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Article:

Ocular sequelae from the illicit use of class A drugs

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Abstract

Aim: **To highlight the changes that may take place in the visual system of the class A drug abuser.**
Methods: **A literature review was carried out of ocular/visual sequelae of the more common class A drugs. These include stimulants (cocaine and crack cocaine), narcotics (heroin, morphine, methadone) and hallucinogenics (ecstasy, lysergic acid diethylamide, magic mushrooms, mescaline, phencyclidine).**
Results: **Ocular sequelae affecting visual acuity, the eye and its adnexa, ocular posture and ocular motility can result from recreational use of these drug(s).**
Conclusions: **Awareness of the consequences of illicit drug use should lead to more pertinent questioning during history-taking.**

Key words: Cocaine and crack cocaine, Heroin, LSD, MDMA (ecstasy), Mescaline, Ocular motility disorders, Phencyclidine, Psilocybin and psilocin (magic mushrooms), Vision disorders

Introduction

This review highlights the changes that may take place in the visual system of the drug abuser and thus may help to alert the clinician to clinical presentations that may be the result of illicit drug use. Awareness of these conditions should lead to more pertinent questioning during history-taking.

The review contains many individual case reports, indicating the rarity of some of the sequelae encountered. However, larger case series or original research articles are also included.

The main and more serious ophthalmological complications arise from the use of cocaine/crack cocaine, ecstasy (methylenedioxymethamphetamine: MDMA) or heroin (diamorphine). However, other narcotics and hallucinogenics are included for the sake of completeness. Class B drugs when prepared for injection become class A but these are not included in this review (Table 1). Whilst the effects are discussed under each individual drug there is overlap as polydrug use is common.

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Stimulants

Cocaine and crack cocaine

Cocaine hydrochloride is a fine crystalline powder that is usually sniffed. If converted into its base form, the pure cocaine is known as 'crack' due to the crackling noise it makes when smoked. Cocaine acts as a sympathomimetic and has vasoactive properties. The sympathomimetic effect (cocaine prevents the reuptake of norepinephrine) leads to dilated pupils. Mitchell and Schwartz[1] report a 55-year-old man who presented with right eye pain and blurred vision which was diagnosed as acute angle closure glaucoma. Three days later a recurrence of the angle closure occurred and the patient admitted intranasal cocaine use through his right nostril. The authors suggest that either transmucosal absorption of the cocaine or a retrograde nasal delivery through the nasolacrimal duct may have been the mechanism, or that topical application from rubbing the eye may have occurred.

In high concentration cocaine may cause exophthalmos, retraction of the upper lid and cycloplegia. In a series of 216 patients who presented to a medical emergency department Brody *et al.*[2] found 6 who complained of blurred vision. This was felt likely to be due to sympathetic stimulation, but further investigation to determine the cause was not reported.

Phenytoin may be added to crack cocaine. This may lead to phenytoin toxicity effects, which include nystagmus, when the crack is smoked.[3,4]

Cerebrovascular disease: ocular motility and retinal problems

Neurological complications include cerebrovascular disease, more frequently haemorrhagic than ischaemic.[5] This may either lead to defects in eye movements or affect visual acuity. A midbrain haemorrhage which

Table 1. British classification of drugs of abuse

Class A	Class B	Class C
Cocaine	Amphetamines	Anabolic steroids
Crack cocaine	Barbiturates	Cannabis/marijuana
Ecstasy	Codeine	Mild amphetamines (e.g. temazepam, valium)
Heroin	DF118 (mild opiate)	
Lysergic acid diethylamide		
Magic mushrooms		
Mescaline		
Methadone		
Phencyclidine (PCP)		

resulted in bilateral internuclear ophthalmoplegia (INO), bilateral ptosis, limited upgaze with convergence-retraction nystagmus, and 4 mm pupils which were unreactive to light but responded normally on accommodation has been reported in a 35-year-old man.[6] The onset occurred a few hours after smoking several vials of crack cocaine and was accompanied by vertigo and incoordination of his right limbs. General examination was unremarkable and visual acuity and fields were within normal limits. Computed tomography showed a haemorrhage in the midbrain tegmentum which had fully resolved on repeat scan 2 months later. At this time all signs had resolved except for limitation of upgaze. The authors suggest that the haemorrhage was due to rupture of a cryptic arteriovenous malformation precipitated by the elevation in blood pressure due to the sympathomimetic action of cocaine. A further three cases of presumed stroke resulting in unilateral INO, bilateral INO and trochlear nerve palsy secondary to use of crack cocaine have been reported.[7]

