

Nystagmus among suspected amphetamine impaired drivers

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ABSTRACT

Clinical signs of drug use can be helpful to identify which drug has been consumed. Amphetamine intake has traditionally not been considered to cause nystagmus. The aim of this study was to explore whether there is a relationship between amphetamine use and nystagmus in a population of apprehended drivers in a naturalistic setting. We evaluated drivers suspected of drug-impaired driving where blood samples were collected and a clinical test of impairment (CTI) was performed. Evaluation of nystagmus is one of the CTI subtests. The samples were analysed for alcohol and psychoactive drugs. Cases with a nystagmus test were recorded and amphetamine-only cases were compared with alcohol-only cases and with cases where alcohol or drugs were not detected, respectively. Samples from 507 amphetamine-only cases were compared to 485 alcohol-only cases and 205 drug-negative cases. The median blood amphetamine concentration was 0.37 mg/L and the median alcohol concentration was 1.57 g/kg. The proportion of cases with nystagmus was similar in amphetamine-only cases (21%) and drug-negative controls (25%), $p = 0.273$, but higher in alcohol-only cases (53%), $p < 0.001$. No association was found between the blood amphetamine concentration and degree of nystagmus (Spearman's $\rho = 0.008$, $p = 0.860$), whereas an association between blood alcohol concentration and degree of nystagmus was demonstrated ($\rho = 0.249$, $p < 0.001$). In conclusion, our study did not find that apprehended drivers using amphetamine had more frequently nystagmus than a control group that tested negative for alcohol and drugs, even at high amphetamine concentrations in blood. Hence, nystagmus should not be considered a tool for identifying amphetamine-induced impairment in drivers.

1. Introduction

Amphetamine is one of the most commonly used illegal drugs globally and is frequently detected in blood samples from drivers suspected of driving under the influence (DUI) of drugs in Norway. In 2020, amphetamines (i.e. amphetamine and/or methamphetamine) were detected in 37% of blood samples from drivers apprehended by the police suspected for DUI of drugs.¹

The use of amphetamines, especially in high doses, is associated with a highly increased risk of being seriously injured or killed in a road traffic crash.² Accordingly, all apprehended drivers suspected of DUI in Norway are tested for the presence of amphetamines in their blood.

To evaluate the suspect's degree of impairment, a clinical test of impairment (CTI) is applied at the time of blood sampling. In Norway, the CTI consists of 25 individual tests, including test of nystagmus.³ A physician performs this clinical examination. The CTI was originally designed to detect alcohol-induced impairment,⁴ but has been modified

to assess impairment by non-alcohol drugs. It has, however, been suggested that the CTI has a low sensitivity to detect impairment following amphetamine intake.

Nystagmus is a condition that causes involuntary, rapid movement of one or both eyes. The most common cause of acquired nystagmus is the use of certain drugs or medicines. Acute alcohol intoxication affects cerebellar function, inducing, among others, gaze instability as gaze-evoked nystagmus.⁵ Nystagmus is also common after the use of many drugs of abuse, including phencyclidine, opiates, cannabis, and barbiturates.^{6–8} Stimulant drugs, like amphetamine, are not known for causing nystagmus.⁹ A clinical study where performance was assessed using the Standardised Field Sobriety Test, which includes nystagmus test, after administration of low doses of dexamphetamine, *d,l*-methamphetamine and *D*-methamphetamine found that the drugs did not significantly impair performance of the horizontal nystagmus test.⁹ Concentrations of amphetamine in blood measured in that study was around 0.07–0.1 mg/L.

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However, it has been claimed that nystagmus might occur after intake of high doses.^{10,11} For ethical reasons, there is a lack of controlled studies on the effect of high-dose intake of amphetamines on nystagmus. In samples from apprehended drivers higher concentrations of amphetamine in blood can be seen than in clinical trials.

The aim of this study was to investigate whether there is a relationship between amphetamine use and nystagmus in apprehended drivers as compared to alcohol-impaired drivers and drivers testing negative for alcohol and drugs in a naturalistic setting.

