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Abnormal Visual-Vestibular Interactions and Smooth Pursuit Tracking in Psychosis: Implications for Cerebellar Involvement.

by Pamela M. Cooper

Thesis submitted to the School of Graduate Studies of the University of Ottawa in partial fulfillment of the requirements for the Doctor of Philosophy Degree in Psychology

Ottawa, Canada, 1986.

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ABSTRACT

This investigation attempted to replicate and extend recent findings regarding abnormal visual-vestibular interactions and pursuit tracking performance which have been observed in psychotic patients. The vestibular ocular response to caloric irrigation and the effect of vestibular activation on eye movements were examined during light (replication) and dark (extension) adaptation--the latter to assess these measures under conditions attenuating cerebellar-vestibular interaction present in the light-adapting condition.

These assessments were conducted in psychiatric patients (23 actively-ill psychotic patients and 23 remitted psychotic patients) and normal controls (23 with no history of psychiatric illness). Standardized clinical electronystagmographic procedures were used, including electrographic recordings of EEG, EOG and EMG together with control for, and assessment of, visual fixation and arousal. All eye movement data were subjected to electronic processing and computer analysis.

During light-adaptation previous findings of impaired smooth pursuit tracking, poor fixation of a stationary target

and reduced fixation suppression in actively psychotic patients were replicated. These patients were also found to exhibit hyperresponsive vestibulo-ocular responses. Remitted patients' performance on test measures was between that of controls and actively-ill patients on the majority of response measures. Remitted patients were, however, found to have impaired smooth pursuit tracking and failure of fixation suppression relative to controls.

Dark adaptation effected a normalization of several measures of patient-control differences including smooth pursuit tracking, fixation of a stationary target and the elimination of vestibular hyperresponsiveness. This constitutes an extension of previous findings of eye movement behaviour in psychotic patients.

In many respects the present results paralleled findings of eye movement aberrations in cerebellar patients. These similarities included an intact but hyperresponsive vestibular system, the normalization of previously disordered pursuit tracking during dark-adaptation, the failure of fixation suppression and the decrease in this measure during dark conditions. These findings are interpreted as indicating that cerebellar dysfunction contributes significantly to the eye movement dysfunctions (smooth pursuit tracking, fixation

suppression and fixation) found in psychotic patients. The replication of vestibular-related deficits in actively-ill patients showing pursuit tracking dysfunction and the extensive evidence involving cerebellar mechanisms in these aberrant oculomotor behaviours argue strongly for subcortical involvement in the eye movement aberrations of psychotic patients.

The results of this investigation are more supportive of a state rather than trait interpretation for the basis of smooth pursuit tracking dysfunction, i.e., remitted patients exhibited fewer aberrations than actively-ill patients. However, it will remain for investigations specifically designed to investigate this issue to resolve the controversy regarding the state or trait status of disordered tracking with respect to psychosis.

CURRICULUM STUDIORUM

Pamela Mary Cooper was born April 22, 1956 in Toronto, Ontario. She received both the Bachelor of Arts degree with honours in Psychology and the Master of Psychology degree from the University of Ottawa in 1980 and 1983, respectively.

Aknowledgments

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Table of Contents

List of Tables

List of Figures

SUMMARY OF BACKGROUND

The critical role played by the vestibular system in normal postural and visual-motor behavior has prompted investigators to consider dysfunction of this system as a potential source of the impaired processing and integration of sensory information characteristically associated with psychotic symptomatology (6,63,80). Still, although studies investigating vestibular reactivity in psychotic and non-psychotic patients spanning a sixty year period have provided evidence of associated vestibular dysfunction (4,5,20,21,27,34,79), a recent and better controlled investigation utilizing standardized electronystagmographic techniques failed to reveal major vestibular dysfunction, reporting instead problems of a modulatory nature, i.e., presence of dysrhythmic vestibular responses (67). These latter findings attest to the functional integrity of the vestibular system in these patients and suggest that if vestibular dysfunction does contribute to psychotic symptomatology, this contribution must reside in the interaction between vestibular and associated systems. Considering the reported presence of eye movement aberrations in psychotic patients (45,84) and the oculomotor involvement of the vestibular system, visualvestibular interaction should be examined as a possible

contributing source of oculomotor dysfunction in these patients.

One index of visual-vestibular interaction may be obtained through measurement of vestibulo-ocular reflexes(VORs). These reflexes are fundamental to normal perceptual-motor behavior; for example, activation of these reflexes during head movement generates compensatory eye movements thereby stabilizing retinal images and maintaining perceptual constancy. This compensatory reaction is effected through numerous three neuron arcs connecting the vestibular end organs to the extraocular muscles. The main pathways involved in these interactions are the medial longitudinal fasciculus, the brachium conjunctivum and the ascending tract of Deiters' (28,41). In the absence of head movement, stabilization of retinal images is dependent upon the suppression of VORs. This suppression is effected through mechanisms associated with visual fixation, and one way of assessing the efficiency of this process is by measuring the degree to which induced nystagmus is suppressed by visual fixation -- i.e., fixation suppression (3,16,62,70,102). Although the central mechanisms responsible for the suppression of caloric nystagmus by visual fixation have not been specified, cerebellar and brainstem structures have been shown to be important in this process (31,59,78,102).

Inadequate VOR suppression has been associated with abnormalities of visual reflexes and with deficits in smooth pursuit tracking performance (18,36), and clinical studies have suggested that impairment of this ability is a sign of CNS disease (1,23, 93). Studies in which subjects were required to read a display coupled to the head during sinusoidal oscillation about the yaw axis found that the range of stimulus frequencies in which the ability to suppress the vestibular response breaks down is similar to that in which the pursuit reflex also becomes ineffective (14). Ethyl alcohol has been reported to degrade the effectiveness of both pursuit and suppression in a similar manner (14). Similarities in the frequency characteristics of suppression and pursuit eye movements have led to suggestions that lesions which give rise to deficits in pursuit should give rise to decrements in suppression (14,18). The association between inadequate VOR suppression and impaired smooth pursuit tracking, taken together with recent reports of disordered smooth pursuit tracking performance in psychiatric patients (45,46,55,83,95) and the known involvement of the vestibular system in the generation of both smooth pursuit and saccadic eye movements (13,16,100), make it appear increasingly likely that some degree of vestibular dysfunction is associated with psychosis.

Recently, Jones and Pivik (59) examined the involvement of

the vestibular system in psychosis by using standardized electronystagmographic techniques, including electro-oculographic recordings of eye movements and computer analysis of eye movement data, to assess: (a) vestibular reactivity, particularly suppression of vestibular nystagmus by visual fixation (fixation suppression); and, (b) the influence of vestibular activation on smooth pursuit tracking performance. Vestibular nystagmus was induced by caloric irrigation of the external auditory canals and the interaction between smooth pursuit tracking performance and vestibular activation was assessed using a technique recently applied to neurological patients to examine the suppression of vestibular nystagmus evoked by visual pursuit (95). In that study it was observed that the suppression of nystagmus was more strongly effected by moving than stationary targets. Furthermore, in patients with central vestibular disorders caloric nystagmus evoked abnormalities in the eye tracking patterns despite the presence of normal eye tracking patterns before caloric irrigation . In normal subjects and patients with peripheral vestibular disorders, caloric nystagmus had little influence on eye tracking patterns.

The main results of the Jones and Pivik study (58,59) were that: (a) indices of reactivity commonly considered to reflect vestibular integrity , namely, slow phase velocity and

bilateral symmetry of response, did not discriminiate patients from controls; (b) response irregularities in the form of dysrhythmia and slower velocity of the nystagmus fast (saccadic) component were present to a significant degree in patients; (c) visual fixation effectively suppressed caloric nystagmus in normal controls, but not in psychiatric patients. This failure of fixation suppression was most marked in patients showing active symptomatology; and, (d)there was a higher incidence of tracking aberrations during both baseline and post- irrigation tracking in actively psychotic patients, but not in comparison groups of normal controls or schizophrenic outpatients with remitted symptomatology. These data are the first using well-controlled standardized procedures to indicate major vestibular-related dysfunction in adult psychiatric patients. Furthermore, the data indicate that the degree of vestibular dysfunction is severe, i.e., the fixation suppression values in the more disturbed patients fell within the range which could be considered pathological (61,93,101).

These results suggest the presence of a central regulatory dysfunction of visual- vestibular interaction in psychiatric patients which varies with intensity of symptomatology. Moreover, the findings of impaired fixation suppression and tracking performance in the same patients suggest that the

central vestibular deficit may contribute to pursuit tracking deficits in psychosis. Obviously, these findings require replication, and it is the purpose of this study not only to reexamine this issue of vestibular activation, psychosis and pursuit tracking performance, but also to extend the assessment with tests designed to more precisely define conditions under which impaired performance occurs. Specifically, in terms of replicating Jones and Pivik's study, the present investigation included: (a) bilateral assessment of parameters of vestibular activation, with emphasis on those variables which proved discriminating in the initial study, namely, velocity of the nystagmus fast phase components and fixation suppression; and, (b) examination of pursuit tracking in conjunction with vestibular activation.

In addition to these replication analyses, the present study included manipulations designed to define factors or processes contributing to the observed oculomotor dysfunction by assessing oculomotor behaviour under light and dark-adapting conditions. The rationale for including the latter conditions is presented below.

Since the vestibular and tracking deficits reported have been observed in patients without other signs of vestibular or oculomotor organicity (e.g., spontaneous nystagmus), the basis for these disorders is likely to be of an interactive or

modulatory nature involving systems responsible for eye movement control. Recent investigations have emphasized the role of cerebellar and brainstem structures in smooth pursuit tracking and in the suppression of caloric nystagmus by ocular fixation (1,8,10,22,57,78). It has also been shown that pursuit eye movements are strongly impaired in patients with cerebellar lesions (103). In fact, several oculomotor abnormalities which have been recorded in psychotic patients have also been recorded in patients with neurological signs of cerebellar dysfunction (Table 1). In this regard it is interesting to note that the cerebellar influence on eye movement control is largely inactive in darkness, a situation which normally prevents optic fixation (48). Significant differences in the caloric response as a function of light-dark testing conditions or with optic fixation have been reported (48), i.e., in darkness the nystagmus response of patients with central lesions approached normal values, and the enhancement of nystagmus in the presence of optic fixation characteristic of central pathology was not apparent. Ritvo et al. (88) observed that in darkness the nystagmus response of autistic children normalized and suggested that interactions between visual and vestibular inputs determine the abnormal suppression of nystagmus in autistic children. Hood and Waniewski (49) found that whereas in normal subjects optic fixation of a target light on an illuminated background suppresses by a factor of two the nystagmus induced by caloric irrigation relative to that when

Table 1. Oculomotor abnormalities related to cerebellar dysfunction. (111)

1. Impaired smooth pursuit and optokinetic nystagmus
2. Hyperactive vestibuloocular responses
3. Impaired suppression of caloric-induced nystagmus
4. Saccadic dysmetria, macrosaccadic oscillations
5. Square-wave jerks (saccadic fixation instability)

the same target is viewed in total darkness, in cerebellar patients the introduction of background illumination does not appreciably suppress further the nystagmus present during fixation in the dark. Dichgans (32) observed that pendular nystagmus present in a patient with cerebellar damage disappeared during fixation in the dark. Hood and Waniewski (49) also noted that patients with cerebellar lesions had aberrant pursuit eye movements and that these were worse in the presence of background illumination. This light-dark recording difference might account for the relatively normal vestibular responses in psychiatric patients in the absence of optic fixation (67). Also of potential relevance to these results are recent reports of cerebellar damage in psychiatric patients (30,37,72,108,99,109). It is important to note that the visual-vestibular abnormalities reported by Jones and Pivik (58,59) were based on recordings taken during continuous illumination. In the present study the contribution of light-dark conditions and opportunity for fixation were determined by assessing vestibular reactivity and tracking performance under conditions of light and dark adaptation, respectively. This differentiation will provide new data relative to considerations of cerebellar involvement in oculomotor deficits accompanying psychoses.

Another way of assessing the effitiency of

vestibular-ocular reflex suppression is by measuring the accuracy of visual fixation of a stationary target. The cerebellum has also been reported to play a modulatory role in this process and the presence of aberrant fixation in conjunction with failure of fixation suppression and poor pursuit tracking in the same subjects would provide even stronger evidence for a central regulatory dysfunction involving the cerebellum. Previous studies (74,75,77) which have evaluated the ability of psychotic patients to fixate a stationary target have reported inconsistent results. Although Mather reports that psychotics did not have stability problems during fixation (74), she did note that poor premorbids had more departures from fixation than good premorbids whose performance was similar to that of controls. Mialet and Pichot (77) found that schizophrenics made significantly more fixation saccades than normal controls and Matsue et al. (75) found differences of a similar nature but they did not reach statistical significance. Based on these findings and the potential for providing additional data regarding possible cerebellar involvement in oculomotor dysfunction in psychotics, this study examined the ability of psychotics to fixate a stationary target during both light and dark adapting condition in the absence of vestibular activation.

Areas of Special Concern

Investigations of the type proposed are vulnerable to multiple sources of confounding influences. Four such areas of particular concern in this study are: 1) patient selection and diagnosis; 2) attentional factors; 3) effects of medication; and, 4) light-dark related variations in the corneoretinal potential (CRP). Each of these topics will be briefly discussed below.

Patient Selection and Diagnosis

The correct diagnosis of psychosis is crucial to the hypothesized results of this study and therefore was stringently controlled. In order to insure the validity and reliability of the patient diagnoses, classification was bassed on the DSM III criteria and was independently determined by two psychiatrists. The presence of active psychotic symptomatology, also crucial to this investigation, was determined through patient interviews and by referring to hospital records, included the presence of delusions, hallucinations and behaviour patterns inconsistent with reality testing. Since relatives of psychotic patients have also been found to have aberrant pursuit tracking, control subjects were screened for a family as well as personal history of psychiatric illness and were required to have a normal profile on the MMPI.

To insure that the results are not attributable to other obvious variables, such as age, gender and intelligence level, -- even though these variables are not reported to be related to eye movement aberration -- efforts were made to match subjects on these factors.

Attentional Factors

The maintenance of sustained attention has been shown to be important both in smooth pursuit tracking performance (43,83,96) as well as in the response to vestibular activation (23,24,25,26). Furthermore, an attentional deficit has been indicated in mental disorders, particularly schizophrenia (38,81,106,110). Consequently, when assessing these oculomotor responses in a population with an indicated attentional deficit it is essential that procedures be implemented which facilitate attentiveness yet do not compromise performance. Moreover, there should be objective measures of such procedures to provide an index of attentiveness. It is particularly difficult in the smooth pursuit tracking paradigm to introduce a measure which monitors attention to the task without interfering with tracking performance. Attempts to control for attentional processes during tracking have consisted of realerting the subject to the tracking task by giving verbal instructions during testing (17,45,46,83,95), and having subjects read numbers presented on the tracking target (43,96). In the verbal

realerting condition, subjects, after an initial series of trials, were again instructed to carefully watch the target. Subsequent to these instructions another series of trials was administered. This procedure has resulted in slight (17) or no (46,83,95) improvement in tracking performance. In the number reading paradigm, subjects were instructed to read, either silently or aloud, numbers presented on the tracking target (pendulum bob). Silent number reading has been reported to improve tracking performance (43,96), and the degree of improvement has been related to the accuracy of baseline tracking performance, i.e., the poorer the baseline tracking (no number presentation), the greater the improvement (96).

Another approach to this problem of providing a measure of attention during tracking has been to randomly interrupt power to the target light for brief periods of time (200 msec.)(52,59,83,84). In response to perception of the target-light interruption, the subject is required to press a hand-held button. Using this procedure, the continued presence of tracking deficits has been observed despite close attention to the target in more disturbed patients (83,84). This procedure was employed in Jones and Pivik's study (59) of tracking performance and vestibular activation, and is included in this study.

The vestibular response to caloric irrigation is reduced by diminished arousal, and consequently it is recommended that exercises designed to effect and maintain arousal and attention be included when assessing the vestibular system using caloric irrigation. One simple manipulation commonly used which quite effectively enhances vestibular reactivity is engagement in mental arithmetic, i.e., counting backwards serially from a given number by a constant (12,25,70) This procedure--which was utilized by Jones and Pivik (58) and resulted in an increased vestibular response in both patients and control subjects during mental alerting relative to measures taken in the absence of this procedure--is also used in the present study.

Medication

It is virtually impossible to avoid the potentially confounding effects introduced by medication when studying psychiatric populations, particularly actively-ill patients. This issue has been considered quite extensively with respect to tracking performance in these patients, and the consensus is that psychotropic medication at the dosage levels generally prescribed in these patients does not interfere with eye tracking performance (44,53,83,95).

The influence of medication on vestibular reactivity in psychiatric patients has not been widely investigated. Shuster

(97) noted some depression in vestibular response in patients on phenothiazines, but the results in schizophrenics tested before the advent of tranquilizers also showed this tendency toward hyporeactivity. A more recent study (79) which employed electrophysiological measures of eye movements also noted hyporeactive vestibular responses in chronic schizophrenics who had been medication free for over a year. Chlorpromazine, a commonly used neuroleptic, reportedly produces a slowing of the fast phase of nystagmus (76). However, a recent report of normal saccadic velocities in medicated psychotic patients (66), and other recent studies of vestibular reactivity in such patients (67), including the Jones and Pivik study (58), suggest that while it is not possible to conclusively rule out deleterious effects of medication on vestibular reactivity, such effects, if present, either do not affect all individuals, or interact in some complex manner with clinical variables to effect the observed deficit. In the present investigation medication parameters were closely monitored. For example, the recent medication history of each patient was carefully documented, with attention paid to amount of, and time on, medication, and subjects receiving medications known to affect eye movements or vestibular responses (e.g., barbiturates, tranquilizers from the benzodiazepine group, stimulants or antihistamines) were not accepted into this study.

Corneoretinal Potential

The amplitude of the corneoretinal potential has been reported to decrease in dark relative to light-adapted conditions (40). To evaluate possible effects of variations in this measure on light- and dark-adapting oculomotor measures, calibration values were obtained in both conditions when baseline and fixation measures were taken.

SYNOPSIS AND HYPOTHESES

The role of the vestibular system in the generation of both pursuit and saccadic eye movements makes it possible that this system is involved in deviant smooth pursuit tracking observed in psychoses. Only three studies have used clinically reliable assessments of vestibular activation in psychiatric patients (58,67,79), and only one has examined the interaction between smooth pursuit tracking and vestibular activation in such patients (59). Futhermore, only one of these investigations (58) examined the vestibular response parameters of fixation suppression and fast phase velocity. These studies all agree that vestibular functioning is intact (as indicated by normal slow phase velocity -- the measure commonly taken as an index of vestibular integrity; 11) -- but evidence of a visual-vestibular dysfunction has been provided by the additional analyses conducted in the study cited above (58).

The latter investigation also found evidence of enhanced tracking deficits following vestibular activation in the same patients showing failure of fixation suppression, thereby suggesting a relationship between these two deviant responses in psychotics. These findings, which have important implications for our understanding of the neurophysiological correlates of psychosis and which may be of eventual use in the treatment of these disorders, require replication. A major intent of this study is to reexamine the vestibular response to caloric irrigation in psychiatric patients with particular attention paid to those variables which have proved discriminating, including the relationship between vestibular reactivity and pursuit tracking performance.