Orbital infarction has been reported in a 36-year-old woman who had inhaled cocaine and heroin and lost consciousness with her head down and the left side of her face and orbit pressed against a desk.[8] Magnetic resonance imaging revealed diffuse swelling of the extraocular muscles but magnetic resonance angiography and venography were normal. Complete left ptosis, with severe limitations of ductions of the left eye in all positions of gaze was present. There was no perception of light by the left eye and right visual acuity was 6/6. A relative afferent pupillary defect was present in the left eye but the pupil reacted normally to consensual stimulation. The left fundus showed residual retinal oedema and retinal pigment epithelium disruption throughout, with markedly attenuated arterioles. No other abnormalities were detected and laboratory tests were normal. After 1 month there was a slight improvement in only the ptosis and eye movements. Although compression alone may cause orbital infarction (defined as ischaemia of all intraocular and orbital structures), the authors felt that the increase in sympathetic tone along with vasospasm from the cocaine use was a contributory factor.

Transient loss of monocular vision (episodes lasting 1 minute) has been reported in an intranasal cocaine abuser.[9] Retinal vasospasm was thought to be the most likely cause. Loss of vision lasting for longer periods or persisting, appears to be more frequent.[10–15] Patients may present with markedly reduced vision in both eyes. Vasospasm or an obstruction caused by fibrinoid necrosis within the vessel or atherosclerotic plaques due to hypertensive effects are thought to be the cause. Recovery of visual acuity is variable.

Cocaine-induced cerebral vasculitis may also be the mechanism in some visual effects. Transient blurring of vision was reported as one sign in an intranasal cocaine user who later, following a generalised tonic seizure, had a left gaze palsy.[16] Cerebral angiography showed findings consistent with vasculitis. Krendel *et al.*[17] report 2 cases of vasculitis confirmed by biopsy; one patient had bilateral blindness and the other (who later died) had bilateral papilloedema due to cerebral oedema. Such cases present with other symptoms that may include weakness of one side of the body, headache, slurred speech, confusion and hemianaesthesia.

Microtalc retinopathy with associated retinal nerve fibre layer 'rake' or 'slit' defects has been observed by Rofsky *et al.*[18] in 'approximately 60 cases' where patients had a history of smoking crack cocaine. Three cases are reported in detail, each with acuity of 20/20 either eye. Some patients showed visual field changes which had the appearance of glaucoma-like defects, being inferior nasal steps. The authors suggest that the microtalc dusting of the retina is probably due to very small crystalline deposits from the adulterants of the crack which have become lodged in the inner retinal layers or the retinal circulation. The preference for the superior portions of the optic nerve head is not explained but likened to anterior ischaemic neuropathy, where the field loss is most commonly inferior altitudinal.

Endophthalmitis

Endogenous endophthalmitis has been reported in one cocaine addict who injected cocaine intravenously.[19] This 22-year-old presented complaining of severe pain in the right eye accompanied by loss of vision and watering of the eye. A *Bacillus* species (later identified as *Bacillus cereus*) was grown from blood culture; this is a bacterium found in air, water, soil or dust and was thought to have been introduced from the injection leading to blood-borne endophthalmitis. Despite treatment with local and systemic antibiotics acuity was not saved and follow-up showed a phthisical eye.

Myasthenia gravis

Another aetiology for ocular motility problems from cocaine use is the unmasking or exacerbation of myasthenia gravis. Berciano *et al.*[20] report a 24-year-old woman who had general signs of myasthenia, including diplopia, immediately after sniffing cocaine. The signs lasted for about 15 minutes but a few months later generalised signs occurred again which were exacerbated by cocaine. This led the patient to stop using cocaine; however, myasthenia gravis still developed. In another case, a polydrug user presented to hospital because of abscesses from injecting but also complained of generalised weakness, dysphagia and bilateral ptosis. The 29-year-old woman was using 2 g cocaine daily as well as 1 g heroin and 40 mg methadone.[21] Ophthalmological examination 6 days following the last use of cocaine or heroin revealed bilateral ptosis, left greater than right (palpebral fissures 6.5 mm and 3.5 mm respectively), complete bilateral external ophthalmoplegia with the eyes fixed in downgaze and exotropia of approximately 10°. No eye movements could be elicited by Bell's phenomenon, vestibulo-ocular reflex or optokinetic testing. The pupils barely reacted to light but reacted on accommodation and constricted with 0.1% pilocarpine, confirming a 'pseudotonic' pupil. Neurological investigations were normal (including magnetic resonance imaging) and edrophonium test was positive. Ocular motility and pupillary reactions returned to normal with medication (pyridostigmine 180 mg daily) and remained so with further use of cocaine, heroin and methadone. The authors suggest that the cocaine blocks the sodium

