Disturbances of ocular movements and blinking in schizophrenia

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SUMMARY Neurological examination and electroencephalograms and electro-oculograms, recorded by telemetry, from unmedicated patients with acute and chronic schizophrenia demonstrate a number of abnormalities of extraocular movement including staring, abnormal blink rate, absent glabellar reflex, and increase in horizontal eye movements. As potential clues to the pathophysiology of schizophrenia, these disturbances are analysed in relation to anatomical substrate and dopamine modulation of ocular movement, rapid eye movement sleep, and the neurological disorders in which similar disturbances of ocular movement occur.

In distinguishing dementia praecox from other forms of mental illness, Kraepelin (1913) called attention to a number of ocular signs of the disorder, including pupillary abnormalities, staring, nystagmus, abnormal blinking, and blepharospasm. Widespread use of neuroleptic medications has now induced a variety of neurological side effects and sequelae which obscure the incidence of these signs and their relevance to the pathology of the schizophrenias. Because these ocular signs may provide clues to the pathology of the schizophrenia syndrome, it seemed worth while to document them carefully in medication-free patients.

Subjects and methods

Complete neurological examinations have been performed on 45 patients who were free from medication for periods of one month to four years, and 10 patients who had never received drugs or other physical treatment. Nine patients were seen within a year of diagnosis, 14 had been diagnosed between one and five years, and the remaining 29 patients, longer than five years. The youngest patient was 17 years of age, the oldest, 49 years. Thirty-one were men, 24 were women.

The diagnosis was made by senior staff consensus and required the following five of the seven criteria stipulated by Taylor and Abrams (1975): illness duration greater than six months; clear

consciousness; delusions, hallucinations, or formal thought disorder; restricted affect; absence of signs and symptoms sufficient to make a diagnosis of affective illness or coarse brain disease. In addition to the neurological examination, 36 of the 55 medication-free patients and 12 normal control subjects have had 2–24 hour electroencephalograms (EEG) and electro-oculograms (EOG), recorded by radiotelemetry during which spontaneous behaviour was recorded continuously by a trained observer. Bipolar EEGs were recorded from tin or gold disc electrodes attached to the scalp with collodion at central-parietal (C3–P3; C4–P4) and temporal (T3–T5; T4–T6) positions bilaterally. Lateral eye movement was recorded between electrodes placed at the outer canthus of each eye. Vertical movements and blinks were recorded between electrodes placed immediately above and below one eye. Subjects wore a small multiplexed 8-channel transmitter (weight 90 g, Benton Instrument Company) held firmly to the head by a special cap.

During the recording period, patients were in their rooms or the dayroom within a radius of 40–50 yards of the receiver antenna. They slept in their own beds, and carried on their usual hospital routine. Electroencephalographic and EOG signals were recorded on a 7-channel FM tape recorder monitored by an ink-writing polygraph. Receiving and recording devices were centrally placed in a hallway near the ward dayroom. The polygraph was run at a speed of 15 mm per second and could be correlated continuously with ongoing behaviour and accelerated to 30 mm per second for

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more detailed examination during periods of unusual behaviour. Frequency modulated tape was recorded at $1\frac{1}{8}$ inches per second, and portions of the taped record were played back during behavioural events of particular interest and for subsequent analysis. Behavioural observations were recorded by a trained observer on a written log and were coded by number at the moment of occurrence on a time code placed on one channel of the tape recorder and polygraph, assuring exact correlation between EEG-EOG recording and behavioural events.

Results

Neurological examination of this group of patients demonstrated that, apart from the characteristic abnormalities of mental state and skeletal motor activity (stereotyped behaviours, rocking, bizarre postures), the most common signs were disturbances of ocular contact and movement. These included staring, abnormal blinking, saccades, and ocular pursuit. Prolonged telemetered EEG-EOG confirmed the clinical evidence of abnormal ocular movements. Although slow or sharp activity appeared over the left or right temporal region of one-third of these patients, these abnormalities could not be associated with the clinical changes nor with the appearance of abnormal ocular activity. In contrast, the oculomotor changes were frequently correlated with abnormalities of perception and attention.