Jones and Pivik's findings (58,59) of markedly attenuated fixation suppression and reduced fast phase velocity indicate central dysfunction involving the vestibular system. Although this dysfunction may reside in the vestibular system, it could also involve the interactions between this system and other cortical and/or subcortical oculomotor mechanisms. In this regard cerebello-vestibular interactions should be considered. There is a confluence of data indicating cerebellar pathology in psychosis (37,99) and in the mechanism of fixation suppression (62,78). Of particular interest with respect to the findings regarding failure of fixation suppression in psychotic

patients are the additional observations that: (i) the cerebellar influence on eye movement control is largely inactive in darkness, a situation which normally prevents optic fixation (49); (ii) in darkness the nystagmus response of neurological patients with central brainstem and cerebellar lesions is reported to approach normal levels, and the enhancement of nystagmus in the presence of optic fixation characteristic of central pathology disappears (48); (iii) normalization of the nystagmus response of autistic children occurs in darkness (88); and, (iv) data indicating impairment of fixation suppression in psychiatric patients were obtained under conditions of continuous illumination -- a situation which would allow the expression of cerebello-vestibular interactions (58). If there is a dysfunction in this interaction, then the slow phase velocity of patients during fixation suppression should not differ under conditions of light and dark-adaptation, but that of normal subjects should be suppressed by a factor of two in the light relative to the dark adapting measures. The degree of fixation suppression in psychotics, however, should decline further in the dark-adapting condition. Hood and Konres (48) found that in cerebellar patients suppression of the vestibulo-ocular reflex was better executed against a background than when no background was present. Therefore, vestibular reactivity and fixation suppression will be examined under light- and dark-adapting conditions to test the normality of

cerebello-vestibular interactions in this process.

Pursuit tracking performance and fixation of a stationary target will also be examined under light- and dark-adapting conditions since: (a) the pursuit tracking performance of neurological patients with cerebellar lesions is reported to normalize in the dark (49); and, (b) fixation of a stationary target is also thought to be modulated by the cerebellar system and may, like pursuit tracking and fixation suppression, be affected under dark-adapting conditions.

HYPOTHESES

Based on the preceding literature review, it is hypothesized that:

1. Subsequent to vestibular activation by caloric irrigation under conditions of continuous lighting, patients with active psychotic symptomatology will show: i) impaired values of fixation suppression; ii) reduced fast phase velocity; and, iii) greater impairment of smooth pursuit tracking than either normal controls or patients with remitted psychotic symptomatology. [this constitutes a replication of Jones and Pivik's study (58,59)].;
2. Under conditions of continuous lighting, but independent of vestibular activation, patients with active psychotic symptomatology will show: greater impairment of both smooth pursuit tracking and fixation of a stationary target than either normal controls or patients with remitted psychotic symptomalogy. [this constitutes a replication of Mialet and Pitchot study (77)].;
3. Relative to light-adapting values, the fixation suppression scores, fast phase velocity measures

and smooth pursuit tracking performance occurring subsequent to vestibular activation will normalize in actively-ill psychotic patients when tested under dark-adapting conditions. The slow phase velocity of actively-ill patients during fixation suppression will not increase in the dark, but fixation suppression will become less efficient. (this is a test of the normality of cerebello-vestibular interactions);

4. Relative to light-adapting values and independent of vestibular activation, the smooth pursuit tracking and fixation values will normalize in actively-ill psychotic patients when tested under dark-adapting conditions.

METHODOLOGY

Subjects

Forty-six psychiatric patients [23 inpatients with active psychotic symptomatology (A) and 23 outpatients who previously showed psychotic symptomatology but who were in remission (R) at the time of the recordings] and 23 nonhospitalized controls (C) were studied. The patient population was recruited from the Department of Psychiatry Inpatient and Outpatient Clinics of the Ottawa General Hospital. Nonhospitalized controls were

recruited from among hospital staff, the local university population and the population at large. Upon acceptance into the investigation, subjects signed forms of informed consent and were assigned a randomly determined identity number so that analyses would be conducted without knowledge of subjects' name, group membership or clinical status. This code was broken only after completion of data processing and analyses prior to group analyses.

Diagnosis of psychosis and the presence of psychotic symptomatology (including delusions, hallucinations and behavior patterns inconsistent with reality testing) were based on APA DSM-III criteria and hospital diagnosis independently determined by two psychiatrists. Included in these group were patients with diagnoses of schizophrenia, paranoid type (A: n=11, R: n=6) schizophrenia undifferentiated type (A: n=5, R: n=9), schizoaffective disorder (A: n=4, R: n=2), and atypical psychosis and affective disorders (A: n=3, R: n=5). The operational definition of remitted symptomatology consisted of the absence of active signs of illness as determined from psychiatric evaluations. An additional requirement for patient selection was a normal electroencephalogram determined by examination of neurological records available on each subject.

Control subjects were accepted into the the study only if

they did not have a family or personal history of psychiatric illness, any personal history of head injury and had a normal response profile on the Minnesota Multiphasic Personality Inventory. Control subjects were matched for age with the patient population.

Subjects included a total of 40 males and 29 females (C: m=9, f=14; R: m=14, f=9; A: m=17, f=6). These subjects were between 20 and 60 years of age (C: X = 28 +/- 6 years, R: X = 32 +/- 10 years, A: X = 31 +/- 11 years), had a minimum IQ of 90, bilaterally intact tympanic membranes and 20/20 vision (normally or after correction).

Individuals with a history of organic disease, alcoholism, or motor abnormalities, e.g., tardive dyskinesia, or who were presently receiving medication known to affect eye movements or vestibular responses (e.g., barbiturates, antihistamines, tranquilizers) were not accepted into the study.

Procedures

A variation of the widely accepted Fitzgerald-Hallpike technique of caloric irrigation (33) was used to assess the integrity of the vestibular system. The deviations from that method included (a) electrooculographic recording of eye movements; and, (b) bilateral irrigation with cool (30 C) water only. Generally, warm (44 C) water irrigation is included as well, and results from the additional irrigations are employed

in deriving a measure of response symmetry. However, in view of the absence of asymmetry in two recent studies in psychiatric patients (58,67) and the potential negative effects of an extended testing sequence upon patients, it was decided to irrigate with cool water only. Moreover, bilateral comparisons of other response parameters can provide an index of symmetry.

Prior to recordings, details of the experimental procedure were related and reviewed with each subject with special emphasis on probable behavioral effects of caloric stimulation, e.g., vertigo. An otoscopic examination of the external auditory meatuses and eardrums was conducted to remove excess cerumen and ensure integrity of the tympanic membranes. Each irrigation extended over a 30 second period. Water cooled and maintained at 30 C by a Grant Instrument Circulator was delivered via a double-walled hose from the circulator to the external auditory canal. The total amount of water delivered for each irrigation was 250ml. Beckman miniature silver-silver chloride electrodes were attached to the outer canthus of each eye to record the horizontal electrooculogram (HEOG). Similar electrodes placed above and below one eye monitored vertical eye movement (VEOG) and blink artifact, and a ground electrode was situated mid- forehead. Eye movements were recorded on direct coupled amplifiers with high frequency response characteristics (.03 to 300 Hz). Electrodes were also attached

for monopolar recording of electroencephalographic (EEG: ØZ/A2) activity and facial electromyographic (EMG; orbicularis oris) activity. A general measure of level of arousal, e.g., increased alpha activity against a low amplitude, mixed frequency EEG background indicating lower arousal, was obtained from the EEG recordings, and EMG recordings were scrutinized for changes in facial muscle tension and movement artifact. All electrographic and stimulus-response data (to be specified) were recorded on paper writeout (Grass Model 78D polygraph) and stored on magnetic tape (Hewlett Packard 8868A tape recorder).

Once electrodes were attached, the subject reclined on a cot with his/her head positioned 1 meter from a light panel and elevated at 30 to assume the proper ventroflexed position for caloric testing. All subsequent tests were conducted while subjects were in this position. The light panel consisted of a bank of red light emitting diodes (LEDs; n=128, 1mm wide, spaced 1.5 mm apart) embedded in a black background and covered with clear plexiglass. A microcomputer controlling target presentation was programmed to simulate horizontal sinusoidal oscillation of a single target light at Ø.45 Hz (2.2 second periods) subtending a 20 arc (10 on either side of midline) through the subject's visual field. The combined effect of close spacing of the LEDs, and brief on/off interval between successive LED illumination effected the perception of a continuous motion of single oscillating target light.

Following calibration procedures, spontaneous eye movements with eyes closed were recorded for 30 seconds. This procedure permitted the detection of spontaneous nystagmus and individuals showing such activity were not accepted into the study. By the time the remaining eye movement testing began, the subjects had been positioned for caloric testing for approximately 20 minutes.

Each testing session was conducted under light and dark (light-tight room) adapting conditions (>10 minutes for each condition). Each session consisted of 3 experimental conditions presented in random order. The conditions were: 1) Baseline eye tracking; 2) Caloric eye tracking, left ear irrigation; and, 3) Caloric eye tracking, right ear irrigation (Figure 1). Each caloric condition consisted of:

(a) 0-30" - irrigation with eyes closed;

(b) a 40 second period (30"-70") with eyes closed while performing a mental alerting task (subtracting serially by 3's). The importance of the counting task was emphasized and during mental alerting subjects were periodically questioned as to what number they were at and after each condition they were asked whether they had continued counting throughout the procedure;

(c) a 20 second period (70"-90") of continued mental alerting while focussing on a small target light. Investigations (e.g., 48) examining the postula-

ted inhibitory effect of cerebellar influences on vestibular nystagmus have demonstrated that nystagmus is suppressed in lighted conditions with fixation, but not under dark conditions. The assumption has been that the dark condition does not allow for fixation and that this is critical since continuous visual feedback is considered essential to achieve optimal suppression (61). However, these conditions confound light-dark and fixation-no fixation variables. The present procedure attempted to differentiate between these factors by providing for fixation of a small red target light under dark adapting conditions.

(d) engaging in pursuit tracking of the same target light oscillating at .45 Hz for a 30 second period (90"-120"). The subject had to depress a hand held button whenever the target light was interrupted (off cycle 200ms);and finally,

(e) closing the eyes at the end of the tracking task and reinitiating mental alerting for 30 seconds or until evidence of nystagmus was no longer present.

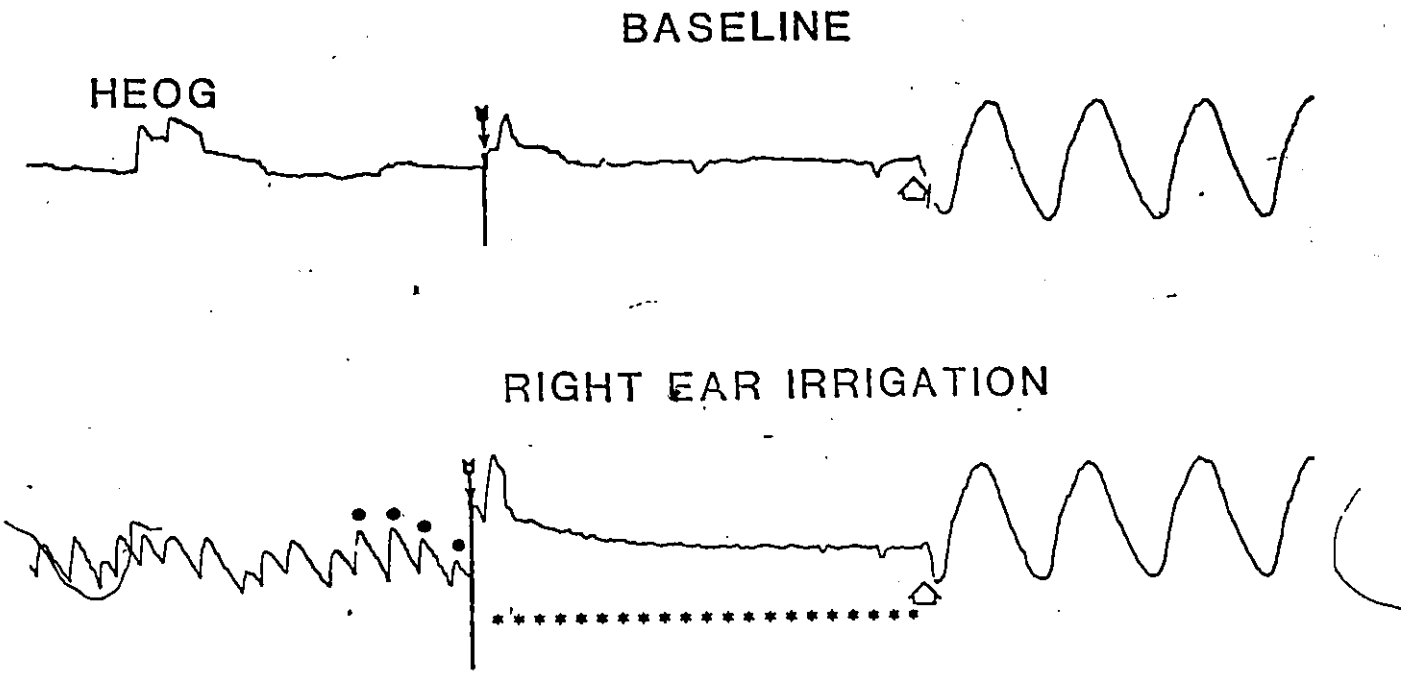


Figure 1: HEOG recording associated with baseline and caloric procedures. Both tracings include the final seconds of the 40 second period with eyes closed while performing mental alerting, a period (only 10 seconds are shown) of continued mental alerting while focusing on a small target light (downward vertical arrow), followed by pursuit tracking of the target light (upward vertical arrow). In the right irrigation tracing filled dots indicate nystagmus beats and the fixation period shows fixation suppression.

Data Analysis

A. Reduction and Analysis of Vestibular Data:

The vestibular response to caloric irrigation was examined for the following parameters:

1) Latency: the time interval from onset of irrigation to the first three beats of nystagmus occurring within three seconds.

2) Duration: the interval between the beginning of irrigation and the last beat of nystagmus. Criteria for the absence of response is the last time two nystagmus beats are seen within a 15 second interval.

3) Peak nystagmus frequency: the average frequency of nystagmus beats during a ten second interval in which the nystagmus is most intense;

4) Response strength: the maximum slow-phase eye velocity (Figure 2).

5) Fast phase velocity: a measure of velocity of rapid return (saccadic) eye movements.

6) Fixation suppression: the measure of effectiveness of visual fixation in suppressing the nystagmus is calculated by the following formula:

$$FS = \frac{\text{slow phase eye speed (eyes closed - eyes opened)}}{\text{slow phase eye speed (eyes closed)}} \times 100$$

where the numerator is the mean slow phase velocity of 10 seconds of nystagmus occurring just before eyes are opened minus 10 seconds of any nystagmus occurring while eyes are opened and fixating, and the denominator is the mean slow phase velocity of 10 seconds of nystagmus occurring just before eyes are opened.

7) Dysrhythmia: a measure of nystagmus irregularity, assessed for a 30 sec. period beginning 30 sec. after the onset of irrigation. Two individuals rated coded recordings of nystagmus according to the scale devised by Lidvall (68). A high interrater reliability index (> .9) achieved on pilot recording data was maintained during analysis of the experimental data.

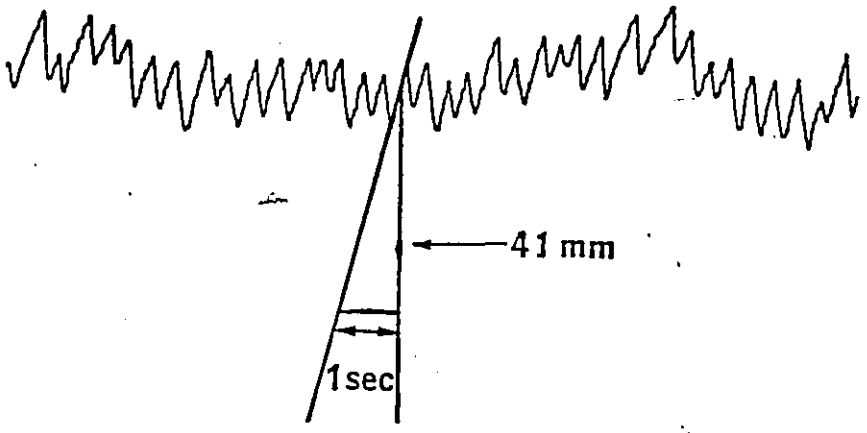


Figure 2: Determination of nystagmus slow phase velocity in degrees/sec. If the eyes moved 41 mm in 1 sec and 25 mm was equivalent to a 20° eye movement, the calculation of slow phase velocity would be as follows:

$$\frac{41\text{mm}}{1\text{ sec}} \times \frac{20}{25\text{mm}} = 32.8/\text{sec}$$

In this study the maximum slow-phase eye speed; i.e., the average slow-phase velocity during the 10 sec interval in which the response is most intense, was determined by computer analysis.

B. Reduction and Analysis of Pursuit Tracking and Fixation Data:

Pursuit tracking patterns were analyzed for the incidence of velocity arrests (VAs), as well as for global deviation of tracking from target patterns (root-mean square error: RMS). The former measure was determined by the following methodology which has been frequently used in the analysis of smooth pursuit tracking patterns in psychiatric patients (43,45,46,83,84,95,96): the tape recorded horizontal EOG tracing was filtered (low pass filter, 5.5Hz; attenuated 3 db at cutoff; 48 db rolloff/octave), amplified and differentiated (Grass 7P21-A differentiator) to obtain the first derivative (velocity) of the sinusoidal tracking pattern. The differentiator output was calibrated at a sensitivity of 20 /sec/cm. Half-wave differentiator tracings were scored for VAs according to previously established criteria (83,95). These three channels of data (ie., filtered HEOG and two differentiated HEOG signals) as well as the target motion indicator were simultaneously input into a PDP11/34 computer via A/D conversion at a sampling rate of 200 points / second / channel and stored on hard disk. The computer scored the differentiated channels for VAs. A VA constituted a slowing of eye velocity to less than 2 /second for greater than or equal to 40 msec. If eye velocity slowed to this level twice within

40 msec only the first slowing was scored. A return of the differentiator tracing to this level for 90 msec was scored as two VAs. VAs detected within 200 msec of a blink or EMG artifact were deleted from further analysis. Mandatory VAs due to the halfwave analysis and target turn around points were eliminated from statistical analyses.

The measure of global deviation of tracking from target patterns (RMS) was determined as follows: subsequent to correction for phase lag, a point by point determination of percent deviation of eye from target position was derived by subtracting eye data values from target signal values and dividing this difference by target signal value to yield percent deviation of eye position from target position. This provided global measures of percent deviation as a function of target velocity.

A similar procedure was followed to obtain a measure of global eye deviation during fixation of a stationary target, ie., a point by point determination of percent deviation of eye from fixation position was derived by subtracting eye data values from the fixation point value and dividing this difference by the fixation point value to yield percent deviation of eye position from target position.

Analogue EOG nystagmus responses, pursuit eye movement patterns, and tracking signal data were digitized at the rate of 200 samples/second and analyzed by computer to determine: 1) nystagmus slow and fast phase velocities; and, 2) phase lag between target and pursuit tracking patterns.

C. Corneoretinal Potential

The amplitude (microvolts) of the calibration signal for a 20 eye movement (averaged over 10 oscillations) was used as a reference measure of the corneoretinal potential. To obtain a light-dark adapting difference score, the dark-adaptation value was subtracted from that taken during the light-adapting condition.

RESULTS

Unless otherwise indicated, group and subject differences across conditions and testing sessions were analyzed using repeated measures analyses of variance (82; UCLA Medical School BMDP2V program), and indicated post-hoc analyses were conducted using the Newman-Keuls procedure. Correlations were performed using the Pearson Product Moment correlation coefficient.

VESTIBULAR RESPONSES: GROUP AND LIGHT-DARK COMPARISONS

No significant main effects were found between left and

right ear irrigations for any of the dependent variables except fixation suppression. Therefore, except for this variable, only results from right ear irrigations will be reported. Figures illustrating left ear responses can, however, be found in the appendix.

Slow Phase Velocity

Mean group slow phase velocity values are presented in Figure 3. There were no significant group differences for this parameter, and the average values for the separate groups correspond to those observed by Jones and Pivik (58) and to normative values reported in the literature (11). When measured under the dark-adapting condition, between-group comparisions of slow phase velocity values remained non-significant. However,relative to their light-adapting responses, the mean slow phase velocity measures of both patient groups decreased significantly in the dark (R:$p<.05$, A:$p<.025$). Consistent with the literature (11), the speed and amplitude of the nystagmus slow phase response were significantly correlated across groups in both the light ($r=.67$ $p<.001$) and dark ($r=.75$ $p<.001$).