channels and causes a slowing in presynaptic neuronal transmission. Daras et al.[22] report a 33-year-old myasthenic man who had eight hospital admissions during a 13 month period: three related to non-compliance with medication and 5 within 24 hours of intranasal cocaine use. Diplopia is listed amongst the symptoms that occurred during these exacerbations.

Destruction of bony tissue

The destruction of the nasal septum due to intranasal cocaine use has been given press coverage in recent times. Intense vasoconstriction and anaesthesia is induced and this leads to mucoperichondrial ischaemia. However, the destruction may extend to the bony walls of the orbit, which can lead to nasolacrimal duct obstruction due to inflammation and orbital cellulitis.[23,24] Common presenting features in a series of 7 patients were epiphora, periorbital pain, oedema, and erythema associated with fever.[23] The authors emphasise the importance of anterior rhinoscopy in correct diagnosis of the cause in this group of patients. Underdahl et al.[24] suggest that the destruction may be exacerbated by microvascular changes from diabetes mellitus and report a 40-year-old man with medial wall destruction and preseptal cellulitis.

The loss of the bony structures around the optic nerve and chronic inflammation in the sinuses have been postulated to be the cause of optic neuropathy in cocaine users[25,26] and the development of a pneumocoele secondary to nasal obstruction has been reported.[27]

Corneal problems

Several single cases have been reported where the use of crack cocaine has affected the cornea.[13,28–31] A series of 12 patients[32] illustrates the various corneal problems that may occur, including corneal ulcers, superficial punctate keratitis and corneal epithelial defects. The presentation in these patients tended to be either a relatively painless loss of vision, redness and purulent discharge associated with infectious corneal ulceration or painful loss of vision, redness, photophobia and tearing. The latter was associated with sterile epithelial defects after eye rubbing. Five of 10 patients tested showed reduced corneal sensitivity. No corneal perforations occurred. In some patients microbial (e.g. Staphylococcus epidermidis, Streptococcus pneumoniae) or fungal (e.g Candida albicans) organisms were identified. Various suggestions are made regarding the mechanism: direct toxic effect from the smoke; decreased corneal sensitivity resulting in reduced blinking and exposure keratopathy; neurotrophic changes; subclinical alkali burn from the smoke; eye irritation leading to vigorous rubbing. A single case report suggesting an increased risk of microbial keratitis in cocaine abusers who wear soft contact lenses has been reported.[33] The 23-year-old woman accidently administered cocaine powder to her left eye which she then rubbed. On examination the following day, a corneal ulcer 3.5 mm by 4 mm was seen. The authors suggest that the direct toxic effect of the cocaine on the cornea combined with vigorous rubbing increased the risk of infection in a patient whose wearing of soft weekly disposable contact lenses had already placed her in a higher-risk group.

One 32-year-old patient instilled cocaine into her conjunctival fornix, rather than sniffing it, and developed corneal ulcers bilaterally with Staphylococcus aureus infection. Extensive scarring resulted and final acuities were 20/70 in her right eye and light perception in her left. The left eye was enucleated 4 months later due to high intraocular pressure and severe pain.[34]

One patient had floppy eyelids and papillary conjunctivitis. It was suggested that these conditions contribute to the formation of corneal ulcers.[35]

Injury from self-abuse

After use of marijuana, amphetamines and cocaine one 25-year-old felt he could only 'get oxygen' by pushing a signet ring into his eye. On presentation there was periorbital oedema and severe conjunctival swelling. Skull radiograph and CT scan revealed the ring in the maxillary antrum, with possible fracture of the roof, haemorrhaging, surgical emphysema and enophthalmos. The ring was removed via the Caldwell-Luc approach but vision was lost.[36]

Madarosis

Smoking crack cocaine from a glass tube resulted in bilateral loss of the eyebrows and eyelashes due to singing. The hair grew back once the 17-year-old abstained from smoking.[37]

Sequelae from prenatal exposure

Chiriboga et al.[38] studied 30 babies who had been exposed prenatally to cocaine and concluded that this was associated with tone and movement disorders. Neurological abnormalities included hypertonia, plantar extension and coarse tremor. Smaller head size was also found in the cocaine-exposed group. Two babies showed persistent tonic downgaze, which resembled the setting sun sign, but was overcome by head movements. The duration of the sign reduced from about 75% of the time to 66% of the time over a 3 week period; however, one baby examined at age 6 months still demonstrated 'rare and brief tonic downward gaze'.

