



## Analysis of stimulant drugs in the wastewater of five Nordic capitals

Arndís Sue Ching Löve<sup>a,\*</sup>, Jose Antonio Baz-Lomba<sup>b</sup>, Malcolm J. Reid<sup>b</sup>, Aino Kankaanpää<sup>c</sup>, Teemu Gunnar<sup>c</sup>, Maria Dam<sup>d</sup>, Kristín Ólafsdóttir<sup>a</sup>, Kevin V. Thomas<sup>b,e</sup>

<sup>a</sup> University of Iceland, Department of Pharmacology and Toxicology, Hofsvallagata 53, 107 Reykjavik, Iceland

<sup>b</sup> Norwegian Institute for Water Research (NIVA), Gaustadalléen 21, 0349 Oslo, Norway

<sup>c</sup> National Institute for Health and Welfare (THL), Forensic Toxicology Unit, Mannerheimintie 166, FI-00300 Helsinki, Finland

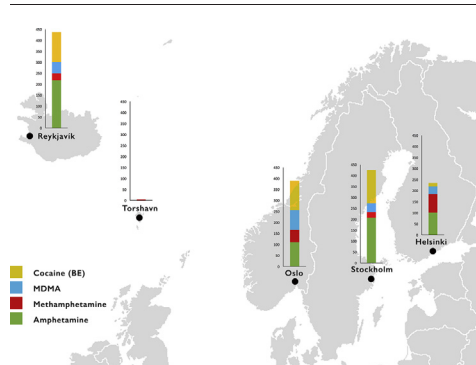
<sup>d</sup> Environment Agency, Traðagøta 38, FO-165 Argir, Faroe Islands

<sup>e</sup> Queensland Alliance for Environmental Health Sciences (QAEHS), 39 Keesels Road, Coopers Plains, 4108, Queensland, Australia

### HIGHLIGHTS

- First Nordic comparison based on wastewater analysis of stimulant drugs in five capital cities
- Analytical performance was ensured by inter-laboratory comparison studies.
- Results revealed high use of amphetamines but not cocaine, compared with other European cities.
- Recreational use of cocaine and MDMA indicated by higher levels during weekends.

### GRAPHICAL ABSTRACT



### ARTICLE INFO

#### Article history:

Received 24 November 2017

Received in revised form 23 January 2018

Accepted 26 January 2018

Available online 3 February 2018

Editor: Jay Gan

#### Keywords:

Nordic countries

Wastewater-based epidemiology

Amphetamine

Methamphetamine

MDMA

Cocaine

### ABSTRACT

Wastewater-based epidemiology is an efficient way to assess illicit drug use, complementing currently used methods retrieved from different data sources. The aim of this study is to compare stimulant drug use in five Nordic capital cities that include for the first time wastewater samples from Torshavn in the Faroe Islands. Currently there are no published reports that compare stimulant drug use in these Nordic capitals. All wastewater samples were analyzed using solid phase extraction and ultra-high performance liquid chromatography coupled to tandem mass spectrometry. The results were compared with data published by the European Monitoring Centre for Drugs and Drug Addiction based on illicit drugs in wastewater from over 50 European cities. Confirming previous reports, the results showed high amphetamine loads compared with other European countries. Very little apparent abuse of stimulant drugs was detected in Torshavn. Methamphetamine loads were the highest from Helsinki of the Nordic countries, indicating substantial fluctuations in the availability of the drug compared with previous studies. Methamphetamine loads from Oslo confirmed that the use continues to be high. Estimated cocaine use was found to be in the lower range compared with other cities in the southern and western part of Europe. Ecstasy and cocaine showed clear variations between weekdays and weekends, indicating recreational use. This study further demonstrates geographical trends in the stimulant drug market in five Nordic capitals, which enables a better comparison with other areas of the continent.

© 2018 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

\* Corresponding author.

E-mail address: [asl2@hi.is](mailto:asl2@hi.is) (A.S.C. Löve).

## 1. Introduction

Increasing use and higher potency of drugs of abuse poses a continuing threat to human health (European Monitoring Centre for Drugs and Drug Addiction, 2016b). Illicit drug use is known to have negative effects on crime rates and can cause serious public health issues such as higher risk of premature death and transmission of infectious diseases. These effects can lead to high economic and social costs (United Nations Office on Drugs and Crime, 2016). Monitoring drug use is crucial in order to fully understand the problem and develop efficient countermeasures (European Monitoring Centre for Drugs and Drug Addiction, 2016b).

Drug use and availability is known to show both temporal and geographical variations (Kankaanpää et al., 2014; Ort et al., 2014; Thomas et al., 2012). For example, amphetamines have a higher prevalence of use in northern and eastern Europe, as opposed to cocaine in western and southern Europe (European Monitoring Centre for Drugs and Drug Addiction, 2016b). National population surveys, information on drug seizures and clinical data have traditionally been used to monitor drug consumption. According to national reports based on population surveys that have been commissioned and compiled by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), cannabis is the most commonly used illicit drug followed by amphetamines and cocaine in Denmark, Finland, Norway and Sweden (European Monitoring Centre for Drugs and Drug Addiction, 2017a, 2017c, 2017d, 2017e). Similar patterns in use have been reported for Iceland and the Faroe Islands, according to the European School Survey Project on Alcohol and Other Drugs (ESPAD) (European Monitoring Centre for Drugs and Drug Addiction, 2016a). However, these survey methods have shown significant limitations such as reporter bias, low response rates and struggle to provide information on rapidly changing trends in the drug market. Therefore, other measures are needed to complement these methods to ensure a more comprehensive assessment (Castiglioni et al., 2014).

