Supranuclear gaze palsy and opsoclonus after Diazinon poisoning

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A 52 year old man developed a supranuclear gaze palsy and opsoclonus after Diazinon poisoning. The diagnosis was confirmed by low plasma and red blood cell cholinesterase activity and urine mass spectroscopy. Saccadic control may be mediated in part by acetylcholine. Opsoclonus in the setting of organophosphate intoxication may occur as a result of cholinergic excess which overactivates the fastigial nuclei.

Various central eye movement abnormalities have been described after organophosphate poisoning. Diazinon, an organophosphate, acts as a cholinesterase inhibitor. Accumulation of acetylcholine at muscarinic, nicotinic, and central sites results in the acute toxic effects. Often the well recognised findings such as delirium, convulsions, and paralysis overshadow such eye findings. We report a patient with supranuclear gaze palsy and opsoclonus from Diazinon poisoning and speculate on the possible underlying mechanisms.

CASE REPORT

A 52 year old man with a history of hypothyroidism and anxiety disorder was admitted to a local hospital with acute confusion, dysarthria, and ataxia. Shortly after admission, he had a convulsion and was intubated for airway protection. Computed tomography (CT) of the head was normal. EEG was noted. He was transferred to our hospital for further evaluation.

Pupillary miosis, copious secretions, and diarrhoea were noted. He was admitted to our hospital for further evaluation. Although opsoclonus has been previously described in association with organophosphate poisoning, our patient was unique in that he demonstrated both supranuclear gaze palsy and saccadic oscillations. Ocular flutter is a saccadic oscillation similar to opsoclonus, characterised by involuntary horizontal eye movements without an intersaccadic interval. Although the exact mechanism and localisation of saccadic oscillations is uncertain, it has been suggested that opsoclonus and ocular flutter occur as a result of dysfunction of omnipause neurones that reside in the nuclei raphé interpositus. During normal fixation, these neurones are thought to inhibit the activity of burst neurones that drive normal saccades. However, pathological studies of patients with opsoclonus have not shown consistent abnormalities in the omnipause region. Furthermore, experimental lesions of omnipause neurones have been shown to cause slowing of horizontal and vertical saccades, but not saccadic oscillations.
or flutter, fastigial and vermal lesions have been shown to lead studies of the cerebellum have not demonstrated opsoclonus under appropriate conditions. The brain stem saccade system that could account for oscillations in omnipause dysfunction there is inherent instability in the saccade generator are partly mediated by acetylcholine. We propose that the source of input may arise from brain stem cholinergic nuclei such as the pedunculopontine segmental nucleus (PPTN). This paired cell group has been traditionally linked to a variety of functions including locomotion, arousal, and sleep. Its location adjacent to the brain stem saccadic system and the fastigial nucleus raises the possibility of a functional connection between these structures. PPTN neurones have been shown to project to the contralateral fastigial nucleus and intermediate layers of the superior colliculus.

In our case of organophosphorus intoxication, excess acetylcholine could have led to enhanced fastigial output resulting in inhibition of omnipause neurones and release of burst neurones (fig 1). Activation of the fastigial nucleus along with the inherent instability and delay in the saccade generator could have led to opsoclonus. The signal for voluntary gaze control may have been inhibited by the effect of excess acetylcholine on other supranuclear projections.

Our patient’s constellation of eye findings suggests that saccadic control may be mediated in part by acetylcholine. A similar combination of supranuclear gaze palsy and saccadic intrusions manifesting as square wave jerks often occurs in progressive supranuclear palsy. In contrast to our case, it is a loss of cholinergic cells in the PPTN, interstitial nuclei of Cajal, rostral interstitial nucleus of the MLF, and superior colliculus that is thought to lead to the hallmark eye movements of progressive supranuclear palsy. Whether it is a loss of acetylcholine or an excess in brain stem nuclei, it is conceivable that an imbalance of acetylcholine may lead to simultaneous release and inhibition of supranuclear structures involved in gaze control. The role of acetylcholine in gaze control is not well understood, and study of these cholinergic pathways may provide further insight into disorders of ocular motility. Furthermore, the diagnosis of organophosphorus poisoning may be aided by the recognition of these eye findings.

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The fastigial ocular motor region has a well known role in the control of saccade accuracy. It is known to project to omnipause neurones and burst neurones. Although lesion studies of the cerebellum have not demonstrated opsoclonus or flutter, fastigial and vermal lesions have been shown to lead to saccades with highly variable gains and velocities. Wong and colleagues created a model of opsoclonus by incorporating the fastigial ocular motor region into the brain stem saccade system. By introducing a slight delay and increase in the fastigial output (gain) into the feedback loop, they produced hypermetria. With further increases in the gain, they produced indefinite oscillations with a frequency and amplitude consistent with opsoclonus.

The fact that the eye findings occurred after organophosphate intoxication suggests that the pathways involved in saccade generation are partly mediated by acetylcholine. We propose that the source of input may arise from brain stem cholinergic nuclei such as the pedunculopontine segmental nucleus (PPTN). This paired cell group has been traditionally linked to a variety of functions including locomotion, arousal, and sleep. Its location adjacent to the brain stem saccadic system and the fastigial nucleus raises the possibility of a functional connection between these structures. PPTN neurones have been shown to project to the contralateral fastigial nucleus and intermediate layers of the superior colliculus.

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