ABNORMALITIES OF EYE CONTACT

A fixed penetrating stare directed into the examiner's eyes, at a distant point, or avoidance and failure of eye contact were noted in 34 patients. These signs were equally common in acutely and chronically ill individuals, and usually responded promptly to neuroleptic treatment in patients with acute psychosis. Interrogation of the patient rarely provided a clear explanation for staring or diversion of gaze. A few individuals indicated that staring or avoidance of eye contact was a response to perceptual change as indicated by the following examples:

A 21 year old man with chronic paranoid schizophrenia, who stared fixedly at the examiner, explained "your face is turning into an animal."

The mother of a 20 year old schizophrenic girl reported: "when I go to the hairdresser I tell her I'll be right back. When I come back an hour later and walk in she just stares at me like I'm a new person to her. At other times she stares at her father like a stranger and shouts 'Get him out of here, he's doing things to me. Who is he? Get him out!'"

A 17 year old boy avoided eye contact because "I'm afraid you'll read my thoughts."

No change in simultaneous EEG accompanied these clinical events.

ALTERED BLINK RATE

Although both Kraepelin (1913) and Bleuler (1950) remarked upon increased blinking in dementia praecox, quantitative studies of blinking in this illness are lacking. Abnormalities of blinking in this group of unmedicated schizophrenic patients fell into three categories: (1) decreased blinking, staring, and absent eye contact, most commonly seen in acute exacerbations of the disorder; (2) steady increase in blinking at rest in patients with chronic schizophrenia; (3) episodic paroxysms of rapid rhythmical blinking associated with hallucinations, sudden impulsive acts, or deluded speech.

Sixteen patients demonstrated episodes of rhythmic or paroxysmal blinking at rates up to 2.5-3 per second, and seven patients, four of whom had never received neuroleptic treatment, displayed absent or decreased blinking (0-1 per minute).

Eight patients showed abrupt change in blink rate during delusional excitement, while speaking in response to hallucinated voices, or during autistic reveries.

A 26 year old former college student, in hospital for nine years with an unrelenting dementia praecox, sat indolently in the dayroom of the hospital blinking steadily two and a half times per second. He reported that he was in a "waking nightmare" of frightening sexual experiences (Fig. 1).

A patient with acute catatonia who was studied before all treatment blinked only two to three times per minute during the day, but exhibited 2-10 second epochs of rhythmic blinking two and a half to three times per second associated with a posture of supplication or deep sighing respiration at intervals during a sleepless night (Fig. 2).

ABNORMAL BLINK (GLABELLAR) REFLEX

In response to gentle taps of the glabella repeated at one second intervals, most normal adults respond by single blinks to the first two to five taps, then stop blinking unless stimulation is discontinued for 10-20 seconds, after which the response returns and again habituates after repetition (Overend, 1896). Twelve of the 50 patients in this study had no response to glabellar tap, six failed to habituate the reflex after 10 or more taps, and 14 patients displayed paroxysmal bursts of rapid blinking to each tap on repetition. Absent blink reflex was most common in patients with acute exacerbation of psychosis, while persistent or

Fig. 1 EEG-EOG by radiotelemetry in a 26 year old man shows steady rhythmic blinking which almost obliterates EEG on the top two panels. Note brief "spike" discharge at 4:02 pm from right parieto-occipital region while patient is dozing. No clinical signs detected. EEG shows asymmetrical temporal function with theta activity on the left, high voltage alpha spindles on the right as patient lies quietly with eyelids fluttering in a "waking nightmare."

paroxysmal response was more characteristic of chronic or less florid psychoses in patients withdrawn from neuroleptics. Six of the 10 patients who had received no previous treatment had no blink reflex to glabellar tap. Return and persistence of the glabellar reflex was one of the earliest effects of neuroleptic drug treatment in these patients.

LATERAL EYE MOVEMENTS

Abnormalities of three types were recorded: (1) rapid, irregular, searching movements; (2) spontaneous, rhythmic, horizontal saccades; (3) single, sustained, lateral glances.

Darting, rapid, irregular searching movements were exhibited by 12 patients, and were observed most commonly during acute exacerbations of the illness or before all treatment. During such behaviour, patients appeared to be hypervigilant

and looking in all directions for the source of auditory or visual stimuli imperceptible to the observer. Characteristically this was accompanied by speech arrest or drivelling. In contrast to psychomotor seizures, which such ocular automatisms may resemble, the darting eye movements of the psychosis usually can be readily, if briefly, interrupted by speaking to or touching the patient. Although the patient can thus be made aware of the activity, an explanation is rarely forthcoming (Fig. 2).

