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LA THÈSE A ÉTÉ
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The Effects of Vestibular Stimulation on
Eye Movements in Psychiatric Patients

by Anne Marie Jones

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
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ABSTRACT

The present investigation which examined possible vestibular involvement in impaired smooth pursuit tracking in psychiatric patients was prompted by: (a) the history of suggested abnormal vestibular functioning in schizophrenia; (b) known vestibular involvement in smooth pursuit and saccadic eye movement systems; and, (c) the recent demonstration that neurological patients with central vestibular disorders show significantly less suppression of calorically induced nystagmus during smooth pursuit tracking than patients with peripheral vestibular disorders or normals.

Forty psychiatric patients (20 inpatients-IP: psychotics requiring intensive psychiatric care; 20 outpatients-OP: psychotics in remission) and 20 non-hospitalized controls (C: no history of psychiatric illness) were subjects. All gave informed consent and were free from organic disorders and medication known to affect vestibular or oculomotor systems or tracking performance. Otoscopic examinations ensured that external auditory canals were unobstructed and tympanic membranes were normal and intact.

5 Bipolar horizontal and vertical EOG activity were recorded before (baseline) and during serial bilateral caloric irrigation (250 ml; 30°C water) while subjects tracked a target light oscillating at .45Hz for 30 seconds. Subjects responded (button-press) to random 200 msec target light interruptions as a monitor

of attentiveness. Tracking trials were randomized across subjects. Horizontal EOG recordings were electronically differentiated to obtain the first derivative (eye velocity). Both slow phase velocity of the vestibular nystagmus--eye movements characterized by a slow deviation and fast return and induced by caloric irrigation--and deviant tracking--instances of eye velocity slowing to $\leq 2^\circ/\text{sec}$ (velocity arrests: VAs) were determined from these tracings. The fast phase velocity was determined by computer digitization of EOG voltage. All other parameters of the vestibular response, including fixation suppression, were assessed by standardized procedures. Data were analyzed using univariate procedures with post-hoc tests where warranted.

The usual measures of vestibular reactivity, including bilateral comparisons, were normal for all groups, reflecting basic integrity of the vestibular system. Those parameters which reflected CNS input and control of the vestibular response--i.e., fast phase velocity, dysrhythmia and fixation suppression--however, were within the range of pathology for the inpatient group. The outpatient group did not differ significantly from the normal control group on these measures with the exception of the dysrhythmia rating on the second irrigation.

Baseline eye tracking of controls was superior to that of the inpatient group ($C > IP$, $p < .05$). Outpatient tracking was less accurate than that of normal controls, but the differences were

not significant. Vestibular activation increased VAs, but only inpatients showed a significant increase in tracking deviations from baseline to the second irrigation. Significant order effects were not found, and baseline VA scores were stable regardless of order of presentation.

The present results suggest that repeated activation of the vestibular system selectively enhances tracking deviations in actively ill psychotics. Indices reflecting central, rather than peripheral, nervous system functioning were found to account for the differences between patients with active psychotic symptomatology and patients with remitted symptomatology and normal controls. It is suggested that the deficits in eye tracking and vestibular response noted in this study could be transitory, and that the CNS effects reflect the severity of the psychotic symptoms rather than any psychotic diathesis.

CURRICULUM STUDIORUM

Anne Marie Jones was born July 10, 1947 in Temiscaming, Quebec. She received the Bachelor of Arts degree from Carleton University, Ottawa, Ontario, in 1966. She received the Masters of Psychology degree from the University of Ottawa, Ottawa, Ontario, in 1976.

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Table of Contents

	page
Abstract.....	ii
Curriculum Studiorum.....	v
Acknowledgments.....	vi
List of Tables.....	ix
List of Figures.....	x
Introduction.....	1
Oculomotor Systems.....	1
Eye Tracking and Schizophrenia.....	3
Vestibular System.....	7
Caloric Stimulation.....	9
Vestibular System and Schizophrenia.....	12
Synopsis and Hypotheses.....	15
Methodology.....	18
Subjects.....	18
Procedure.....	20
Data Analysis.....	27
Vestibular Data.....	27
Pursuit Tracking Data.....	31
Statistical Analysis.....	34
Results.....	35
Vestibular Responses.....	35
Fixation Suppression.....	43
Velocity Arrests.....	45

	page
Button Press and Blinks.....	47
Subcategories of Schizophrenia.....	49
Neuroleptic Medication.....	53
Discussion.....	55
Vestibular Responses.....	55
Pursuit Tracking.....	61
References.....	69
Appendix A	
Dysrhythmia Rating Scale (Lidvall).....	79

List of Tables

Table		page
1	Demographic Characteristics of Subject Groups.....	21
2	Conditions and Procedures for Baseline, Vestibular Activation and Smooth Pursuit Tracking Measurement.....	25
3	Mean Fast Phase Velocity for all Subjects grouped by Dysrhythmia Rating.....	41
4	Means of Significant Dependent Variables by Subject Group (Hospital Diagnosis).....	50

List of Figures

Figure		page
1	Caloric Nystagmus and Associated Procedures Electrographic Recordings.....	22b
2	Slow Phase Velocity Differentiated.....	28
3	Measurement of Nystagmus Slow Phase Velocity.....	30
4	Measurement of Velocity Arrests by Differentiation.....	32
5	Mean Slow Phase Velocity across Caloric Conditions.....	36
6	Mean Fast Phase Velocity across Caloric Conditions.....	37
7	Mean Frequency of Nystagmus Beats across Caloric Conditions.....	39
8	The Effects of Mental Alerting on Slow Phase Velocity.....	42
9	Mean Percent Suppression of Nystagmus by Visual Fixation.....	44
10	Mean Velocity Arrests across Baseline and Caloric Conditions for all groups.....	46
11	Mean Velocity Arrests for Patients grouped by Rorschach Classification.....	52

INTRODUCTION

Visual perception requiring foveal fixation of the target is achieved by the interaction of two different oculomotor systems: the saccadic and the smooth pursuit. The two systems differ in many respects, the most obvious being in terms of their velocity-amplitude characteristics. The velocity of the saccade is related to the distance the eye has to travel, and during a large amplitude eye movement the eye can reach $700^{\circ}/\text{sec}$ (Baloh, 1975). Smooth pursuit velocity approximates the speed of the target (Henriksson, 1955), provided that the latter is less than $30^{\circ}/\text{sec}$. The upper limit of this system is $50^{\circ}/\text{sec}$ (Robinson, 1975). Saccadic eye movements are also ballistic and generally beyond voluntary control once begun, whereas during smooth pursuit adjustments in angular velocity are continuous (Rashbass, 1961). The stimulus for saccades is generally a retinal position error (Rashbass, 1961). For smooth pursuit tracking the stimulus is almost exclusively a moving target, though tracking can occur in REM sleep (Fuchs & Ron, 1968), and subjects can learn to make tracking eye movements in the absence of a moving stimulus (Westheimer & Conover, 1954). Functionally, the two systems also differ, (e.g.), during saccadic eye movements vision and the pupillary reflex are suppressed (Zuber & Stark, 1966), while vision is continuously present during smooth pursuit.

Although saccades and smooth pursuit eye movements may serve different functions, they do not occur independently. Recent studies indicate that the same oculomotor neurons participate in both types of eye movement, with the site of regulation for both being in the cerebellum and the paramedian pontine reticular formation (PPRF) (Robinson, 1975; Cohen, Komatsuzaki & Bender, 1968). Saccades control the onset, duration and location of fixation and tracking movements. A regulated coordination and mutual dependence between the two systems is found during a rhythmical pattern of eye movement--nystagmus--one type of which may be produced by stimulation of the vestibular system. The simple sequence of slow (pursuit) and quick (saccadic) phases of vestibular nystagmus serves as a neuronal model for sequential regulation of tracking and saccades. During voluntary fixations the coordination is more complex, irregular and selective, but saccadic, fixation and tracking eye movements are nonetheless regulated in their sequential role for the sensorimotor basis of visual information (Jung, 1972).

Standardized methods for the evaluation of pursuit and saccadic eye movements are used as clinical tools in the diagnosis of neurological disease. Accordingly, impairments in eye movements associated with central pathology are well documented. For example, the pursuit eye tracking response achieved by following the pendular movement of a visual stimulus is highly sensitive to injury (Corvera, Torres & Lopez, 1973), and deviant tracking is found in neurological

patients, in alcohol and barbituate intoxication, and frequently in the aged.

Deviant eye tracking patterns have also been reported in psychiatric patients, and one of the first observations of this phenomenon was made by Diefendorf and Dodge (1908). The authors noted aberrations of smooth pursuit tracking in their schizophrenic patients, and suggested that this represented a central nervous system deficit in processing perceptual data. An early replication of the original study (Couch & Fox; 1934) observed deviant tracking in the most severely ill psychiatric patients, irrespective of diagnosis of schizophrenia, and related the aberrant tracking to inattention. It was not until the early 1970s that the tracking anomalies noted in these early studies were reinvestigated (Holzman, Proctor & Hughes, 1973; Holzman, Proctor & Levy, 1974; Holzman, 1975). As in the first study, pursuit disorders were found to be more frequent among schizophrenics than among other psychiatric patients.

In subsequent investigations (Holzman & Levy, 1977; Shagass, Amadeo & Overton, 1974; Pivik, 1979) there has been consensus that hospitalized schizophrenics showed deviant tracking relative to normal controls. In an attempt to differentiate between good trackers and poor trackers within the schizophrenic population, Holzman et al., (1974) focused upon a single component of the schizophrenic process, i.e., thought disorder. A stronger

relationship between deviant tracking and thought disorder was found than that which obtained between deviant tracking and the general category of schizophrenia. Tracking deficits have been noted in patients with affective psychoses (Shagass et al., 1974), in major functional psychoses (Lipton, Levin, Holzman, 1980), and have been correlated with scales measuring psychoticism (Iacono & Lykken, 1979), which suggests that the tracking dysfunction is not exclusive to schizophrenia.

There is no evidence to suggest that neuroleptic drugs cause these eye tracking anomalies. This has been adduced from studies which have shown that cognitive tasks improved tracking in normal controls and in patients administered drugs known to produce strong sedative effects (Holzman, 1975). Furthermore, tracking abnormalities were reported in psychiatric patients previous to the use of major tranquilizers (Diefendorf & Dodge, 1908; Couch & Fox, 1934). Nonpsychotic patients who had received neuroleptics did not show the eye tracking aberrations (Holzman & Levy, 1977), and no relationship, irrespective of diagnostic category, was found between medication and tracking impairments (Shagass et al., 1974). These findings have been proposed as indirect evidence that medication effects do not account for the smooth pursuit tracking deviations.

The basis for the deviant tracking in psychiatric patients has not yet been determined. In addition to the influence of medication discussed above, other possibilities which have been proposed

(Holzman et al., 1973) include: 1) failure of cognitive centering mechanisms, i.e., an attentional deficit; 2) visual system pathology, particularly of the retina or the extraocular muscles; and 3) dysfunctioning of central nervous system control mechanisms underlying accurate tracking. Of these, examination of attentional factors has been most intense, because of the importance of attention in visual fixation and since attentional deficits have been reported in schizophrenia.