Four cases of congenital exotropia in drug-exposed babies led Dominguez et al.[39] to further identify 6 other cases with developmental delay and congenital cerebral anomalies where prenatal drug exposure was present. In 7 the drug was cocaine, and in the remaining 3 it was heroin, amphetamines or phenylpropanolamine (diet pills). Nine of the 10 babies had ophthalmological abnormalities including 5 with exotropia (one with nystagmus in addition), 2 with esotropia, 1 with absent upgaze, and 1 with unilateral 3rd nerve palsy and nystagmus (diet pills). Two of these 9 also had hypoplastic or atrophic optic discs (1 cocaine-exposed, 1 amphetamine-exposed). All babies showed global or motor delay and congenital malformations of the brain on neuroimaging. These authors estimate that 0.8–1.2% of infants with prenatal drug exposure have congenital malformations of the brain. The mechanisms for these defects are poorly understood but could be due to vasoconstriction causing diminished fetal perfusion or effects on the central nervous system due to a direct effect on the brain related to the dopaminergic sytem.[38] Hand et al.[40] found no difference in the incidence of

retinopathy of prematurity in very low birth weight infants who had been cocaine-exposed compared with those who had not.

Isenberg *et al.*[41] reported that slit lamp examination of 13 cocaine-intoxicated neonates showed that most had iris blood vessel abnormalities. Five were followed up and they showed gradual resolution without any apparent long-term visual sequelae.

Changes in eye movement systems

No differences have been found in saccadic velocity, amplitude or duration between cocaine-abusers and non-drug-users,[42] nor in smooth pursuit, optokinetic nystagmus, vestibulo-ocular reflex, visual suppression of the vestibulo-ocular reflex, or caloric testing.[43] Tracking accuracy, however, has been reported as superior to that of non-drug-users due to a small increase in eye movements at target frequency.[44] Attention fixations and antisaccades have been examined with relation to craving and foraging for cocaine.[45,46] An inverse correlation was found between cocaine craving scores and the number of pre-attentive fixations.

Electroretinogram changes

The dopamine-altering effect of cocaine, which leads to increased dopaminergic neurotransmission, led Roy *et al.*[47] to hypothesise that cocaine-dependent subjects would show abnormalities in electroretinogram (ERG) recordings. Twenty subjects admitted to a rehabilitation unit were tested, all of whom had been drug-free for a minimum of 3 days prior to the test. None were dependent on opiates, barbiturates, alcohol or marijuana. Cone ERGs to a white flash were not different between normals and the patient group; however, blue cone ERG showed significant reduction, the mean amplitude being about half that of the normal subjects. The changes identified persisted for at least 8 weeks without regression.[48] Further, this reduction has been found to relate to cocaine craving, such that the ERG could be an indicator of subjects more vulnerable to future relapse.[49,50]

Defects in colour vision

As dopamine plays a role in colour vision Desai *et al.*[51] investigated colour vision using the Farnswell-Munsell 100-hue and Lathony desaturated D-15 colour vision tests. Thirty-one inpatients who had recently stopped using cocaine were tested and compared with a control group matched for age and gender. The cocaine-withdrawn group showed a significantly higher error score on both tests, with 23 and 15 showing blue–yellow vision loss on the Farnswell-Munsell 100-hue and Lathony desaturated D-15 test, respectively. There were no significant differences for either red–green or mixed colour deficiencies. The authors consider the impairment due to the effect of cocaine on retinal neural transmission, and dismiss the possibility that vasoconstrictive effects on the retina are responsible, as no patient showed any evidence of retinal lesions.

