High Thresholds for Movement Perception in Schizophrenia May Indicate Abnormal Extraneous Noise Levels of Central Vestibular Activity

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A theoretical argument proposes that thresholds for visual perception of movement should be abnormally high in schizophrenia. This may reflect a central vestibular dysfunction, consisting of abnormally high levels of extraneous noise within the neural activity of the central vestibulo-cerebellar complex. Two experiments are reported with results that support the hypothesis. To some extent, the disorder may explain the smooth pursuit eye movement dysfunction in schizophrenia. Relations to the dopamine hypothesis in schizophrenia are discussed.

Introduction

There have been consistent reports suggesting the presence of pathology within the central vestibular and cerebellar areas in schizophrenic patients (e.g., Shilder 1933; Levy et al. 1973, 1978, 1983; Buckley 1981; Ottenbacher 1982; Seidman 1983). The assumption is based mainly on evidence from so-called “soft signs” of vestibular malfunction (see Seidman 1983), and on a relatively high incidence of cerebellar atrophy in schizophrenic patients (Heath et al. 1979; Snider and Snider 1979; Weinberger et al. 1979, 1980; Coffman et al. 1981; Luchins et al. 1981; Nasrallah et al. 1981; Reyes and Gordon 1981; Koller 1982; Lippmann et al. 1982; Snider 1982; Dewan et al. 1983; Seidman 1983). The assumption is consistent with the dopamine hypothesis of schizophrenia, because lesions in the cerebellum or vestibular nuclei reportedly affect dopaminergic activity (e.g., Glowinski et al. 1978; Nicoll et al. 1979; Snider and Snider 1979; Shima and Hassler 1982; Snider 1982).

However, the hypothesis that such a neural disorder exists in schizophrenia is still somewhat controversial because of contradictory indications. A diminished orderliness...
of caloric nystagmus (e.g., Levy et al. 1978) and an impaired ability to perform smooth pursuit eye movements (e.g., Holzman 1983; Lipton et al. 1983) have a high incidence among schizophrenic patients, but both full-field optokinetic nystagmus (Latham et al. 1981) and the vestibulo-ocular reflex (Levin et al. 1982) seem to be normal. As all these types of eye movements are monitored by the vestibulo-cerebellar complex (Granit and Pompeiano 1979; Henne et al. 1981; Cohen 1981; Lennerstrand et al. 1982; Leigh and Zee 1983) some authors (e.g., Levin 1983; Stark 1983) have doubted whether the abnormalities do indeed indicate pathology at the level of these mechanisms (see also, Levy et al. 1983).

On the other hand, the resting activity of vestibular neurons, presumably maintained by mossy and climbing fiber excitation (Chez and Fahn 1981), is controlled by the inhibitory action of Purkinje cell axons from the cerebellum, in particular in the areas of the vermis cortex and the flocculonodular lobe (Ito et al. 1968a,b; Precht 1974a,b; Barmack and Pettorossi 1980; Pettorossi et al. 1982; see also, Chez and Fahn 1981). Interestingly, data reported in at least one paper (Pettorossi et al. 1982) suggest that cerebellectomy may have the effect of significantly increasing the variability within the spontaneous resting activity of vestibular neurons, although it does not affect its mean level. Thus, cerebellar malfunction resulting from atrophy or other abnormalities within the vermis, the flocculus, the fastigial nucleus, or any other relay station through which cerebellar afferents reach the vestibular nuclei, could conceivably remove certain constraints on the tonic resting activity of vestibular nucleus neurons. The dysrhythmic response to caloric stimulation and the "soft signs" of vestibular malfunctioning could reflect some behavioral consequences of an abnormally noisy tonic resting discharge of the central vestibular system. The hypothesis that this is the nature of the vestibular disorder in schizophrenia would be appealing, as it does not necessarily imply that the mean discharge rate of such neurons is also affected. Hence, normal responsiveness to vestibular or optokinetic stimulation may well remain intact.