Wastewater-based epidemiology (WBE) is an approach where urinary excretion products are quantified to assess illicit drug use of a large population (Zuccato et al., 2005). WBE can give reliable results that may quickly reveal short and long-term trends in the scale of drug use. This approach can therefore provide a valuable source of complementary data to support more traditional epidemiological methods (Ort et al., 2014; Terzic et al., 2010; Thomas et al., 2012; van Nuijs et al., 2011; Zuccato et al., 2011). The EMCDDA has published the findings of the European inter-disciplinary network “Sewage analysis CORE group – Europe” (SCORE) (SCORE, 2017). This network brought scientists from relevant disciplines together to support research and innovation in Europe based on the analysis of biomarkers in wastewater. The main aim was to ensure that novel technologies were transferred to full-scale applications in order for authorities to be able to utilize the information gathered. Furthermore, the goal was to establish protocols for wastewater analysis by coordinating international studies with inter-laboratory comparisons. This European-wide network has organized measurements of illicit drugs in wastewater each year since 2011 in over 50 cities (Ort et al., 2014; SCORE, 2017; Thomas et al., 2012).

WBE studies have been performed in most Nordic countries to complement other methods (Bramness et al., 2015; Kankaanpää et al., 2014; Ort et al., 2014; Östman et al., 2014; Thomas et al., 2012). Results have shown that amphetamines have been more dominant than cocaine on the stimulant drug market in Northern Europe (Bramness et al., 2015; Kankaanpää et al., 2014; Ort et al., 2014; Östman et al., 2014; SCORE, 2017; Thomas et al., 2012). Amphetamine is excreted unchanged in urine (30–74%) and is also an urinary metabolite of methamphetamine (4–7%) (Baselt, 2014). It is therefore important to assess the use of these two chemicals in parallel (Ort et al., 2014). WBE studies have demonstrated that methamphetamine use is prominent in central Europe and is reportedly produced in Lithuania or the Czech Republic before being exported to Scandinavian countries (Griffiths et al., 2008;

Mackul'ak et al., 2014; Ort et al., 2014). Amphetamine use has generally been higher than methamphetamine use in the Nordic countries with the exception of Denmark where the use of both drugs is low compared with cocaine (Baz-Lomba et al., 2016; SCORE, 2017). However, in recent years Norway and Finland have also showed high methamphetamine loads with continued high loads of amphetamine in parallel (Bramness et al., 2015; Ort et al., 2014; SCORE, 2017). Trends in 3,4-methylenedioxymethamphetamine (MDMA) use, based on interview surveys, have indicated that the drug is becoming more common in Europe among young people (European Monitoring Centre for Drugs and Drug Addiction, 2016b). Most recent reports based on WBE show that the largest MDMA loads are measured in northern European countries such as the Netherlands, Belgium, Norway and Denmark (Baz-Lomba et al., 2016; SCORE, 2017). WBE studies have demonstrated that cocaine use is most prominent in western European countries such as Belgium, the United Kingdom, Switzerland, Spain and the Netherlands (Baker et al., 2014; Baz-Lomba et al., 2016; Been et al., 2016; SCORE, 2017).

For the first time, this study aims to compare and discuss trends in stimulant drug use based on WBE in the capital cities of Norway, Iceland, Finland, Sweden and the Faroe Islands. Never before have illicit drugs in wastewater been analyzed from Torshavn in the Faroe Islands. Chosen for this study were the stimulant illicit drugs amphetamine, methamphetamine, MDMA and cocaine. Due to analytical difficulties it was not possible to include cannabis in this study (Causanilles et al., 2017). By using similar sample preparation methods, instrumental analysis and data processing, it was possible to achieve harmonized results that can be compared with reports from other European countries in the SCORE network (SCORE, 2017). The analytical performance of methodologies was also evaluated by external quality control cycles, which were performed by different laboratories (van Nuijs et al., 2018).

## 2. Materials and methods

### 2.1. Chemicals, reagents and materials

The following materials were used for the preparation and analysis of samples from Oslo, Reykjavik, Stockholm and Torshavn: reference standards for eight illicit drugs and/or major metabolites were amphetamine, methamphetamine, MDMA, cocaine, benzoylecgonine (BE), and cocaethylene. Reference standards were dissolved in methanol (MeOH) or acetonitrile (ACN) at concentrations of 1 mg/mL or 100 µg/mL. Corresponding isotope-labeled internal standards (ILIS) used were amphetamine- $d_8$ , methamphetamine- $d_{11}$ , MDMA- $d_5$ , cocaine- $d_3$ , BE- $d_3$  and cocaethylene- $d_3$  dissolved in MeOH or ACN at concentrations of 100 µg/mL. All reference standards and ILIS were purchased from Cerilliant (Round Rock, TX, USA). Standard stock solutions for reference standards were prepared at concentrations of 100 µg/mL in either MeOH or ACN. Mixed working solutions were prepared for the reference standards and the ILIS at concentrations of 1.0 µg/mL in MeOH. All standard and working solutions were stored at  $-20\text{ }^{\circ}\text{C}$ . HPLC-grade MeOH was from Rathburn Chemicals Ltd. (Walkerburn, SCT, UK) and HPLC-grade ACN was from VWR Chemicals (Oslo, NOR). Ammonium hydroxide ( $\text{NH}_4\text{OH}$ ) solution  $\geq 25\%$  in water was from Fluka - Sigma-Aldrich (Oslo, NOR) and formic acid (FA) 98–100% (p.a.) was from Merck - Millipore (Billerica, MA, USA). Oasis HLB µElution plates (30 µm) were purchased from Waters (Milford, MA, USA).