Narcotics

Heroin (diamorphine), morphine, methadone

The main abuse with this group of opiates occurs with heroin and methadone. Although heroin can be sniffed or taken orally, it is usually smoked or injected. The effects of heroin are feelings of euphoria, peace and freedom from fear. It is a powerful analgesic. One sign of opiate use is miosis.[52] There has been some dispute as to whether tolerance develops, as pupils are still found to be miosed in long-term addicts; however, Tress and El-Sobky[53] found that to produce the same amount of constriction a much lower dose was necessary in non-dependent subjects than dependent subjects. Pupillary dilation has been shown to last for 5 days following withdrawal of heroin[54] and anisocoria may occur in some subjects (18% compared with 4% in the control group), usually during the first or second day of withdrawal.[55] In a systematic study of the effect of daily methadone use (50–60 mg) on pupil size under different light intensities, Weinhold and Bigelow[56] found that peak miosis was 90 minutes after methadone administration and was best detected under moderately dim lighting conditions.

Visual acuity loss

Buyers will often taste the heroin, which is bitter, to test quality. Quinine is sometimes used as a cutting agent, because of its bitter taste, to disguise dilute heroin. Toxic amblyopia due to quinine may occur.[57–60] Brust and Richter[57] report a patient taking about 5 g of quinine per day. Whilst vision did improve from the initial RE: hand movements and LE: 5/200 when on heroin without quinine, it deteriorated when the patient started using a heroin supply with quinine again. Pruzon *et al.*[60] found positive Amsler chart results in 3 of 14 addicts with blurred vision.

Quinine causing temporary visual loss was reported in another heroin user,[58] who started on a home-based detoxification programme and took quinine to help with muscle cramps. On presentation (after taking 20×6 g quinine sulfate tablets over a 12 hour period) acuities were limited to light perception; fundal examination showed attenuation of retinal arterioles and pallor. Eight days later acuities were 6/6 in either eye.

With overdose, respiratory function is depressed and one case of delayed postanoxic encephalopathy is reported where death eventually occurred.[61] However, prior to this pupils were reactive but visual acuity was limited to perception of large images. Optic discs were normal in appearance and presumably the visual defect was cortical.

Endophthalmitis

Metastatic endophthalmitis, due to *Candida albicans*, may occur where lemon juice has been used to dissolve the heroin and injected; or some cutting agents may embolize to the eye.[62] Martinez-Vazquez *et al.*[63] report a series of 15 cases, 12 with severe vitritis and 3 with uveitis. Seven patients underwent early vitrectomy and all had favourable responses. Late vitrectomy or no vitrectomy led to blindness in most cases. The authors concluded that early vitrectomy preceded and followed

by antifungal therapy should be the treatment method. Candidiasis may affect several parts of the body. Of 9 young men who used the same heroin, 7 (the other 2 having boiled the heroin preparation before injection) presented with hepatitis, followed by skin lesions, osteomyelitis, costochondritis (pain and tenderness in costal cartilage) and ocular lesions (chorioretinitis in 5 and episcleritis in 2).[64] Whilst no comment is made on the mechanism in this series, Hoy and Speed[65] report 8 cases over 4 years of candidiasis, in which 5 had ocular involvement (chorioretinitis and/or episcleritis). All had used lemon juice and at least 5 used a lemon which had been cut open more than 24 hours previously. The interior of lemons can support *Candida albicans* growth. Intralenticular abscess may also develop.[66] Another cause of metastatic endophthalmitis in drug users has been identified as *Aspergillus* (an air-borne fungus).[67]

Strabismus and ocular motility disorders

Himmelsbach in 1941[68] stated that patients, when withdrawing from heroin, sometimes complain of double vision or some impairment of vision. The incidence of 'diplopia/blurred vision' during both previous and current attempts at withdrawal in US soldiers who had served in Viet Nam[69] was found to be between 10% and 33.3% depending on the mode of heroin use.

Small case series of esotropia following heroin detoxification have appeared in the recent literature[70–72] and diplopia, in the absence of extraocular paresis, has been associated with the use of chlorpromazine (Largactil) during withdrawal in one patient.[73] Exotropia has been reported on intake of heroin in 2 cases.[72]

In a prospective study of patients attending a detoxification programme Firth *et al.*[74] reported a significant change in horizontal angle of deviation at distance, demonstrating a change in the eso direction (median 6^Δ) with about one-third of patients complaining of diplopia immediately post-detoxification. No statistical difference existed in the total prism fusion range before and after detoxification for near or distance and sixth nerve involvement was not implicated. Stereo-acuity, visual acuity (near; distance; reduced contrast) and convergence were found to be reduced in the immediate post-detoxification period. Subjective accommodation did not reduce but a small decline was found in objective accommodation at 20 cm. No changes in refractive error or objective accommodation at 33 cm were found. Further, no difference was found in the accommodation of the heroin users and a control group. Contrary to this Perez *et al.*[75] reported decreased or abnormal accommodation in 10 of 15 heroin users; however, the mechanism is suggested to be due to the sympathomimetic effect of cocaine, as 12 of the 15 subjects also used cocaine.