Seven patients, including three without previous treatment, displayed episodes of sustained horizontal lateral oscillations of the eyes at rates of one to two per second lasting for 10–20 seconds. These rhythmic ocular movements resembled nystagmus in amplitude of excursion and return of eyes to midposition after each lateral movement. Rarely observed during conventional neurological ex-

Fig. 2 Telemetered EEG-EOG from a 21 year old man with acute catatonia for three days with no previous treatment. Top: EEG is unremarkable in dark room at night. Blinking occurs in showers accompanied by lateral eye movements. Middle: 11 am, lighted room. Patient is mute, statuesque, appears frightened. There are rapid, darting, searching, horizontal eye movements. Bottom: midnight in lighted room. Patient is unable to sleep or respond, and is blinking rhythmically and rapidly. EEG shows only low voltage fast activity.

amination, spontaneous horizontal oscillations usually occurred during autistic reveries or psychomotor blocking. These episodes usually lasted for less than 10 seconds, and continued for 30–60 seconds in severely disturbed patients, particularly those with intense delusory and hallucinatory experiences (Fig. 3).

Unexplained single sustained lateral glances interrupted the speech or attention of 14 patients, and, in their most extreme form, constituted a continuous stereotyped automatism in two patients with far advanced schizophrenia.

A 37 year old man in hospital for nearly 20 years after adolescent onset of schizophrenia stood by the hour against the wall in the hospital day-room repeatedly turning his eyes from side to side as though following a tennis match. Meanwhile he twisted his hands together steadily, flicking his fingers, making signs to himself, smiling and laughing vacuously. On reclining at bedtime his

head remained flexed on the neck several inches above the mattress ("psychological pillow"), and lateral eye movements continued for several hours until sleep supervened.

IRREGULAR OCULAR PURSUIT

Using simple bedside examination of extraocular muscle function in which the patient was asked to fix his eyes on the examiner's moving finger, flashlight, or the movement of his own finger, 24 patients demonstrated one or more abrupt arrests or coarse saccades during each trajectory of horizontal ocular movement. Four patients, all with severe chronic schizophrenia, were entirely unable to follow the moving object with the eyes, and two patients with previously untreated acute schizophrenia repeatedly lost ocular contact with the moving object as their eyes returned from pursuit to staring at the examiner's face.

Fig. 3 EEG-EOG recorded by telemetry from a 22 year old man demonstrates rhythmic 1 cps lateral saccades associated with spindled alpha activity during autistic reverie.

Discussion

SPONTANEOUS BLINKING: CLINICAL AND EXPERIMENTAL STUDIES

In contrast to normal control subjects, whose blink rates varied from 8–22 per minute (Zametkin *et al.*, 1978), 17 patients in this series had resting blink rates in excess of 60 per minute. Sustained high blink rates were more common in patients with previously treated chronic schizophrenia, while blink rates of less than five per minute were found in five of six patients with catatonic schizophrenia. There are many studies of reflex blinking and the glabellar reflex in the literature, but very few address the clinical significance of spontaneous blinking. Ponder and Kennedy (1928), in one of the few published studies of quantitative blink rate in man, noted that the rate of blinking tends to be remarkably constant in a given individual, and remains essentially unchanged by darkness, temperature, humidity, anaesthesia of the cornea, or deafferentation of the fifth cranial nerve. Observing that one of the earliest features of postencephalitic Parkinsonism was the almost complete absence of blinking, Ponder and Kennedy proposed that normal blinking depends on the integrity of the basal ganglia.

The centres responsible for initiation and modulation of spontaneous blinking are poorly defined. Van Buren (1963) reported rapid bursts of blinking after stimulation of the caudate nucleus in man. Nashold (1969, 1970) elicited eye closure and rhythmic lid flutter in response to stimulation ventral to the superior colliculus and central grey matter, a region from which sensations of burning chest pain and intense emotional reactions were also elicited.