The following materials were used for the preparation and analysis of samples from Helsinki: reference standards purchased from Sigma-Aldrich (St. Louis, MO, USA) were amphetamine sulphate, cocaine hydrochloride and MDMA hydrochloride. A reference standard donated by the UN Narcotics Laboratory (Vienna, Austria) was methamphetamine hydrochloride. Reference standards and ILIS purchased from Cerilliant (Round Rock, TX, USA) were BE, amphetamine- $d_6$ , cocaine- $d_3$ , MDMA- $d_5$ , methamphetamine- $d_{14}$  and BE- $d_3$  dissolved in MeOH or ACN at concentrations of 1 mg/mL or 100 µg/mL. Carbon 13-labeled

internal standards purchased from Chiron AS (Trondheim, NO) were  $^{13}\text{C}_6$ -amphetamine sulphate,  $^{13}\text{C}_6$ -methamphetamine hydrochloride and  $^{13}\text{C}_6$ -MDMA hydrochloride. A Direct-Q® system with a LC-Pak™ from Merck - Millipore (Billerica, MA, USA) was used to purify water to a UHQ grade. A  $\text{C}_{18}$  reverse-phase silica cartridge was used to minimize interferences due to organic impurities in the mobile phase. Oasis MCX Vac RC solid phase extraction (SPE) cartridges (60 mg) were purchased from Waters (Milford, MA, USA).

## 2.2. Sample collection and storage

Sample collection details and map of all cities included in the study are presented in Fig. 1. Samples from Oslo were collected from the VEAS wastewater treatment plant (WTP) over seven consecutive days from March 11–17, 2016 (including a 3-day weekend composite sample and four 24 h samples). Seven scattered 24 h wastewater samples (five weekdays and two days during the weekend) were collected in Stockholm in May 2016 in the Henriksdal WTP from two separate locations, Henriksdal I and II. Sampling in Reykjavik was conducted in two WTPs, Skerjafjarðarveita and Sundaveita, which collect wastewater from the majority of the Reykjavik metropolitan area. Seven 24 h samples were collected consecutively at both locations in Reykjavik from

August 17–23, 2016. Sample collection from Sersjantvíkin WTP in Torshavn consisted of seven 24 h consecutive samples from April 2–8, 2016. 24 h wastewater samples from Viikinmäki WTP in Helsinki were collected over seven consecutive days from March 16–22, 2016.

Samples from Helsinki were acidified on site after collection with hydrochloric acid (pH 2) to prevent degradation (Kankaanpää et al., 2014, 2016). Samples were transported to the National Institute for Health and Welfare (THL) in Helsinki and stored at  $-20\text{ }^\circ\text{C}$  until analysis in April 2016. Samples from Oslo, Reykjavik, Stockholm and Torshavn were shipped frozen without acidification to the Norwegian Institute for Water Research (NIVA) in Oslo, and stored at  $-20\text{ }^\circ\text{C}$  until analysis in September 2016 (Baz-Lomba et al., 2018).

## 2.3. Sample extraction procedure

Samples from Oslo, Reykjavik, Stockholm and Torshavn were pre-treated according to Baz-Lomba et al. (2018) as follows: prior to extraction, influent wastewater samples were spiked with a mixed working solution of ILIS at a concentration of 500 ng/L. 1 mL of sample was centrifuged at 13000 rpm for 5 min at  $4\text{ }^\circ\text{C}$  and the supernatant was used for analysis. Solid phase extraction (SPE) was performed using Oasis HLB  $\mu$ Elution plates, 30  $\mu\text{m}$ . The plate was conditioned by washing and

	Name of WTP	Number of inhabitants	Month of sampling	Flow range ( $\text{m}^3/24\text{h}$ )	Sampling mode
Helsinki	Viikinmäki	800000	March 2016	283800 - 353837	Volume proportional
Oslo	VEAS	607651	March 2016	250830 - 391527	Flow proportional
Reykjavik	Skerjafjarðarveita and Sundaveita	186000	August 2016	64725 - 73333	Time proportional
Stockholm	Henriksdal I and II	784000	May 2016	101500 - 136000	Flow proportional
Torshavn	Sersjantvíkin	820	April 2016	600 - 960	Time proportional



Fig. 1. Map of cities and sample collection details for the five locations included in this study.

rinsing with 1 mL of MeOH and 1 mL of purified water under suction. The supernatant of the wastewater samples after centrifugation was loaded onto the plate under suction and washed with 1 mL of ultrapure water. The plate was vacuum dried for 5 min. Analytes were eluted into a 96 well plate using 50  $\mu$ L of 1%  $\text{NH}_4\text{OH}$  in MeOH, 50  $\mu$ L of 1% FA in MeOH and 100  $\mu$ L of MeOH. Eluents were combined and analysis was performed by injecting 37  $\mu$ L into the ultra-high performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS) system.