Attempts to control for attentional processes have consisted of re-alerting subjects during tracking (Holzman et al., 1973; 1974), having subjects silently read numbers on the pendulum bob while tracking (Shagass et al., 1976), and having subjects respond to variations in target characteristics during tracking (Pivik, 1979). Re-alerting had no significant effect on the number of tracking errors. Although silent number reading improved the performance of both patients and controls, the group differences still remained (Holzman, Levy & Procotor, 1976). The silent number reading task normalized only certain types of eye tracking impairments, i.e., tracking where pursuit movements are replaced by saccades (Holzman & Levy, 1977). In patients who demonstrated tracking with small amplitude saccadic movements superimposed on the general pursuit tracking pattern only slight improvement was noted with the additional cognitive demand (Holzman & Levy, 1977). Requiring subjects to respond to periodic interruptions in the tracking

target--a manipulation designed to heighten attention--resulted in improved tracking in control subjects, but further impaired tracking in inpatients (Pivik, 1979). Generally, it appears that temporary improvement in eye tracking may result from directly controlling attention. The quality of the tracking of schizophrenics, however, remains significantly impaired relative to normal controls regardless of aids to direct cognitive attention. It has been suggested (Holzman et al., 1974) that if attention is involved in aberrant tracking then it would seem to represent a form of involuntary and phasic interrupting of centering of focus, i.e., a disorder of nonvoluntary attention.

To date, the investigations have presented no evidence regarding a further suggested locus for impaired eye tracking, i.e., dysfunction of central nervous system control mechanisms. The present study is focused upon central nervous system involvement in deviant eye tracking in psychiatric patients. Specifically, the involvement of the vestibular system in eye tracking deviations is examined. The major considerations upon which the present study is based are the following:

7

The vestibular system is intimately involved in mechanisms underlying control of both smooth pursuit and saccadic eye movements.

The central pathway of the vestibular system which is directly involved in eye movement control involves a three neuron arc consisting of: the vestibular afferent fibers, the straight through fiber pathway from the premotor system, and the oculomotor neuron (Lorenté de No, 1933; Barber & Stockwell, 1976). There are no neurons originating in the semicircular canals or in the otolith organs which project directly to oculomotor nuclei. Instead, an intermediate synapse within this arc in the vestibular nuclei or in the cerebellum is the most direct link between the vestibular apparatus and the eye muscles (Lorenté de No, 1933). The vestibular system projects into the paramedian portion of the pontine reticular formation, where mechanisms which generate gaze and horizontal eye movements reside (Gernandt, 1964, 1968; Ladpli & Brodal, 1968), and to the cerebellum where these eye movements are regulated (Carpenter et al., 1959; Carpenter, 1960). Quantitatively, the most significant number of brain stem projections to the nuclei of the extraocular muscles arise from the vestibular nuclei (Cohen, 1971).

The vestibulo-ocular reflex and the pursuit or fixation reflex are the two neural control systems used by man to stabilize the foveal image. The pursuit reflex alone is unable to preserve visual acuity when the head is moving, or when the velocity of the target movement is too great, or when the frequency of a direction changing movement is too high (Benson & Barnes, 1978). The vestibulo-ocular reflex, meanwhile, preserves visual acuity in the frequency domain where the pursuit reflex is largely ineffective. In situations where the pursuit and the vestibulo-ocular reflex interact, the vestibular responses must be suppressed if visual acuity is not to be impaired. Therefore, it has been proposed that the pursuit and the vestibulo-ocular reflexes converge before neural signals are transmitted to the motoneurons of the extraocular muscles. It follows then that suppression of an inappropriate vestibular response is dependent upon the generation of an antagonistic signal by the pursuit system. The combination of the two responses compensates for the limited working range of either.

Experimental evidence (Stark, 1971) has shown that both visual and vestibular systems share a common input to the mechanisms of saccadic generation. Experiments on visual target acquisition (Barnes, 1976) indicate the existence of a hierarchical system for the control of saccadic eye movements in which the vestibulo-ocular reflex acts in a subsidiary manner to retinal

afferent information. Saccades also occur in the absence of visual stimuli, i.e., in the dark, and to auditory and tactile stimuli. This suggests that these eye movements are coded in the brain within a body or head co-ordinate system (Chun & Robinson, 1978), and it is the vestibular system which specifies the location of any eye movement in the head co-ordinate system.

The basis for the coordination of pursuit and saccadic eye movements with vestibular input has largely centered around the concept of a neural integrator subserving these systems. Recently, it was shown that quick phases of nystagmus and saccades shared the same neural integrator (Ron, Robinson & Shavenski, 1972). Although anatomical evidence is not available, it has been proposed that the pursuit system also shares this same integrator, and that all visual commands for eye movements descend to the level of the vestibular nucleus and are processed along with vestibular signals (Chun & Robinson, 1978). The need for a common mechanism subserving these systems is essential so that whatever system is being used, the net eye movement response will be similar in form and will not lead to difficulties in, for example, spatial orientation.

Standardized stimulation techniques and assessment methods have been developed to study the vestibular system.

Peripheral stimulation of the vestibular system by caloric irrigation or rotation induces movement of the endolymphatic

fluid contained in the semicircular canals. Caloric unlike rotatory stimulation offers the advantage of testing each labyrinth separately and is the method of choice in this investigation. Caloric stimulation deviates the cupula through heat transfer, density changes in the endolymph, and production of a convection current. As calories are transferred from inner ear fluids to the bone of the posterior-superior annulus, the endolymph condenses and resulting changes in specific gravity produce endolymph flow. This endolymph flow bends the cupula in the ampulla, producing a change in the impulses to the vestibular nuclei, which in turn induce nystagmus. Nystagmus is a distinct and patterned deviation of the eyes (the slow phase) which is periodically interrupted by a rapid movement in the opposite direction (the fast phase).

The parameters of nystagmus that are used herein and listed below include both standard indicators of vestibular reactivity (Kosoy, 1977; Barber & Stockwell, 1976), as well as those which reflect central nervous system input.

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

Duration: the interval between the onset of irrigation and the last beat of nystagmus.

Peak frequency: mean frequency of nystagmus beats per unit time (10 secs) when the nystagmus is most intense.

Maximum slow phase velocity: average slow phase speed during the most intense response interval.

Maximum fast phase velocity: average fast phase speed during the most intense response interval representing the quick saccadic return.

Fixation suppression: a measure of the effectiveness of visual fixation in suppressing caloric nystagmus.

Dysrhythmia: a measure of the regularity of the nystagmus response.

It is generally accepted that the slow phase speed of nystagmus provides the most sensitive index of vestibular reactivity. The slow component is a linear function of the difference between the temperature of the stimulus and the body, and so is the parameter most closely related to the stimulus. Bilateral symmetry of the slow phase speed is preferred as a more reliable measure of vestibular reactivity than latency, duration or intensity since these latter indices show considerable variability in the normal population (Kosoy, 1977). The fast phase velocity, fixation suppression and dysrhythmia represent central nervous system input to the vestibular response.

Sakata and Umeda (1976) used a procedure (termed the Caloric Eye Tracking Pattern Test) which combined pursuit tracking and suppression of vestibular nystagmus to examine the suppression mechanism evoked by visual pursuit. The authors observed that

the suppression mechanism was evoked more strongly by a moving target than a stationary one. The usual response in normal subjects and patients with peripheral vestibular damage is a suppression or disappearance of caloric nystagmus. In patients with central vestibular abnormalities there was insufficient suppression and vestibular nystagmus was superimposed on the tracking pattern. With this procedure the authors were able to detect patients with central vestibular dysfunctioning with 95% accuracy (Sakata & Umeda, 1976).

Models of schizophrenia have long posited abnormal vestibular functioning in the schizophrenic process.

The history of studies examining vestibular functioning in schizophrenia and related processes spans nearly six decades, beginning with a study by Pekelsky in 1921 in which inconsistent nystagmus responses to caloric and rotatory stimuli were observed. A variety of abnormalities have since been observed, from hyporeactivity in catatonia (Claude et al., 1927) through various abnormalities in catatonic and noncatatonic patients (Angyal & Blackman, 1940; Angyal & Sherman, 1942; Claude et al., 1932; Fitzgerald & Stengel, 1945; Myers et al., 1973), to normal vestibular responses (Rosenblum & Friedhoff, 1961). Studies of autistic children, while also indicating vestibular abnormality (Ornitz, Brown, Mason et al., 1974; Pollack & Krieger, 1958;

Ritvo, Ornitz, Eviatar et al., 1969; Ornitz, 1970), have shown the importance of arousal and visual fixation in defining variability in the vestibular response. Levy, Holzman & Proctor, (1978) emphasized the importance of controlling the variables of arousal and visual fixation in providing reliable measurement of vestibular reactivity, and noted that not only has the majority of studies examining vestibular reactivity in schizophrenia not employed clinically reliable procedures, but only one study (apart from their own) has controlled for fixation and none for level of arousal. The results of their study--which followed acceptable clinical procedure, used electrophysiologically recorded eye movement activity, and controlled for arousal and fixation--failed to replicate previous studies in finding lower response intensity, latency, culmination time or a prevalence of significant asymmetry. However, significantly greater dysrhythmic responses were observed in both chronic deteriorated and recent schizophrenics. Dysrhythmia represents the interruption of orderly nystagmus, and the degree of dysrhythmia has been assessed using a four grade rating scale devised by Lidvall (1961). Levy et al., (1978) could not determine whether the observed dysrhythmia represented CNS malfunctioning, methodological artifact or psychological factors in schizophrenia, but thought that peripheral vestibular disease was unlikely. The authors suggested, however, that the dysrhythmia might be related to

the existence of a suspected core attentional dysfunction in schizophrenia.

The effects of drug therapy on vestibular responses of psychiatric patients is uncertain. Shuster (1965) noted some depression in vestibular responses of patients on phenothiazines, but the results in schizophrenics tested before the advent of tranquilizers also showed this tendency to hyporeactivity. A later study (Myers et al., 1973) which employed electrophysiological measures of eye movement noted the same hyporeactive vestibular responses in chronic schizophrenics who had been medication free for over a year.

The fragmentary and often contradictory reports of the existence of a vestibular deficit in schizophrenics makes interpretation of findings difficult. The study by Levy et al., (1978) which failed to find evidence of vestibular dysfunctioning other than dysrhythmia, may reflect the emphasis placed on peripheral indicators of vestibular reactivity. The integration by the vestibular system of visual and other sensory input, and the effect of afferent vestibular discharges on other oculomotor systems remain to be explored in these patients.

SYNOPSIS AND HYPOTHESES

The consistently reported observation of deviant eye tracking in psychotic patients has been interpreted (Holzman & Levy, 1977) as reflecting a "disorder of non-voluntary attention" (page 22). The deviant tracking is expressed as disruption of visual focus continuity. The fundamental role of eye tracking in visual perception, and its potential use as a diagnostic tool, underscores the importance of defining the specific mechanisms underlying impaired tracking in psychoses.

The involvement of the vestibular system in the control of pursuit and saccadic eye movements, together with the frequently reported vestibular abnormalities in schizophrenia, suggest possible involvement of the vestibular system in the aberrant tracking observed in psychoses. Standardized stimulation and evaluation techniques, combined with the specialized technique capable of differentiating between peripheral and central vestibular dysfunctioning, make it possible to assess the nature of vestibular involvement in tracking aberrations in psychiatric patients.

The present study investigates the vestibular responses of psychiatric patients following vestibular activation alone and in conjunction with smooth pursuit tracking, within the context of a general standardized electronystagmographic examination. It is expected that vestibular and smooth pursuit tracking

aberrations will be related. More specifically it is hypothesized that:

1. Psychiatric patients will evidence more general abnormal vestibular responses than normal controls, and patients with active psychotic symptomatology will show more abnormal vestibular responses than patients with remitted symptomatology or normal controls. The parameters of vestibular reactivity to be examined for irregularities will include: speed of slow phase, speed of fast phase, peak nystagmus frequency, duration, latency and dysrhythmia.
- 2a. On baseline recordings patients with active psychotic symptomatology will show a higher frequency of tracking aberrations than either a remitted group or normal controls. This represents a replication of previous work.
- b. These same patients will show an enhancement of tracking aberrations during vestibular activation relative to either comparison group. Aberrations in tracking will be operationally defined as velocity arrests.
3. In contrast to either patients with remitted psychotic symptomatology or to normal controls, patients with active psychotic symptomatology will show evidence of

a vestibular deficit indicative of central disorder, i.e., failure of suppression of vestibular nystagmus with visual fixation.