Of course, the hypothesis cannot be examined directly at the neural level, but it does have theoretical consequences for certain perceptual phenomena that can be tested. To make this clear, we should first describe how objects that are moving or are stationary in space are visually perceived. To do this, we use the conceptual framework of what is known as cancellation theory (for a more elaborate treatment see Sperry 1950; von Holst 1954; MacKay 1973; Wertheim 1981; Wertheim and Bles 1984). The theory explains how it is possible to maintain the percept of a stationary visual world around us during movements of our visual gaze. The point is that when a shift in visual gaze direction causes the retinal surface to move across a stationary scene (or any stationary visual stimulus), the image of the scene does in fact move across the retina. In order to maintain a perception that the scene remains stationary, the perceptual apparatus must evaluate such retinal image motion in terms of the available evidence that the retinae themselves have moved, i.e., evidence for concurrent gaze changes. This evaluation may be conceptualized as a comparison process between two neural signals: an afferent retinal signal (encoding the movement characteristics of the retinal image) and a reference signal (encoding the movement characteristics of the visual gaze change). The stimulus is perceived as moving only when a difference is detected between the two signals. The threshold for the perception of stimulus motion thus depends on the detectability of this difference (MacKay 1958; Wallach and Lewis 1965; MacKay 1973; Wertheim 1981; Wertheim and Bles 1984). It is reasonable to assume that this detectability, in turn, depends on the amount of extraneous noise within the neural firing patterns that define the two signals.
If either of them is very noisy, it would take a relatively large difference to be detectable with any confidence, and consequently, the threshold for the visual perception of stimulus motion will be high.

As many movement characteristics of a visual gaze change can be recognized quite accurately in the firing pattern of particular cells in the vestibulo-cerebellar complex (e.g. Fuchs and Kim 1975; Lisberger and Fuchs 1978a, b; Henn et al. 1980; Berthoz et al. 1981; McCrean et al. 1981; Yoshida et al. 1981; Miles and Lisberger 1981; Baker 1982; Lopez-Barneo et al. 1982; Leigh and Zee 1983), it is likely that the reference signal somehow derives from these firing patterns (see Lisberger and Fuchs 1978a, b; Baker 1982; Wertheim and Bles 1984). Hence, if, as postulated above, the neural activity in the vestibular nuclei is very noisy in schizophrenia, reference signals are likely to become noisy too. Consequently, thresholds for the visual perception of motion should become abnormally high.

At the Department of Psychiatry of New York University Medical Center, this prediction was tested using an experimental set-up in which the thresholds for the perception of movement could be determined for schizophrenic patients.

**Experiment I**

**Method**

Subjects were asked to report whether or not they perceived the motion (and direction) of a visual stimulus that was presented on a fast phosphor CRT screen. During the task, ocular fixation was maintained using a stationary fixation point continuously present at the center of the screen. The stimulus consisted of a computer-generated 24 x 32" random dot \( n = 90 \) pattern. It remained visible for a period of 60 msec, during which the whole pattern moved either to the left (leftward conditions) or to the right (rightward conditions), thus enabling the determination of two independent thresholds. Thresholds were obtained with the standard staircase method of limits. A threshold measurement sequence started with the presentation of a stimulus moving at the clearly perceivable velocity of 19.3%/sec. On each following trial, stimulus velocity was reduced by 2.1%/sec steps, until the subject reportedly perceived a stationary stimulus. Stimulus velocity was then increased again until motion was perceived, after which it was reduced again, and so on. The threshold was defined as mean stimulus velocity across the first six consecutive turning points within each staircase. Subjects were seated in an easy chair with their head held steady by a head and a chin rest so that they faced the screen 35 cm away from the eyes. Standard electrooculographic (EOG) equipment (using two Ag–AgCl electrodes positioned at the outer canthi of the eyes and an earth electrode at mid-frontal position) yielded horizontal eye movement records that were stored on-line by computer. This enabled trials in which fixation was lost to be excluded from further analysis on a post-hoc basis. To prevent lapses of attention, subjects were always verbally warned by the experimenter about 1 sec prior to the onset of a stimulus. The range of stimulus velocities over which motion could not be perceived (i.e., the distance between the thresholds for stimulus motion to the left and to the right), is henceforth referred to as the no-motion range. This served as the index that should reflect the amount of neural noise within the central vestibular apparatus. As illumination of the retinal surface may reduce (or even suppress) central vestibular activity (Dichgans and Brandt 1978; Waespe and Henn 1979a, b; Büttner and Büttner 1979; Horn et al. 1983), and thereby affect the reference signal (Wertheim and
Bles 1984), the experiment was performed twice, once in a dimly illuminated experimental cabin and once in a completely darkened environment, during which only the signals on the screen remained visible. In the latter case, the lights were extinguished prior to the verbal warning at the beginning of each trial.