Pre-treatment of samples from Helsinki was, according to Kankaanpää et al. (Kankaanpää et al., 2014, 2016), carried out as follows: 40 mL aliquots of acidified water samples were mixed with a phosphate buffer (adjusted to pH 2.5 with  $\text{H}_3\text{PO}_4$ ), ILIS was added and centrifuged. Solid phase extraction was performed using Oasis MCX cartridges. The cartridges were first conditioned with 5 mL MeOH and 5 mL of purified water. The supernatant of the wastewater sample after centrifugation was loaded into the cartridges and washed with 3 mL of purified water, 2 mL of 0.01 M hydrochloric acid (pH 2) and 3 mL toluene consecutively. The cartridges were vacuum dried with a stream of nitrogen before the compounds of interest were eluted with 5 mL of MeOH:  $\text{NH}_3$  (100:3). 140  $\mu$ L of formic acid was added to acidify the solution and ionize the compounds in order to protect vulnerable basic analytes during the evaporation process. The eluate was then evaporated at 75 °C to approximately 100  $\mu$ L. 50  $\mu$ L of 0.2 M hydrochloric acid was added to the residue prior to injection (2  $\mu$ L) into the UHPLC-MS/MS system.

#### 2.4. Instrumental conditions

Samples from Oslo, Reykjavik, Stockholm and Torshavn were analyzed according to Baz-Lomba et al. (Baz-Lomba et al., 2018) as follows: a Waters Acquity UPLC system (Milford, MA, USA) coupled to a Waters Quattro Premier XE Micromass triple quadrupole mass spectrometer (Milford, MA, USA) was used with a T-wave collision cell. Electrospray ionization interface (ESI) was operated in positive ionization mode. Chromatographic separation was carried out using a Waters Acquity UPLC BEH C8 column, 1.7  $\mu$ m, 2.1  $\times$  100 mm (Milford, MA, USA). The column temperature was kept at 50 °C and the temperature of the sample manager was 4 °C. A constant flow rate of 0.5 mL/min was used with a mobile phase consisting of 0.1% ammonium hydroxide (solvent A) and ACN (solvent B). The UHPLC system was equilibrated with 2% of solvent B. The gradient elution started by increasing solvent B to 13% over 5 min and held for 0.5 min. Solvent B was increased to 50% over 3.5 min and to 95% in 0.5 min, held for 1.0 min. Solvent B was decreased to 2% over 0.2 min and held for 0.3 min for equilibrium of the column. The cone and desolvation gas was nitrogen, with flow rates of 50 L/h and 800 L/h, respectively. The collision gas was argon, with a flow rate of 0.15 mL/min. Other operational parameters were capillary voltage, 3.2 kV; source temperature, 100 °C and desolvation temperature, 450 °C. Limits of quantification (LOQ) for all analytes was 5 ng/L.

Instrumental conditions for the analysis of samples from Helsinki were according to Kankaanpää et al. (Kankaanpää et al., 2014, 2016) as follows: an Agilent Technologies Series 1290 Infinity LC system (Santa Clara, CA, USA) connected to an Agilent Technologies 6460 Triple Quad LC/MS tandem mass spectrometer (Santa Clara, CA, USA) was used. Jet stream ESI was operated in positive ionization mode. Chromatographic separation was performed using a Waters Acquity CSH™ C18 column, 1.7  $\mu$ m, 2.1  $\times$  75 mm (Milford, MA, USA), and a Waters Acquity CSH™ C18 VanGuard™ guard column, 1.7  $\mu$ m, 2.1  $\times$  5 mm (Milford, MA, USA), with a column temperature of 40 °C. A flow rate of 0.5 mL/min was used with a mobile phase consisting of 5 mM aqueous ammonium formate/0.05% formic acid at pH 3.4 (solvent A) and ACN (solvent B). The UHPLC system was equilibrated with 7% solvent B. The gradient started with 7% solvent B held for 1.0 min then solvent B was increased to 18.3% at 3.0 min, 32.1% at 6.96 min, 80% at 8.0 min and 95% at 10.0 min. Other operational parameters were drying gas, nitrogen (8 L/min, 305 °C); nebulizer gas, nitrogen (30 psi); sheath gas, nitrogen (12 L/min, 350 °C) and capillary voltage, 3 kV. Dynamic multiple

reaction monitoring mode (dMRM) was used. LOQ's of analytes were the following: amphetamine 5 ng/L, cocaine 5 ng/L, BE 5 ng/L, methamphetamine 2 ng/L and MDMA 1 ng/L.

#### 2.5. Calculations

The concentrations (ng/L) of the chosen compounds were analyzed in daily samples of wastewater. The concentrations were multiplied by the daily average of the wastewater flow (L/day) to achieve daily mass loads (g/day). The mass loads were normalized with respect to the population connected to the catchment area to give mg/day/1000 people for comparable results. Further details on all parameters used in the back-calculations can be found in Table S1 in the Supplementary information. Statistical analysis on the difference between two averages was performed by using the Student's *t*-test with a significance level of  $p < 0.05$ .