METHODOLOGY

Subjects:

Forty psychiatric patients and twenty non-hospitalized normal controls were studied. The patient population was recruited from the Department of Psychiatry Inpatient and Outpatient Clinics of the Ottawa General Hospital. Non-hospitalized controls were recruited on a voluntary basis from among hospital staff and the local population.

The psychiatric population consisted of twenty hospitalized patients and twenty patients receiving treatment on an outpatient basis. The inpatients were individuals diagnosed actively psychotic and in need of intensive psychiatric care. Diagnosis of psychoses and psychotic symptomatology was based on two independent psychiatric evaluations according to DSM III criteria, hospital diagnosis and patient history charts. Information regarding length of illness, medication history, premorbid precipitating factors and subtypes of schizophrenia were obtained from the patient charts. Additionally, 34 of the patients (six could not be tested) were administered the Rorschach Ink Blot test and the vocabulary subtest of the Wechsler Adult Intelligence Scale (WAIS). Verbatim responses to the Rorschach were used as a separate measure of psychotic symptomatology. Schizophrenic thought disorder measured by this test was

independently rated by two clinical psychologists employing criteria outlined by Rappaport et al., (1968). The WAIS was included to provide a further index of bizarre or inappropriate thought.

Included in the inpatient group were four new patients with no previous history of psychosis, ten patients with a precipitating onset and acute course, and six patients with chronic conditions. None of the patients had been hospitalized for more than a year, or was then currently hospitalized for longer than six months. All patients were receiving medication, i.e., phenothiazines, butyrophenones or lithium carbonate. All patients in the outpatient group had been previously diagnosed schizophrenic, and all were receiving injections of the depot phenothiazine--fluphenazine decaonate. This group contained five patients with the diagnosis of remitting psychoses, five with chronic courses and ten patients with an acute course of illness. All outpatients were free from acute psychotic symptomatology.

Control subjects were questioned in detail with respect to medical history, medication, alcohol intake, and personal and family history of mental illness. The Rorschach Ink Blot test and the vocabulary subtest of the WAIS were administered to the normal controls, and were scored according to procedures described above for similar data from the patient population.

All subjects met the following criteria for inclusion in the study: 20-60 years of age, minimum I.Q. of 80, and bilaterally intact tympanic membranes. Individuals with a history of alcoholism, audiological deficits, peripheral vestibular damage, and motor abnormalities (e.g., tardive dyskinesia), were not included. Individuals on medication known to affect eye movements or vestibular responses such as, barbituates, tranquilizers from the benzodiazepine group, stimulants or antihistamines were not included. An additional requirement for patient selection was a normal EEG, this was determined by examination of the neurological report available on each patient. The demographic characteristics of subjects in this study are listed in Table 1. There is no difference in mean age or gender distribution across subject groups.

Procedure:

A variation of the widely accepted Fitzgerald-Hallpike technique of caloric irrigation (1942) 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. In view of the absence of asymmetry in a recent large scale study of

TABLE 1
Demographic Characteristics of Subject Groups

Group	Subtype	n	Diagnosis	n	Medications	n	Age		Gender		Duration of Illness		
							M	SD	Male	Female	n	Time	
<u>Inpatients</u>	New	4	Schizoaffective	6	Phenothiazines	10					5	< 6 mos.	
	Acute	10	Paranoid Schizophrenia	5	Butyrophenones	5							
			Nonparanoid Schizophrenia	5	Lithium Carbonate	5	30.2	8.6	9	11	3	< 2 yrs.	
	Chronic	6	Schizophrenia	5									
			Manic Depressive	4									12
	<u>Outpatients</u>	Acute	10	Schizoaffective	4							2	< 1 yr.
Chronic		5	Paranoid Schizophrenia	9	Modecate (Depot Phenothiazine)	20	30.8	8.8	10	10	3	< 2 yrs.	
			Nonparanoid Schizophrenia	7								15	> 2 yrs.
<u>Controls</u>		20					30.3	9.8	7	13			

psychiatric patients (Levy et al., 1978), and considering the additional discomfort engendered by the extended testing sequence upon patients, it was decided to irrigate with cool water only. An index of response symmetry could still be ascertained from bilateral comparisons of other test parameters.

Prior to recordings all subjects signed forms of informed consent and details of the experimental procedure were related and reviewed with special emphasis on probable behavioural effects of caloric stimulation, (e.g., vertigo). An otoscopic examination was conducted to ensure integrity of the tympanic membranes, and excess cerumen was removed from the external auditory meatuses. Beckman miniature silver-silver chloride electrodes were attached to the outer canthus of each eye for recording the horizontal electrooculogram (HEOG), and placed above and below one eye for monitoring vertical eye movements (VEOG) and blink artifact. A ground electrode was placed in the mid-forehead region. All eye movements were recorded on DC-35Hz amplifiers (Grass Model 7P122). Electrodes were also attached for monopolar recording of electroencephalographic (EEG: O_2/A_2) activity, and recording of facial electromyographic (EMG) activity. All electrographic and stimulus-response data were recorded on paper write-out (Grass Model 78D polygraph) (see Figure 1) and stored on magnetic tape (Hewlett Packard 8868A tape recorder).

Once electrodes were attached, the subject reclined on a cot with head elevated 30° to assume the proper ventroflexed position for caloric (vestibular) testing. Following calibration procedures, spontaneous eye movements with eyes closed were recorded for a period of 30 seconds. By the time caloric testing began, the subjects had been in the lighted room for approximately 20 minutes. Each irrigation extended over a 30 second period. Water cooled and maintained at 30°C by a Grass Instruments 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 250 ml.

The primary experimental task required subjects to track a light emitting diode (2 mm in diameter) attached to the arm of a motorized pendulum. In the caloric testing position the tracking target was viewed in a mirror positioned approximately 18 cm from the subject's eyes, with a distance of 84 cm between the center of the mirror and the pendulum. Effectively, the target light was situated at eye level one meter from the subject. The pendulum was programmed to oscillate at the rate of one excursion every 2.2 seconds (.45Hz). This frequency permits effective tracking, and fixation of targets moving at $<.5\text{Hz}$ effectively suppresses vestibular nystagmus. During pendulum tracking the subject's head was stabilized by head supports attached to the side of the testing table.

Subjects were instructed to depress a hand-held button whenever the target light was interrupted (off cycle, 200 msec). Six to ten interruptions were distributed throughout each eyes-opened period. Since it has been demonstrated repeatedly that the performance of mental tasks, especially mental arithmetic, augments the vestibular response (Collins, 1964; Barber & Stockwell, 1976), a mental alerting task was incorporated into the vestibular testing procedure. This procedure involved serial subtraction by threes. Subjects were instructed to start performing the mental alerting task at the beginning of each period not involving pendulum tracking, i.e., following irrigation, continuing for 50 seconds, including a 20 second period of fixation on the target, and continuing after tracking until signalled by the experimenter to stop. This point of cessation occurred when the last nystagmus beat was detected. The tracking task was presented at the point of maximum culmination of nystagmus (Torok, 1972), approximately 60 seconds after irrigation. The total recording time required for one subject to complete all procedures was approximately one hour.

Three experimental conditions were presented in random order (Table 2). The conditions were: 1) baseline eye tracking; 2) caloric eye tracking; left ear irrigation; and 3) caloric eye tracking; right ear irrigation. Each condition consisted of:

TABLE 2

Conditions and Procedures for Baseline, Vestibular Activation and

Smooth Pursuit Tracking Measurement

Conditions	Eyes Closed	Eyes Closed	Eyes Open	Eyes Open	Eyes Open	Eyes Closed
Baseline		Mental Alerting	Fixation	Tracking	Tracking	Mental Alerting
			Mental Alerting	Button Press	Button Press	
Caloric			Mental Alerting			
Left Ear	Irrigation	Mental Alerting	Fixation	Tracking	Tracking	Mental Alerting
			Button Press	Button Press	Button Press	
Caloric			Mental Alerting			
Right Ear	Irrigation	Mental Alerting	Fixation	Tracking	Tracking	Mental Alerting
			Button Press	Button Press	Button Press	
	0	30	60	80	110	

Continuous Time (secs)

a) an initial 30 second period with eyes closed; b) a 30 second period with eyes closed while performing the mental alerting task; c) a 20 second period of continued mental alerting while focusing on the small target light and responding to periodic interruptions of this target light with a button press; d) engaging in pursuit tracking of the same target light oscillating at .45Hz for a 30 second period; 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 not present. A minimum of eight and one half minutes elapsed from the onset of the first irrigation to the onset of the second. This time period permits the system to regain a resting state.

A third irrigation (referred to as Caloric III) was administered to determine the effects of mental alerting on the vestibular nystagmus. This condition was presented last, did not include the tracking task, and the order of the mental alerting/no mental alerting task was balanced within and across subjects.

DATA ANALYSIS

A. Reduction of vestibular data

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

1. Latency: the interval between the beginning of irrigation and the onset of nystagmus. Criterion for the presence of response was the first time three nystagmus beats were seen within a 3 second interval.
2. Duration: the interval between the beginning of irrigation and the last beat of nystagmus. Criterion for the absence of response was the last time two nystagmus beats were seen within a 5 second interval.
3. Peak nystagmus frequency: the average frequency of nystagmus beats during the 10 second interval (usually 50-60 seconds after onset of irrigation) in which the nystagmus was most intense.
4. Response strength: the maximum slow phase speed during the 10 second interval in which the response was most intense (usually 50-60 seconds after onset of irrigation). The procedure for calculating the slow phase speed by differentiation was as follows (see Figure 2): the tape recorded calibration signal of the corneo-retinal potential for each subject for a 10^0 visual arc was adjusted to yield a sensitivity of 10^0 /cm. The Grass Model 7P21 differentiator (velocity)