Four groups of subjects participated. One group, serving as controls, consisted of 10 healthy, paid volunteer subjects (7 men, 3 women) between 22 and 45 years of age. The first experimental group consisted of nine male schizophrenic subjects from the Department of Psychiatry of the New York Veterans Administration Hospital. They were selected according to DSM-III criteria and were between 23 and 56 years old. These patients all received antipsychotic medication (phenothiazine, i.e., chlorpromazine, perphenazine, and fluphenazine HCL; daily doses in chlorpromazine equivalents ranged between 200 and 3200). All had been hospitalized over a period ranging from 1 to 10 months (the duration of the hospital course at the time of the trial).

A second experimental group consisted of five more schizophrenic patients (four men and one woman) from the same department who were similarly diagnosed. One male patient had no history of prior neuroleptic medication. The other patients had been taken off antipsychotic medication for a period ranging from 1 to 4 weeks. The duration of prior medication history of these patients ranged from 1 to 5 years, during which period their daily dose in chlorpromazine equivalents was between 300 and 1200. Patients in this group were between 29 and 39 years old. One of them had been hospitalized for a period of 1 month. The others were formally hospitalized outpatients.

A third experimental group of subjects consisted of three outpatients, two men and one woman, none of them schizophrenic, from the Department of Otolaryngology of New York University Medical Center. They were between 52 and 65 years of age. They had been selected on the basis of diagnoses that suggested that their central vestibular apparatus may have been more noisy than is the case with healthy normal subjects. They suffered from a variety of symptoms and neural deficiencies, such as acoustic neuroma, vestibular neuronitis, tinnitus, presbycusis, benign positional vertigo, dizziness, positional nystagmus, and decrease of caloric response. If the results of these patients were similar to those of the schizophrenic patients, this would provide additional support for the assumption that effects observed in the schizophrenic groups do indeed reflect a vestibular malfunction.

All subjects were informed in advance about the method of experimentation, although not about the nature of the hypothesis, and only those who voluntarily signed a written consent statement participated. All patients gave voluntary informed consent. Permission for experimentation was also obtained from the commissions of ethical affairs of the participating hospitals.

**Results and Discussion**

The results, presented in Figure 1, show that, in general, the no-motion range in the control group was much smaller than in any of the patient groups, and that this difference was larger in darkness than in conditions of low illumination. These effects were statistically significant: ANOVA on all scores yielded a significant main effect of groups (\(F = 12.66; \text{df} 3,23; p < 0.001\)) and of room illumination (\(F = 40.66; \text{df} 1,23; p < 0.001\)), and their interaction was also significant (\(F = 6.34; \text{df} 3,23; p < 0.003\)). ANOVA performed on the scores of only the three patient groups revealed only a significant effect of room illumination (\(F = 35.95; \text{df} 1,14; p < 0.001\)), indicating that these groups could
not be distinguished from each other on the basis of their results. ANOVA carried out between the control group and all patients pooled together showed that the mean no-motion range in the control group was indeed significantly smaller than in the patient population ($F = 30.28; \text{df} 1,25; p < 0.001$), with the difference being significantly enhanced in darkness ($F = 11.38; \text{df} 1,25; p < 0.002$), although the main effect of illumination remained significant across all subjects ($F = 35.19; \text{df} 1,25; p < 0.001$).