### 3. Results and discussion

#### 3.1. Amphetamine

Amphetamine was detectable in samples from all cities with the exception of Torshavn (Fig. 2). Amphetamine loads from Reykjavik (217 mg/day/1000 people) and Stockholm (208 mg/day/1000 people) were the highest, followed by Oslo (110 mg/day/1000 people) and Helsinki (101 mg/day/1000 people). Full summary of calculated amphetamine loads can be found in Table S2 in the Supplementary information.

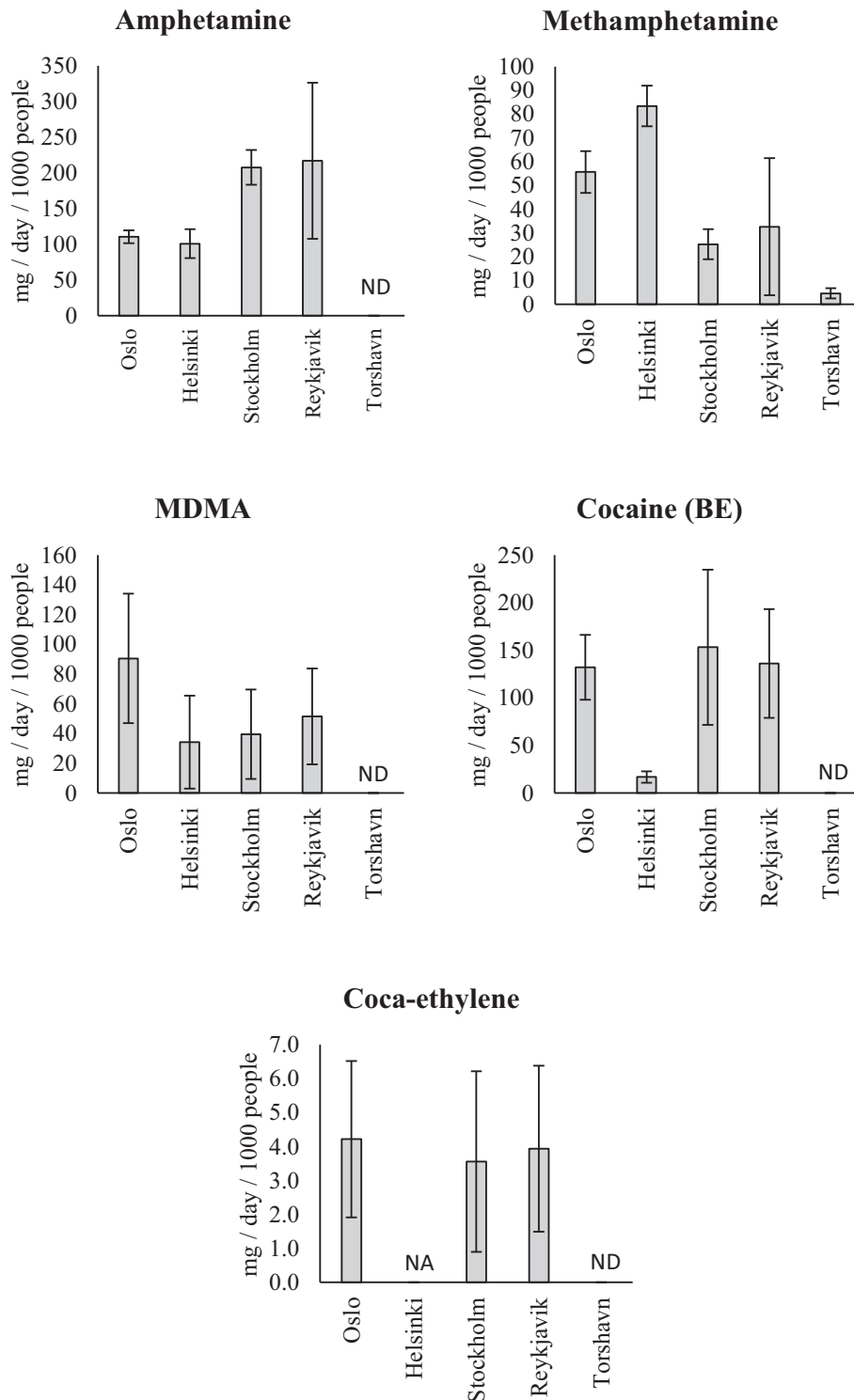
Amphetamine is known to have dominated the stimulant drug market in Iceland in recent years according to the number of driving under the influence cases (data from the Department of Pharmacology and Toxicology, University of Iceland) and seized amounts (National Police Commissioner of Iceland, 2016). All cities except Reykjavik collected samples in the spring of 2016. Sampling in Reykjavik took place during a summer week when a festival was held and therefore does not represent a normal week. The SCORE study presented results from Reykjavik collected in March 2016, which indicate lower amphetamine loads (123 mg/day/1000 people) (SCORE, 2017), similar to those from Oslo and Helsinki. High number of social events during the summertime in Reykjavik is a likely cause for increased amphetamine use and high variability of results.