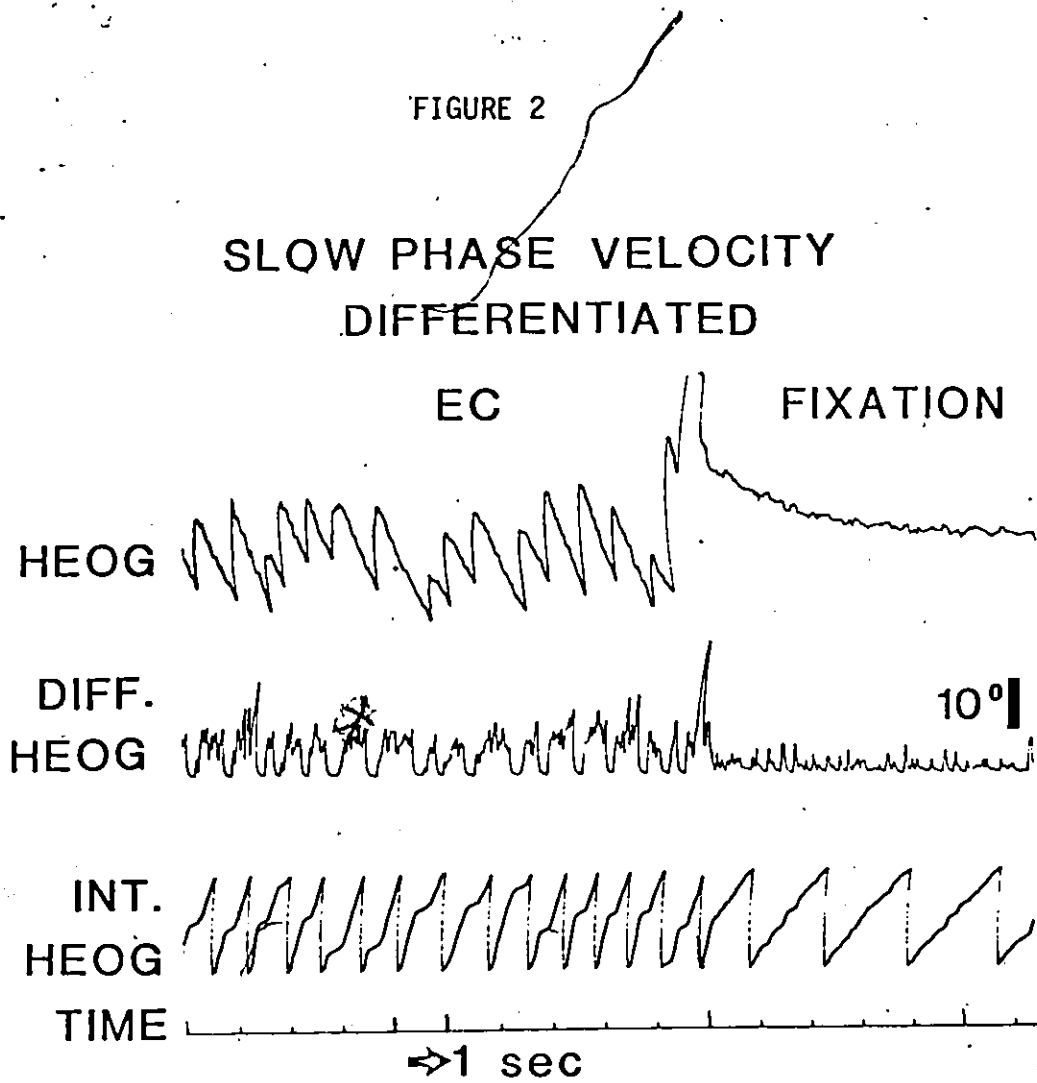


Figure 2: Measurement of nystagmus--slow phase velocity--by differentiation. HEOG--horizontal electrooculogram depicting nystagmus in the eyes closed (EC) condition and suppression in the eyes opened fixation condition. Diff. HEOG--differentiated nystagmus. The amplitude of the trace represents the velocity of the slow component of nystagmus. Int. HEOG--integrated nystagmus, the number of resets reflects variations in amplitude of the HEOG trace.

channel was calibrated for 10^0 /sec/cm. The nystagmus recordings were input directly from the tape recorder into the nystagmus differentiator, and the speed of the slow phase was read directly from the velocity channel. The computational procedure for calculating the slow phase speed is depicted in Figure 3. This method was compared to the differentiator output. The averaged slow phase velocity for the 10 second period of maximum intensity was used as an indicator of response strength.

5. Fast phase velocity: the maximum fast phase speed was measured during the 10 second interval in which the response was most intense (usually 50-60 seconds after beginning of irrigation). This measure of saccadic velocity was analyzed using a PDP 11/34 minicomputer. The tape recorded horizontal EOG voltage transient corresponding to a 20^0 saccade initiated by the subject transferring gaze from one point to another was used to calibrate corneo-retinal potential. The EOG data were digitized at the rate of 200 points/second, and the computer generated a series of digital values corresponding to number, amplitude, duration and velocity of the EOG activity.
6. Fixation suppression: the measure of the effectiveness of visual fixation in suppressing nystagmus was calculated by the following procedure:

FIGURE 3

MEASUREMENT OF NYSTAGMUS: SLOW PHASE VELOCITY

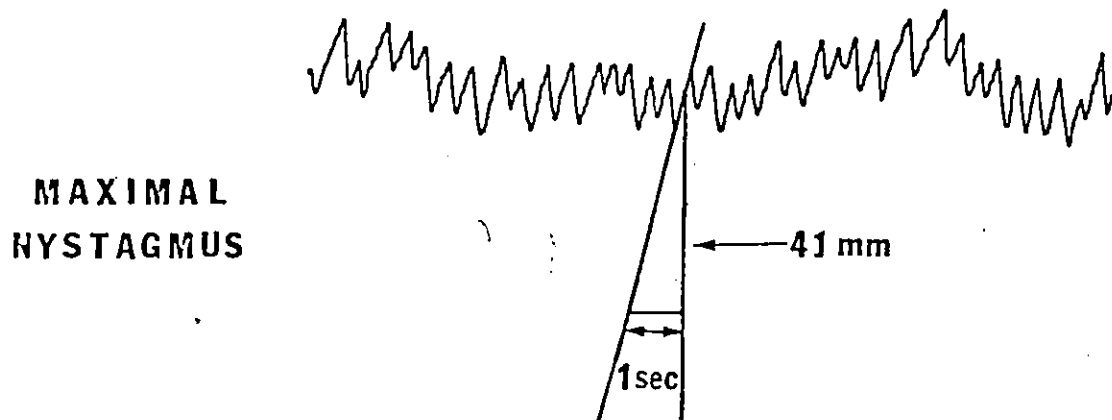


Figure 3: Measurement of slow phase velocity of nystagmus response:
conventional determination of slow phase velocity.

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

The percent reduction is denoted as the fixation suppression (FS) value. This value was obtained by subtracting the mean slow phase velocity of 10 seconds of nystagmus occurring while eyes were opened and fixated from the mean slow phase eye speed of 10 seconds of nystagmus occurring just before the eyes were opened, and dividing by this same control value. Fixation suppression was reported as a percentage.

7. Dysrhythmia: this measure of nystagmus irregularity was assessed for a 30 second period beginning 30 seconds after the beginning of irrigation. Two individuals naive with respect to subjects' group membership rated coded recordings of nystagmus according to the scale devised by Lidvall (1961) (see Appendix A). Interrater agreement for this analysis was 96.5%.

B. Reduction of pursuit tracking data

Pursuit tracking patterns were analyzed for the incidence of velocity arrests (VAs) using a methodology commonly employed in the analysis of smooth pursuit tracking patterns in psychiatric patients (Holzman et al., 1973, 1974, 1978; Shagass et al., 1974, 1976; Pivik, 1979). In this procedure the tape recorded HEOG tracing was filtered (low pass filter, 5.5Hz; attenuated 21 db at cutoff; 48 db rolloff/octave), amplified and differentiated

(Grass 7P21A Differentiator) to obtain the first derivative (velocity) of the sinusoidal tracking pattern (see Figure 4). The differentiated output was calibrated at a sensitivity of $20^{\circ}/\text{sec}/\text{cm}$. Half wave differentiator tracings were scored according to previously established criteria (Shagass et al., 1974; Pivik, 1979), such that a VA constituted a slowing of eye velocity to $\leq 2^{\circ}/\text{sec}$. 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. Each half wave differentiator tracing contained two obligatory VAs, which occurred at the end points of the oscillation. Accordingly, the half wave method of analysis artificially doubles the number of obligatory arrests. These were included in the analysis. The number of VAs present during perfect tracking of ten oscillations would be 40 - 2 VAs for each of 20 half waves. Two individuals naive with respect to subjects' group membership independently scored coded records of the differentiated playbacks after establishing a high level of interrater agreement (95.8%). Interscorer agreement for the 3,600 comparisons was 94.5%, and discrepancies in the scoring of the coded data were discussed and resolved.

The differentiated recordings were also examined for the presence of positive saccadic eye movements. During such movements, eye velocity exceeds the maximum target velocity and

FIGURE 4

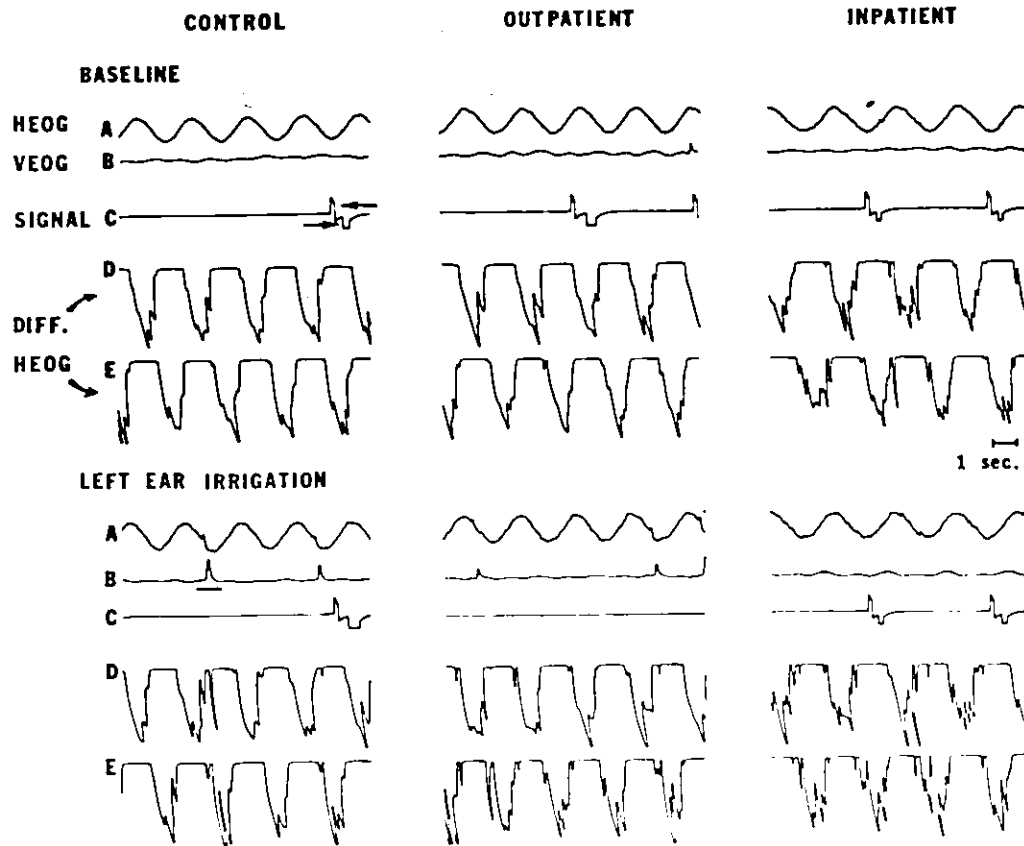


Figure 4: Determination of velocity arrests by half-wave differentiation of the sinusoidal pursuit tracking pattern. A) HEOG--horizontal electrooculogram. B) VEOG--vertical electrooculogram--the underscored signal represents a blink. C) SIGNAL--the arrows designate target light interruptions (upward deflection), and the subject's response (downward deflection). D and E) DIFF. HEOG--half-wave differentiated display of HEOG signal. Each column represents one experimental group, and recordings obtained during baseline, and following caloric irrigation.

overshoots the tracking target. A positive saccade was scored when tracking velocity exceeded maximum pendulum velocity by 33.3%. Additionally, vertical EOGs were played back with the differentiated horizontal EOG information to permit time related analysis of blinking and VAs. Eye deviations in the vertical EOG recordings of 1 mm (50 uv) lasting 200-500 msec were scored as blinks. Blink related VAs, and VAs which occurred during head movement (EMG channel) were excluded from the data analysis.

C. Statistical Analysis

Unless otherwise indicated, data for the dependent variables were analyzed using Analysis of Variance with Repeated Measures (BMDP2V, 1977), with the Scheffé post-hoc procedure for multiple contrasts applied if the F ratio was significant at the .05 level. All other statistical treatment of data are specified in the text. Level of statistical significance was based on two-tailed criterion.

Independent variables consisted of groupings according to hospital and psychological test diagnosis, medication, performance on the attention monitor task, as well as the various conditions of testing (e.g., order of irrigation, baseline, alerting condition).

RESULTS

VESTIBULAR RESPONSES: GROUP COMPARISONS

Slow Phase Velocity

The mean group differences across testing conditions for the slow phase velocity of the vestibular response are presented in Figure 5. There were no significant group or condition effects for this parameter. The values obtained for all subject groups corresponded to normal values reported in earlier studies (Henriksson, 1955; Stahle, 1958; Brookler & Pulec, 1970). All bilateral comparisons of the vestibular response were within the normal range of variability (Barber & Stockwell, 1976).