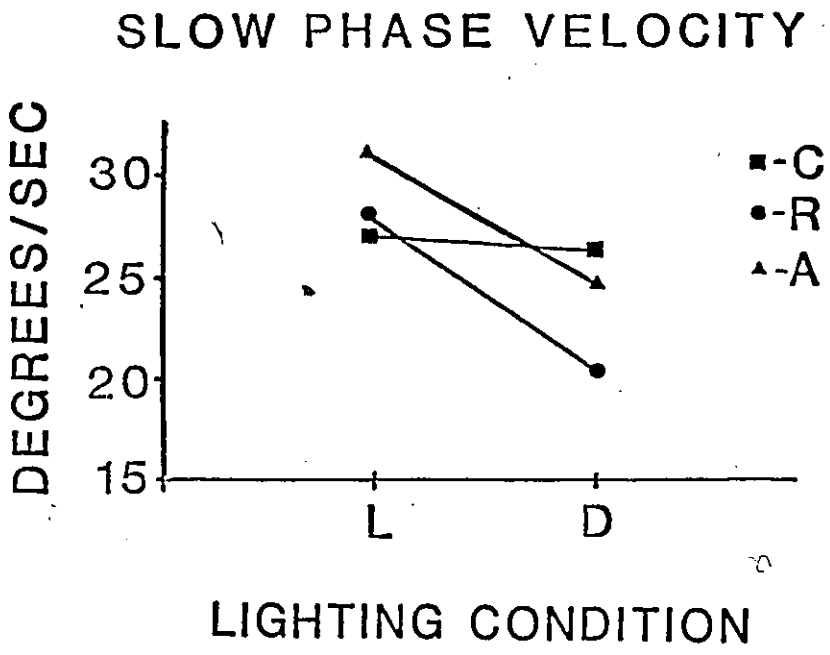


Figure 3: The maximum nystagmus slow phase velocity in degrees/sec following right ear irrigation in both the light-(L) and dark-adapted (D) conditions. Values for both patient groups decreased significantly in the dark ($p < .05$). In this and all subsequent figures the symbols C, R and A refer to control, actively-ill and remitted subjects, respectively, and the symbols L and D to Light and Dark-adapted conditions, respectively.

Fast Phase Velocity

No significant between-group differences were found for the fast phase velocity comparisons (Figure 4). The values reported here are slower than those reported by Jones and Pivik (58), but do, however, conform with the 3.5 to 1 ratio found to exist between fast and slow phase nystagmus velocity (76,91). The fast phase values in the present study also agree with those reported by Pyykko et al (86) for nystagmus beats of similar amplitude (Table 2). These authors (86) also reported that the peak velocity increased with increases in amplitude. In the present data, speed and amplitude of nystagmus fast phase were significantly correlated across groups (light: $r=.72$, $p< .001$, dark: $r=.79$, $p<.001$). The average fast phase velocity for each group decreased during dark adaptation, but this decrease was significant only for the patient groups R,$p<.05$; A,$p<.001$). As with slow phase velocity, the mean group differences for this measure remained non-significant in the dark. Fast and slow phase velocities are reported to correlate positively (91), and the data from this investigation corroborate that report, ie, these measures were significantly

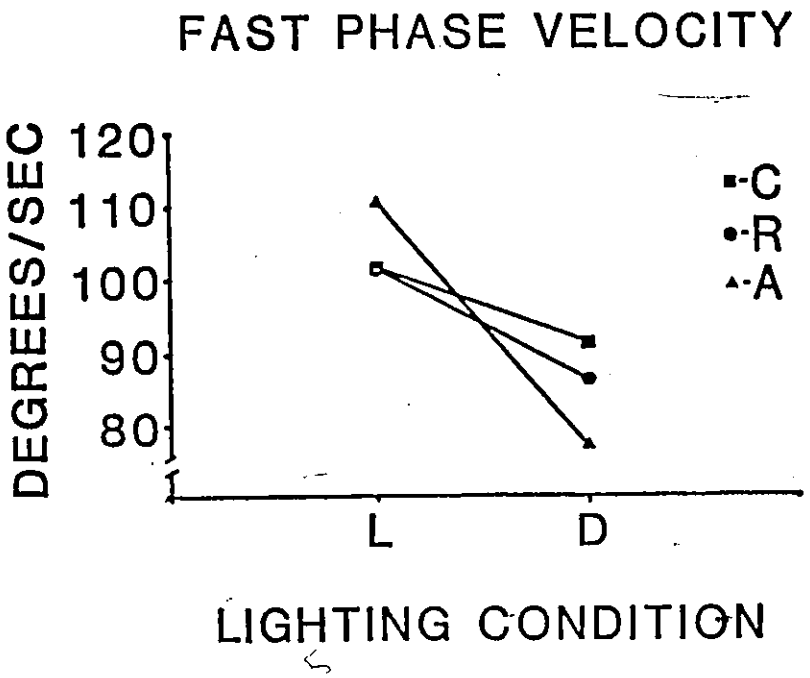


Figure 4. Average maximum fast phase velocity of nystagmus (degrees/sec) by group across lighting conditions. The frequency of nystagmus for both patient groups significantly decreased in the dark-adapted condition (R, $p<.05$; A, $p<.001$).

Table 2. Group means and standard deviations for velocity and amplitude of vestibular nystagmus.

Condition	Group	Slow phase velocity (degrees/sec	Amplitude (degrees)	Fast phase velocity (degrees/sec)	Amplitude (degrees)
LIGHT	C	27.29 +/- 11.74	11.33 +/- 4.69	101.63 +/- 34.10	11.35 +/- 5.12
	R	28.35 +/- 11.21	8.96 +/- 3.55	106.49 +/- 35.28	8.88 +/- 3.74
	A	31.29 +/- 14.25	9.50 +/- 4.16	112.62 +/- 46.26	9.34 +/- 4.26
DARK	C	26.92 +/- 12.01	9.67 +/- 3.85	91.24 +/- 31.43	9.46 +/- 4.09
	R	20.42 +/- 9.71	7.16 +/- 2.16	90.74 +/- 31.62	6.83 +/- 2.76
	A	24.44 +/- 12.88	7.00 +/- 2.81	82.06 +/- 29.59	6.39 +/- 2.70

correlated across groups in both the light ($r=.77$, $p<.001$) and dark ($r=.74$, $p<.001$).

Peak Frequency, Duration and Latency

The subject groups did not differ significantly with regard to the peak frequency of the nystagmus response. Although patients had higher frequencies of nystagmus beats than normals (C:X=16, R:X=18, A:X=21), these differences did not reach statistical significance (Figure 5).

A lighting-condition by group interaction effect [$F(2,65) = 3.54$ $p<.0346$)] was obtained for nystagmus frequency. Post-hoc analyses revealed that the actively-ill patients peak frequency was significantly ($p<.01$) decreased in the dark- compared to the light-adapting condition. Despite this reduction, there were no significant group differences for the dark-adapting data.

Significant main effects were not present for latency to nystagmus onset or duration of nystagmus under either lighting condition. There was, however, a trend in the light-adapting data for nystagmus to begin later and end earlier in actively-ill patients relative to controls (Table 3).

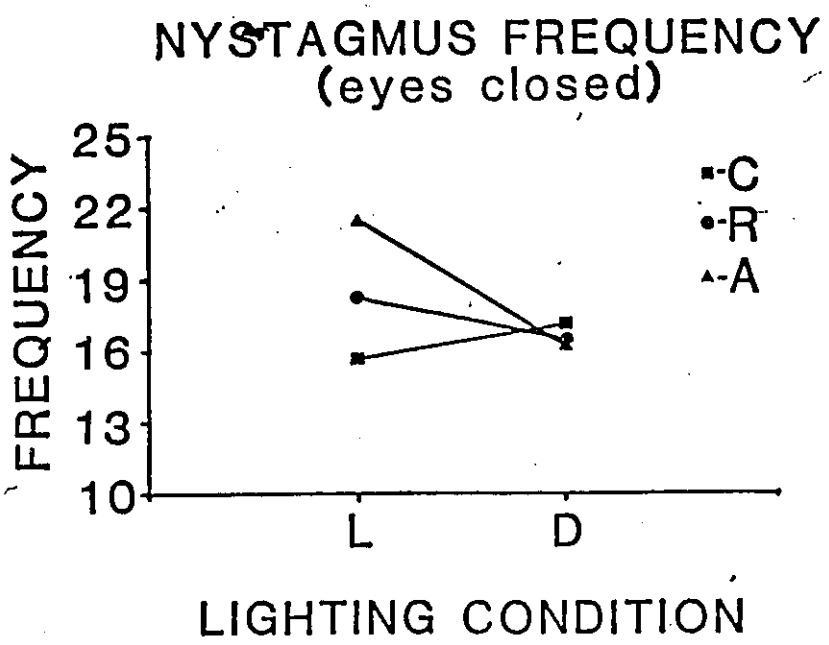


Figure 5. Group nystagmus frequency, i.e., average maximum number of nystagmus beats, during eyes closed across lighting conditions. Actively-ill patients had significantly lower frequencies during dark-adaptation ($p < .01$).

Table 3. Means and standard deviations obtained across groups for vestibular response measures.

Condition	Group	Frequency (beats/10sec)	Latency (sec)	Duration (sec)
LIGHT	C	14.95 +/- 5.98	27.22 +/- 8.45	188.13 +/- 34.33
	R	18.09 +/- 9.26	33.78 +/- 17.37	173.74 +/- 23.04
	A	20.74 +/- 7.14	35.27 +/- 15.78	171.19 +/- 18.27
DARK	C	16.27 +/- 6.38	34.09 +/- 7.93	182.95 +/- 34.06
	R	19.65 +/- 8.28	35.00 +/- 13.96	170.35 +/- 19.26
	A	16.91 +/-10.27	33.50 +/- 8.34	175.23 +/- 19.04

Dysrhythmia

No significant differences in dysrhythmia ratings were found across groups in the light or dark adapting conditions (analyses based on Kruskal Wallis non-parametric procedures). Although there was a trend towards increasing dysrhythmia across irrigations (Figure 6), analyses performed to test for the possible influence of order on these results were non significant. When order is considered, there were still no significant group differences. However, patients received a higher percentage of grade 2 and 3 dysrhythmia ratings than controls (Figure 7).

Dysrhythmia ratings did show the same linear relationship with fast phase velocity as reported by Jones and Pivik (58) i.e., the higher the dysrhythmia rating the slower the fast phase velocity. However, in this study that relationship was obtained for slow phase velocity as well. The mean slow and fast phase velocities were slowest when the nystagmus was rated as most dysrhythmic (grade 3, Table 4).

Based on results from comparisons using the Wilcoxon Matched-Pairs test, no significant within-group differences were found for light-dark adaptation dysrhythmic values.

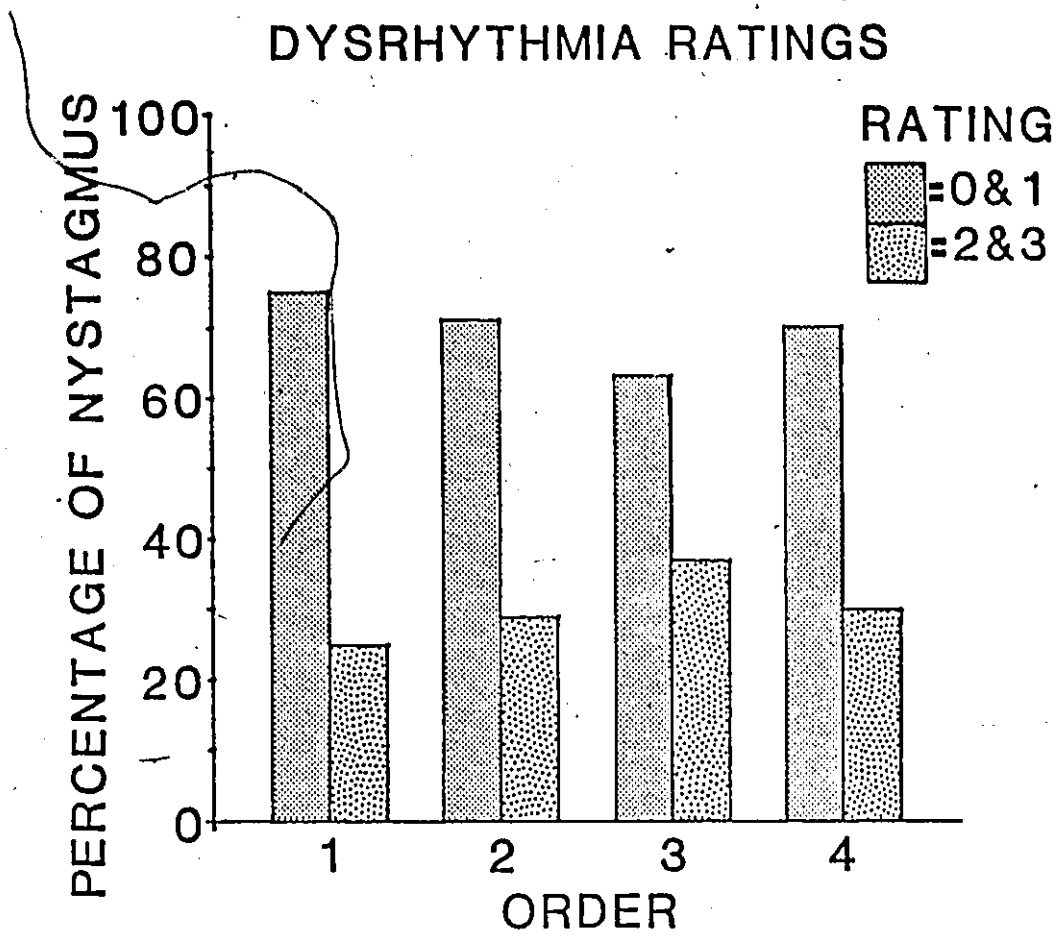


Figure 6. The bar graph shows the percentage of nystagmus for all subjects following caloric irrigation receiving normal (0 or 1) or abnormal (2 or 3) dysrhythmia ratings. The results are divided by order of irrigation irrespective of side of irrigation. Note the tendency for grade 2 and 3 ratings to increase across irrigations.

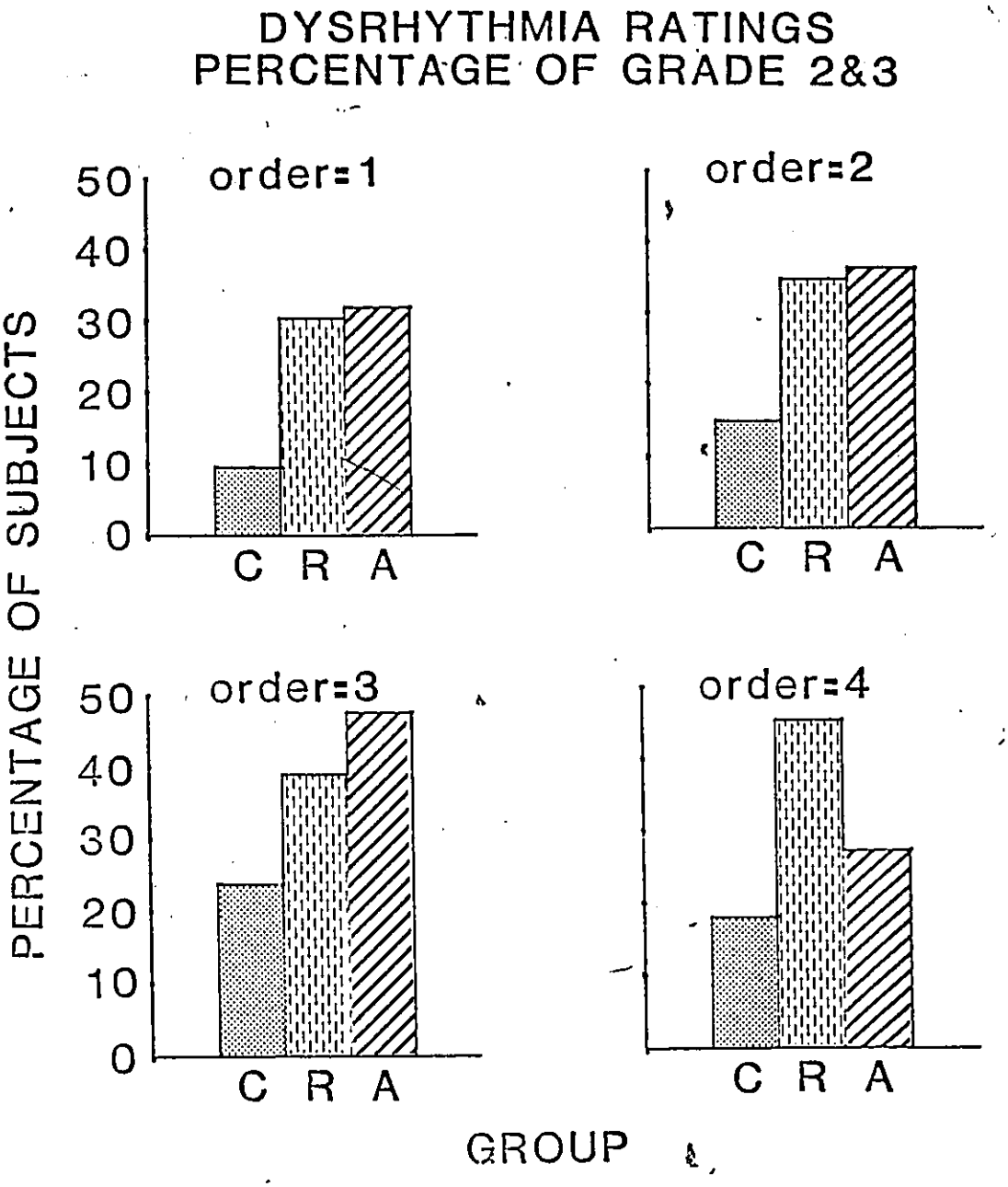


Figure 7. The bar graphs illustrate the percentage of subjects with grade 2 and 3 dysrhythmia ratings within each group for the first, second, third and fourth irrigations.

Table 4. Mean slow and fast phase values (degrees/sec) for subjects grouped by dysrhythmia ratings.

Measure	Grade	n	Light	Dark
SLOW PHASE	3	4	14.62	12.18
	2	6	25.74	19.48
	1	24	24.93	24.96
	0	29	26.61	35.28
FAST PHASE	3	4	58.47	57.96
	2	5	81.88	83.47
	1	21	92.62	83.44
	0	28	127.83	97.62

Fixation Suppression

Separate ANOVAs on the two fixation suppression conditions--i.e., following right and left ear irrigations--were performed since a main effect for these conditions was found ($F(1,59)=7.99$, $p< .006$). Post-hoc analyses performed on data from light-adapting conditions revealed no significant lateralized effect for controls, but remitted patients showed significantly greater suppression following left ear irrigation (right-64.25%, left-76.30%, $p<.01$), while actively-ill patients showed significantly higher suppression following right ear irrigation (right-67.15, left-60.15, $p<.01$). Similar analyses conducted on data from the dark-adapting condition revealed significantly greater fixation suppression for all groups following the left ear irrigation.(C,$p<.05$; R,$p<.01$; A,$p<.01$).

During the light-adapting condition, irrigation of either ear was associated with significant group effects (right, $F(2,61)=12.65$, $p< .0001$; left, $F(2,61)=10.50$, $p< .0001$). Following right ear irrigation, controls had significantly greater fixation suppression than either remitted ($p< .01$) or actively-ill patients ($p<.01$). When the left ear was irrigated, controls remained significantly different from actively-ill ($p .01$) but not from remitted patients --although the latter still showed less suppression than controls. In these analyses,

however, remitted patients exhibited significantly greater fixation suppression than actively-ill patients ($p<.05$, Figure 8).

During the dark-adapting condition, between-group analyses indicated that controls had significantly higher mean percent suppression than either patient group (C > A: $p<.01$; C > R: $p<.01$), and that the patient groups did not differ significantly from each other.