LATERAL SACCADIC GLANCES

The darting glances displayed by these patients are strikingly similar to the ocular searching movements termed "checking" displayed by cats and monkeys in strange environments, when intensely frightened, or after administration of amphetamine and cocaine (Ellinwood, 1974). Sato (1977) described visual searching movements after stimulation in the nucleus accumbens in cats. Similar movements are reported in encephalitis, alcoholic encephalopathy, pretectal lesions, and temporal lobe seizures (Mayanagi and Walker, 1974; Escueta *et al.*, 1977). Shimazano *et al.* (1965) noted that, in contrast to normal subjects who characteristically increase horizontal saccades in response to external stimuli, patients with schizo-

phrenia decrease or arrest rapid horizontal eye movements in response to the same stimuli. These investigators proposed that the increased horizontal eye movements of schizophrenia, which they termed "waking REM," do not simply reflect arousal but represent a mechanism closely related to the psychotic state.

We observed similar ocular movements after stimulation of the mesolimbic dopaminergic pathway in cats and in response to apomorphine and other dopaminergic agents (Stevens *et al.*, 1974; Stevens and Livermore, 1978). These stereotyped responses were abolished by neuroleptic agents or by elimination of visual stimuli, suggesting that the ocular movements represent dopamine-mediated automatisms elicited by visual stimuli (Stevens *et al.*, 1977).

Wallach and Wallach (1964) described episodic rapid regular horizontal oscillations of the eyes at rates of 60–100 per minute in children and adults with severe forms of schizophrenia. Regularly associated with severe thought disturbance, preoccupation with endogenous percepts, and a sense of personal dissolution, rhythmic lateral saccades in their patients were also abolished by fixation of attention and by remission of the illness. Recurrence of rhythmic saccades coincided with deterioration or recurrence of psychosis.

OCULAR PURSUIT

First described and illustrated graphically in patients with dementia praecox by Diefendorf and Dodge in 1908, interruption of smooth ocular pursuit movements has more recently been recorded again in a high percentage of patients with schizophrenia and mania (Holzman *et al.*, 1973, 1976; Shagass *et al.*, 1976). Savitsky and Winkelman (1947) described similar cogwheel motion on deviation of the eyes in patients with disease of the corpus striatum, and Luria *et al.* (1966) reported similar saccades in patients with frontal lobe lesions and severe cognitive disorders. Interruption in smooth pursuit can be overcome partially by increasing the patient's attention to the task (Shagass *et al.*, 1976).

SCHIZOPHRENIA, DOPAMINE BLOCKADE, AND THE LIMBIC SYSTEM

Evidence that the effectiveness of neuroleptic agents against the symptoms of schizophrenia is related directly to the capacity of these agents to block dopamine receptors in the brain has implicated central dopaminergic systems in the pathophysiology of schizophrenia (Carlsson and Lindquist, 1963). Striking similarities between the subjective disturbances and stereotypes of

schizophrenia, and the auras and automatisms of psychomotor epilepsy suggest that schizophrenia, like psychomotor epilepsy, is associated with abnormal function in the limbic system (Stevens, 1973). The dopamine innervation of the limbic system derives principally from the most medial units of the pars compacta of the substantia nigra (SN), and from the ventral tegmental area (VTA, A10), located just medial and rostral to SN. From VTA, axons of the dopaminergic neurones of the mesolimbic system ascend to the nucleus accumbens, olfactory tubercle, nucleus of stria terminalis, diagonal band, lateral septum, and the central nucleus of the amygdala (Ungerstedt, 1971). Abnormal electrical activity has been reported from these regions in schizophrenic patients by Heath (1954), Hanley *et al.* (1970), and others. In keeping with a more medial position in the forebrain, the nucleus accumbens projects to more axial structures of the diencephalon and mesencephalon than the caudate nucleus, including the paramedian pontine reticular formation and tectum (Domesick *et al.*, 1976), regions closely associated with regulation of extraocular movement, arousal and attention.

Species specific stereotyped exploratory behaviours released by dopaminergic agents, consisting of sniffing, licking, and chewing in rodents, depend on the integrity of the neostriatum (Randrup and Munkvad, 1967), while increased exploratory activity induced by these agents is attributed to activation of the nucleus accumbens and other components of the limbic striatum (Iversen, 1977). The disturbances in eye movement demonstrated by schizophrenic patients are usually attributed to the heightened state of fear or arousal associated with the acute psychosis. However, the occurrence of these disturbances in patients with longstanding psychosis, the modulation of these signs by agents which alter central dopamine function, and the appearance of similar signs after stimulation of the mesolimbic dopaminergic system in experimental animals and during temporal lobe seizures of man suggest that these ocular signs may represent abnormal function of the mesolimbic dopamine system.

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