Fast Phase Velocity

A significant overall main effect for group was found across all conditions for the fast phase velocity ($F(2,114) = 7.88, p < .01$, Figure 6). Post-hoc procedures revealed that inpatients showed a significant slowing of mean fast phase velocity relative to normal controls for all conditions: caloric I ($p < .01$); caloric II ($p < .005$); caloric III ($p < .005$). Outpatients showed a similar reduction in fast phase velocity, but it was not significantly different from either comparison group. No significant differences for condition effect were found. The slowing of the fast phase velocity following caloric irrigation has been previously observed (Ron et al., 1972) and was therefore expected. However, the

FIGURE 5

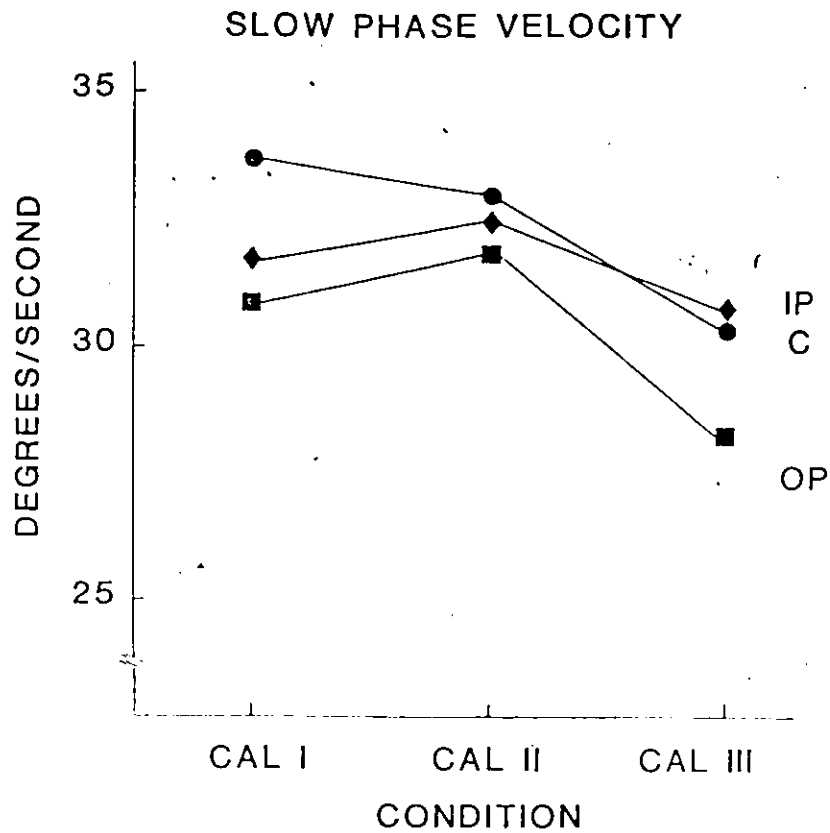


Figure 5: Mean slow phase velocity of nystagmus across caloric conditions. The response was obtained for a 10 second period (50-60 seconds after onset of irrigation) while subjects' eyes were closed and they were engaged in mental arithmetic. The abbreviations IP, OP, and C which appear in this and subsequent figures refers to Inpatients, Outpatients and Controls, respectively.

FIGURE 6

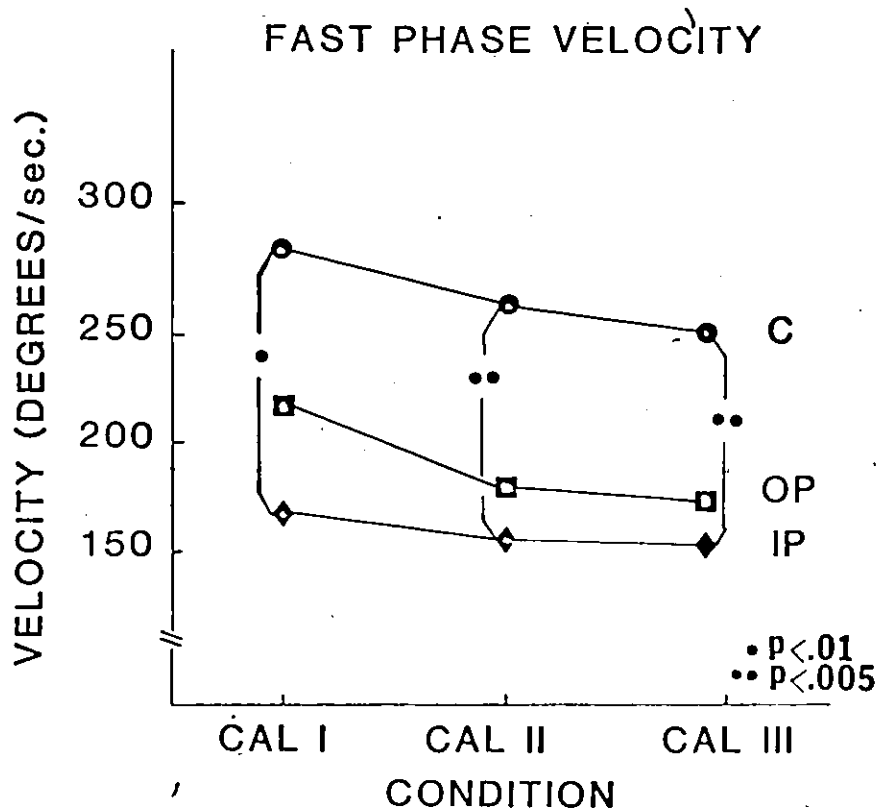


Figure 6: Mean velocity measurement of the fast phase component of nystagmus taken during caloric irrigation procedures. The measure reflects the mean velocity of the quick component for a 10 second period during the maximum nystagmus response (50-60 seconds after onset of irrigation) while subjects' eyes were closed and they were engaged in mental arithmetic.

values reported for the inpatient group lie outside the limits found for normal control subjects in this study.

Peak Frequency, Duration and Latency

No significant overall main effect for frequency (mean number of beats in 10 seconds) was obtained for the nystagmus response across conditions. Separate one-way analyses of variance (ANOVAs) procedures performed for each condition revealed significant group effects particular to each condition (see Figure 7); caloric I ($F(2, 57) = 8.96, p < .001$); caloric II ($F(2, 57) = 11.02, p < .001$); and caloric III ($F(2, 57) = 4.49, p < .025$). Post-hoc analyses revealed that outpatients had significantly higher frequency of nystagmus beats than normal controls for all conditions (caloric I and II, $p < .001$; caloric III, $p < .002$). Inpatients had a significantly higher frequency of nystagmus beats than normal controls on caloric I and caloric II ($p < .01$). Nystagmus frequency measurements of inpatients and outpatients did not differ significantly. The values obtained for all subject groups for the peak frequency response are within the normal limits (Barber & Stockwell, 1976). The values obtained for latency and duration of the nystagmus response did not vary significantly across groups or conditions, and were within the normal limits previously reported (Stahle, 1958).

FIGURE 7

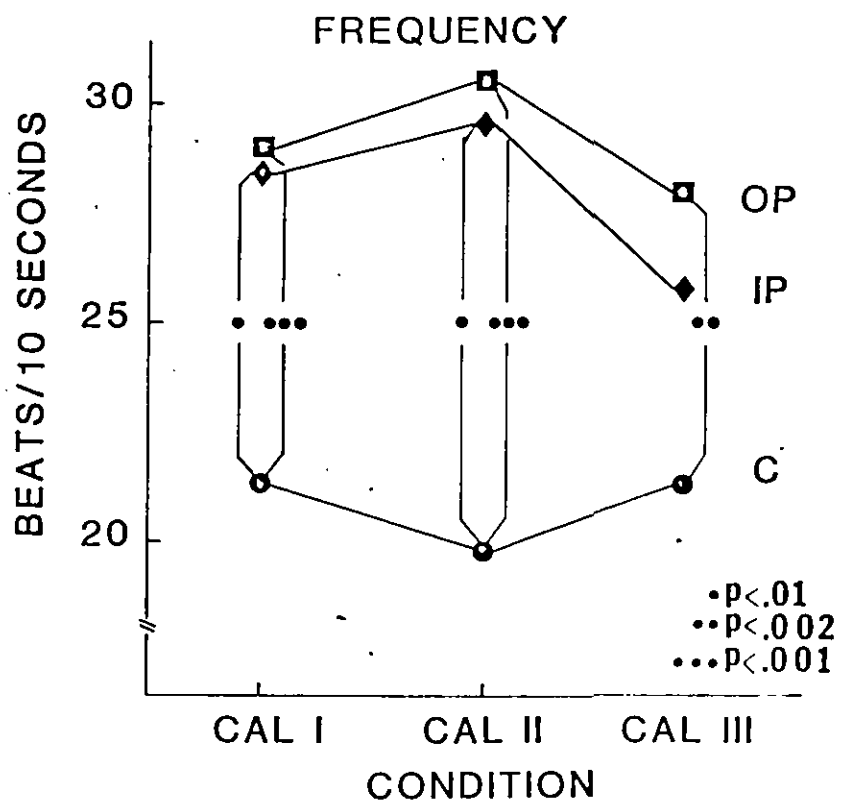


Figure 7: Group variations in frequency of nystagmus beats during a 10 second period (50-60 seconds after onset of irrigation), while subjects' eyes were closed and they were engaged in mental arithmetic.

Dysrhythmia

Sixty-five percent ($n = 39$) of all subjects showed some evidence of dysrhythmia (grades 1 to 3). Only 16 percent ($n = 10$) had ratings reflecting significant (grade 3) dysrhythmia. No significant differences between groups were noted for the first irrigation, but t tests revealed significantly higher dysrhythmia ratings for both patient groups than for normal controls for the second irrigation: inpatients ($t(38) = 2.60, p < .02$), outpatients ($t(38) = 3.61, p < .001$). Dysrhythmia rating generally showed a linear relationship with fast phase velocity (see Table 3), and subjects with ratings reflecting grade 3 dysrhythmia had the slowest fast phase velocities across all three caloric conditions.

Mental Alerting

Reduction of the variability of the vestibular response not due directly to vestibular function by performance of simple tasks requiring sustained mental activity is thought to reflect a psychological state of alertness or concerted attending (Collins, 1974). The effect of the mental arithmetic task employed in this study was evaluated by measuring its effect on slow phase velocity--the most accurate measure of nystagmus intensity (Henriksson et al., 1972). A rise in the mean slow phase velocity while subjects were engaged in the mental arithmetic task as contrasted to performance during the no mental alerting condition was noted for all subject groups (Figure 8). No significant differences between conditions were found.