Comparisons of fixation suppression values across light-dark adapting conditions following right ear irrigation revealed an across-group consistency in demonstrating less suppression in the dark (C, $p<.025$; R, $p<.05$; A, $p.001$). Although this trend was maintained following left ear irrigation , only the remitted patients' light-dark mean suppression comparison attained statistical significance ($p<.05$).

To compare the present results with those of Hood and Waniewski (49) the speed of the slow phase velocity with eyes open and fixating in the light-adapting condition were compared to that with eyes open and fixating in the dark-adapting condition. It was found that in the light controls suppressed the slow phase velocity of nystagmus by a factor of 1.6

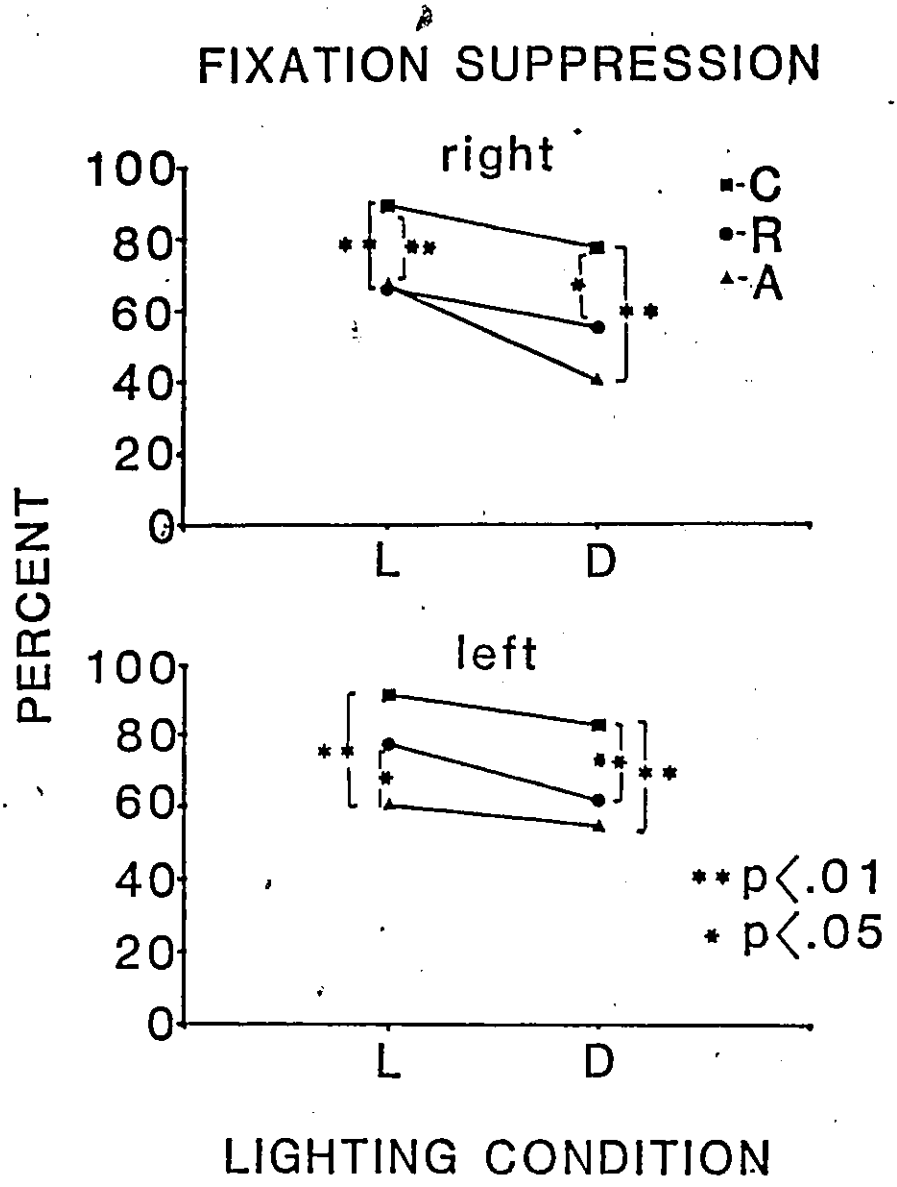


Figure 8. Mean percent suppression of caloric nystagmus by fixation . (see text for fixation suppression calculation. The decrease in fixation suppression was significant (C: p<.03, R: p<.05, A: p<.001) for all groups following right ear irrigation, but only for remitted patients (p<.01) following left ear irrigation.

relative to when the target was viewed in total darkness. For this group slow phase velocity in the dark was 68% faster than in the light. Actively-ill patients were virtually unaffected by background illumination, suppressing by a factor of .97, with their slow phase velocity actually being 8% lower in the dark. Patients in remission suppressed by a factor of 1.21, with variable responses between irrigations, increasing 3% in the dark following right ear irrigation and 42% following left ear irrigation. (Figure 9)

FIXATION : GROUP AND LIGHT-DARK ADAPTED COMPARISONS

A significant main effect for group was found ((F2,62)=4.10, p< .02) for percentage fixation RMS during baseline. Post-hoc analyses revealed that during the light-adapting condition actively-ill patients were significantly worse than either controls (p< .01) or remitted patients (p<.01) at suppressing extraneous eye movements during fixation of a stationary target. Following dark-adaptation there was no longer any significant between-group differences on this measure. Actively-ill patients maintained fixation significantly better in the dark than in the light (p<.001 Figure 10). It should be noted that even though the

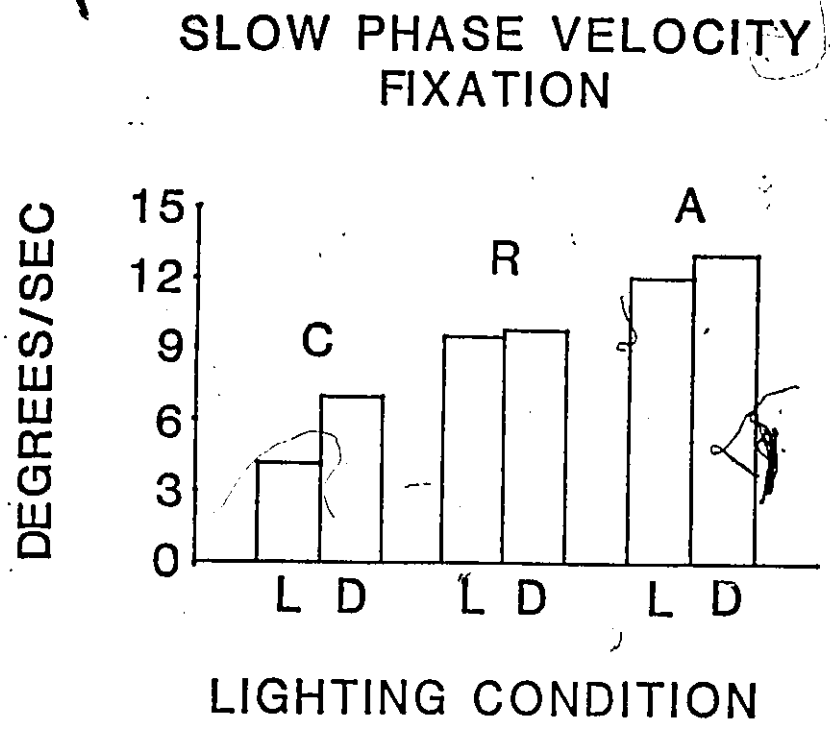


Figure 9. Mean nystagmus slow phase velocity (degrees/sec) during fixation for each group across lighting conditions.

between-group difference was not significant, both controls and remitted patients had higher RMS scores in the dark than in the light-- indicating that they had greater difficulty maintaining fixation under the dark adaptation condition.

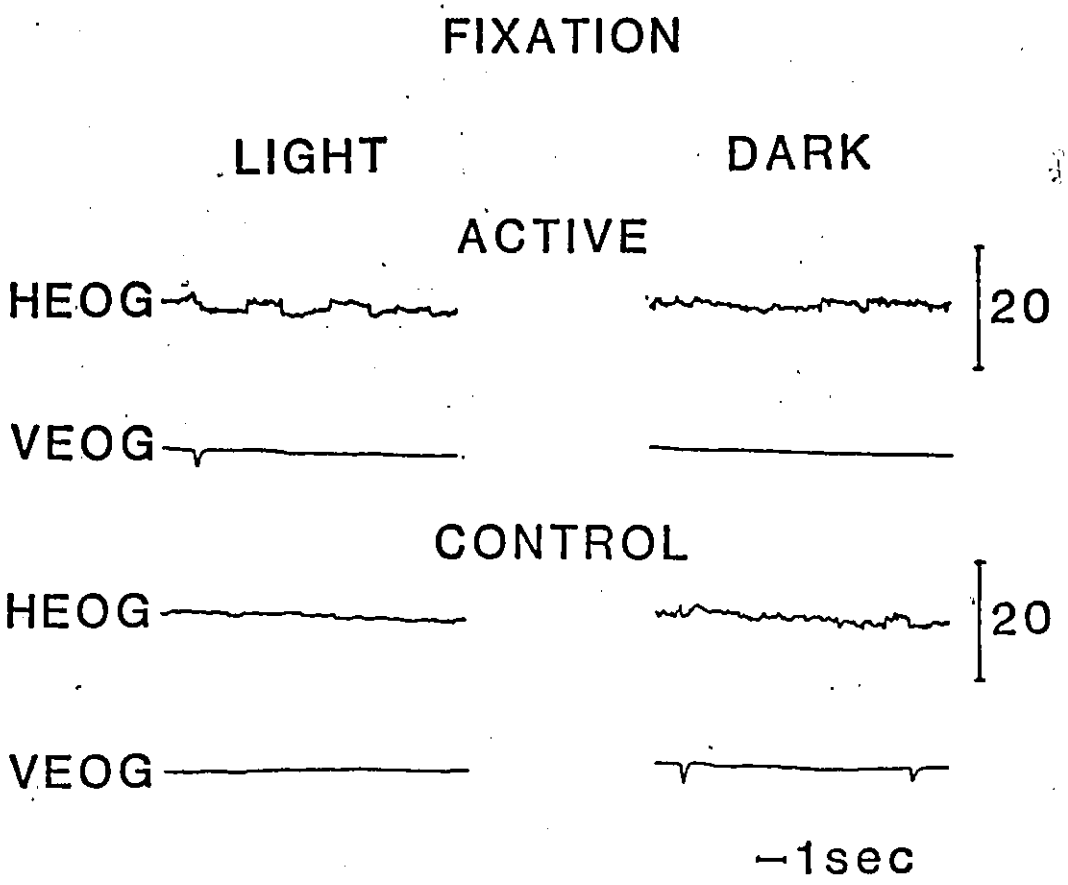
To provide an estimate of the relationship between poor tracking and poor fixation, fixation RMS was correlated with VAs and pursuit RMS (PRMS). In both cases the correlations were significant in both the light (VAs, $r=.38$; PRMS, $r=.44$; $p<.001$, respectively) and dark (VAs, $r=.41$, $p< .001$; PRMS, $r=.32$, $p<.006$).

TRACKING : GROUP AND LIGHT-DARK ADAPTED COMPARISONS

Velocity Arrests

A significant main effect for group was found ($F(2,58)=14.55$, $p< .001$) for the average number of VAs for baseline and vestibular irrigation conditions. Post-hoc analyses revealed that under light-adapting conditions baseline recordings from actively-ill patients contained a significantly higher frequency of VAs than those of either controls ($p<.01$) or remitted patients ($p< .01$). Furthermore, patients in remission also had significantly more VAs than controls ($p<.01$)

A



B

Group	Light	Dark
Control	4.58 +/-3.05	5.36 +/-3.40
Remitted	6.02 +/-3.98	7.07 +/-5.41
Active	10.90 +/-7.95	7.60 +/-6.74

Figure 10. A. Electrographic tracings of fixation during light and dark adaptation taken from a control and actively-ill patient. B. Mean and standard deviation of percent fixation root mean square for each group across lighting conditions. Channel designations: HEOG: horizontal electrooculogram: VEOG: vertical electrooculogram.

under these conditions (Figure 11). Following dark-adaptation, however, these between-group differences disappeared (Figure 11), i.e., dark-adaptation reduced VAs from levels present during the light-adapting condition to the extent that group values were statistically similar. There was a significant light-by-group interaction effect, and subsequent analyses indicated that when comparing baseline tracking there was no significant light-dark difference in the mean number of VAs for controls. For both patient groups, however, the mean number of VAs significantly decreased in the dark ($p<.05$; Figure 12).

Post-irrigation tracking in light-adapting actively-ill and remitted patients was characterized by significantly more VAs than that of controls ($p<.01$ and $p<.05$ respectively, Figure 13). In the dark, actively-ill patients still evidenced significantly more VAs than controls ($p<.01$), but also had a significantly higher VA frequency than remitted patients ($p< .01$). During the post-irrigation condition , however, the mean number of VAs did not change significantly as a function of lighting condition for any group.

No overall main effect was evident in baseline to post-irrigation tracking comparisons.. However, there was a light by condition effect [$F(1,58)=10.98$ $p<.0016$]. Post Hoc

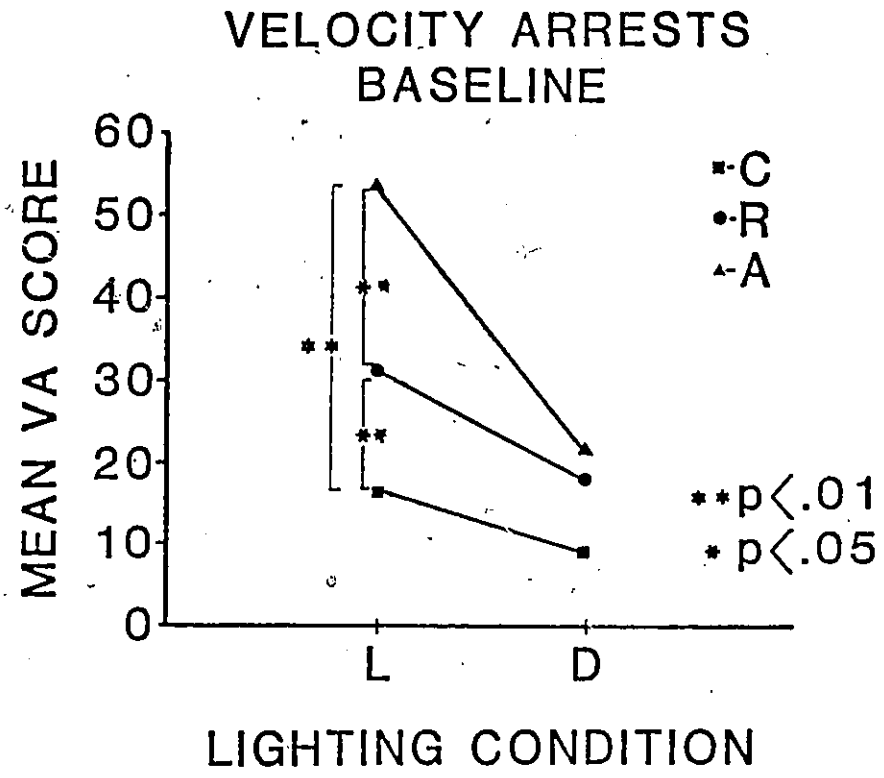


Figure 11. The mean number of VAs is presented for each group across lighting conditions. In addition to the indicated significant differences the mean number of VAs for both patient groups, but not controls, decreased significantly in the dark-adapted condition ($p<.05$, respectively).

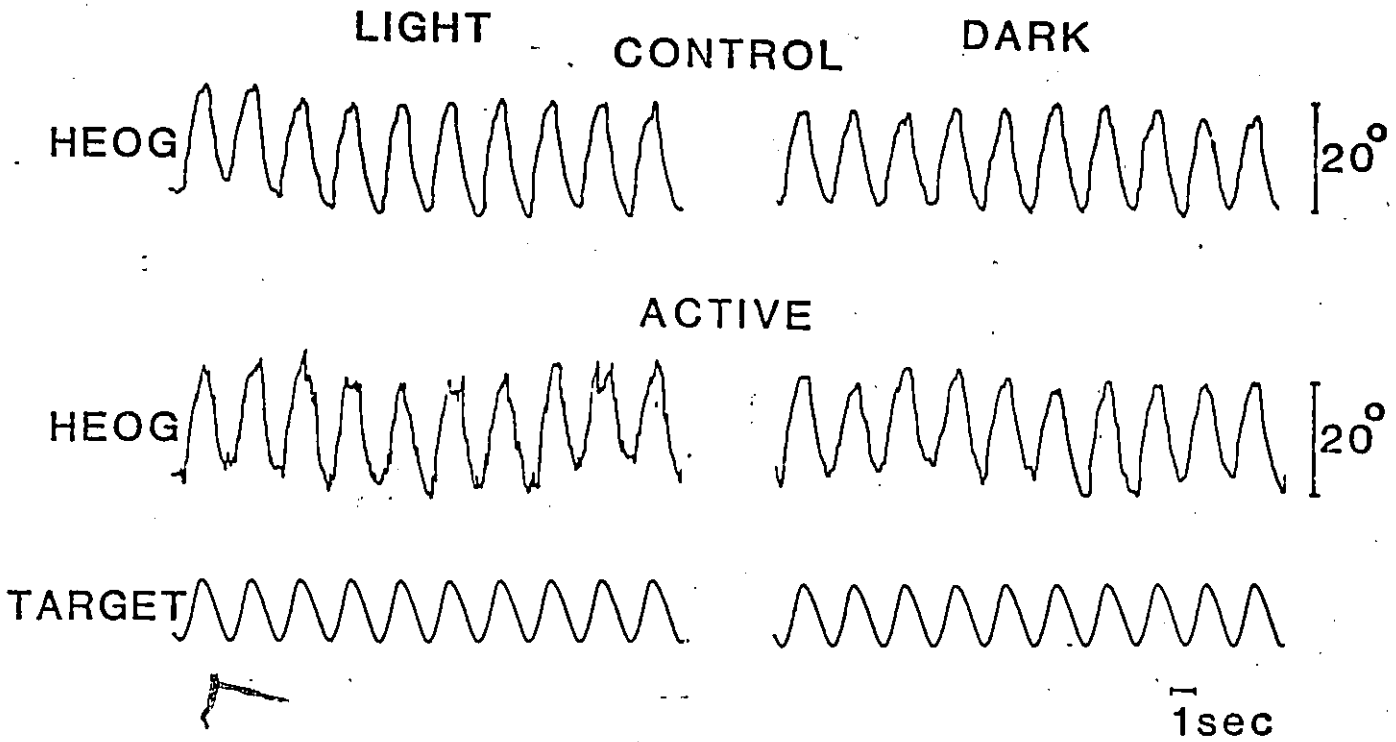


Figure 12. Electrographic tracings of pursuit tracking during light and dark-adaptation taken from a control and actively-ill patient. These tracings illustrate the more regular and accurate tracking exhibited by patients during dark adaptation. Channel designations: HEOG: horizontal electrooculogram; Target: target light excursions.