Wound botulism has been reported in 2 intravenous heroin users.[76,77] Diplopia, dysphagia, dysphonia and descending paralysis occur. Effects are reversed with anti-toxin administration.

Cases of internuclear ophthalmoplegia following opiate overdose have been reported.[78,79] Rizzo and Corbett[80] report one case of bilateral internuclear ophthalmoplegia in a known polydrug user (currently using methadone, diazepam, propoxyphene, and pheny-

toin sodium irregularly for generalized seizures co-incident with the multiple drug use). On presentation there was a decreased level of responsiveness; he was complaining of headaches, blurred vision and lethargy. Ecchymosis was present from a punch to the left eye 2 weeks earlier, and the eyes appeared exotropic. Limitation of both eyes on adduction with nystagmus of the abducting eye was present; convergence was normal. Speech was slurred. Naloxone (narcotic antagonist) was administered and within 5 minutes the patient was alert and eye movements returned to normal. This response to naloxone is suggestive that the opiate was responsible for the eye movement defect, although no opiate receptor sites have yet been identified in the region of the medial longitudinal fasciculus. The bilateral INO returned about 3 hours later but resolved completely by day 4 following presentation.

Stroke has been reported as a sequela of heroin use; however, no reports were found which specifically included ocular defects.

Nystagmus

Downbeat nystagmus has been observed after intravenous injection of opioids (100 mg pethidine or 0.1 mg fetanyl).[81] Mild cerebellar syndrome developed with ataxia, dysarthria and intention tremor. Similar effects occurred from both drugs, and have been reported previously with methadone. The mechanism may be related to the presence of opioid receptors in the cerebellum.

Injury from self-abuse

Self-injury was suspected in a supposed former heroin addict, now using methadone and barbituates.[82] The 24-year-old woman presented with a left hyphaema. Once the hyphaema had cleared a needle track was seen through the lens and vitreous to a rent in the retina. Perforating corneal scars were also present. The injury may not always be intentional. Hawkins *et al.*[83] report Horner's syndrome in a user following injection into the neck area and presumed damage of the sympathetic fibres (neck or groin area was used for injection as the arms were no longer able to be used).

Prenatal exposure

A higher number of strabismic children are born to heroin/methadone-dependent women than in the normal population.[84,85] Of 29 infants born to mothers at a methadone hydrochloride maintenance programme centre, 7 developed strabismus.[84] Four esotropic cases had a mean age at diagnosis of 10.5 months (range 6–12 months) and 3 exotropic cases had mean age at diagnosis of 15 months (range 6–27 months). The babies who developed strabismus showed a lower birth weight and their mothers had higher use during pregnancy of other drugs (e.g. antidepressants). There were no other differences in aspects studied (e.g. Apgar score, size, head circumference). Dominguez *et al.*[39] (as above) reported one heroin-exposed baby who had exotropia, and global delay with truncal ataxia and hypertonicity.

Changes in eye movement systems

Studies have been inconclusive regarding fixations

during reading[86] and tracking accuracy,[87] due to poor control of studies. Rothenberg *et al.* measured saccadic[88] and smooth pursuit[89] movements in a group of adults who were not drug-abusers after administration of 10 mg of oral methadone. The gain in smooth pursuit was reduced and an undershoot of saccades occurred which increased with increasing horizontal displacement of the target. The latency from target displacement to initiation of saccade was retarded. The authors suggested that the opiate binding sites identified in the area of the superior colliculus may have a role in causing the changes in the saccades. They point out that their findings were similar to those reported by others where lesions had been created in this area in animal models.

