in an "acute care facility", while the data in the present study were obtained from patients admitted to a more chronic, "long-term care facility". Most of the patients in the

present study had a history of previous hospital admissions, and thus those with HHPO may have had this chemical state for years. Therefore, in terms of this "longitudinal effect", Hoffer's and Osmond's patients may have been largely acute HHPO patients undergoing a changing HHPO state "imposed" upon a wide range of cerebral augmenting -reducing, and thus could be experiencing greater perceptual instability (higher HOD scores) than HHPO-free schizophrenic patients who may also have a similar condition of neurological augmenting - reducing, but not the additional changes associated with HHPO. The present study, consisting largely of chronic patients, who may have had a relatively constant HHPO state for years, and thus a narrower range of augmenting - reducing than HHPO-free patients, would be expected to have more stable perceptions (lower HOD scores), though as shown earlier, greatly distorted due to extreme neurological attenuation of their sensory environment.

Naturally, it is possible that some acute patients may stabilize their HHPO state for a period of time which could temporarily stabilize their perceptions (lower HOD scores), and some chronic patients may at times have fluctuating HHPO levels and consequently have elevated HOD scores during these periods. Therefore, it would be important to monitor both the HHPO and perceptual states over an extended period of time in the same patients. Control of this hypothesized longitudinal variable in future HHPO-HOD-VFA studies may help resolve what may only be an apparent discrepancy between Hoffer's and Osmond's data and the present study.

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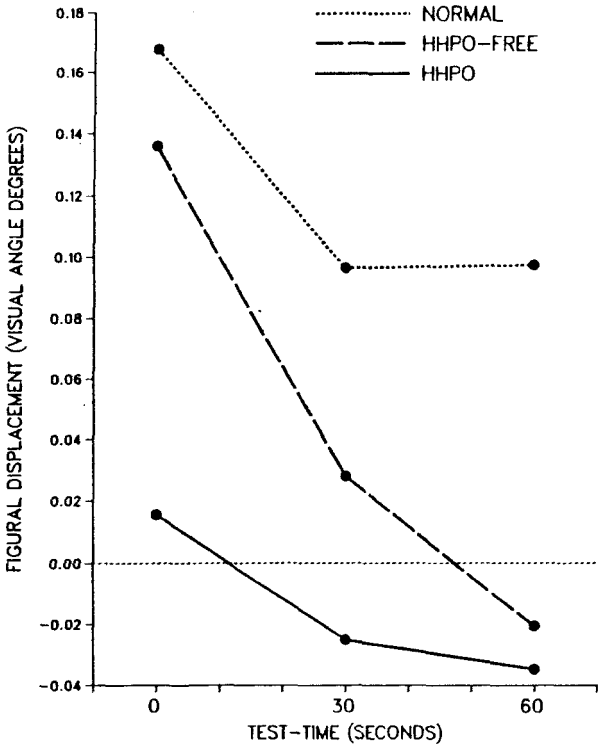

Figure 1. VFAs of Normal Individuals, HHPO-free and HHPO Schizophrenic Patients as a function of test time.

Table 1. Summary of Analysis of Variance for HHPO and HHPO-free Schizophrenic Patients with Three Test-times

Source	**SS**	**df**	**MS**	**F**
A: HHPO/HHPO-free	0.02940	1	0.02940	12.250*
Error (a)	0.01920	8	0.00240	
B: Test-time	0.05687	2	0.02844	27.233**
A x B	0.01447	2	0.00723	6.927*
Error (b)	0.01671	16	0.00104	
Total	0.13665	29		

*p < .01; **p<.001