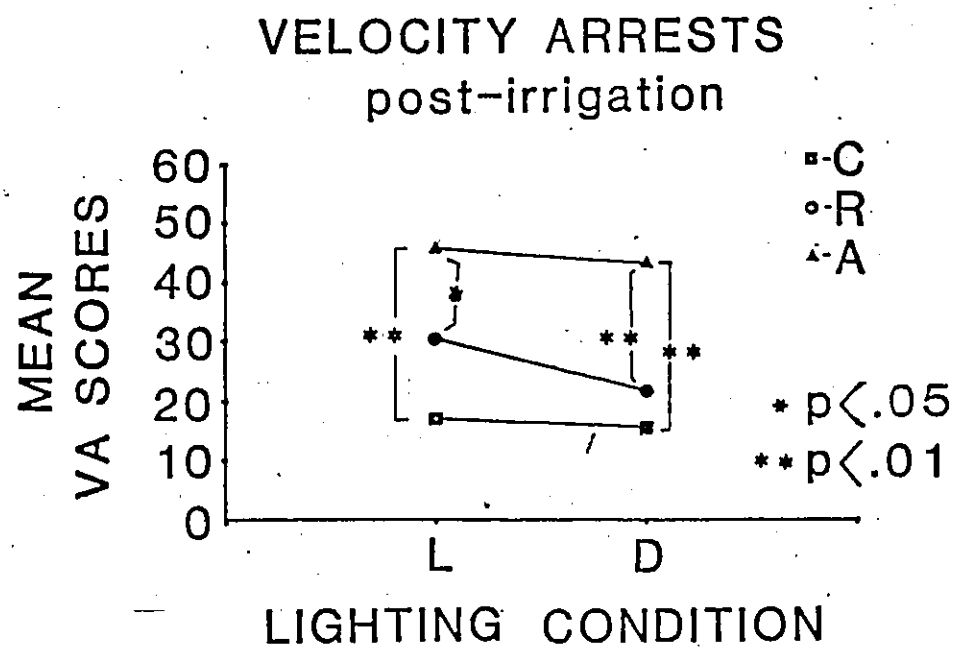


Figure 13. The mean number of VAs for each group following caloric irrigation under both lighting conditions.

comparisons revealed that in the dark actively-ill patients evidenced significantly more VAs following irrigation than during baseline tracking.

To determine whether deficits in baseline tracking were related to failure of fixation suppression, correlation coefficients between these variables were obtained. Significant negative correlations were found between the mean number of VAs and fixation suppression measures (Table 5). Significant negative correlations were also found between the mean number of VAs post-irrigation and fixation suppression measures. In other words, low fixation scores were correlated with poor tracking (Left,light: $r=-.47$, $p<.001$; Right,light: $r=-.23$, p .028; Left,dark: $r=-.49$, $p<.001$; Right,dark: $r=-.44$, $p<.001$). These results suggest a relationship between disordered pursuit tracking and failure of fixation suppression which has been previously reported in both neurological (18,34) and psychiatric patients (59).

Table 5.Correlation between baseline tracking and fixation suppression measures [pooled across groups]

		Fixation suppression	
Condition	Measure	Right	Left
LIGHT	VA	- .161 p<.101	- .275 p<.013
	PRMS	- .072 p<.281	- .252 p<.020
DARK	VA	- .365 p<.002	- .345 p<.003
	PRMS	- .261 p<.019	- .276 p<.015

Pursuit RMS

A significant main effect for group was found ((F 2,56) =8.46, p<.005) for percentage pursuit RMS for both baseline and post- irrigation conditions. Post-hoc analyses indicated that for light-adapting data: 1) actively-ill patients' values were significantly greater (p<.01) than controls in both baseline and post-irrigation conditions, and significantly greater than remitted patients (p<.05) during baseline; and, 2) remitted patients' values were significantly greater than controls (p<.01) on the post-irrigation condition. Following dark-adaptation there were no significant between- group differences for either baseline or post-irrigation conditions. Relative to their light-adapting baseline condition, actively-ill patients improved (p< .05) in the dark. Remitted patients showed improvement (p<.05) in the dark relative to light-adapting condition during post-irrigation tracking. No significant between-group differences were found between the pursuit RMS scores obtained during baseline tracking and those during post-irrigation tracking (Figures 14, 15).

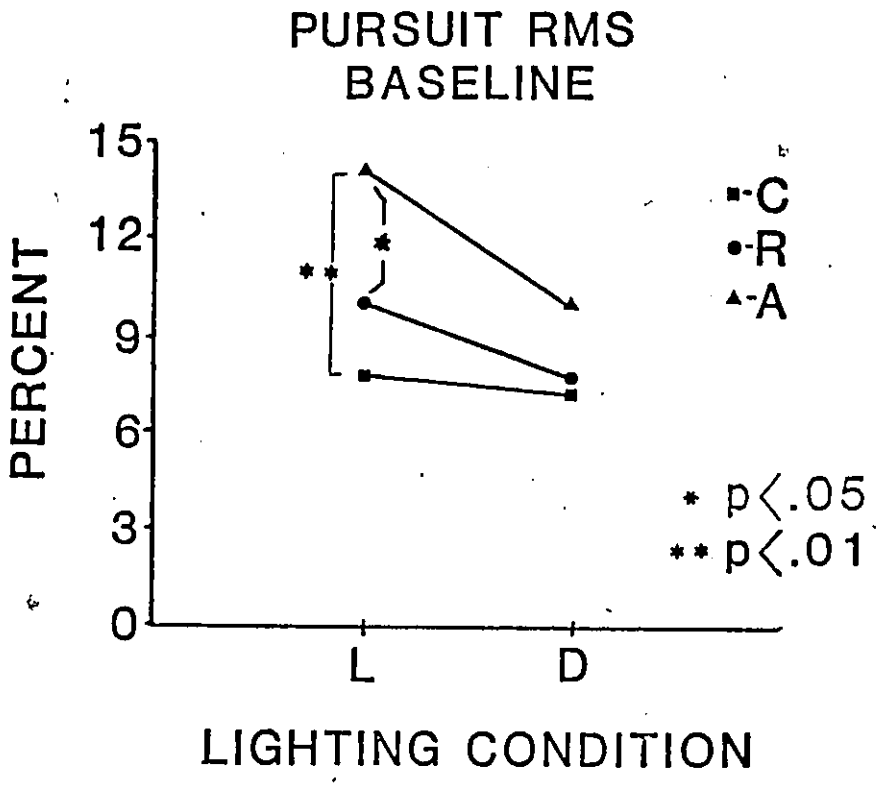


Figure 14. Mean percent root mean square during baseline tracking for each group across lighting conditions. In addition to the indicated significant differences noted in the figure, the PRMS of actively-ill patients decreased significantly during the dark-adapted condition ($p<.02$).

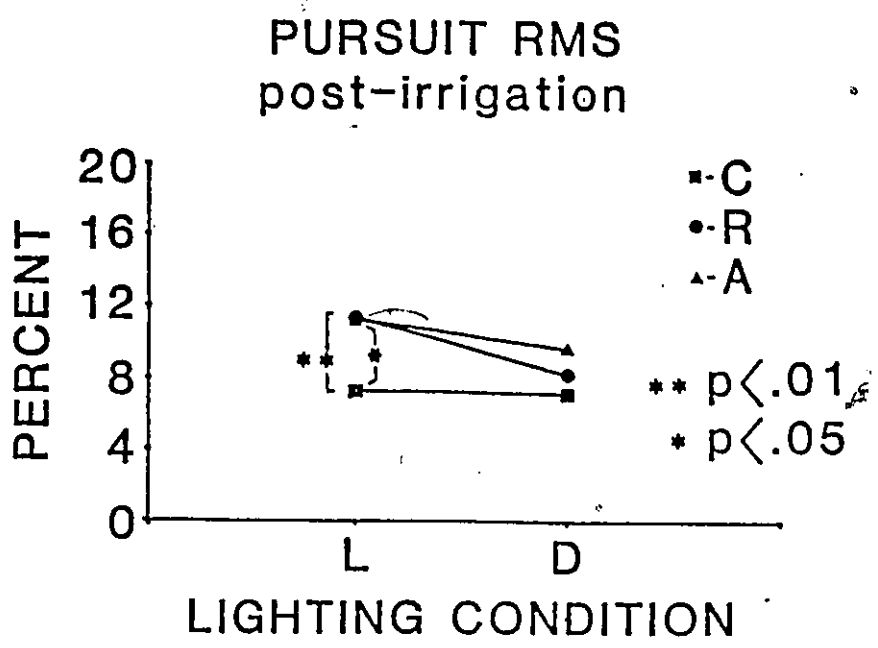


Figure 15. Mean percent root mean square during post irrigation tracking for each group across lighting conditions. In addition to the designated statistical differences, the PRMS value for remitted patients decreased significantly ($p < .01$) during dark-adaptation.

The presence of aberrant eye movements was related to the presence or absence of psychotic symptomatology with approximately twice as many actively-ill patients showing abnormal tracking, fixation suppression and fixation than remitted patients. Similarly, twice as many remitted patients showed aberrant eye movements relative to controls (Table 6).

To determine whether deficits in baseline tracking, fixation and fixation suppression were present in the same subjects, a descriptive breakdown of those subjects who showed deficits on all these measures was obtained. Sixty-five percent of actively-ill patients showed aberrations on both baseline tracking and fixation suppression, whereas only seventeen percent of remitted and four percent of controls showed aberrations on both measures. Only actively-ill patients exhibited aberrations on all three eye movement measures (Table 7).

Button Press: Group and light-dark comparisons

During the light-adapting condition, controls responded more frequently than patients with a button-press response to target light interruptions, but significantly so only relative

Table 6. Percentage of subjects (n in parentheses) in each group who were at least one standard deviation from the mean score obtained by the control group on VAs, PRMS, fixation suppression and fixation during light-adaptation.

Group	VAs	PRMS	Fixation suppression		Fixation
			R	L	
C	8%(2)	26%(6)	17%(4)	13%(3)	8%(2)
R	39%(9)	22%(5)	52%(12)	39%(9)	22%(5)
A	70%(16)	74%(17)	70%(16)	82%(19)	50%(11)

Table 7. Percentage of subjects (n in parenthesis) in each group who, during the light-adapting condition, were at least one standard deviation from the mean on: a) both baseline tracking and fixation suppression measures; and, b) baseline tracking, fixation suppression and fixation RMS measures.

	(a)	(b)
CONTROLS	4% (1)	0% (0)
REMITTED	17% (4)	0% (0)
ACTIVE	65% (15)	43% (10)

to actively-ill patients ($p<.05$; C = 95.00 +/- 8.55%, A = 78.20 +/- 22.98%, R = 88.21 +/- 26.13%; mean number of failures: C= .27 +/- .45, A= 1.09 +/- 1.19, R= .42 +/- 1.01). These group differences vanished following dark-adaption when actively-ill patients' responding improved significantly (11% increase in correct responses, $p<.01$).

During post-irrigation tracking controls were significantly more accurate in responding (98.62 +/- 4.43%) than either remitted (74.35 +/- 37.43, $p<.01$) or actively-ill (82.38 +/- 24.21, $p< .05$) groups. In the dark during post-irrigation tracking, significant between-group differences for this measure were no longer present. Remitted patients' button press accuracy increased significantly in the dark compared to their performance in the light (15% increase in correct responses, $p<.01$).

To evaluate the relationship between button-press response accuracy and the dependent variables found to significantly differentiate the groups ,ie., velocity arrests, fixation suppression and fixation RMS measures, a separate ANOVA was performed comparing only those subjects whose response accuracy was 100% (C,n = 20, R,n = 13, A,n = 11). This analysis revealed that despite perfect detection of target light interruptions,

actively-ill patients continued to exhibit significantly more tracking disruptions than comparision groups during light-adapting conditions. The dark adapting improvement previously noted was also present in these patients. However, the tracking performance of remitted patients with 100% button-press accuracy was not significantly different from that of controls under either light- or dark-adapting conditions.

During post-irrigation tracking this group of actively-ill patients continued to exhibit significantly more VAs than controls in both lighting conditions. Whereas in the pooled group data actively-ill patients had only been significantly different from remitted patients in the dark, the 100%-accuracy subgroup was significantly different from remitted patients in both the light and dark. The tracking performance of remitted patients with 100% detection of target light interruptions was not different from that of controls.

Analyses of the fixation suppression measures for these 100% accuracy subgroups did not reveal any significant change relative to the pooled data analyses. In the light following right ear irrigation, controls showed significantly ($p<.05$) higher fixation suppression (91.79%) than either actively-ill or remitted patients (61.63%, 71.27%, respectively). In the dark, controls continued to be significantly different from

both patient groups (C, 79.44%; R, 55.23%; A, 48.18%) However, in the dark, patient groups were no longer significantly different from one another.

The fixation RMS measure also continued to show significant differences between controls and actively-ill patients ($p < .05$) during light-adaptation when only those subjects with 100% accuracy on button press were compared. Remitted patients, however, were no longer significantly different from either controls or actively-ill patients. The dark-adapting improvement previously noted was also present in this subgroup of subjects.

Gender

Since there was a increased number of males in the patient groups relative to the control group the eye movement data were re-analyzed using gender as an independent variable. No significant main effects were found between males and females for any of the dependent variables.

Neuroleptic medication

To evaluate the effects of neuroleptic medication on the dependent measures, the daily dosage of medication was correlated with these variables. Dosage level across medication was made equivalent to an approximate daily dosage of chlorpromazine (90). None of the correlations attained the .05 level of significance.

Corneoretinal potential

Relative to values during light adaptation, there was a mean CRP decrease for control subjects during dark-adaptation (55.26 uv or 15%). The CRP of remitted and actively-ill patients, however, increased in the dark (35.59uv and 37.93uv, respectively-- representing a 9% mean increase for remitted and 12% mean increase for active psychotics). Corneoretinal potential changes in the dark were not significantly correlated with VA differences ($r = -.18$, ns).

DISCUSSION

The results of this investigation corroborate previous reports of abnormal visual-vestibular interaction and abnormal smooth pursuit in psychotics and indicate further that the disordered tracking can be statistically normalized by dark

adaptation. However, before discussing these findings it is important to identify and evaluate potential sources of confounding which might have influenced the outcome of the present investigation. Obvious areas of concern in this respect include artifact in the electrophysicological recordings, variations in level of attention and arousal, and medication effects.

In general, the present findings cannot be attributed to the selective presence of artifact in the recordings since these data were screened for the presence of both movement and blink related disruptions. Furthermore, the EOG data were electronically processed to minimize EEG influences. Variations in the CRP across lighting conditions -- which could influence the sensitivity with which tracking disruptions were detected--can also be discounted as a significant influence since a consistant lighting-condition related variation in this measure was not found in the patient groups, and the changes that did occur were not correlated with improvements in tracking or fixation.

Variations in arousal and attention were also monitored and no evidence was found indicating the systematic influence of these variables on the observed group effects. Finally,

although the patients participating in this study were on drug therapy, examination of the relationship between medication levels and the results provided no evidence for a medication-dependent variable relationship.

Based on the above condiderations it is reasonable to conclude that the physiological results of the present investigation were not significantly influenced by these methodological, procedural or pharmacologic variables.

Vestibular Reactivity

The results of the present assessment of vestibulo-ocular functioning in psychotic patients is in agreement with previous reports indicating that the vestibular apparatus is intact in these patients (58,67). For all subject groups the maximum slow phase velocity -- the response measure commonly accepted as a gauge of vestibular integrity -- was within normal limits (7,11,39,60). The other indexes of response strength, i.e, duration and latency of nystagmus and the peak nystagmus frequency, were also within normal limits (11) and did not differentiate among groups. Patients did receive a higher percentage of ratings indicating increased dysrhythmia, but unlike previous reports (67,58) their nystagmus was not judged to be significantly more dysrhythmic than that of normal controls.

The speed and amplitude of the nystagmus during both slow and fast phase measures were highly related -- a finding in agreement with previous reports of a strong linear relationship between these two nystagmus measures (19). However, contrary to the findings reported by Jones and Pivik (58), significant between group differences were not found for the fast phase velocity measure. This finding may not be surprising considering that slow phase velocity did not differentiate between groups in either this or Jones and Pivik's study and that fast and slow phase velocities are thought to be intimately related (91). In Jones and Pivik's study (58), slowing of the fast component was associated with dysrhythmic nystagmus. The fact that patients were not significantly more dysrhythmic than controls in the present investigation might be related to this between-study difference. In both investigations, slower fast phase responses were associated with higher dysrhythmic scores.

Although the above discussed vestibular measures did not statistically differentiate between groups, actively-ill patients did exhibit faster mean slow (17% faster) and fast (11% faster) phase velocities than controls during the light-adapting condition. Patients also showed a higher peak frequency of nystagmus beats relative to controls -- a finding

which replicates in direction, but not intensity, an observation reported by Jones and Pivik (58). These findings suggest the presence of some degree of vestibular over reactivity in these patients. Vestibular hyperresponsiveness -- generally quantified in terms of vestibular-ocular gain and total amplitude of caloric nystagmus which is highly correlated with the velocity of the nystagmus (32,112) -- is thought to result from a reduction of normal cerebellar inhibition of caloric activity (11).

During dark adaptation patients and controls continued to show signs of normal vestibular functioning,i.e., slow and fast phase velocities, and nystagmus duration, latency, and peak frequency and dysrhythmia measures were all within normal limits. The trend towards hyperresponsiveness present in actively-ill patients in the light-adapting condition was no longer evident when these patients were dark-adapting, i.e., the slow and fast phase velocities and nystagmus frequency of these patients significantly decreased in the dark-adapting condition. However, velocity measures of control subjects decreased only slightly in the dark and nystagmus frequency actually increased. There is no published information regarding variations in these measures in dark-adapting cerebellar patients, but since dark adaptation reduces the cerebellar effects on eye movements, it is not unreasonable to

suggest that cerebellar dysfunction may be associated with the noted trend towards hyperresponsiveness in patients.

Fixation Suppression

A main focus of the present investigation was the reexamination of the influence of optic fixation on nystagmus suppression among patients with active psychotic symptomatology. The failure of fixation suppression among these patients, initially reported by Jones and Pivik (58), was replicated in this study. Furthermore, there are indications that this abnormal response may characterize remitted patients as well -- but not as consistently. Both patient groups continued to show failure of fixation suppression during dark adaptation when compared to normals. However, fixation suppression for all groups was less efficient in the dark than in the light, suggesting that target background information generally assists in the suppression of caloric nystagmus. The fact that fixation suppression was affected similarly in all groups during dark-adaptation i.e., decreased efficiency in the dark, underscores the observation that the mechanism for fixation suppression is generally impaired in the patient groups.

The finding of significant levels of abnormal fixation suppression in remitted patients only following right ear irrigation , along with the fact that in the dark nystagmus

suppression was more efficient in all groups when the left ear was irrigated, suggests the presence of lateralized influences on this aspect of eye movement control. Vestibulo-cerebellar projections to the brainstem are predominantly ipsilateral (85), and purkinje cells project to the ipsilateral medial vestibular nucleus. Takemori and Cohen (104) report that after unilateral lesions of the flocculus, visual suppression of slow phase velocity was lost when the quick phases were directed to the ipsilateral side and visual suppression of nystagmus following caloric irrigation of both sides vanished after bilateral floccular lesions. It is conceivable, therefore, that the differences found between the fixation suppression measures following right and left ear irrigations in this investigation may have been influenced by hemispheric dominance. Since fast phase eye movements are toward the left following left ear irrigation with cool water, then, based on the findings of Takemori and Cohen (104) the efficiency of suppression should be related to the left cerebellar hemisphere. Since ninety percent of the subjects in this study were right-handed, left cerebellar dominance might account for the higher level of fixation suppression following left ear irrigation.

During the light-adapting condition, however, actively-ill patients had greater difficulty suppressing nystagmus following left ear irrigation. This finding is compatible with reports of

left hemispheric defects in psychotic, mainly schizophrenic, patients. Several studies have advanced the notion that subtle variations in lateralization of brain organization may exist in schizophrenia and other psychoses (97,105). This hypothesis has been examined in studies using pneumoencephalographic, computer tomographic, cerebral blood flow, EEG and sensory asymmetry techniques. Although the results of such studies have often been ambiguous and contradictory, the evidence generally supports a left hemisphere dysfunction in schizophrenics (97,105). Accordingly, the higher fixation suppression following left ear irrigation exhibited by actively ill patients' during dark-adaptation may reflect a reduced influence of the cerebellum, i.e., an attenuation of the postulated cerebellar laterality dysfunction.

When level of visual attention was maximized by comparing only subjects with 100% accuracy on the button press response, actively-ill, but not remitted, patients continued to show significantly reduced fixation suppression relative to controls. These data suggest that although level of attention may have been a contributing factor for the remitted group, this variable cannot account for the aberrant fixation suppression of the actively-ill group.

