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Sir,

Primary position upbeat nystagmus associated with amitriptyline use

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This case illustrates that amitriptyline withdrawal may be responsible for the onset of primary position upbeat nystagmus. This is not a recorded side effect of the drug and it has not been previously reported in the literature.

Case

A 42-year-old man was seen in the West Suffolk Eye Department complaining of blurred vision for 5 days. His Snellen visual acuity was 6/60 in the primary position, and on down gaze it improved to 6/6. He had no medical history of eye problems; however, he did suffer from asthma and had had a basal skull fracture in 1996. A computerized tomography scan from 1996 showed right posterior temporal and left subfrontal region gliosis.

Eye examination revealed a primary position vertical nystagmus, and the fast phase was up. The nystagmus reduced on down gaze. He had no relative afferent pupillary defect; his eye movements were full; his colour vision, measured with Ishihara plates, was intact; and fundal examination showed no abnormalities. An examination of his central nervous system was normal. A magnetic resonance scan of his brain showed no new changes.

He had been taking salbutamol and flixotide inhalers for a number of years to control his asthma. At 6 months before the onset of nystagmus, he had started taking amitriptyline 150 mg once daily, for depression. At 2 weeks before the nystagmus commenced, he reduced his amitriptyline dose down to 100 mg. At 2 weeks after the start of the nystagmus he cut the dose to 50 mg, under the guidance of his GP. The dose was reduced to 25 mg a week later, and stopped after a further week. With the reduction of the drug, he found that his nystagmus gradually resolved.

The medicines control agency was informed of a possible association between amitriptyline and the induction of nystagmus; the agency reported two previously documented cases.

Comment

Upbeat nystagmus is a type of central vestibular nystagmus. It can be caused by lesions from the medulla to the midbrain. It usually increases in up gaze, but not on lateral gaze, and fixation does not dampen it. Causes of upbeat nystagmus include: cerebellar degeneration, multiple sclerosis, infarction of the medulla, tumours, Wernicke's encephalopathy, brain stem encephalitis, Behcet's syndrome, meningitis, congenital, middle ear disease, and drugs. This condition is often seen with medullary lesions; these involve the perihypoglossal nuclei, medial vestibular nuclei, nucleus intercalatus, and the ventral tegmentum. It is also reported in lesions of the anterior vermis of the cerebellum, the brachium conjunctivum, and midbrain.

Primary position upbeat nystagmus has been reported secondary to organophosphate toxicity[1] and tobacco.[2]

We propose that amitriptyline withdrawal may cause upbeat nystagmus by the following mechanism. Acetylcholine and histamine are found in the vestibular system; acetylcholine is a central vestibular agonist. Amitriptyline blocks histamine and muscarinic acetylcholine receptors and is therefore a vestibular suppressant. We suggest that withdrawal of amitriptyline removes this inhibition and may result in nystagmus owing to receptor hypersensitivity; this is a temporary symptom. If this is the case, there may be a role for amitriptyline in the control of nystagmus.

References

1 Jay WM, Marcus RW, Jay MS. Primary position upbeat nystagmus with organophosphate poisoning. *J Pediatr Ophthalmol Strabismus* 1982; **19**): 318–319.
2 Sibony PA, Evinger C, Manning KA. Tobacco-induced primary-position upbeat nystagmus. *Ann Neurol* 1987; **21**(1): 53–58.

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