TABLE 3
Mean Fast Phase Velocity for all Subjects
Grouped by Dysrhythmia Rating

Fast Phase Velocity
Degrees/second

Grade of Dysrhythmia	<u>n</u>	Caloric I	Caloric II	Caloric III
3	10	143.5	108	123.9
2	5	219	219	158.
1	23	218	200	189.6
0	22	243	227	206

FIGURE 8

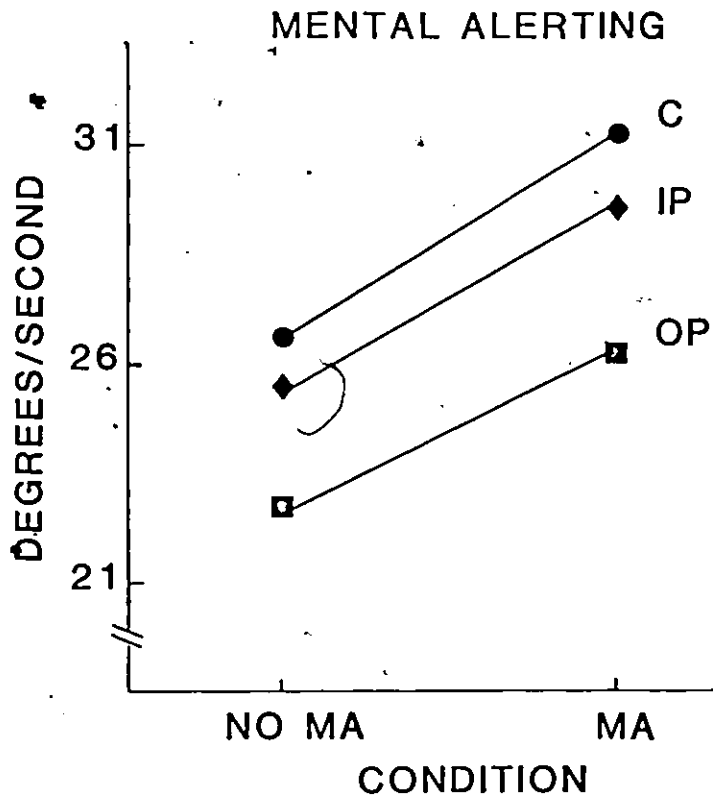


Figure 8: The effects of mental alerting on slow phase velocity following caloric irrigation.

Of the five dependent variables reflecting vestibular reactivity, inpatients differed significantly from normal controls on three: fast phase velocity, frequency and dysrhythmia. Outpatients differed from normal controls on two: frequency and dysrhythmia. There were no significant differences between inpatients and outpatients on any of these parameters.

FIXATION SUPPRESSION: GROUP COMPARISONS

The groups were compared with respect to the amount nystagmus (slow phase speed) was suppressed during the eyes-open-fixation condition. Mean percent suppression for all groups is presented in Figure 9. Separate Analyses of Variance for the two fixation conditions revealed a significant group effect for caloric I ($F(2,57) = 3.43, p < .05$), and caloric II ($F(2, 57) = 4.79, p < .025$). Post-hoc procedures revealed that the mean differences between inpatients and normal controls were significant for both conditions ($p < .05$). The outpatient group showed slightly less total suppression than normal controls, but the differences were not significant. The mean percent reduction reported in humans following 30°C caloric irrigation ranges from 84.2% (Kato, Kimura et al., 1977) to 50% (Takemori, 1977). Others report abnormal fixation suppression when the mean percent reduction is less than 60% (Kato et al., 1977; Sato, Kato et al., 1980). Demanez and Ledoux (1970) found that normal human slow phase velocity Ocular Fixation Indices (OFIs)--i.e., ratio of eyes open to eyes closed--

FIGURE 9

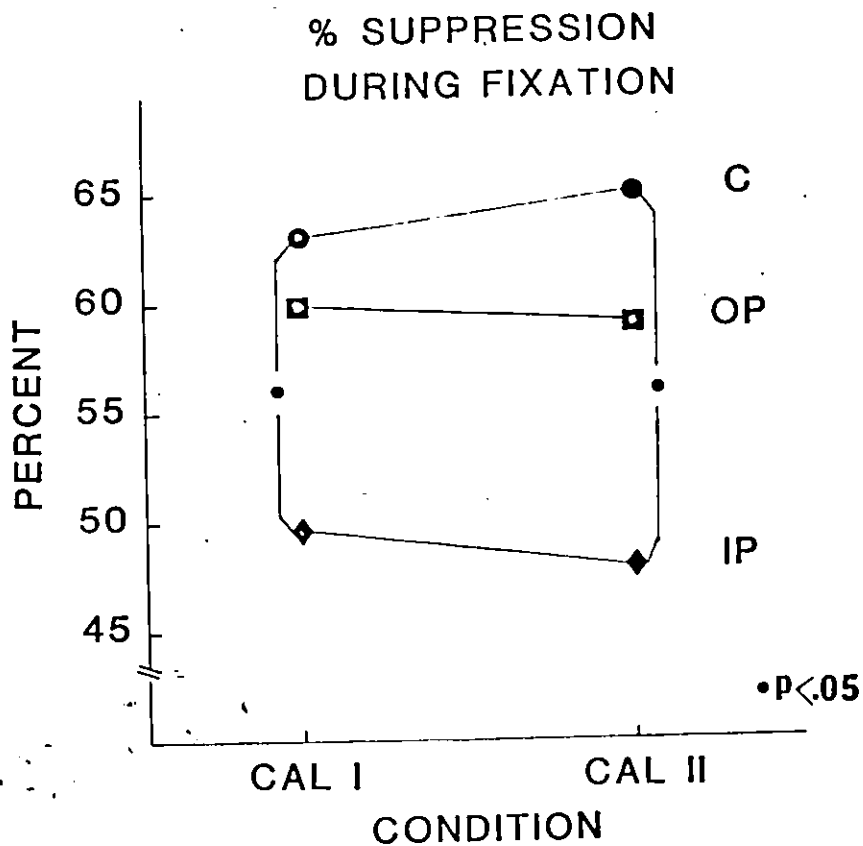


Figure 9: Mean percent suppression of nystagmus by fixation after caloric irrigation. The percent reduction in the slow phase velocity was determined by the following procedure:

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

ranged between 8 and 25%, and were always less than 50%. The inpatients in this study had OFIs which ranged between 23 and 100%, with an average mean of 53% (S.D. 20%). This might be compared with normal controls with a range between 15 and 75%, and an average mean OFI of 36% (S.D. 13%), and outpatients with an OFI range between 17 and 80%, with an average mean of 39% (S.D. 17%). t tests between the OFIs of inpatients and normal controls revealed significant differences for both caloric conditions ($t(38) = 2.34, p < .05$; $t(38) = 2.84, p < .01$). Inpatients had significantly higher OFIs than outpatients for the second caloric condition ($t(38) = 2.39, p < .05$). Additionally, 50% ($n = 10$) of inpatients had OFIs above 60%, whereas 15% ($n = 3$) of outpatients, and 5% ($n = 1$) of normal controls were above that level. Given the variability in the parameters defining normal/abnormal fixation suppression, the mean percent reduction and the OFIs of normal control subjects observed in this study would appear to be the most valid index against which to compare the performance of the patient populations.

VELOCITY ARRESTS: GROUP COMPARISONS

Group differences in mean VAs for all conditions are presented in Figure 10. A significant overall main effect for group was found ($F(2, 114) = 3.41, p < .05$). Post-hoc procedures revealed

FIGURE 10

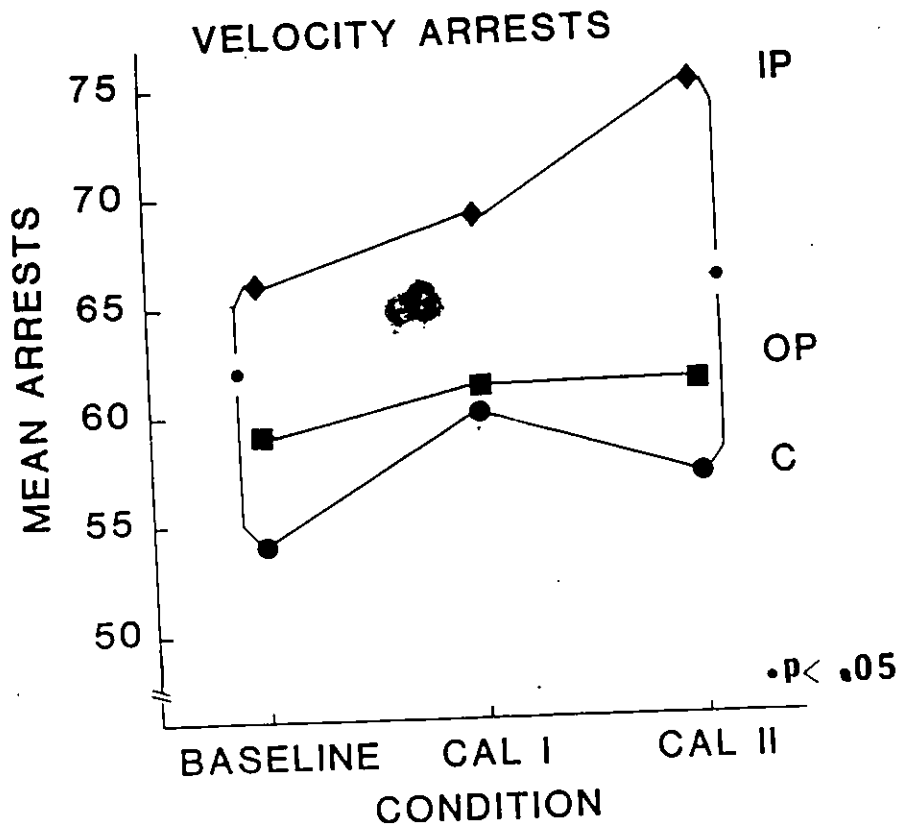


Figure 10: Mean number of velocity arrests (VAs) across conditions for patient groups and normal controls. The scores represent the number of VAs for 10 complete oscillations, or 20 half waves, and include obligatory arrests.

that inpatients had a significantly higher frequency of mean VAs relative to normal controls for baseline and caloric II conditions ($p < .05$). The outpatient group tracked less accurately than normal controls, but these differences were not significant. No significant differences were found between inpatients and outpatients for any of the conditions. Although there was no significant overall condition effect, the increase in the number of mean VAs for inpatients from baseline to caloric II ($t(38) = 1.72$) was significant at the .05 level for the one-tailed test.

A separate Analysis of Variance was performed on baseline measurements to determine whether, despite randomization of conditions, VAs were associated with presentation order in a systematic manner. This separate analysis was intended to provide information on the possibility that an increase in mean VAs with repeated irrigation might have reflected tonic excitability. The baseline condition, however, did not differ in total number of VAs across testing positions, and there was no group effect for presentation order.

BUTTON PRESS AND BLINKS: GROUP COMPARISONS

One measure of attention used in this study was the number of times subjects failed to respond with a button press to

interruptions of the target light. The mean number of failures to respond across all conditions was higher for inpatients (3.0 ± 1.86) than for either outpatients (1.95 ± 2.44), or normal controls (0.5 ± 0.83). Both patient groups made significantly more errors than normal controls on caloric I and caloric II (I > C: $p < .005$, $p < .005$; O > C: $p < .005$, $p < .01$). There were no significant differences between inpatients and outpatients.

To evaluate the effects of accuracy of button press response on the dependent variables separate ANOVAs compared those subjects from each group who responded with 100% accuracy to target light interruptions. These procedures revealed no change in the relative position of inpatients, who continued to show significant differences from normal controls, i.e., slower fast phase velocities ($p < .025$, $p < .005$), less fixation suppression ($p < .01$, $p < .025$), and more VAs ($p < .05$, $p < .025$, $p < .025$). Outpatients who made zero errors in responding to target light interruptions performed like normal controls in number of VAs and fixation suppression scores. No significant within group differences were found.

For all groups blinking increased, but not significantly during caloric tracking relative to baseline levels. The mean rate (across the three tracking conditions) for inpatients (9.45 ± 10.33) was higher than that for either normal controls (5.80 ± 7.20), or outpatients (4.74 ± 8.60). Of the total number of VAs, those associated with blinks (i.e., occurring within 200 msec from blink

onset) for the three groups were as follows: inpatients, 18.6%; outpatients, 11.1%; controls, 21%. Positive saccades had a low frequency across all groups and were not significantly related to VAs.