With regards to slow phase velocity during eyes open, the

controls in this study behaved in the same manner as did the normal subjects in Hood and Waniewski's study (49), i.e., relative to tracking during darkness, in the light slow phase velocity was suppressed by a factor of 1.60. The actively-ill patients' results were comparable to those of the cerebellar patients, ie., the slow phase velocity was virtually unaffected by background illumination. The remitted patients' performance was intermediate between that of controls and actively-ill patients. The similarities between the performance of cerebellar and psychotic patients provides further evidence suggestive of vestibulo-cerebellar dysfunction in these patient groups.

Fixation

The difficulty experienced by light-adapting actively ill-patients in fixating a stationary target in this investigation has been previously observed (74,75,77). However, the present study relates this finding to the occurrence of aberrant pursuit tracking and failure of fixation suppression in these subjects. The high positive correlation between the fixation RMS and pursuit tracking measures is of interest since in the pooled data fixation RMS did not correlate with fixation suppression in either light- or dark-adapting conditions. This apparent inconsistency probably reflects the fact that a relationship between aberrant

tracking, fixation suppression and fixation of a stationary target during the baseline condition existed only in the actively-ill group. Forty-three percent of actively-ill patients showed evidence of dysfunction on all three measures while none of the controls or remitted patients had aberrations in all three areas.

The lack of significant between-group differences on the fixation RMS measure during dark adaptation parallels the smooth pursuit tracking results. Controls and remitted patients had greater difficulty fixating a stationary target in the dark than in the light, suggesting that background illumination normally enhances this ability. Since background illumination appears to be important in fixation, one would expect that the performance of actively-ill psychotics would deteriorate further in the dark-adapting condition. The findings to the contrary are consonant with the idea that the attenuation of the cerebellar influence must contribute significantly to this improvement in actively-ill patients. As with fixation suppression, maximizing attention (by comparing only subjects with 100% accuracy on button-press response) does not change the direction of the results, indicating that it is unlikely that level of attention could account for these findings.

Tracking

The findings of disordered smooth pursuit tracking in actively-ill patients along with the significant correlation between smooth pursuit performance and degree of fixation suppression in these patients replicates the Jones and Pivik findings (59) and strengthens the evidence indicating an association between dysfunction in these systems. Subjects who showed significantly reduced fixation suppression had a correspondingly higher frequency of VAs and a higher percentage pursuit RMS. Seventy percent of those subjects showing aberrant pursuit tracking also demonstrated failure of fixation suppression.

With regard to the differential sensitivity of VAs and PRMS measures, it would appear that VAs are more sensitive to group differences than PRMS. Velocity arrests differentiated between active, remitted and control groups during light adaptation, whereas PRMS only differentiated between actively-ill and control subjects and did not show a significant differences between these two groups and remitted patients. The PRMS measure gives a global measure of the accuracy of smooth pursuit tracking whereas a VA is a more discrete measure of tracking aberration. The nature of the PRMS measures allows positive and negative eye position deviations from the target to cancel each other out. In so doing the PRMS measure may be masking the presence of certain eye movements

which are apparently being picked up by VAs. Thus, there is a need to assess the nature of eye movement behaviour during VAs to more precisely determine the oculomotor correlates of psychosis.

As hypothesized, tracking patterns of patients during dark adaption were no longer significantly different from those of controls. This normalization of aberrant pursuit tracking of psychotic patients is unprecedented and the role of dark-adaptation in this finding should provide insights into the basis for this dysfunction. Hood and Korres (48) observed that neurological patients with central vestibular lesions suppressed the vestibulo-ocular reflex better when fixating a target against a textured (light),relative to uniform (dark) background. They also found that the pursuit tracking in these patients improved in the dark. These authors felt that since execution of these oculomotor behaviors were not comparable in the dark, disordered tracking could not be attributed to the lack of vestibulo-ocular suppression. It is of interest to note in this regard that in the present investigation even though fixation suppression worsened and tracking improved in the dark, the significant negative correlation existing between these variables in the light continued to be present in the dark. This finding does not support the suggestion of Hood and Korres (48) that tracking performance and fixation suppression

are not integrally related. Rather, the continued significant correlation between the two measures in the dark rekindles the idea that they are somehow related.

Caloric nystagmus has been reported to have little influence on eye tracking in control subjects free of vestibulo-cerebellar lesions (92). This observation is corroborated by data from the present study showing that for all groups during the light-adapting condition there was no significant difference between the VA or PRMS scores during baseline and post-irrigation tracking. Not confirmed by these findings is the report of increased tracking deficits following vestibular activation in psychotic patients (59). It is possible that the high levels of aberrant pursuit tracking of actively-ill patients masked any effect caused by vestibular activation. Credence is given to this interpretation by the fact that during dark-adaptation when patients' baseline tracking performance was essentially normal, caloric nystagmus evoked abnormalities in the post-irrigation tracking of actively-ill patients.

The initiation of tracking 90 seconds after the start of irrigation rather than 50 seconds as in Sakata and Umeda's study (92) may also account in part for the lack of a significant difference found between baseline and

post-irrigation tracking in this investigation during light adaptation. The intensity of vestibular activation may have already been reduced sufficiently so as not to interfere with tracking in the patient groups. Since the accuracy of pursuit tracking can be considered as a measure of the ability to suppress 'nystagmus' via fixation, and since lower fixation suppression is significantly correlated with increased tracking deficits occurring following vestibular activation, then the fact that fixation suppresssion was less efficient in the dark may account in part for the fact that abnormalities in post-irrigation tracking were present only at this time. A critical level of fixation suppression may be required before tracking aberrations become apparent. This possibility is supported by the observation that during the light-adapting condition, when caloric nystagmus did not further impede the tracking performance of actively-ill patients, their percentage of fixation suppression was in fact 10 points higher than that reported for actively-ill patients in Jones and Pivik's study (59), whereas during the dark-adaptation condition, when their level of fixation had dropped to that reported by Jones and Pivik, their tracking was adversely affected by caloric nystagmus. Thus when the degree of fixation suppression is considered there is agreement between these results and those of Jones and Pivik (59). This response, unmasked in this investigation by the dark-adapting condition, is to some extent

similar to that of patients with central vestibular disorders whose eye tracking patterns, relative to those of normal controls, are affected by caloric nystagmus (92).

THE CASE FOR CEREBELLAR DYSFUNCTION IN PSYCHOSIS

The performance of the patient groups, particularly the actively-ill patients, during light-adaptation is comparable to that of cerebellar patients tested under similar conditions. In the psychotic patients there was abundant evidence of a trend towards vestibular hyperresponsiveness, i.e., fast nystagmus, slow and fast phase velocities, increased nystagmus frequency, failure of fixation suppression, aberrant pursuit tracking and impaired fixation of a stationary target during light-adaptation. In addition, these disorders in eye movement control normalized during the dark adaptation condition. All of these findings are comparable with the eye movement behaviour of cerebellar patients under similar testing conditions. The results indicate that psychotic patients have an intact vestibular system with evidence of vestibular hyperresponsiveness. Vestibular hyperresponsivess has been related to cerebellar lesions (32,112). Barber and Stockwell (11), who use slow phase velocity as the measure for hyper-responsiveness, attribute it to a reduction of normal CNS--mainly cerebellar--inhibition of caloric induced activity.

The lack of significant groups differences for the fast phase velocity measures is consonant with the cerebellar hypothesis since Dichgans and Jung (32) have noted that fast phase velocity appears normal in patients with cerebellar atrophy.

The psychotic patients' failure of fixation suppression during light adaptation is consistant with a central dysfunction (29,48,90) implicating cerebellar --primarily floccular (32,111)--and brainstem structures (61,78). The continued failure of fixation suppression in the dark is also consistent with the performance of patients with central pathologies who show failure of fixation suppression when required to fixate on a light target in the dark (without background) (48). During fixation suppression the effects of background on nystagmus slow phase velocity in the actively-ill patients were comparable to those reported for cerebellar patients, ie., the slow phase velocity during fixation was virtually unaffected.

With respect to the cerebellar implications of these data, it should be noted that 2 active and 1 remitted subjects did not exhibit any nystagmus when their eyes were closed following irrigation, but suddenly had very prominent nystagmus when they opened their eyes and fixated. The data from these subjects could not be analyzed on all measures because of these results.

Similar observations have been reported to occur uniquely in some cerebellar patients (48) and its presence in some psychotic patients provides further evidence suggestive of cerebellar involvement in the noted eye movement dysfunctions in psychosis.

The inferior ability of the psychotic patients to fixate a stationary target is also linked to cerebellar functioning since instability of visual fixation is commonly associated with defective cerebellar mechanisms (50). Hotson (50) states that the cerebellum modulates both the saccadic and slow eye movement generators, and functions during precise fixation in normal subjects to reduce and miminize fluctuations in these systems.

The normalization of pursuit tracking during dark adaptation mimicks the performance of Hood and Waniewski's cerebellar patients (49). Since tracking normalized when the cerebellar influence was attenuated during dark-adaptation and since a similar normalization has been reported to occur in cerebellar patients, cerebellar mechanisms would appear to be implicated in the aberrant tracking of psychotic patients, i.e., the noted deviant tracking during light-adaptation may reflect the failure of cerebellar mechanisms to inhibit saccadic eye movements at this time.

Potential support for these findings comes from the study by Mather (73) in which she reported that schizophrenics had ocular phase lag--eyes lagged behind the target during pursuit tracking--with normal illumination but not in the dark. Furthermore, in the present investigation the increased aberrations during tracking in the dark following caloric irrigation are similar to those of patients with central vestibular disorders, including cerebellar patients, whose eye tracking patterns, unlike those of normals, are affected by caloric nystagmus (92).

The high correlation between fixation and smooth pursuit eye movement measures and the similar effects of dark-adaptation on these measures in the patient group suggest that whatever mechanism is common to these functions may be impaired in psychosis-- and the preceding discussion offers multiple arguments implicating cerebellar dysfunction in these behaviours.

Despite the prominence of arguments and data supportive of cerebellar involvement in oculomotor dysfunctions in psychosis, other factors must be considered for their potential role in eye movement performance during dark-adaptation. Most obvious among these is the enhancement during dark-adaptation of target salience resulting from the reduction of potentially

distracting background stimuli. However, the fact that fixation suppression deteriorated further in dark-adapting actively-ill patients argues against this notion. Based on the significant negative correlation of fixation suppression with pursuit tracking measures, an increase in fixation suppression measures would have been expected if target salience alone were responsible for the improvement in pursuit tracking.

Dark adaptation and the use of a punctate light source as a tracking target also effectively reduce activation of peripheral retinal processes which, through feedback mechanisms, normally improve target fixation during during both smooth pursuit and during supression of vestibular nystagmus by visual fixation (35,49). Based on these considerations, a deterioration in tracking and fixation (as in the normal control group) would have been expected if the results were determined predominantly by peripheral retinal mechanisms. Increasing attention by removal of distracting stimuli might also be suggested as an influential factor, but the assessment of measures controlling attention, as previously mentioned, do not support this hypothesis.

Another argument advanced against cerebellar involvement in aberrant eye movements in psychosis is the absence of evidence of impairment in other oculomotor parameters under

subcortical control, e.g., reaction time and velocity of saccades are not impaired (74). However, these variables have not been found to be disturbed in cerebellar patients. Dichgans and Jung (32) report that cerebellar lesions might result in saccadic dysmetria and Baloh et al. (10) found that although the peak velocity and latency measures for cerebellar patients was normal, some of these patients exhibited dysmetria of horizontal saccades. Similarly Selhorst et al. (94) reported that saccadic overshoot dysmetria occurred in patients with cerebellar disorders. Lesion experiments indicate that the cerebellum is not responsible for initiation and execution of saccades, but contributes to the precision with which a saccade localizes a visual target within a high acuity retinal region (56). It is perhaps noteworthy that saccadic dysmetria in cerebellar patients disappears in the dark (94). Schizophrenics have been reported to overshoot visula targets more often and by greater amounts than normals. (73,74). These findings in fact support, rather than contradict, the hypothesis that dysfunctions at the level of the cerebellum may be involved in the aberrant eye movements found in psychotic patients.

Cortical or Subcortical Basis for Oculomotor Disorder in Psychosis?

Several investigators (71,42,64) have proposed that the

pursuit abnormalities seen in psychotic patients represents cortical and not subcortical dysfunction. This conclusion is based on observations that eye movement behavior generated by vestibular and brainstem mechanisms are normal in psychotics. These authors, arguing from a standpoint of clinical symptomatology and distractability in these patients, suggest that the eye tracking disorder is related to dysfunction in frontal cortex. In the present investigation, the poorer detection by actively-ill patients of target light interruptions during light adaptiation and the corresponding significant increase in this measure during dark adaptation suggests that their level of attention varied as a function of lighting condition. However, since the light-related significant differences on the dependent variables and their normalization during dark-adaptation persisted even in those subjects showing 100% accuracy on button press response, attention alone cannot account for the present results . In addition, the findings that fixation suppression did not improve and that fixation of a stationary target, although normalized, actually decreased in efficiency during dark-adaptation do not support an attentional hypothesis. Both measures were significantly correlated with tracking performance and would have been expected to improve if attention alone were responsible for the aberrations.

Of importance in this regard, as well, is the fact that the arguments in support of an exclusive cortical localization for oculomotor dysfunction have not incorporated the presence of aberrant fixation suppression in these patients (58,59)--a finding which is replicated in this study along with observations of impairments of both smooth pursuit tracking and fixation. The finding that 90% of the actively-ill patients who had aberrant tracking also had low fixation suppression scores provides evidence for the idea that these aberrations result from a common or associated influence. Additional support for this notion of an interrelatedness and subcortical involvement in oculomotor dysfunction comes from the fact that even though only 50% of actively-ill patients had aberrant fixation RMS, 90% of this subgroup also had high tracking errors and low fixation suppression values while none of the control or remitted patients was aberrant on all three of these eye movement control measures. Collectively, these findings argue forcibly for subcortical involvement in eye tracking dysfunction and draw attention to possible vestibulo-cerebellar involvement in this disorder.

State-Trait Implications

Impaired pursuit tracking has been proposed as a trait factor which may even serve as a genetic marker for schizophrenia (42,47,51). The bases for this belief have

included the high occurrence of aberrant tracking in schizophrnic patients (50-80%; 47,48), the high concordance rate between monozygotic twins for quality of tracking even when clinically discordant for schizophrenia (42), and reports of poor tracking in remitted schizophrenics (55). The stability of eye tracking performance taken together with the above findings makes it tempting to accept this measure as a potential genetic marker for vunerability to schizophrenia. Strictly considered, a trait phenomenon should continue to be expressed in the absence of active clinical symptomatology. However, reports indicating that the level of tracking impairment in remitted schizophrenics is generally lower than that of actively-ill schizophrenics and often does not differ from that of normal controls (59,83,84) are inconsistent with the trait characterization of tracking impairment. These latter observations ,in fact, suggest that tracking performance may vary as a function of the clinical state of the patient.

The results of the present investigation indicate that the tracking performance of both actively-ill and remitted patients were significantly worse than controls on fixation suppression and VAs during the light adapting condition-- findings consistent with a trait interpretation. However, active, but not remitted, patients were significantly different from controls on the PRMS measure. Furthermore, actively-ill

patients were significantly worse than remitted patients on fixation suppression, VAs and fixation of a stationary target and more than twice as many actively-ill patients had abnormal (one standard deviation from the mean score obtained by control subjects) VAs, PRMS scores, fixation suppression and fixation RMS scores relative to remitted patients whose scores fell between those of normal controls and actively-ill patients. These results indicate a deterioration of eye movement responses of actively-ill patients compared to remitted patients. The presence of increasing evidence of oculomotor abnormalities associated with worsening of clinical symptomatology and the fact that only actively-ill patients had abnormal responses on all the discriminating dependent variables , argues for a state--rather than trait--basis for these oculomotor phenomena. State-trait differentiations however, are difficult to support since they may reflect fluctuations along a continuum which may at times be operationally indistinquishable. It is likely that the state-trait controversy will remain a point of contention in this area for some time.

Conclusions

The following statements summarize the results of this investigation as they relate to the hypotheses.

--- As hypothesized, during continuous lighting patients with active psychotic symptomatology showed greater impairment of smooth pursuit tracking and fixation than either normal controls or patients with remitted psychotic symptomatology. These findings replicate previous findings of such aberrations in psychotic patients (58,74) and their presence in conjunction with failure of fixation suppression indicates a central regulatory dysfunction.

--- The hypothesis that the baseline smooth pursuit tracking and fixation values of actively-ill psychotic patients would normalized under dark-adapting conditions was supported. This normalization of pursuit tracking in psychotic patients--which is unprecedented in the literature-- cannot be accounted for by methodological, procedural, or pharmacological variables. These findings, in conjunction with the presence of reduced fixation suppression in the same subjects , supports the argument for cerebellar involvement in the eye movement aberrations of psychotic patients.

--- Visual-vestibular abnormalities previously reported by Jones and Pivik (59) were partially replicated in this investigation. As predicted, during light-adaptation psychotic patients showed failure of fixation suppression. However, the anticipated greater impairment of smooth pursuit tracking

subsequent to vestibular activation was not observed. The latter effect may have been related to the overall higher level of fixation suppression of the subjects in this study.

--- Neither fixation suppression nor the smooth pursuit tracking scores of actively-ill psychotic patients subsequent to vestibular activation normalized during the dark-adapting condition. These findings, though not in the predicted direction, further support the hypothesis of abnormal visual-vestibular activation in psychotic patients. The findings that the slow phase velocity of the actively-ill patients during fixation suppression did not change with background illumination, and that fixation suppression became less efficient in the dark, support the hypothesis that cerebellar mechanisms are involved in these aberrant eye movements.

In conclusion, striking parallels between results from studies of neurological patients with cerebellar disease and the results of the present strongly suggest that cerebellar dysfunction may contribute significantly to disordered pursuit in psychiatric patients. These parallels include : a) an intact vestibular system, the presence of vestibular hyperresponsivity, impaired fixation of a stationary target, failure of fixation suppression and the presence of impaired

smooth pursuit tracking; b) the normalization of impaired smooth pursuit following removal of target background by dark adaptation (49); c) during post-irrigation fixation the failure of background illumination to further decrease the velocity of the slow phase of nystagmus relative to that during fixation when no background illumination is present (49); d) the normalization of fixation RMS in both psychiatric and cerebellar patients (32); d) the normalization during dark adaptation of the trend towards hyperresponsive vestibular responses generally reported in cerebellar patients; and, e) post-mortem and computed tomography findings of cerebellar damage in schizophrenics (30,108). Deficiencies in cerebellar control of saccadic eye movements have been suggested as a source of impaired tracking in schizophrenics (65,59), and the present results strongly reinforce this notion.

REFERENCES

1. Alpert, J.N. Failure of fixation suppression: A pathologic effect of vision on caloric nystagmus. Neurology, 24: 891-895, 1974.

2. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, ed 3. Washington, DC, 1980.

3. Anderson, P.J., Diamond, S.P., Bergman, P.S., Nathanson,M. Electrooculographic investigation of the caloric response. Neurology, 8: 741-799, 1958.

4. Angyal, A., Blackman, N. Vestibular reactivity in schizophrenia. Archives of Neurology and Psychiatry, 44: 611-620, 1940.

5. Angyal, A., Sherman, M. Postural reactions to vestibular stimulation in schizophrenic and normal subjects. American Journal of Psychiatry, 98: 857-862 1942.

6. Ayres, A.J., Heskett, W.M. Sensory integrative dysfunction in a young schizophrenic girl. Journal of Autism Childhood Schizophrenia, 2: 174-181, 1972.

7. Baloh, R.W., Honrubia, V. Clinical neurophysiology of the vestibular system. F.A. Davis Co., Philadelphia, 1979

8. Baloh, R.W., Jenkins, H.A., Honrubia, V., Yee, R.D., Lau, C.G.Y. Visual-vestibular interaction and cerebellar atrophy. Neurology, 29:116-119, 1979.

9. Baloh, R.W., Kumley, W.E., Sills, A.W., Honrubia, V., Konrad,

H.R. Quantitative measurement of smooth pursuit eye movements. Annals of Otology, Rhinology and Laryngology, 85: 111-119, 1976.