Defects in colour vision

Colour vision was found to be reduced in the blue–purple range in heroin addicts compared with controls. The level of defect (scored on the Farnsworth-Munsell 100-hue test) did not correlate with how the heroin was used (inhalation or intravenously). No macular lesions were found in the users and the pathogenesis was not explained; the defect could be retinal or within the visual pathway.[90]

Hallucinogenics

LSD (lysergic acid diethylamide)

LSD is a mood-altering drug which alters the state of perception and produces hallucinations and illusions that may be visual, auditory, related to the body or time. Visual changes include[91] blurring of vision (LSD dilates the pupils), imagery of patterns, fog, smoke which fills the visual field, changes in faces or body parts, changes in size and shape of objects/image distortion, heightened colours, false perception of movement, and trailing phenomena (i.e. discontinuous stationary images that trail behind the moving object).[92] LSD users may also experience hallucinogen persisting perception disorder (HPPD), that is either flash-backs or longer-lasting alterations of perceptions, after use of LSD.[93] Woody[94] reports 3 subjects, all of whom had used LSD along with other drugs (from amongst cannabis, heroin, amphetamines), who each reported a visual hallucination or prolonged after-image whilst driving. Physiological nystagmus has been shown to increase in frequency and amplitude after oral administion of 120 µg of LSD.[95] Sun-gazing whilst under the influence of LSD, leading to solar retinopathy, has been reported.[96–98]

Palinopsia

Kawasaki and Purvin[99] report palinopsia (the visual preservation of a recently seen object, usually associated with infarction, tumour, trauma or arteriovenous malformation) during acute LSD intoxication in 3 patients, each of whom also suffered the effect following discontinuation of the drug. The palinopic images were of a complementary colour in 2 patients and consisted of a trailing image in the third. All showed a normal neurological examination. The mechanism is not fully understood but failure of inhibition in an activated visual circuit can be considered.

Accommodative convergence/accommodation (AC/A) ratio

Payne[100] measured the AC/A ratio by a gradient method before and after varying doses of LSD in 10 male healthy volunteers. Mydriasis was noted in all subjects. The mean AC/A ratio increased from 4.83 ± 0.844 to 6.08 ± 0.973 ($p < 0.01$) but the change was not related to dose. The authors interpret this as due to a cycloplegic effect of the LSD, but were not able to determine whether this was due to sympathomimetic or parasympatholytic effects of the drug.

Ecstasy (methylenedioxymethamphetamine: MDMA)

MDMA acts by increasing the net release of the monoamine neurotransmitters (mainly serotonin and noradrenaline, with increased release of dopamine to a lesser extent).[101] Adverse reactions include: headache, loss of appetite, dry mouth, muscular tension, hyperthermia, cerebral oedema, hepatopathy, tachycardia, hypertension, and intracerebral haemorrhage (frequently related to an underlying vascular malformation such as aneurysm or arteriovenous malformation[102]).

One common complaint during use is blurred vision.[101] The mechanism for this is not stated but visual disturbances are a side effect of amphetamines and the blurred vision may arise from the increase in noradrenaline causing a dilated pupil or affecting accommodation. Two of 37 cases reported to the Poisons Information Centre in Ireland over an 18 month period were reported to have dilated pupils;[103] no other ocular symptoms were reported in this group.

Flashbacks have also been reported in two ecstasy users, one of whom had occasionally used LSD in the past.[104]

Ocular motility problems

One case of bilateral sixth nerve palsy has been reported in a 17-year-old man who had been taking ecstasy tablets (80–160 mg) at 5 to 7 day intervals over a period of 2 months.[105] Diplopia occurred approximately 24 hours after taking two tablets and resolved within 5 days. Abduction was mildly limited and a deviation of 10^Δ was present in the primary position increasing to 15^Δ on right and left gaze. In addition minimal paresthesia was present in both arms and legs and there was mild sleepiness. All neurological investigations were normal, and there were no other signs of central nervous system or neurodegenerative disease. The mechanism for the sixth nerve involvement is speculative but the authors propose either a mild cerebral oedema not detectable by magnetic resonance imaging or interaction of MDMA with serotonin metabolism in the sixth nerve, if serotoninergic interneuronal fibres exist in humans as found in the cat.

Visual acuity loss

Sudden loss of vision due to a retinal haemorrhage has been reported in a 22-year-old woman 30 minutes after taking an ecstasy tablet.[106] Examination revealed visual acuity of 1/60 in the affected eye with a subinternal limiting membrane haemorrhage at the centre of the left macula with retrohyaloid haemorrhages above and

below the macula. No other abnormalities were found and 3 months later the visual acuity was 6/9 and the haemorrhages had resolved. The cause is suggested to be a sudden rise in blood pressure affecting the retinal circulation, which is vulnerable to sudden changes in blood pressure.