Amphetamine loads from Stockholm were high. Previously reported amphetamine loads from Stockholm in 2013 showed similar loads (215 mg/day/1000 people) indicating stable use since that time (Ort et al., 2014; SCORE, 2017). Seizure numbers indicate that amphetamine and cannabis dominate the Swedish drug market. Amphetamine seizures in the last decade seem to be decreasing in Sweden but have shown similar numbers since 2013 (European Monitoring Centre for Drugs and Drug Addiction, 2017b, 2017e). These trends support the presented findings that the use of amphetamine in Stockholm has been relatively stable in recent years.

Amphetamine loads from Oslo were in the higher range of European cities and were similar to what was reported in 2015, indicating stable availability of the drug since that time (SCORE, 2017). Amphetamine and cannabis are the most commonly seized drugs in Norway. Long-term trends indicate an increase in the number of amphetamine seizures with the highest amounts seized in 2015 (European Monitoring Centre for Drugs and Drug Addiction, 2017b, 2017d). This is in accordance with the SCORE study, which reported an increase in amphetamine loads in 2015 (SCORE, 2017).

Amphetamine loads from Helsinki were in the higher range when compared to other cities in the SCORE study (SCORE, 2017). According to Kankaanpää et al. amphetamine loads have significantly increased from 2012 to 2015 which was in accordance with driving under the influence and drug seizure data (European Monitoring Centre for Drugs and Drug Addiction, 2017c; Kankaanpää et al., 2016). The SCORE



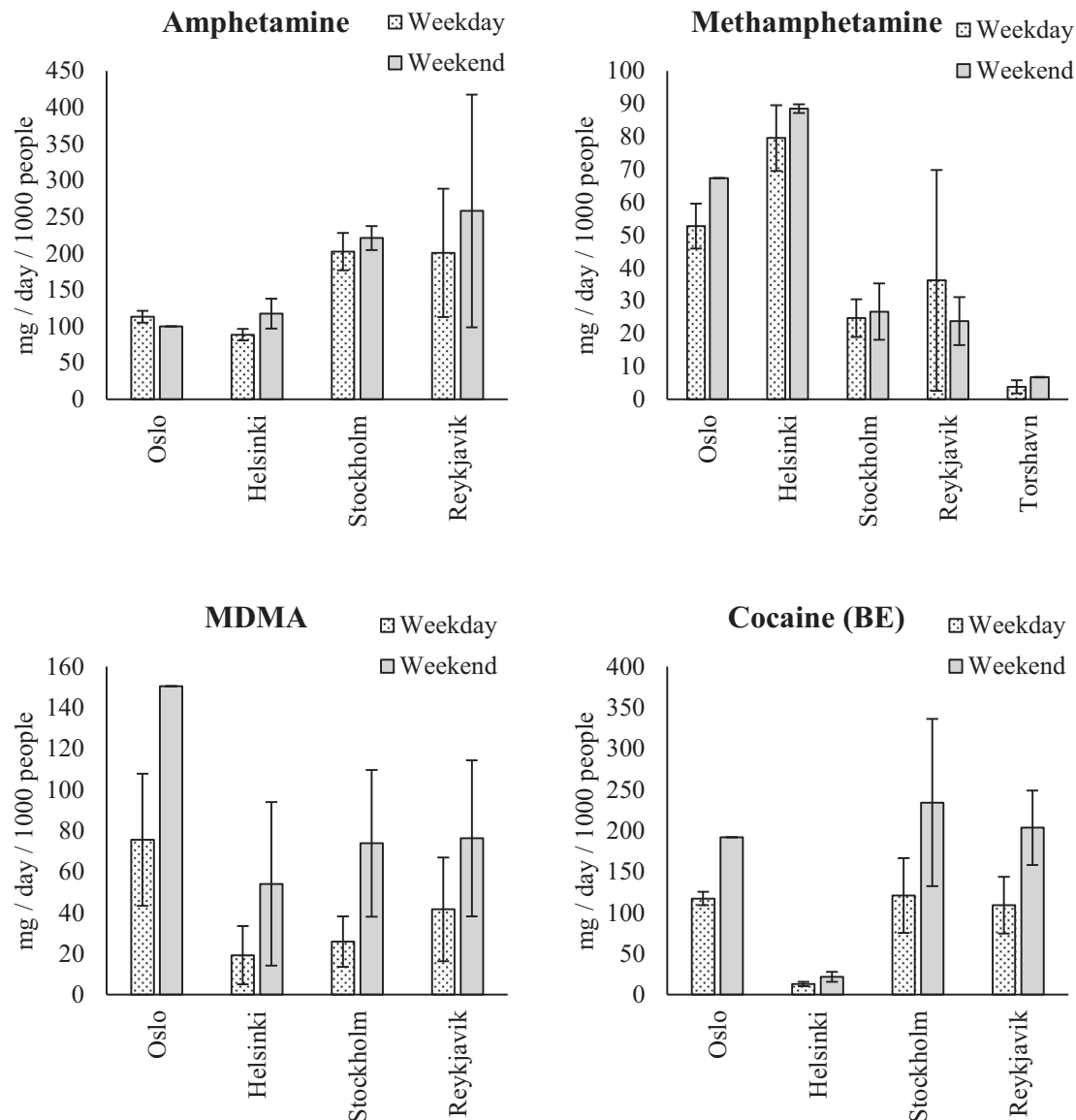


**Fig. 2.** Loads of illicit drugs in the different cities: Average loads  $\pm$  standard deviation (SD) of amphetamine, methamphetamine, MDMA, cocaine (calculated from BE loads) and coca-ethylene in mg/day/1000 people. ND = not detected. NA = not analyzed.

study further indicated that amphetamine loads were relatively stable from 2015 to 2016 (SCORE, 2017).