10. Baloh, R.W. Yee, R.D., Kimm, J., Honrubia, V. Vestibular-ocular reflex in patients with lesions involving the vestibulocerebellum. Experimental Neurology, 72:141-152, 1981.

11. Barber, H.O., Stockwell, C.W. Manual of Electronystagmography. C.V. Mosby Co., St. Louis, 1980.

12. Barber, H.O., Wright, G. Release of nystagmus suppression in clinical electronystagmography. Laryngoscope (St. Louis), 77: 1016-1027, 1967.

13. Barnes, G.R. The role of the vestibulo-ocular reflex in visual target acquisition. Journal of Physiology, 258:64-65, 1976.

14. Barnes G.R., Physiology of visuo-vestibular interactions: discussion paper. Journal of the Royal Society of Medicine. Vol. 76, Sept 83.

15. Barnes G.R., Edge A., Non linear effects in visual suppression of vestibular nystagmus. Experimental Brain Research, 52: 9-19, 1983.

16. Benson, A.J., Barnes, G.R. Vision during angular oscillation: the dynamic interaction of visual and vestibular mechanisms. Aviation, Space, and Environmental Medicine, pp. 340-345, January 1978.

17. Brezinova, V., Kendell, R.E. Smooth pursuit eye movements of

schizophrenics and normal people under stress. British Journal of Psychiatry, 130:59-63, 1977.

18. Chambers, B.W., Gresty, M.A. The relationship between disordered pursuit and vestibular ocular reflex suppression. Journal of Neurology, Neurosurgery and Psychiatry, 46: 61-66, 1983.

19. Chun, K.S., Robinson, D. A. A model of quick phase generation in the vestibulo-ocular reflex. Biological Cybernetics, 28: 209-221,1978.

20. Claude, H., Baruk, H., Aubry, M. Contribution a l'etude de la demence precoce catatonique: Inexcitabilite labyrinthique au cours de la catatonie. Revue Neurologique, 1: 976-980, 1927.

21. Claude, H., Bourguignon, G., Baruk, H. Essai sur les variations spontanees et experimentales de la chronaxie vestibulaire au cous du sommeil cataleptique, et de la catalepsie dans l'hysterie, dans la catatonie, et dans l'hebephrenic. Annales of Medico-Psychologiques, 90: 611-651, 1932.

22. Coats, A.C. Central electronystagmographic abnormalities. Archives of Otolaryngology, 92: 43-53, 1970.

23. Collins, W.E. Manipulation of arousal and its effects upon human vestibular nystagmus induced by caloric irrigation and angular accelerations. Aerospace Medicine, 34: 124-129, 1963.

24. Collins, W.E.. Arousal and vestibular habituation. In:Handbook of Sensory Physiology, ed. H.H. Kornhuber, Springer Publishing Co. Inc., New York, 6:361-368, 1974.

25. Collins, W.E., Crampton, G.H., Posner, J.B. Effects of mental activity upon vestibular nystagmus and the electroencephalogram. Nature (Lond.) 190:194-195, 1961.

26. Collins, W.E., Guedry, F.E. Arousal effects and nystagmus during prolonged constant angular acceleration. Acta Otolaryngologica, (Stockh.) 54: 349-362, 1962.

27. Couch, F.H., Fox, J.C. Photographic study of ocular movements in mental disease. Archives of Neurological Psychiatry, 34:556-578, 1934.

28. Demanez. J.P. Anatomie et physiologie du reflexe vestibulo-oculaire. Acta Otol-Rhino-Laryngologica Belgium, 31:317-535,1977.

29. Demanez, J.P., Ledoux, A. Automatic fixation mechanisms and vestibular stimulation. Advances in Otorhinolaryngology, 17: 90-98.

30. Dewan, M.J., Pandurangi A.K., Lee S.H., Ramachandran T., Levy B.F., Boucher M., Yozawitz A. and Major L. Cerebellar morphology in chronic schizophrenic patients: A controlled computed tomography study. Psychiatric Research, 10: 97-103, 1983.

31. Dichgans, J., Buettner, V.W. The vestibular-ocular reflex. Neuro-Opthamology, Vol 1, 178-195, 1980.

32. Dichgans, J., Jung, R. Oculomotor abnormalities due to

cerebellar lesions, In: Basic Mechanisms of Ocular Motility and their Clinical Implications, Eds. G. Lennerstrand and P. Bach-y-Rita, Pergamon, Oxford, 281-298, 1975.

33. Fitzgerald, G., Hallpike, C.S. Studies in human vestibular function: I. Observations on the directional preponderance (Nystagmusbereitschaft") of caloric nystagmus resulting from cerebral lesions. Brain, 65: 115-137, 1942.

34. Fitzgerald, G., Stengel, E. Vestibular reactivity to caloric stimulation in schizophrenics, Journal of Mental Science, 91: 93-100, 1979.

35. Guedry, F.E., Davenport, K.S., Brewton, C.B. and Turnispeed, G.T. The pendular eye tracking test under two background viewing conditions. NAMRL 1257 Naval Aerospace Medical Research Laboratory, Pensacola, FL. 1979.

36. Halmagyi, G.H., Gresty, M.A. Clinical signs of visual-vestibular interactions. Journal Neurology, Neurosurgery and Psychiatry, 42:934-939, 1979.

37. Heath, R.G., Franklin, D.E., Walker, C.F., Keating, J.W., Jr. Cerebellar vermal atrophy in psychiatric patients. Biological Psychiatry, 17:569-583.

38. Hemsley, D.R., Zawada, S.L. 'Filtering' and the cognitive deficit in schizophrenia. British Journal Psychiatry, 128:456-461, 1976.

39. Henriksson, N.G., Speed of slow component and duration in caloric nystagmus, Acta Orolaryngol. Supp. 125, 1956.

40. Hickson, F.S. Illuminance and recording of eye movement by electro-oculography. British Journal of Audiology, 17: 11-16, 1983.

41. Highstein, A.M., Reisine, H. Synaptic and functional organization of vestibuloocular reflex pathways. In: Control of Posture and Movement, Progress in Brain Research, Eds. R. Granit and O. Pompeiano, Vol. 50, Elsevier/North Holland Biomedical Press, New York, 431-442, 1979.

42. Holzman, P.S. Eye movement dysfunctions and psychosis. International Review of Neurobiology 27: 179-209, 1986.

43. Holzman, P.S., Levy, D.L., Proctor, L.R., The several qualities of attention in schizophrenia. In: The Nature of Schizophrenia, New Approaches to Research and Treatment. Eds. L.C. Wynne, R.L. Cromwell, S. Matthysse, J. Wiley and Sons Inc., New York; 295-306, 1978.

44. Holzman, P.S., Levy, D.L. Uhlenhuth, E.H. Smooth-pursuit eye movements and diazepam, CPZ , and secobarbital. Psychopharmacologia, 44: 111-115,1975.

45. Holzman, P.S., Proctor, L.R., Hughes, D.W. Eye tracking patterns in schizophrenia. Science, 181: 171-181, 1973.

46. Holzman, P.S., Proctor, L.R., Levy, D.L., Yasillo, N.J.,

Meltzer, H.Y., Hurt, S.W. Eye tracking dysfunctions in schizophrenic patients and their relatives. Archives of General Psychiatry, 31: 143-151, 1974.

47. Holzman P.S., Solomon C.M., Levin S., Waternaux C.S., Pursuit eye movement dysfunctions in schizophrenia., Archives of General Psychiatry, 41: 136-139, 1984.

48. Hood, J.D., Korres, S. Vestibular suppression in peripheral and central vestibular disorders. Brain, 102: 785-804, 1979.

49. Hood, J.D., Waniewski, E., Influence of peripheral vision upon vestibulo-ocular reflex suppression. Journal of Neurological Science, 63:27-44, 1984.

50. Hotson, JR. Cerebellar control of fixation eye movements. Neurology, 32:31-36, 1982.

51. Iacono, W. Psychophysiologic markers of psychopathology: A review. Canadian Psychology, 26:(2) 96-111, 1985.

52. Iacono, W., Lykken, D.T. Electro-oculographic recording and scoring of smooth pursuit and saccadic eye tracking: A parametric study using monozygotic twins. Psychophysiology, 16: 94-107, 1979.

53. Iacono, W., Lykken, D.T. Eye tracking and psychopathology. Archives of General Psychiatry, 1361-1369, 1979.

54. Iacono, W., Lykken, D.T. Two-year retest stability of eye tracking performance and a comparison of electro-

oculographic and infrared recording techniques: Evidence of EEG in the electro-oculogram. Psychophysiology, 18:49-55, 1981.

55. Iacono, W., Tuason, V.B., Johnson,R.A. Dissociation of smooth pursuit and saccadic eye tracking in remitted schizophrenics. Archives of General Psychiatry, 38:991-996, 1981.

56. Ito, M., Cerebellar control of the vestibulo-ocular reflex -around the flocculus hypothesis. Annual Revue of Neuroscience, 5: 275-296, 1982.

57. Ito, M., Nisimaru, N., Yamamoto, M. Specific neural connections for the cerebellar control of vestibulo-ocular reflexes. Brain Research, 60:238-243, 1973.

58. Jones, A.M., Pivik, R.T. Abnormal visual-vestibular interactions in psychosis. Biological Psychiatry, 18:45-61,1983.

59. Jones, A.M., Pivik, R.T. Vestibular activation, smooth pursuit tracking and psychosis. Psychiatry Research, 14:291-308, 1985.

60. Jongkees, L.B.W, and Philipszoon, A.J. Electronystagmography. Acta Otolaryngologica, Supplement. 189, 1964.

61. Kato, I., Sato, Y., Aoyagi, M., Mizukoshi, K., Kawasaki, T. Visual suppression of caloric nystagmus in normal individuals. Acta Otolaryngologica, 83: 245-251, 1977.

62. Kato, I., Sato, Y., Aoyagi, M., Mizukoshi, K., Kimura, Y.,

Koike, Y., Hayano, N. Caloric pattern test with special reference to failure of fixation-suppression. Acta Otolaryngologica, 38: 97-104, 1979.

63. King L.J. A sensory-integrative approach to schizophrenia. American Journal of Occupational Therapy, 28: 529-536, 1974.

64. Lathan C., Holzman P.S., Monschreck M.C., Tole J., Optokinetic nystagmus and pursuit eye movements in schizophrenia. Archives of General Psychiatry, 38: 997-1003, 1981.

65. Levin, S., Frontal lobe dysfunction in schizophrenia, 1. Eye movement impairments. Journal of Psychiatric Research, 18: 27-55, 1984.

66. Levin, S., Holzman, P.S., Rothenberg, S. J., Lipton, R.B. Saccadic eye movements in psychotic patients. Psychiatric Reseach, 5:47-58, 1981.

67. Levy, D.L., Holzman, P.S., Proctor, L.R. Vestibular responses in schizophrenia. Archives of General Psychiatry, 35: 972-981, 1978.

68. Lidvall, H.F. Vertigo and nystagmus response to caloric stimuli repeated at short and long intervals. Acta. Otolaryngologica, 53: 507-518, 1961.

69. Lipton, R.R., Frost, L.R., Holzman, P.S. Smooth pursuit eye movements, schizophrenia, and distraction. Perceptual and Motor Skills, 50:159-167, 1980.

70. Lipton, R.B., Levin, S., Holzman, P.S. Horizontal and vertical pursuit eye movements, the oculocephalic reflex, and the functional psychoses. Psychiatric Research, 3: 193-203, 1980.

71. Mahoney, J., Harlan, W., Bickford, R. Visual and other factors influencing caloric nystagmus in normal subjects. Arch. Otolaryngologica. 65:46-53, 1957.

72. Mantosh J.D, Pandurangi, A.K., Lee, S.H., Ramachandran T., Levy, B.F., Bougher, M., Yozawitz A., Major L. Cerebellar morphology in chronic schizophrenic patients, A controlled computer tomography study. Psychiatry Research, 10: 97-103 1983.

73. Mather J. Saccadic eye movements to seen and unseen targets: Oculomotor errors in normal subjects resembling those of schizophrenics. Journal of Psychiatric Research, 20: (1) 1-8, 1986

74. Mather J., Putchat C. Motor control of schizophrenics-I. Oculomotor control of schizophrenics : a deficit in sensory processing, not strictly in motor control. Journal of Psychiatric Research, 17:343-360 1983.

75. Matsue Y., Okuma T, Saito H., Aneha S., Veno T., Chiba H., Matsuoka H. Saccadic eye movements in tracking, fixation, and rest in schizophrenic and normal subjects. Society of Biological Psychiatry, 21:382-389, 1986.

76. McCabe, B.F. The quick component of nystagmus. Laryngoscope,

75:1619-1646, 1965.

77. Mialet J.P., Pichot P., Eye-tracking patterns in schizophrenia. Archives of General Psychiatry, 38: 183-186, Feb. 1981.

78. Miles, F.A., Lisberger, S.G. Plasticity in the vestibulo-ocular reflex: A new hypothesis. Annual Revue of Neuroscience, 4:273-299, 1981.

79. Myers, S., Caldwell, D., Purcell, G. Vestibular dysfunction in schizophrenia. Biological Psychiatry, 71:255-261,1973.

80. Ornitz, E. Vestibular dysfunction in schizophrenia and childhood autism. Comparative Psychiatry, 11:159-173, 1970.

81. Orzack, M.H., Kormetsky, D. Attention dysfunction in chronic schizophrenia. Archives of General Psychiatry, 14:323-326, 1966.

82. Overall, J.E., Gorham, D.R. The Brief Psychiatric Rating Scale. Psychological Report, 10:799-812, 1962.

83. Pivik, R.T. Smooth pursuit eye movements and attention in psychiatric patients. Biological Psychiatry, 14:859-879, 1979.

84. Pivik, R.T. Target velocity and smooth pursuit eye movements in psychiatric patients. Psychiatric Research, 1:313-323, 1979.

85. Precht, W. Cerebellar influence on eye movements In: Basic Mechanisms of Ocular Motility and their Clini-

cal Implications, Eds. G. Lennerstrand and P. Bach-y-Rita Pergamon, Oxford, 261-280, 1975.

86. Pyykko, I., Wennmo, C., Henrickson, N.-G., Schalen L. Velocity of rapid eye movements and vertigo of central origin. Annals of Otology, Rhinology and Laryngology, 90: (2) 164-168, 1981.

87. Rapaport, D., Gill, M., Schafer, R. Diagnostic Psychological Testing. New York: International Universities Press, 1968.

88. Ritvo, E., Ornitz, E., Eviatar, A. Decreased postrotatory nystagmus in early infantile autism. Neurology, 19:653-658, 1969.

89. Robinson D.A., Control of Eye Movements, In: Handbook of Physiology--The Nervous System, Eds. S.R. Geiger, V.B. Brooks, J.M Brookhart, V.B. Mountcastle, American Physiological Society, Bethesda, Maryland, 1275-1320, 1981.

90. Rodman, M.J., Smith, D.W. Clinical Pharmacology in Nursing, J.B. Lippincott Co. Philadelphia, 1984.

91. Ron, S., Robinson, D.A., Skavenski, A.A., Saccades and the quick phase of nystagmus. Vision Research, 12: 2015-2022, 1972.

92. Sakata, E., Umeda, Y. Caloric eye tracking pattern test. 1. Visual suppression and the possibility of simplified differential diagnosis between peripheral and central vertigo. Annals of Otolaryngology, 85: 261-267, 1976.

93. Sato, Y., Kato, I., Kawasaki, T., Mizukoshi, K., Hayano, M. Failure of fixation suppression of caloric nystagmus and ocular motor abnormalities. Archives Neurology, 37: 35-38, 1980.

94. Selhorst, J.B., Stark L., Ochs A.L. and Hoyt W.F., Disorders in cerebellar occular motor control, 1. Saccadic overshoot dysmetria and oculographic control systems and clinico-anatomical analysis. Brain, 99, 497-508, 1976.

95. Shagass, C., Amadeo, M., Overton, D.A. Eye-tracking performance in psychiatric patients. Biological Psychiatry, 9: 245-260, 1974.

96. Shagass, C., Roemer, R.A., Amadeo, M. Eye-tracking performance and engagement of attention. Archives of General Psychiatry, 33: 121-125, 1976.

97. Shuster, A.R. The psychotropic drugs: Considerations relative to the vestibular pathways and testing. Laryngoscope, 75: 707-734, 1965.

98. Siedman, L.J. Schizophrenia and brain dysfunction: An integration of recent neurodiagnostic findings. Psychological Bulletin. 94: (2) 195-238, 1983.

99. Snider, S.R. Cerebellar pathology in schizophrenia- Cause or consequence? Neuroscience Biobehavioral Reviews, 6:47-53, 1982.

100. Stark, L. The control system for versional eye movements. In: The Control of Eye Movements, Eds. P. Bach-Y-Rita,

C.C. Collins, J.E. Hyde, Academic Press Inc., New York, 363-428, 1971.

101. Takemori, S. Visual suppression test. Annals Otolaryngology, 86:80-85, 1977.

102. Takemori, S., Visual Suppression Test. Advances in Oto-Rhino-Laryngology, 29:102-110, 1983.

103. Takemori, S., Aiba, T., Siozawa; R., Saccade and pursuit eye movements. Advances in Oto-Rhino-Laryngology, 33:8-82, 1983.

104. Takemori, S., Cohen B. Loss of visual suppression of vestibular nystagmus after flocullus lesions. Brain Research, 72, 213, 1984.

105. Tanguay, P.E., Implications of Hemishpheric Specialization for Psychiatry. In: The Dual Brain, Eds. F.D. Benson and E. Zaidel, New York, The Gail Ford Press, 1985.

106. Torok, N. Standard evaluation of the reactive nystagmus. Archives of Otolaryngology, 96:448-452, 1972.

107. Walker, E. Attentional and neuromotor functions of schizophrenics, shizoaffectives, and patients with other affective disorders. Archives of General Psychiatry. 38: 1355-1358, 1981.

108. Weinberger, D.R., Klenman, J.E., Luchins, D.J., Bigelow L.B., Wyatt, R.J. Cerebellar pathology in schizophrenia: A controlled post mortem study. American Journal of Psychiatry, 137:359-361, 1980.

109. Winer, B.J. Statistical Principles in Experimental Design. McGraw-Hill Book Co., New York, 1962.

110. Wohlberg. G.W., Kornetsky, C. Sustained attention in remitted schizophrenics. Archives of General Psychiatry, 28: 533-537, 1973.

111. Zee, D.S. Cerebellar control of eye movements. In: Nystagmus and Vertigo, Clinical Approaches to the Patient with Dizziness, Eds. U. Honrubia and N.A.B. Brazier, Academic Press, N.Y., 1982.

112. Zee, D.S. Ocular motor control: The cerebellar control of saccadic eye movements. In: Neuro-ophthalmology, volume 3, Eds. S. Lessell and J.T.W. Van Dalen, 141-156. Elsevier, New York, 1984.