2. Methods

We used data from an existing database at the Department of Forensic Medicine, Oslo University Hospital, consisting of analytical test results for all blood samples taken from apprehended drivers suspected of DUI of drugs in Norway. Cases from the period 2016–2021 were reviewed and the results of a nystagmus test was recorded in a total of 507 cases testing positive for amphetamine only, 485 cases of alcohol only, and 205 cases where alcohol or drugs were not detected.

The following parameters were registered: concentration of alcohol or amphetamine, age, sex, and horizontal gaze nystagmus. Nystagmus was scored as either ‘no’, ‘slight’ or ‘obvious’. The amphetamine or ethanol positive cases were divided into five groups based on the concentration in blood.

All blood samples from apprehended drivers were routinely screened for ethanol and drugs of abuse (approximately 50 drugs including amphetamines, cocaine, MDMA, benzodiazepines, THC, opioids, and others). Amphetamine concentrations were determined by ultra-high performance liquid mass spectrometry (UHPLC-MS/MS) and alcohol by head-space gas chromatography.^{12–14} The cut-off values of the analysis were set to 0.03 mg/L for amphetamine and 0.04 g/kg for ethanol.

Microsoft Excel was used for manual data preparation and figures. A Chi-Square Test was applied to compare the presence of nystagmus in amphetamine-positive cases to alcohol-positive cases and to cases testing negative for alcohol and drugs. For correlation between concentrations and degree of nystagmus, a bivariate Spearman’s correlation was applied. A multiple linear regression model using degree of nystagmus as dependent variable was implemented to correct for age and gender in the relation between drug concentration and degree of nystagmus. All statistical analyses were conducted using SPSS Statistics version 28 (IBM Corporation, Armonk, NY).

The study was approved by the Norwegian Higher Prosecuting Authority (21/1392), which is the data owner, and by the Data Protection Officer at Oslo University Hospital (21/11520).

3. Results

The data included 507 cases of apprehended drivers where only amphetamine was detected in the blood sample (hereafter referred to as amphetamine-only cases). The drivers were aged 17–71 years with a median age of 39 years, see Table 1. A total of 485 alcohol-only cases were included, with drivers aged 16–80 years with a median age of 35 years. Finally, 205 drug-negative cases were included with drivers aged

Table 1
Number of cases with gender (%) and median (range) age, and median (range) concentrations of amphetamine and alcohol in blood.

| | Amphetamine-only | Alcohol-only | Alcohol and drug negative |
|--|------------------------|-------------------------|---------------------------|
| n | 507 | 485 | 205 |
| Number of males (%) | 431 (85) | 387 (80) | 186 (91) |
| Median age (range) | 39 years (17–71) | 35 years (16–80) | 31 years (16–72) |
| Median concentration in blood (range) | 0.37 mg/L (0.027–3.65) | 1.57 g/kg (0.005–0.397) | – |

16–72 years with a median age of 31 years.

The median blood amphetamine concentration was 0.37 mg/L and the median blood alcohol concentration was 1.57 g/kg, see Table 1.

The proportion of cases with nystagmus was similar in amphetamine-only cases (n = 107, 21%) and drug-negative controls (n = 51, 25%), p = 0.273, see Fig. 1. The proportion of cases with nystagmus was higher in alcohol-only cases (n = 255, 53%) than in amphetamine-only cases and drug-negative controls, p < 0.001 for both

No association was found between the blood amphetamine concentration and degree of nystagmus (Spearman’s $\rho = 0.008$, p = 0.860), whereas an association between blood alcohol concentration and degree of nystagmus was demonstrated ($\rho = 0.249$, p < 0.001). Also when correcting for age and sex in a multivariate regression analysis, there was no relation between concentration of amphetamine and degree of nystagmus ($R^2 = 0.004$, F(3,503) = 0.691, p = 0.558). There was still a relation between concentration of ethanol and degree of nystagmus after correction for age and sex ($R^2 = 0.080$, F(3,481) = 14.011, p < 0.001).