An increase in amphetamine loads was observed during weekends in Reykjavik and Helsinki, a decrease was detected in Oslo and negligible difference in Stockholm (Fig. 3). An increase in amphetamine loads in Reykjavik by 29% during the weekend indicates that the drug is recreationally used to some extent. Nevertheless, the difference between average amphetamine loads during weekdays and weekends

showed high variability, which was consistent at both WTPs. A likely cause is that sampling took place during the summertime with a high number of scattered special events, which included a festival during the weekend. A significant increase ( $p < 0.05$ ,  $t$ -test) in amphetamine loads by 33% was observed in Helsinki, indicating recreational use of the drug similar to Reykjavik. Unlike other cities in this study, weekly patterns in Oslo showed a decrease during the weekend by 12%. A decrease in the population of the catchment in Oslo by approximately



**Fig. 3.** Comparison of loads between weekdays and weekends: Average loads  $\pm$  SD of amphetamine, methamphetamine MDMA and cocaine (calculated from BE loads) in mg/day/1000 people during weekends (Friday–Sunday) compared with weekdays (Monday–Thursday). Only methamphetamine was detected in samples from Torshavn.

15% has been observed during weekends, based on mobile device data (Thomas et al., 2017). This could at least partly explain the drop in amphetamine use during weekends in the area. Only one composite sample was collected during the weekend in Oslo and therefore statistical analysis on the significance of variations between weekdays and weekends was not possible. A comparison between amphetamine loads during weekdays and the weekend in Stockholm show a small increase during the weekend. This is in accordance with previous reports that have demonstrated negligible variations between days or a minimal increase during weekends in Stockholm (Baker et al., 2012; Kankaanpää et al., 2014; Thomas et al., 2012).

### 3.2. Methamphetamine

Methamphetamine was detected in wastewater samples from all cities included in this study (Fig. 2). Substantial geographical differences of methamphetamine loads were observed between the five sampling locations. Helsinki showed the highest average methamphetamine loads (83.4 mg/day/1000 people), followed by Oslo (55.7 mg/day/1000 people), Reykjavik (32.6 mg/day/1000 people), Stockholm (25.3 mg/day/1000 people) and Torshavn (4.6 mg/day/1000 people). Full

summary of calculated methamphetamine loads can be found in Table S2 in the Supplementary information.

Methamphetamine loads from Helsinki were high in comparison with other cities in the SCORE study in 2016, below cities in Slovakia, the Czech Republic and the eastern part of Germany (SCORE, 2017). Similar loads were also measured in the Finnish cities of Espoo (89.5 mg/day/1000 people) and Jyväskylä (63.7 mg/day/1000 people) (SCORE, 2017). Kankaanpää et al. described a decrease in methamphetamine use from 2012 to 2015 in Helsinki (Kankaanpää et al., 2014, 2016). However, methamphetamine loads from Helsinki reported in the SCORE study have increased significantly ( $p < 0.05$ ,  $t$ -test) since 2015, from 5 mg/day/1000 people (SCORE, 2017). These results demonstrate that there are substantial fluctuations in methamphetamine use in Helsinki, most likely depending on the availability, season, purity and price of the drug (European Monitoring Centre for Drugs and Drug Addiction, 2016b).

Methamphetamine loads from Oslo were also in the higher range when compared with other cities in the SCORE study, below Espoo, Helsinki and Jyväskylä in Finland. Bramness et al. demonstrated that the drug market in Norway has shifted from amphetamine to methamphetamine with an extensive increase since 2000, but has stabilized with a

small decrease from 2010 to 2012 (Bramness et al., 2015). This study further demonstrates a drop in the methamphetamine market in Oslo compared with previous years (Bramness et al., 2015; Ort et al., 2014; SCORE, 2017; Thomas et al., 2012). The number of methamphetamine seizures in Norway increased from 2009 to 2013 but decreased from 2014 to 2015 (European Monitoring Centre for Drugs and Drug Addiction, 2017d). These findings support the previously discussed results based on wastewater analysis.

Methamphetamine use is minimal in Reykjavik according to the number of driving under the influence cases (data from the Department of Pharmacology and Toxicology, University of Iceland) and seized amounts (National Police Commissioner of Iceland, 2016). Methamphetamine loads from Reykjavik were in the lower range, compared with other cities included in this study. Average methamphetamine loads increased by 186% from March 2016 (11.4 mg/day/1000 people) to August 2016 when compared with the SCORE study. Results from March 2016, representing a normal week, indicate that methamphetamine use in Reykjavik is low compared with other Nordic cities (SCORE, 2017). Results from Reykjavik show high variability, which is due to an unexplained spike in methamphetamine loads during the sampling week in only one of the two WTPs. Summer festivities is a likely cause for this unusual rise in methamphetamine loads on a weekday.