APPENDIX A

Figure A

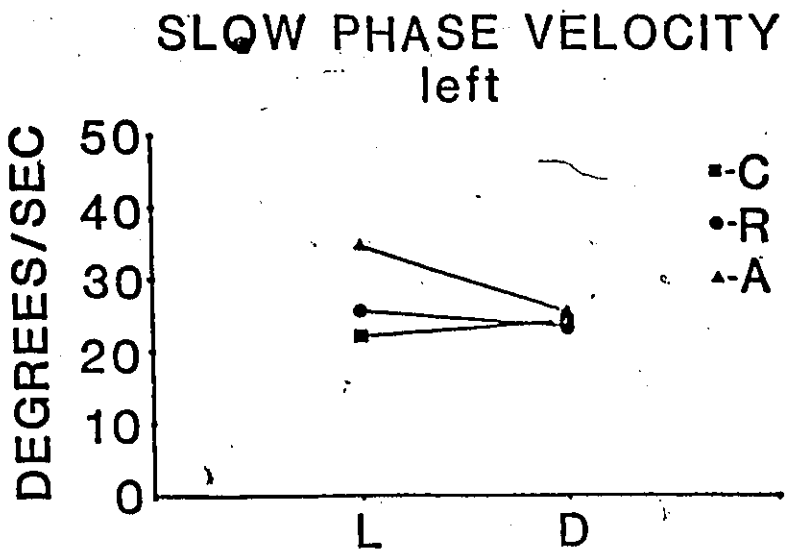


Figure B

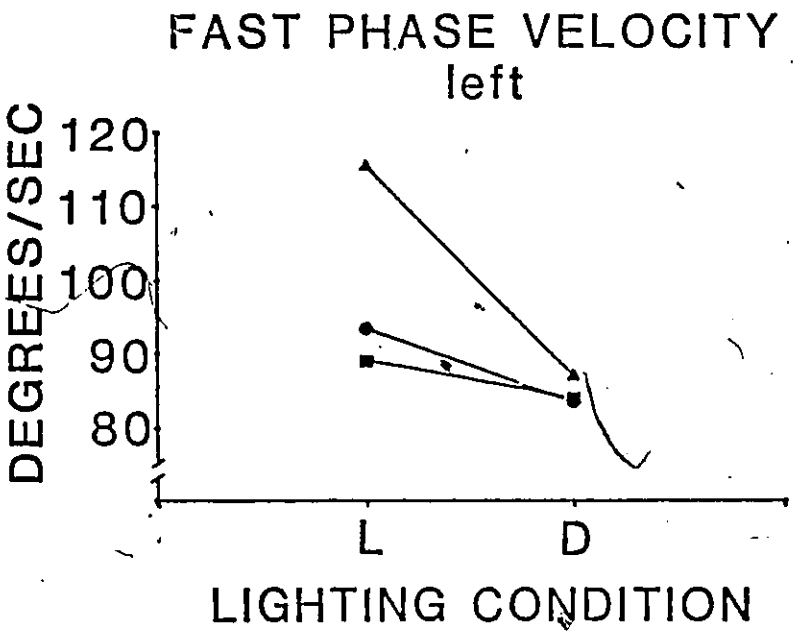


Figure A: The maximum nystagmus slow phase velocity, in degrees/sec, following left ear irrigation across lighting conditions.

Figure B: The maximum nystagmus fast phase velocity, in degrees/sec, following left ear irrigation across lighting conditions.

Figure C

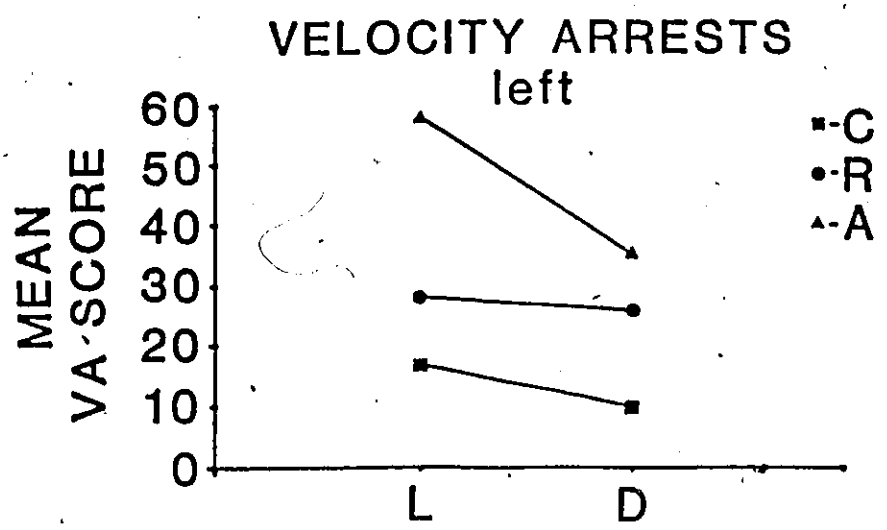


Figure D

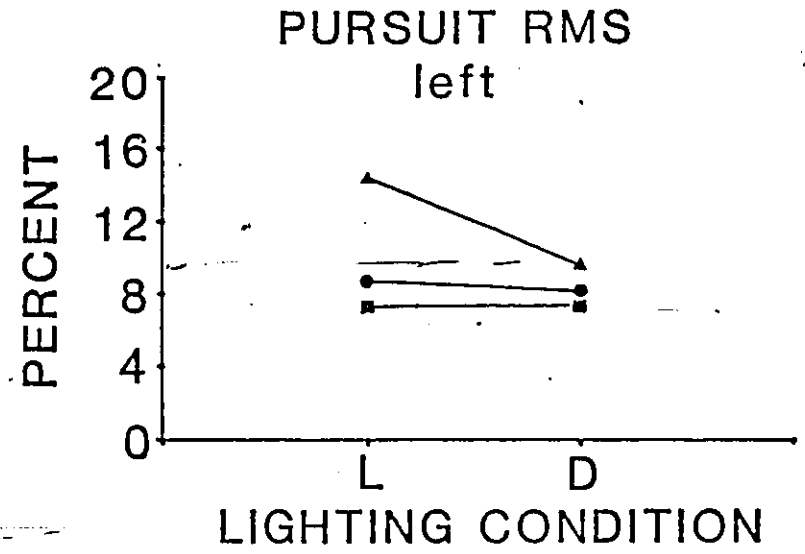


Figure C: Mean number of VAs for each group following left ear caloric irrigation and across lighting conditions.

Figure D: Mean percent root mean square during post-irrigation (left ear) tracking for each group across lighting conditions.

APPENDIX B

Statistical Design

To determine whether variations in the oculomotor functioning of the three groups (i.e., controls, remitted psychotic patients and active-ill psychotic patients) varied significantly across groups or testing situations, the following design was used. Each subject was tested and his performance on the various independent variables examined under both light and dark conditions and for certain variables following both right and left ear irrigations. The statistical designs being used, therefore, are; 1. a two-factor design repeated over one factor (grouping x lighting repeated over lighting); and, 2. a three-factor design repeated over two factors [(grouping x lighting) x irrigation repeated over both lighting and irrigation]. Subsequently, unless otherwise indicated, group and subject differences across conditions and testing sessions were analyzed using repeated measures analyses of variance (82; UCLA Medical School BMDP2V program), and indicated post-hoc analyses were conducted using the Newman-Keuls procedure. The Power of the Analysis of Variance F test was calculated for key variables and is included in the ANOVA Tables (see Appendix C). Due to the elevated number of analyses of variance being conducted a Bonferonni test was performed. On the basis of results from the latter, the accepted significance level was decreased from $p<.05$ to $p<.022$. Correlations were performed using the Pearson Product Moment correlation coefficient (see Appendix D).

APPENDIX C

ANOVA TABLES

SLOW PHASE VELOCITY

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL PROB.
MEAN	89700.57711	1	89700.67711	454.38	0.0000
GROUP	229.28862	2	114.64431	0.58	0.5626
ERROR	11844.89689	60	197.41495		
LIGHT	766.54673	1	766.54673	8.29	0.0055
LG	345.56544	2	172.78272	1.87	0.1634
ERROR	5551.26604	60	92.52110		

FAST PHASE VELOCITY

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL PROB.
MEAN	1082530.35224	1	1082530.35224	575.84	0.0000
GROUP	99.96855	2	49.98427	0.03	0.9738
ERROR	103395.64344	55	1879.92079		
LIGHT	10177.72431	1	10177.72431	18.88	0.0001
LG	1948.48493	2	974.24246	1.81	0.1737
ERROR	29652.48357	55	539.13606		

FREQUENCY

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL
MEAN	41757.18394	1	41757.18394	351.28	0.0000
GROUP	131.86024	2	65.93012	0.55	0.5770
ERROR	7726.63241	65	118.87127		
LIGHT	121.14265	1	121.14265	4.54	0.0369
LG	252.95022	2	126.47511	4.74	0.0120
ERROR	1733.66008	65	26.67169		

DURATION

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL
MEAN	4126667.61609	1	4126667.61609	4066.93	0.0000
GROUP	4944.18977	2	2472.09489	2.44	0.0957
ERROR	63925.39356	63	1014.68879		
LIGHT	74.99049	1	74.99049	0.25	0.6195
LG	512.91347	2	256.45673	0.85	0.4315
ERROR	18966.85168	63	301.06114		

LATENCY

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL PROB.
MEAN	147960.07957	1	147960.07957	627.19	0.0000
GROUP	353.18934	2	176.59467	0.75	0.4771
ERROR	15098.18979	64	235.90912		
LIGHT	123.56219	1	123.56219	1.48	0.2284
LG	368.45664	2	184.22832	2.20	0.1186
ERROR	5347.27470	64	83.55117		

FIXATION SUPPRESSION

POWER OF .99 AT p<.01
AND p<.05

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL PROB.
MEAN	1169231.32514	1	1169231.32514	746.65	0.0000
GROUP	39953.84787	2	19976.92394	12.76	0.0000
ERROR	92392.70455	59	1565.97804		
LIGHT	9551.13636	1	9551.13636	27.00	0.0000
LG	385.87104	2	192.93552	0.55	0.5825
ERROR	20873.71364	59	353.79176		
EAR	2059.78182	1	2059.78182	7.99	0.0064
EG	782.26166	2	391.13083	1.52	0.2279
ERROR	15216.96818	59	257.91471		
LE	802.57514	1	802.57514	5.60	0.0212
LEG	1283.34787	2	641.67394	4.48	0.0154
ERROR	8449.20455	59	143.20686		

FIXATION RMS

POWER OF .60 AT p<.01
.80 AT p<.05

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL PROB.
MEAN	6209.54062	1	6209.54062	130.77	0.0000
GROUP	389.59996	2	194.79998	4.10	0.0212
ERROR	2943.99128	62	47.48373		
LIGHT	7.92623	1	7.92623	0.89	0.3501
LG	123.78378	2	61.89189	6.92	0.0019
ERROR	554.33552	62	8.94090		

VELOCITY ARRESTS
BASELINE

POWER OF APPROX. .99
AT p<.01 AND p<.05

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL PROB.
MEAN	77052.02675	1	77052.02675	107.94	0.0000
GROUP	12468.79227	2	6234.39614	8.73	0.0005
ERROR	42828.65217	60	713.81087		
LIGHT	9699.11583	1	9699.11583	23.60	0.0000
LG	3055.17649	2	1527.58825	3.72	0.0301
ERROR	24659.69652	60	410.99494		

VELOCITY ARRESTS
(POST IRRIGATION AND BASELINE)

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL PROB.
MEAN	169361.36894	1	169361.36894	191.04	0.0000
GROUP	25835.95061	2	12917.97531	14.55	0.0000
ERROR	51500.46742	58	887.93909		
LIGHT	8897.38143	1	8897.38143	22.14	0.0000
LG	2649.31982	2	1324.65991	3.30	0.0441
ERROR	23312.62281	58	401.94177		
COND	513.10905	1	513.10905	1.43	0.2362
CG	101.76482	2	-50.88241	0.14	0.8679
ERROR	20772.80075	58	358.15174		
LC	2260.30034	1	2260.30034	10.94	0.0016
LCG	773.71252	2	386.85626	1.87	0.1629
ERROR	11982.70551	58	206.59837		

PURSUIT RMS
BASELINE

POWER OF .74 AT p<.01
POWER OF .89 AT p<.05

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL PROB.
MEAN	11606.91860	1	11606.91860	361.04	0.0000
GROUP	410.01547	2	205.00774	6.38	0.0030
ERROR	1993.21079	62	32.14856		
LIGHT	151.22394	1	151.22394	7.55	0.0078
LG	52.14029	2	26.07014	1.30	0.2794
ERROR	1241.72908	62	20.02789		

PURSUIT RMS
(POST-IRRIGATION AND BASELINE)

SOURCE	SUM OF SQUARES	DEGREES OF FREEDOM	MEAN SQUARE	F	TAIL PROB.
MEAN	20204.49972	1	20204.49972	392.10	0.0000
GROUP	567.84605	2	283.92302	5.51	0.0065
ERROR	2885.58478	56	51.52830		
LIGHT	215.66300	1	215.66300	8.46	0.0052
LG	56.28044	2	28.14022	1.10	0.3389
ERROR	1428.20319	56	25.50363		
COND	5.32602	1	5.32602	0.64	0.4270
CG	35.52491	2	17.76246	2.13	0.1278
ERROR	465.90334	56	8.31970		
LC	4.41855	1	4.41855	0.66	0.4192
LCG	6.18089	2	3.09044	0.46	0.6316
ERROR	373.56680	56	6.67804		

BUTTON PRESS RESPONSE

MEAN	972183.96649	1	972183.96644	1278.29	0.0000
GROUP	4670.52985	2	2335.26493	3.07	0.0540
ERROR	44110.99474	58	760.53439		
LIGHT	640.55420	1	640.55420	6.44	0.0139
LG	472.07256	2	236.03628	2.37	0.1022
ERROR	5770.46842	58	99.49083		

APPENDIX D

CORRELATIONS BETWEEN ALL INDEPENDENT VARIABLES
DATA POOLED ACROSS ALL GROUPS

CONDITION = BASELINE

	PURSUIT RMS	FIXATION RMS
VELOCTIY ARREST	0.789 P=0.00	0.376 P=0.00
PURSUIT RMS		0.383 P=0.00

CONDITION = IRRIGATION

	PURRMS	FIXRMS	LATENC	DURAT	DISRHYT	SLOW	FAST	FREQ	FIXSUP
VELOCITY ARREST	0.616 P=0.00	0.500 P=0.00	0.005 P=0.46	0.087 P=0.08	-0.011 P=0.42	0.393 P=0.00	0.271 P=0.00	0.220 P=0.00	-0.364 P=0.00
PURSUIT RMS		0.431 P=0.00	0.068 P=0.13	0.071 P=0.12	0.089 P=0.06	0.224 P=0.00	0.120 P=0.03	0.021 P=0.38	-0.253 P=0.00
FIXATION RMS			-0.018 P=0.38	0.074 P=0.11	-0.101 P=0.05	0.367 P=0.00	0.335 P=0.00	0.148 P=0.00	-0.276 P=0.00
LATENCY				-0.258 P=0.00	0.519 P=0.00	-0.282 P=0.00	-0.201 P=0.00	-0.492 P=0.00	-0.281 P=0.00
DURATION					-0.243 P=0.00	0.149 P=0.00	0.141 P=0.01	0.179 P=0.00	0.062 P=0.15
DISRHYTHMIA						-0.375 P=0.00	-0.402 P=0.00	-0.597 P=0.00	-0.207 P=0.00
SLOW PHASE VELOCITY							0.749 P=0.00	0.595 P=0.00	-0.043 P=0.24
FAST PHASE VELOCITY								0.465 P=0.00	0.011 P=0.42
FREQUENCY									0.035 P=0.20

CORRELATIONS: WITHIN GROUP

GROUP = CONTROL
CONDITION = BASELINE

	PURSUIT RMS	FIXATION RMS
VELOCITY ARREST	0.607 P=0.00	0.349 P=0.01
PURSUIT RMS		0.282 P=0.03

GROUP = CONTROL
CONDITION = IRRIGATION

	PURRMS	FIXRMS	LATENC	DURAT	DISRHYT	SLOW	FAST	FREQ	FIXSUP
VELOCITY ARRESTS	0.344 P=0.00	0.156 P=0.07	0.020 P=0.42	0.227 P=0.01	-0.226 P=0.01	0.104 P=0.16	0.035 P=0.37	0.104 P=0.16	-0.067 P=0.26
PURSUIT RMS		0.378 P=0.00	0.210 P=0.02	0.192 P=0.03	-0.146 P=0.08	0.160 P=0.06	0.098 P=0.18	0.205 P=0.02	-0.114 P=0.14
FIXATION RMS			-0.058 P=0.29	-0.036 P=0.36	-0.140 P=0.09	0.020 P=0.42	0.119 P=0.13	0.127 P=0.12	-0.144 P=0.09
LATENCY				-0.331 P=0.00	0.340 P=0.00	-0.307 P=0.00	-0.175 P=0.04	-0.403 P=0.00	-0.203 P=0.02
DURATION					-0.342 P=0.00	0.146 P=0.08	0.164 P=0.06	0.227 P=0.01	0.082 P=0.21
DISRHYTHMIA						-0.369 P=0.00	-0.348 P=0.00	-0.501 P=0.00	0.166 P=0.05
SLOW PHASE VELOCITY							0.689 P=0.00	0.674 P=0.00	-0.277 P=0.00
FAST PHASE VELOCITY								0.407 P=0.00	-0.219 P=0.01
FREQUENCY									-0.184 P=0.04

CORRELATIONS: WITHIN GROUP

GROUP = REMITTED
CONDITION = BASELINE

	PURSUIT RMS	FIXATION RMS
VELOCITY ARREST	0.818 P=0.00	0.302 P=0.02
PURSUIT RMS		0.186 P=0.11

GROUP = REMITTED
CONDITION = IRRIGATION

	PURRMS	FIXRMS	LATENC	DURAT	DISRHYT	SLOW	FAST	FREQ	FIXSUP
VELOCITY ARREST	0.664 P=0.00	0.360 P=0.00	0.063 P=0.27	0.156 P=0.07	0.123 P=0.12	0.329 P=0.00	0.161 P=0.07	-0.019 P=0.42	-0.191 P=0.04
PURSUIT RMS		0.235 P=0.01	0.289 P=0.00	-0.038 P=0.36	0.229 P=0.01	0.079 P=0.24	-0.038 P=0.36	-0.228 P=0.01	-0.099 P=0.18
FIXATION RMS			0.044 P=0.33	0.033 P=0.37	0.040 P=0.35	0.083 P=0.22	0.070 P=0.26	-0.005 P=0.47	-0.364 P=0.00
LATENCY				-0.293 P=0.00	0.679 P=0.00	-0.398 P=0.00	-0.335 P=0.00	-0.645 P=0.00	-0.382 P=0.00
DURATION					-0.139 P=0.09	0.177 P=0.05	0.070 P=0.26	0.267 P=0.00	0.009 P=0.46
DISRHYTHMIA						-0.341 P=0.00	-0.447 P=0.00	-0.702 P=0.00	-0.332 P=0.00
SLOW PHASE VELOCTIY							0.677 P=0.00	0.588 P=0.00	0.114 P=0.14
FAST PHASE VELOCITY								0.418 P=0.00	0.146 P=0.09
FREQUENCY									0.359 P=0.00

CORRELATIONS: WITHIN GROUP

GROUP = ACTIVE
CONDITION = BASELINE

	PURSUIT RMS	FIXATION RMS
VELOCITY ARREST	0.769 P=0.00	0.288 P=0.03
PURSUIT RMS		0.404 P=0.00

GROUP = ACTIVE
CONDITION = IRRIGATION

	PURRMS	FIXRMS	LATENC	DURAT	DISRHYT	SLOW	FAST	FREQ	FIXSUP
VELOCITY ARREST	0.653 P=0.00	0.476 P=0.00	-0.129 P=0.12	0.266 P=0.00	-0.166 P=0.06	0.490 P=0.00	0.369 P=0.00	0.301 P=0.00	-0.258 P=0.00
PURSUIT RMS		0.471 P=0.00	-0.105 P=0.17	0.243 P=0.01	-0.023 P=0.41	0.316 P=0.00	0.243 P=0.01	0.086 P=0.21	-0.208 P=0.02
FIXATION RMS			-0.115 P=0.15	0.287 P=0.00	-0.259 P=0.00	0.560 P=0.00	0.535 P=0.00	0.175 P=0.05	-0.102 P=0.17
LATENCY				-0.083 P=0.22	0.387 P=0.00	-0.218 P=0.02	-0.093 P=0.21	-0.398 P=0.00	-0.251 P=0.01
DURATION					-0.272 P=0.00	0.218 P=0.02	0.331 P=0.00	0.154 P=0.07	-0.087 P=0.21
DISRHYTHMIA						-0.475 P=0.00	-0.443 P=0.00	-0.638 P=0.00	-0.179 P=0.05
SLOW PHASE VELOCITY							0.840 P=0.00	0.526 P=0.00	0.146 P=0.17
FAST PHASE VELOCITY								0.594 P=0.00	0.129 P=0.12
FREQUENCY									0.066 P=0.26