SUBCATEGORIES OF SCHIZOPHRENIA

The comparison of hospitalized patients with nonhospitalized patients and normal controls yielded an estimate of the relationship between severe psychiatric illness and the various measures of vestibular reactivity and VAs. Statistically significant differences between hospitalized patients and normal controls were found for fast phase velocity, frequency, dysrhythmia, fixation suppression and VAs. Of concern here is whether diagnostic category, as determined from psychiatric evaluation and hospital charts (DSM III criteria), affects these measures. A series of statistical procedures (ANOVAs and t tests) was applied to determine the difference between normal controls and each diagnostic group with respect to vestibular reactivity and VAs.

The results of the analyses produced general overall differences between diagnostic categories and normal controls, but the degree of these differences varied across dependent measures (see Table 4). Of interest, was the high number of VAs associated with the schizo-affective subgroup, and the abnormally low fixation suppression scores for the manic-depressive subgroup. However, 80 percent of these patient subgroups were hospitalized, while only 38 percent of the paranoid schizophrenics, and 45 percent of the nonparanoid schizophrenics

TABLE 4
Means of Significant Dependent Variables by Subject Group (Hospital Diagnosis)

Subject Groups	n	VAS		Fast Phase °/sec.		Fixation Suppression %	
		Mean	SD	Mean	SD	Mean	SD
Schizoaffective	10	72.9	15.0	188	86.3	54	20
Manic-Depressive	4	65.1	6.7	163	90.0	26	23
Paranoid Schizophrenia	14	64.2	17.3	182	68.0	55	17
Nonparanoid Schizophrenia	12	58.9	12.8	187	125.0	57	19
Controls	20	57.0	9.0	264	91.0	63	13

were hospitalized. This effect may therefore be attributable to severity of illness rather than diagnostic category.

A series of ANOVAs performed to determine whether diagnosis by course of illness (acute, chronic, remitting) would provide a stable and significant index of the relationship between psychiatric illness and the various dependent measures revealed no significant relationships. This finding possibly reflects the non-deteriorated condition of the chronic patients, and the inclusion of hospitalized and non-hospitalized patients in both the acute and chronic categories.

An analysis based on psychological test diagnosis was performed in a further attempt to isolate characteristics of the patient population contributing to the significant group differences. When the patients were re-classified into groups characterized by active or remitted symptomatology (two records could not be classified in either category) as assessed by the Rorschach, consistent differences between the groups were found for fast phase velocity, fixation suppression, and mean VAs. The only significant difference was found on the baseline measure of mean VAs ($p < .05$) (Figure 11). The group differences were in the expected direction, that is, patients classified as actively psychotic had more response variables significantly different from normal controls than did the remitted group. Seventy-five percent of patients classified actively psychotic by the Rorschach were in the hospitalized group, whereas only 31 percent of the hospitalized patients were contained in the remitted

FIGURE 11

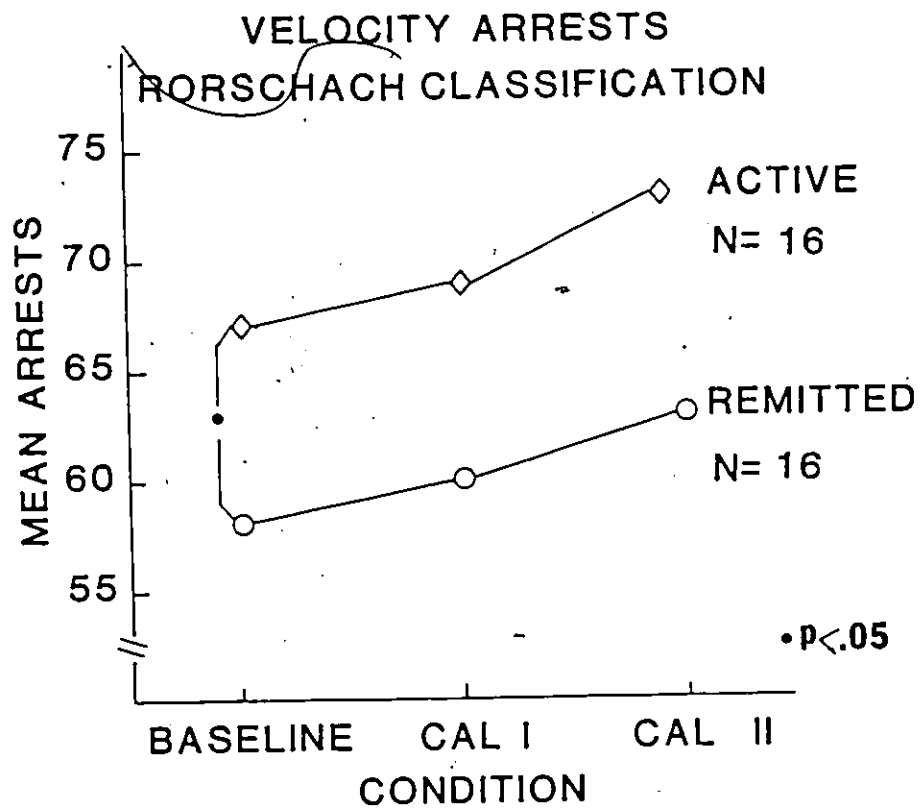


Figure 11: Variations in mean number of velocity arrests across conditions for patients regrouped by Rorschach classification. The captions Active and Remitted refer to the presence or absence of psychotic symptomatology in the Rorschach record.

group. The composition of the groups as classified by the Rorschach was generally similar to that of the original groupings of hospitalized, non-hospitalized and normal controls. None of the normal control subjects was rated psychotic. General interrater agreement was 96 percent.

NEUROLEPTIC MEDICATION

To evaluate the effects of neuroleptic medication on the dependent measures, the patients were subdivided according to length of time on medication. The results of the ANOVAs suggested that this variable did not significantly differentiate among the groups. However, this re-classification which combined hospitalized and non-hospitalized patients in each of the divisions confounded the effects of severity of illness, and this may have influenced the medication-related analysis.

A second series of analyses correlated amount of medication with the dependent variables. Dosage level across medications (except for lithium) was made equivalent to an approximate daily dosage of chlorpromazine (Koda-Kimble, Catcher, Young, 1978). None of the correlations was significant, suggesting that amount of medication, per se, did not account for the differences observed. Of the five patients receiving lithium carbonate three were also receiving neuroleptics. A comparison of the performance means across the dependent variables between the lithium only and lithium plus neuroleptic group revealed similar values. t tests performed

to determine whether the performance of patients receiving lithium carbonate differed from patients receiving neuroleptics did not reveal significant differences.

A further point with respect to medication effects is the lack of significant differences between the outpatient group--all of whom received a depot phenothiazine (Modecate)--and normal controls on number of VAs and fixation suppression. Inpatients who received this same depot phenothiazine ($n=4$) had consistently higher numbers of VAs, slower fast phase velocities, and lower fixation suppression scores than the outpatient modecate group. t tests revealed that the inpatient modecate group had significantly more VAs for both baseline ($t(22) = 3.20, p < .01$) and caloric II ($t(22) = 2.68, p < .02$) conditions. In summary, it appears that neuroleptic medication alone did not account for the differences between patients and normal controls, but some interaction between medication and clinical status (severity of psychiatric illness) appears possible.

DISCUSSION

Vestibular Responses

The present study provided an assessment of the vestibulo-ocular response to caloric irrigation in psychiatric patients and also focused upon the possible contribution of the vestibular system to deviant pursuit eye tracking. The usual measures of the response to caloric irrigation such as slow phase velocity, duration, latency, frequency and bilateral symmetry of the response, were found to be within the normal limits for all subject groups when compared with values reported elsewhere (Stahle, 1956; Henriksson, 1972; Gulick & Pfaltz, 1964). Additional response measures, however, revealed significantly reduced fast phase velocities, and reduced suppression of nystagmus with visual fixation for the hospitalized psychotic patients--findings which have not been previously reported for this group of patients.

It is generally agreed that normal slow phase velocity, including the absence of asymmetry or distortions of this measure, reflects integrity of the vestibular-labyrinth system. It is noteworthy, however, that whereas in this study and others involving psychiatric patients (Levy et al., 1978) these measures indicate normal vestibular functioning, there have been consistent reports of absent or diminished or dysrhythmic nystagmus which have not been explained (Angyal & Blackman, 1940; Myers et al.,

1973; Levy et al., 1978). In the present study, absent vestibular responses were not found, in fact, patients showed a higher frequency of nystagmus beats than normal controls. An increase in the frequency of nystagmus beats coincided with lower amplitude slow eye deviations, but does not support reports of hyporeactivity in psychiatric patients (Angyal & Blackman, 1940; Fitzgerald & Stengel, 1945; Ornitz, 1970; Myers et al., 1973). Coincident with higher frequency-lower amplitude slow deviations, the patient populations had significantly more dysrhythmia and slower fast phase velocities.

In the vestibular response, the fast phase is the eye movement which returns the eyes to the periphery between the slow deviations. The fast phase takes the eyes into the direction in which the head is turning and occurs before the slow phase has brought the eyes back to midline (Melvill Jones, 1964). The function of the fast phase is to put the visual apparatus into that orientation of the visual world into which the head or body is turning. It has been shown that fast phases, like all rapid eye movements, including saccades, refixation saccades, microsaccades are regulated by the same neural mechanisms (Goto et al., 1968; Ron et al., 1972; Sharpe et al., 1975). These eye movements are thought to be generated by closed feedback loops in the pons which compare instantaneous eye position to desired eye position and drive the eyes until they are equal (Robinson, 1975). Evidence that quick phases of nystagmus are generated in the pons is mainly

derived from lesion studies. The strongest evidence that the paramedian pontine reticular formation (PPRF) is the site of origin of fast phases of nystagmus is that fast phases are profoundly affected or abolished by lesions of this area (Cohen et al., 1968; Lorenté de No, 1933).

Slowing of saccadic eye movements has been related to dysfunctioning of brain stem nuclei, especially of the pontine reticular formation (Giesenberg & Robinson, 1977), as a result of lesion or physiological modulation of this region. In the absence of other conspicuous CNS manifestations, it is doubtful that the slowing of the fast phase velocities in patients arises from lesion or structural damage. A number of other factors affect the triggering and amplitude of rapid eye movements, including the fast phase of nystagmus. Initial eye position, ongoing eye movement, head position and level of alertness are the most striking (Goto et al., 1968). Many of the patients had low amplitude-high frequency slow phase nystagmus which would require a smaller amplitude (and slower velocity) return movement. Saccadic eye movements and the fast phase are also differentially sensitive to decreased alertness (Sharpe et al., 1975; Bahill & Stark, 1975; Henriksson, 1972). During drowsiness the fast phase can be markedly attenuated, while slow movements or tonic deviations persist unchanged (Collins, 1962; McCabe, 1965). The slowing of

the fast phase of nystagmus for the patient groups might then be related to the amplitude-frequency characteristics of the nystagmus response, or the level of alertness rather than to any defect in the pontine system controlling eye movements.

A significant number of the patient population had dysrhythmic nystagmus which coincided with periods when the fast component velocity was slowed. It is suggested that the same mechanisms underlie the deficits in these response parameters, but their presence seems incompatible with peripheral vestibular disease, motivational issues or inattentiveness. A possible explanation is that the dysrhythmia and the slowing of the fast phase velocity represent a central attenuation of total eye displacement following caloric irrigation. Conspicuous attenuation of the vestibular response has been frequently reported among catatonic patients, but this response is transitory and disappears with clinical improvement. This observation lends support to a state-related modulation, one associated with severity of psychiatric illness.