Visual perception disorder

Destruction of serotonergic nerve terminals has been suggested as the mechanism for a persistent visual perception disorder in a 22-year-old man with a 3 year history of drug abuse.[107] The patient reported 'hundreds of transparent dots moving chaotically over his whole visual field'. The phenomenon increased in the dark, and with his eyes closed small coloured dots were seen. This patient had also used cannabis regularly and had used LSD on between five and seven occasions.

Palinopsia

Palinopsia was reported in 2 patients in a series of 13 who presented with psychiatric problems.[108] One had previously used LSD on several occasions and had used ecstasy on one occasion only. The other had not used any other drugs.

Magic mushrooms

Common varieties of mushrooms used are Liberty Cap (*Psilocybe semilanceata*) and Mexican mushroom (*Psilocybe mexicana*). The active ingredients in mushrooms are psilocybin and psilocin. The effects are similar to those of LSD, the main ones being psychological – feeling euphoric, giggly and happy. The senses are increased so that colours are more intense and music sounds richer. Heart rate and blood pressure increase slightly and the pupils dilate. At higher doses hallucinations occur. Anxiety, fear and paranoia are less pleasant effects. Malitz and Kanzler[91] found the perceptual distortions following administration of psilocybin in a normal population to be similar to those of LSD (see above), and similar changes in physiological nystagmus to those produced by LSD have been reported.[95] Fischer *et al.*[109] found contraction or closing in of nearby visual space in a group of normal subjects under psilocybin.

Another mushroom used as a drug is the European Fly Agaric (*Amanita muscaria*, which is poisonous when uncooked), which contains a high concentration of muscarine. Ocular side effects of its use are blurred vision (due to reduced accommodation)[110] and runny eyes.

Mescaline

Mescaline is a hallucinogenic found in several types of cactus that has effects similar to LSD. Whilst a liquid form can be prepared it is usually available as a powder. It is extremely rare in the UK. Malitz and Kanzler[91] found that visual hallucinations occurred slightly more frequently with mescaline than with LSD, although the content of illusions was similar. Euphoria did not occur with mescaline. Physiological nystagmus may increase.[95]

Phencyclidine (PCP)

PCP is a stimulant with hallucinogenic properties. It is bought in white crystalline powder form which may be sniffed, smoked, swallowed or prepared for injection. Mild hallucinations may occur and the user feels dreamy and may experience distortions of time and space.

Amaurosis fugax

One case has been reported of amaurosis fugax associated with PCP inhalation.[111] The 45-year-old diabetic man with hypertension and a history of coronary artery disease presented with two episodes of sudden, transient right vision loss in 3 days. The visual loss had occurred 6–8 hours after smoking an unknown substance. Urine toxicology was positive for PCP. Fundoscopy was normal and no retinal pallor seen.

Nystagmus

Liden *et al.*[112] reported nystagmus in 5 of 9 cases of PCP poisoning: 1 horizontal, 3 horizontal and vertical, and 1 horizontal, vertical and rotary. No further detail is given. Miotic pupils were also listed as a sign. Herskowitz and Oppenheimer[113] suggest that nystagmus is an important sign in distinguishing PCP poisoning from other drug intoxications. In their two teenage cases 'striking bursts of irregular, shuddery, jerky nystagmus in the direction of gaze' were present, with the amplitudes being greatest on upgaze. General signs were red cheeks, inflamed nasal mucosae, dry tongue, increased lacrimation and marked ataxia on walking. In another report 7 patients admitted to an intensive care unit for PCP intoxication all showed nystagmus, along with disorientation, delusions and disorganised thoughts. The focus of the paper was on use of physostigmine as an antidote and the nystagmus did reduce following injections of this drug.[114]

Method of literature review

Relevant articles were identified by a MEDLINE search (1966 to June 2003) using the combined search terms visual acuity, blindness, retinal haemorrhage, vision disorders, eye diseases, diplopia, strabismus, eye movements, ocular motility disorders, and the individual terms cocaine and crack cocaine, MDMA (ecstasy), heroin and heroin dependence, LSD, psilocybin and psilocin (magic mushrooms), mescaline, phencyclidine. The search was limited to human. Additionally, articles of relevance, from peer-reviewed journals, that were referenced in the articles identified from the MEDLINE search have been included.

Conclusion

The main problems following use of class A drugs that may present to the ophthalmologist or orthoptist include cerebrovascular disease, retinal or corneal problems, strabismus and ocular motility defects. Clinical examination will reveal the condition present but illicit drug use should be considered in the differential diagnosis where the aetiology is obscure or unexplained.

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