These results are all as predicted: In the schizophrenic patients, the threshold for the perception of movement is significantly elevated. The absence of significant differences between the medicated and unmedicated schizophrenic groups implies that effects of medication were not observed. However, it remains possible that antipsychotic medication may have effects that continue even after cessation of medication. However, correlations between the individual levels of chlorpromazine equivalent daily dose and the magnitude of the observed no-motion ranges were not significant and were neglectable ($r = 0.07$). Interestingly though, the one patient in the present study who had never received medication did in fact have the smallest no-motion ranges of his group, although in the dim illumination condition, it was still larger than any of the no-motion ranges observed with the healthy control subjects. However, one case is insufficient to draw definite conclusions. The question can obviously only be decided upon by further research, using many schizophrenic patients that have never been medicated. Nevertheless, the present data show no difference between the schizophrenic and otolaryngological patients. This strongly sug-
gests that a noisy central vestibular apparatus does not necessarily relate to antipsychotic medication.

Although care was taken to prevent lapses of attention by warning subjects just prior to each stimulus presentation, one should not exclude the possibility that some attentional deficit of the patients, especially in the schizophrenic group (see Baribeau-Braun et al., 1983; Seidman 1983), might have resulted in elevated thresholds. This can be tested because, if a lapse of attention occurs on a particular trial, a turning point in the staircase sequence, used to obtain the threshold, is delayed. This should increase both the mean and the variance of the group of six turning points defining that particular threshold. Thus, if attentional deficits have caused the elevated thresholds, a positive correlation should be observed between the threshold scores and their associated variances. However, no correlation of importance was observed (the highest correlation was observed in the nonmedicated schizophrenic group and was even negative: $r = -0.46$). To eliminate possible biasing effects of these variances, the no-motion range scores were again tested for significance, this time using the variances as covariates in ANCOVAs. However, the resulting pattern of significant effects was identical to the one produced by the ANOVAs. Thus, lapses of attention cannot explain the data.

The present results may be relevant to the explanation of the smooth pursuit eye movement dysfunction in schizophrenia. When the sensitivity for perceiving movement is reduced (i.e., if the threshold for motion perception is elevated), a stimulus moving with an above-threshold velocity will appear to move at a lower velocity than when the threshold for motion perception is lower (see Wertheim 1981; Wertheim and Bles 1984). This reduction of perceived velocity applies equally to any movement in the visual field, i.e., also to a moving target tracked with the eyes. Smooth pursuit eye movements appear to be monitored not only on the basis of retinal errors (the distance between target image and fovea), but also on perceived target velocity (Yasui and Young 1975; Steinbach 1976; Young 1977; Mack et al. 1982). Thus, when the latter is too slow, smooth pursuit eye movements are likely to also become inappropriately slow. Consequently, large retinal errors will occur, necessitating abrupt "catch-up" movements to bring the target image on the fovea again. To some extent, this may explain the smooth pursuit dysfunction in schizophrenia (see Lipton et al. 1983; Stark 1983).

However, if this reasoning is correct, the threshold for motion perception should not only be abnormally elevated in the absence of eye movements, but also during the execution of smooth pursuit eye movements. To test this prediction, a second experiment was designed that was similar to the first one (also using the same subjects), but with a small change in method.

**Experiment II**

**Method**

The fixation point was initially located close to the left rim of the screen. At the beginning of a trial, it began to move (at constant 25.7°/sec velocity) across the screen to the right.

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*The results of Mack et al. (1982) suggest that perceived velocity is a less important factor than assumed by others. However, their evidence is only based on experiments showing that smooth pursuit is not affected when target velocity is perceptually overestimated. Target velocity was underestimated in only one of their experimental conditions from which the data are not reported, because it "failed to produce consistent perceptual results."*
traversing a horizontal 33° visual angle. (To optimize eye tracking performance, this movement was slightly damped at the beginning and endpoints of each sweep.) Subjects were required to track the fixation point with their eyes as well as possible. When the fixation point passed the midpoint of the screen, the moving stimulus pattern was presented on the screen for 300 msec. Thus, the threshold for perceiving the movement of the dot pattern to the left or to the right could be measured during the execution of smooth pursuit eye movements to the right.