The group with highest amphetamine concentrations (>1.08 mg/L) consisted of 60 cases. The prevalence of nystagmus among these drivers (25%) was not statistically significantly different from the prevalence among those with amphetamine concentrations below 1.08 mg/L (20%; p = 0.252). No association between blood amphetamine concentrations >1.08 mg/L and degree of nystagmus was demonstrated ($\rho = 0.009$, p = 0.947).

4. Discussion

The proportion of cases with nystagmus was similar in amphetamine-only cases and drug-negative controls, but higher in alcohol-only cases. No association was found between the blood amphetamine concentration and degree of nystagmus, even at the highest concentration-levels, which contradicts the claim that high doses of amphetamine might cause nystagmus.^{10,11} Correction for age or gender did not affect the relation between degree of nystagmus and drug concentration in any group.

The median amphetamine concentration in blood in the mono-substance cases was 0.37 mg/L, which is relatively high compared to the legal limit, which is 0.041 mg/L, and the graded sanction limits 0.203 mg/L and 0.487 mg/L.¹⁵ Even at the highest concentrations (>1.08 mg/L), no significant association with degree of nystagmus was observed.

Fig. 1 visually give the impression that nystagmus was more frequent in the group with the lowest amphetamine concentrations in blood.

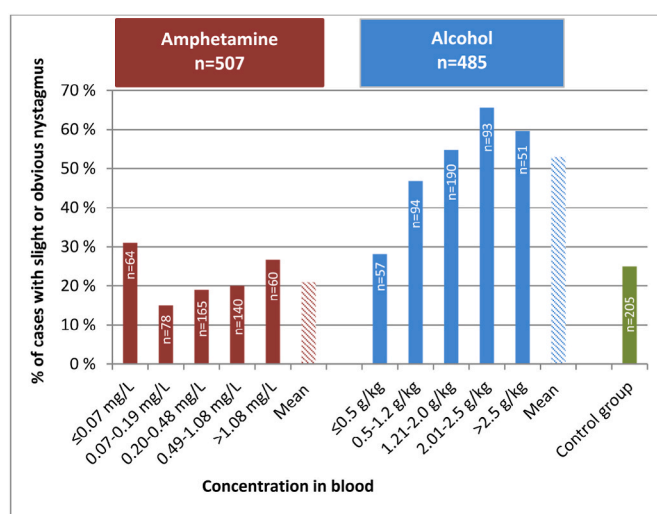


Fig. 1. The proportion of cases with nystagmus in amphetamine-only cases, alcohol-only cases and drug-negative controls, related to amphetamine- and alcohol concentration levels in blood.

However, there was no significant difference in prevalence of nystagmus among drivers with concentrations ≤ 0.07 mg/L than those with concentrations > 0.07 mg/L.

Amphetamine effects in apprehended drivers is depending on whether blood amphetamine concentrations rise or decline, but it is not known if this pertains to nystagmus. Amphetamine typically causes an increased energy level, restlessness, dilated pupils and increased blood pressure and pulse in the first hours after intake.¹⁶ Towards the end of the intoxication, most typically after binge use, depressant effects, such as sleepiness and lethargy, are the prominent effects. A limitation in our study is that our data does not include the time of amphetamine intake and hence the time point of a time-concentration curve is unknown.

In conclusion we did not find that apprehended drivers using high doses of amphetamine had more frequently nystagmus than a control group that tested negative for alcohol and drugs. To the best of our knowledge, there is also no other evidence from other studies to support that nystagmus is a sign of use or impairment of amphetamine. A nystagmus test should therefore not be considered a tool for identifying amphetamine-induced impairment in drivers.

Declaration of competing interest

All authors have declare that: (i) no support, financial or otherwise, has been received from any organization that may have an interest in the submitted work; and (ii) there are no other relationships or activities that could appear to have influenced the submitted work.

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