Modulation of the vestibular response with visual fixation, i.e., the amount the slow component of nystagmus was suppressed with visual fixation, provided evidence of abnormal control of the vestibulo-ocular reflex (VOR) among hospitalized patients. Failure of fixation suppression reflects central dysfunctioning and has been found in various neurological diseases (Coats, 1970; Alpert, 1974; Sato et al., 1980). The explanation for its specificity to functional psychosis could represent either, a failure of active visual

fixation (Sato et al., 1980), or some internal deficit in the regulation of the VOR as a consequence of psychotic disorganization. It is unlikely that failure of active visual fixation can fully explain the modulation, because controls for visual attention did not discriminate good suppressors of caloric nystagmus from poor suppressors. The exact mechanism responsible for the modulation of caloric nystagmus remains unclear. Recent studies have shown that modulation of the VOR with fixation involves the mediation of cerebellar control by the vestibulo-cerebellar and oculomotor pathways in the brainstem. More recently, Miles and Lisberger (1981) have proposed a model of VOR functioning which suggests that ocular instability occurs when the gain of the VOR deviates from unity. Minor diseases, trauma, aging and distorting optical lenses all affect changes in the gain of the VOR; therefore, it seems reasonable that the biochemical and physiological changes reported in psychosis may similarly affect the VOR.

The possibility that psychotropic medication may underlie the deficits is of importance since all patients in this study were on drug therapy. The pharmacological treatment of schizophrenia employs chemical agents which modify, stimulate or inhibit the action of neurochemical transmitters. It is possible, therefore, that these medications in their generalized action on neural mediators may have contributed to the deficits noted in this study. However, antipsychotic medication has not been well investigated with

respect to its effect on the vestibular system. Chlorpromazine, one of the major neuroleptics, has been reported to produce slowing of the fast phase, but to leave the slow phase unaffected (McCabe, 1965). None of the studies of the effects of neuroleptics has examined either the fast component or fixation suppression in the vestibular response of psychiatric patients who received neuroleptics.

It is generally accepted that the drugs which are effective in the treatment of the affective disorders or of schizophrenia exert their principal therapeutic action on catecholaminergic neuronal systems. It seems reasonable, then, to expect that medications common to the patients in this study may have contributed to the observed deficits. One difficulty in accepting medication as the cause of the deficits, however, is that the deficits seemed consistent only among those patients who showed acute psychotic symptomatology. Remitted schizophrenics (outpatients) receiving similar medication, did not differ significantly from normal control subjects on most of these measures--an observation which casts doubt on medication as the sole basis for the observed deficits. If antipsychotic medication affects vestibular responses and tracking patterns, then either all individuals are not susceptible to its effects, or the deficits represent some interaction between pharmacological and clinical variables. It is conceivable that the interaction of psychotic symptomatology and medication might reflect differences in length of time on medication. A high proportion (68%) of patients

with active symptomatology were either receiving medication for the first time, or had only recently been placed back on medication, which might suggest that the drugs had not yet reached their peak of clinical efficiency. It is then possible that the deficits reflect psychotic disorganization, and that they attenuate with remission of active symptomatology or the therapeutic action of antipsychotic medication.

Pursuit Tracking

It is significant that the observation of abnormalities in the vestibular response in those patients with active psychotic symptomatology paralleled observations of smooth pursuit tracking disorders in this same group. It would seem reasonable to expect that poor fixation suppression would correlate well with defective tracking since both require maintained fixation. Furthermore, recent studies with neurological patients have established that the inability to suppress caloric nystagmus with visual fixation correlated well with the occurrence of smooth pursuit deficits (Sato et al., 1980; Halmagyi & Gresty, 1979). It has been hypothesized that the smooth pursuit system counteracts the vestibulo-ocular reflex (VOR) during visual fixation, and is involved in the modulation of this reflex (Benson & Barnes, 1978; Zee, Yee, Cogan et al., 1976; Miles & Lisberger, 1981). Lisberger and Fuchs (1978) have identified neurons that discharge in relation to both suppression of the VOR and smooth pursuit eye movements.

In this study, subjects who showed significantly reduced fixation suppression had a correspondingly higher frequency of velocity arrests (VAs), as well as significantly reduced fast phase velocity and dysrhythmia, but there was no significant one-to-one correlation between individual measures of the vestibular response and number of VAs. The explanation for the failure to find a one-to-one correlation may reflect both limitations in the VA measure, and characteristics of the task demands, i.e., fixation suppression requires maintaining foveal fixation of a stationary target, while VAs were measured during foveation of a moving target--a decidedly more complex oculomotor task. The presence of significantly higher frequency of VAs among subjects who showed reduced fixation suppression suggests that common mechanisms may underlie the deficits.

Further evidence of deviance in response was provided by the significant increase in VAs for the hospitalized patients following the second caloric irrigation. This did not appear to reflect tonic excitation of the vestibular system since there was no increase in VAs for the baseline condition which was randomized across testing positions. Both comparison groups showed a consistency in number of VAs over the two irrigations, a finding which corresponds to consistency in pendulum tracking previously noted in normal control subjects (Shagass et al., 1974). The continued increase in VAs for the hospitalized patients was not correlated with a deterioration in attention or level of performance. Of some interest, however,

is that the increase in VAs for the second irrigation was most evident among schizo affective patients. A consideration with respect to this finding is that the schizo affective subgroup, like manic-depressives, contained disproportionately more patients with active psychotic symptomatology (70%), recent onset (60%), and shorter time on medication (60%) than any of the other subgroups. This observation lends support to the statement made earlier that it is psychotic disorganization which disrupts the mechanisms which underlie ocular stability.

It is noteworthy that the association between clinical status and aberrant vestibular and tracking responses has been consistently supported by the findings of this study. Psychological test diagnosis also supported a difference between patients with active and remitted psychotic symptomatology on these measures. There is some evidence in the literature that clinical improvement is associated with normalization of vestibular responses (Fitzgerald & Stengel, 1945; Rosenblum & Friedhoff, 1961; Rosenfeld, 1926). Furthermore, outpatient status, usually associated with a reduction in acute psychotic symptomatology, was found to be related to a reduction in VAs (Pivik, 1979)--a finding supported in this study. It might well be that the vestibular deficits and the tracking deviations are transitory and reflect a psychological state which corresponds to CNS changes.

The question of specificity and continuity--whether eye tracking

disorders are found only in schizophrenics and occur regardless of functional state--has an obvious bearing on the genetic marker hypothesis (Holzman et al., 1974, 1977). The observation of deviant eye tracking patterns among nonschizophrenic functionally psychotic patients in this study and previously (Shagass et al., 1974), and the absence of data which supports deviant eye tracking patterns in outpatient schizophrenics noted in this study and previously (Pivik, 1979), throws some doubt on this hypothesis.

The consequences of the observed deficits for psychiatric patients are most obvious with respect to visual perception. It has been shown that some alteration of the vestibular and oculomotor response occurs with acute psychotic episodes, especially alterations affecting maintained foveal fixation. Poor fixation or poor eye stability would presumably affect visual information processing, and would lead to errors in perceptual scanning strategies. It seems reasonable that many of the scanning or field articulation dispositions which have been related to Kraepelinian categories of schizophrenia and attributed to inattention (Silverman, 1964), may reflect a more basic alteration of CNS activity.

The observation that severity of psychiatric illness, rather than diagnostic category, provides the most consistent correlation with the deficits lends support to a physiological basis for the deviant tracking behaviour. The findings of this study consistently support a central, rather than a peripheral, basis for the poor

ocular stability. One possible explanation of the findings is based on a model of the functioning of the VOR (Miles & Lisberger, 1981), and was suggested earlier. This hypothesis assumes that the deficits noted in the fixation and tracking patterns of psychotic patients represent retinal image slip. Retinal image slip is corrected by visual feedback mechanisms, which rely on a fixed VOR calibration of unity to protect the preexisting gaze velocity should the head move. If for any reason the gain of the VOR deviates appreciably from unity, ocular stability will be lost. Visual feedback mechanisms could ameliorate the retinal image slip, but because of their long latency never eradicate it. It seems logical that psychosis might affect VOR calibration, and that VAs and poor fixation suppression reflect a regulation deficit in the VOR which visual feedback mechanisms cannot eradicate. The more obvious disturbance in modulation among manic depressive patients, whose illness follows an acute rather than a chronic course, supports a state-related modulation. This interpretation is consistent with the observation of relatively normal performances of patients with remitted symptomatology. This hypothesis which speculates on a possible physiological cause of poor fixation and tracking aberrations among psychotic patients requires validation. Examining patients while actively psychotic and while in remission might resolve the issue of the specificity of the deficits to psychotic disorganization.

A review of the findings of this study in relation to the hypotheses will conclude this discussion.

1. Partial support for hypothesis number 1--that psychiatric patients would evidence more abnormal vestibular responses--was obtained. Evidence of alteration of the vestibular response was noted in the slowing of the fast phase velocity, and the presence of dysrhythmia. The slowing of the fast component velocity had not been previously reported for this group of patients, and its occurrence coincident with the presence of dysrhythmia was considered as indirect evidence that the basis for both lay in modulation of the same central mechanisms. There was some indication of a slowing of the fast phase velocity for outpatients, but the irregularities occurred only in patients who showed symptoms of schizophrenic thought disorder, irrespective of grouping. The reactivity of the vestibular labyrinth system as measured through the slow phase velocity, latency, duration, frequency and bilateral symmetry was found to be within the normal expected range, and this was taken as evidence of the integrity of the vestibular system for all groups.

2. Hypothesis number 2--that tracking deviations would be higher for patients with active psychotic symptoms--was supported, and the findings of this study with respect to VAs and severity of psychotic disorganization corroborated observations previously noted. As anticipated on the basis of previous reports, hospitalized patients had a higher frequency of VAs on baseline measures; however,

the increase in VAs with vestibular stimulation for this group had not been previously reported. The pattern of VAs across the three conditions also differentiated the hospitalized patients from comparison groups, and the increase in VAs on the second irrigation appears related to the effects of psychiatric illness.

3. The reduced suppression of nystagmus during visual fixation among the actively psychotic patients, who also showed significantly more VAs, supports hypothesis number 3. The failure to inhibit caloric nystagmus with visual fixation had not been previously reported for psychiatric patients, and like other signs of central modulation noted in this study, appears related to clinical status.

Improved clinical status seemed to be related to normalization of the vestibular responses, and to reductions in tracking aberrations, which suggests that the deficits are transitory. Further study of vestibular and tracking responses in the same patients while actively ill and in remission is necessary to test this hypothesis. A positive relationship between clinical status and tracking performance would argue against acceptance of eye tracking deviations as a genetic marker for schizophrenia. In this study, deviations in tracking were not common to all schizophrenics, but appeared to be related to severity of psychiatric illness, a finding not clearly articulated in the literature.

The issue of the VA requires further descriptive clarification. A detailed computerized analysis of what constitutes a VA seems warranted, as this measure has been shown to consistently differentiate between hospitalized psychotics and normal controls. It also appears to have some value in differentiating psychiatric patients with respect to severity of illness. The continued use of this measure, however, will demand greater definition of its nature.

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APPENDIX A

Dysrhythmia--this measure of nystagmus irregularity was assessed for a 30 second period (between 30 and 60 seconds after the beginning of irrigation) using the four grades of dysrhythmia devised by Lidvall*. Regularity referred to the nystagmus rhythm and was defined as the presence of continuous nystagmus beats in the appropriate direction which did not contain sudden or pronounced variability in the amplitude or the velocity of the slow phase component. The duration of periods of distinct nystagmus which alternated with periods of less distinct or indiscernible beats was used to determine the grade of dysrhythmia:

Grade 3--Alteration between short periods of distinct nystagmus and considerably longer "nystagmus-free" intervals.

Grade 2--Alternation between about equally long periods of distinct nystagmus and "nystagmus-free" intervals.

Grade 1--Alternation between long periods of distinct nystagmus and considerably shorter "nystagmus-free" intervals.

Grade 0--Regular or almost regular nystagmus.*

* Taken from Lidvall, H. F. Vertigo and nystagmus responses to caloric stimuli repeated at short intervals. Acta Otolaryngologica, 1961, 53, p. 36.