A complicating factor is that, normally, such thresholds increase linearly with ocular velocity (Wertheim 1981; Wertheim and Bles 1984). Thus, to allow for comparability of thresholds between patients (expected to have low smooth pursuit velocity) and controls (having higher smooth pursuit velocity), the thresholds had to be expressed as stimulus velocity over ocular velocity. The difference between this fraction in leftward and rightward conditions then constitutes the no-motion range and thus served as the measure of extraneous noise in the central vestibular apparatus. To obtain these fractions, ocular velocity across the 300-msec stimulus presentation time was calculated from the stored EOG traces. The mean of the ocular velocities measured at the first six consecutive turning points within each staircase served as the ocular velocity score associated with that particular threshold. Trials on which the eyes remained stationary or on which a saccade occurred during the stimulus presentation interval had to be rejected from analyses, and this led to some loss of data, reducing the number of interpretable data (especially in the schizophrenic groups), although not to such an extent as to preclude statistical analysis. In all other respects, this experiment was identical to the first one.

Results and Discussion

The no-motion range (Figure 2) again differed significantly between groups ($F = 3.38; \text{df} 3,18; p < 0.05$) and was again smaller in the illuminated conditions than in the dark ($F = 10.19; \text{df} 1,14; p < 0.007$). This time, however, differential effects of illumination between groups did not reach significance ($p > 0.05$). As in the first experiment, an ANOVA performed on only the patient groups showed no evidence of group differences, but only an effect of illumination ($F = 5.97; \text{df} 1,7; p < 0.05$). However, a comparison between the normal controls and the three patient groups taken together showed, as expected, that the no-motion range was significantly smaller in the control group ($F = 7.76; \text{df} 1,20; p < 0.007$) and was generally largest in darkness ($F = 7.18; \text{df} 1,16; p < 0.02$). The correlation between daily dose chlorpromazine equivalent levels and the no-motion ranges was again insignificantly small ($r = -0.12$). Although this strongly suggests that the no-motion range is unrelated to (level of) medication, again, the one patient who had never received medication appeared to have the smallest no-motion range of all patients, and this time, it did not differ from the no-motion ranges observed in the healthy control group.

At an earlier occasion, an experiment was carried out at the Institute for Perception TNO in The Netherlands (Wertheim and Bles 1984) with conditions similar to the dark conditions of the present experiment, in which only healthy subjects participated. Although, in that study, the target and the stimulus pattern (consisting of a large vertical grating) were projected on a large screen using a complex mirror system, the results were strikingly similar to the present ones obtained with the CRT screen (see Figure 2b). This finding demonstrates the robustness of the present data.

Figure 3 shows that smooth pursuit ocular velocity was indeed higher within the healthy
control group than in any of the patient groups. ANOVA across all groups showed a significant group effect ($F = 3.38; \text{df} 3,18; p < 0.03$), but no significant differences were observed between the three patient groups. When the patient groups were pooled together and compared to the controls, ocular velocity in the control group was again significantly higher ($F = 12.88; \text{df} 1,20; p < 0.002$).

Interestingly, in all three ANOVAs, a significant effect of illumination appeared: In total darkness, smooth pursuit ocular velocity is reduced ($F = 10.15; \text{df} 1,14; p < 0.007$). As darkness also increases the size of the no-motion range, and thus presumably reduces the perceived velocity of the moving fixation point, the reduction of smooth pursuit ocular velocity in the dark is in line with expectations.

If this reasoning is correct, the size of the individual no-motion ranges observed in the first experiment should correlate negatively with the mean of the eye velocity scores (across each pair of leftward and rightward conditions) in the second experiment. This correlation is indeed highly significant ($p < 0.002$), but it is nevertheless rather small ($r = -0.45$), which suggests that noisy vestibular activity may indeed contribute to the pursuit dysfunction, although not to a very large extent. The results of the second experiment thus replicate the finding that in schizophrenia, the threshold for perceived movement is abnormally high, and they provide at least a partial explanation for the smooth pursuit dysfunction that is associated with this illness (see also Figure 4).

If in the two experiments the elevated thresholds are really caused by the same factor (abnormally noisy reference signals, i.e., high levels of extraneous noise in the neural
activity of the central vestibular apparatus), then the individual no-motion ranges observed in the two experiments should correlate. This correlation was indeed observed ($r = 0.68$) and was highly significant ($p < 0.001$).

**General Discussion**

The main conclusion from the two experiments is that in schizophrenia, the sensitivity to visually perceived movement is abnormally reduced. As an attentional explanation was ruled out and the nonschizophrenic patients, who were suspected to suffer from noisy central vestibular activity, showed an identical decrease of sensitivity to motion perception, the results strongly suggest that in schizophrenia, the neural activity of the central vestibular apparatus is pathologically noisy. We do not know of any alternative explanation for these phenomena.

The relationship between this phenomenon and the pathogenesis of schizophrenia is not immediately apparent. However, a few speculations can be made. For example, possible links between this neural disturbance and schizophrenia may be found when more is known about causality in the cerebellar and vestibular associations with dopa-
minergic systems. The typical circling behavior of laboratory animals that is characteristicly produced by injections of apomorphine (a dopamine receptor stimulant) or amphetamine (a dopamine releaser) strongly resembles the famous circling behavior that results from visual inversion of the perceptual world, as induced by surgical rotation of the eyes in fishes and amphibians (Sperry 1950) and in insects (von Holst 1954). This latter circling behavior is generally interpreted as reflecting sustained, but abortive, attempts to stabilize the illusory motion of the visual environment. This illusory environmental motion stems from retinal image movements that are concurrent with visual gaze motions accompanied by an inverse, and thus inappropriate, reference signal. Lesions in the vestibulo-cerebellar complex are likely to affect reference signals, and they are indeed reported to produce circling behavior in the rat. The point to note here is that such lesions, and the circling behavior, have both been associated with either hypersensitivity of dopamine receptors or an increase in dopamine receptor activity (Shima and Hasler 1981). Thus, it is conceivable that dopaminergic pathways are also somehow involved in the perception of motion, i.e., in the generation of reference signals. Such an assumption agrees with evidence that at least some dopaminergic pathways are involved in sensory motor interaction and spatial orientation (see Nicoullon et al. 1979). One possible hypothesis could be that the normal firing pattern of the climbing or mossy fiber excitatory collaterals, which presumably induce the tonic resting discharge in the vestibular nuclei, is disturbed as a result of a dopamine deficiency. The brain stem, from which many mossy fibers originate, contains many clusters of dopaminergic cell groups and a disturbance here could thus affect the noise level of the vestibular nuclei, even if the cerebellar regulatory system is otherwise functioning properly.

On the other hand, the absence of (dose-related) effects of antipsychotic (dopamine blocking) medication on the high threshold for perceiving movement seems to imply that in schizophrenia, neural noise in the central vestibular apparatus may not be caused by a dopamine deficiency. Instead, such noisy neural activity may either cause a dopamine deregulation or be merely a corollary to such a deregulation, in which case both phenomena might stem from the same malfunction (e.g., in the cerebellum).
Another point of relevance could be that, as mentioned before, abnormally high thresholds for motion perception affect the perceived velocity of objects in motion. Therefore, the exact location of objects in space will also be misperceived to a certain extent. This is rather similar to what happens when prismatic goggles are placed before the eyes. Normally, adaptation to such visual distortions is easily achieved. There are indications that the flocculus in the vestibulo-cerebellum provides the relevant error signals that enable a recalibration of the changed relationship between retinal image velocity and gaze or eye velocity signals (Lisberger and Fuchs 1978a; Miles et al. 1980; Miles and Lisberger 1981; Ito 1982). However, visual distortions that stem from increased neural noise in these signals occur in a situation where it is not that relationship itself that is distorted. Thus, in this case, consequent perceptual distortions cannot be made to disappear by recalibration. Put simply, there is no new relationship to learn. Distortions are thus likely to remain unchecked and, especially if this happens in early childhood (and/or in conjunction with floccular lesions), they might conceivably hamper the development of the faculty for reality testing. By this means, the disorder might leave a person more receptive to hallucinatory experiences, i.e., to the development of schizophrenia.

With our present state of knowledge, these hypotheses are of course still rather speculative. However, they illustrate that the elevated threshold for the perception of motion is a suggestive finding and may become a helpful aid in further efforts to discover organic malfunction in schizophrenia.

The authors gratefully acknowledge the inventive technical and programmatic support of Drs. Wai Hon Tsui and Sergey Lebedev, without whose efforts this research would not have been possible, and of Dr. E. Friedman, who helped us to gain insight into some of the theoretical issues related to the dopamine hypotheses in schizophrenia.

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