The average methamphetamine loads in Stockholm were low. These results are similar to previously published results on methamphetamine loads in wastewater from Sweden (Östman et al., 2014). Methamphetamine loads from Stockholm, last included in the SCORE study in 2011, were reported to be even lower (9.4 mg/day/1000 people) (SCORE, 2017; Thomas et al., 2012). Although these methamphetamine loads are both low, they show considerable shifts in the availability of the drug. Reports on the number of seizures support these fluctuations in the methamphetamine market in Sweden, although remaining low, they reached a peak amount in 2009 but have decreased since that time (European Monitoring Centre for Drugs and Drug Addiction, 2017e).

Average methamphetamine loads from Torshavn were very low. The number of people that contributed to the WTP was only 4% (820 inhabitants) of the total population of Torshavn Municipality, resulting in a high degree of uncertainty. The Sersjantvíkin WTP is the only treatment facility in Torshavn with access to influent and effluent wastewater and therefore it was not possible to collect samples that represented a larger portion of the population. It is difficult to compare these results with other countries included in this study due to these limitations. However, they indicate that the use of methamphetamine is not high in Torshavn.

Variable differences in methamphetamine loads between weekdays and weekends were observed in this study (Fig. 3). Although methamphetamine loads from Torshavn were extremely low, they show a significant increase ( $p < 0.05$ ,  $t$ -test) during weekends by 81%. This gives an indication that methamphetamine is recreationally used to some degree in Torshavn. Methamphetamine loads from Oslo increased by 28% during the weekend. Only one composite sample was collected during the weekend in Oslo and therefore statistical analysis on the significance of variations between weekdays and weekends was not possible. In accordance with known patterns of use, both Helsinki and Stockholm showed limited variations in methamphetamine loads between weekdays and weekends as previous reports have described (Kankaanpää et al., 2016; SCORE, 2017; Thomas et al., 2012). Due to the high variability of results as mentioned above, it was not possible to detect significant variations between weekdays and weekends in methamphetamine loads from Reykjavik.

### 3.3. MDMA

MDMA was detected in samples from all cities included in this study except Torshavn (Fig. 2). Average MDMA loads were the largest in wastewater samples from Oslo (91.0 mg/day/1000 people), followed

by Reykjavik (51.5 mg/day/1000 people), Stockholm (39.6 mg/day/1000 people) and Helsinki (34.2 mg/day/1000 people). Full summary of calculated MDMA loads can be found in Table S2 in the Supplementary information.

The results show that MDMA loads from Oslo have increased greatly since 2013 (from 7.4 mg/day/1000 people) (SCORE, 2017; Thomas et al., 2012). Changes in the availability and purity of MDMA in Norway have caused a recent rise in use with the highest number of seizures recorded in 2015 (European Monitoring Centre for Drugs and Drug Addiction, 2017d). This study therefore supports that MDMA use is increasing in Oslo.

The results from this study show that MDMA loads from Reykjavik were 38% higher than in March 2016 (37.4 mg/day/1000 people) when compared to the SCORE study. MDMA loads in March 2016 that represents a normal week are similar to those measured from Stockholm and Helsinki in this study (SCORE, 2017). These results indicate that MDMA is a popular recreational drug in Reykjavik with increased use during the summer time and during special event weekends.

MDMA loads from Stockholm have not been reported in the SCORE study since 2011, where it was not detected (Ort et al., 2014; SCORE, 2017; Thomas et al., 2012). The number of MDMA seizures in Sweden have increased greatly since 2009, with record-breaking numbers in 2015 (European Monitoring Centre for Drugs and Drug Addiction, 2017e). These results indicate that MDMA use in Stockholm has become more prominent in recent years.

MDMA loads from Helsinki were very similar to Stockholm. These amounts were also in the same range as MDMA loads reported from Espoo (31.9 mg/day/1000 people) and Tampere (27.1 mg/day/1000 people) in Finland, according to the SCORE study (SCORE, 2017). Kankaanpää et al. reported that MDMA use has significantly increased in Helsinki both from 2012 to 2014 and from 2014 to 2015 (Kankaanpää et al., 2016). This increase is in accordance with the SCORE study, although it also shows very similar MDMA loads in 2015 and 2016, supporting previously reported fluctuations in the availability of the drug (Kankaanpää et al., 2014; SCORE, 2017). Similar findings on the number of MDMA seizures in Finland also show an increase in recent years (European Monitoring Centre for Drugs and Drug Addiction, 2017c).

MDMA loads increased during weekends compared to weekdays with similar variability of results in all cities included in this study (Fig. 3). Weekly patterns in MDMA loads were evident in Stockholm with a significant increase ( $p < 0.05$ ,  $t$ -test) by 186% during the weekend. Similar trends were observed in Helsinki with an increase ( $p = 0.051$ ,  $t$ -test) by 180% during the weekend. Clear variations between days were observed in Oslo with a 99% increase in MDMA loads during the weekend. Only one composite sample was collected during the weekend in Oslo and therefore statistical analysis on the significance of variations between weekdays and weekends was not possible. MDMA loads from Reykjavik also increased significantly ( $p < 0.05$ ,  $t$ -test) by 83% during the weekend. These results are in accordance with previous studies that have also shown notable variations between days in accordance with known patterns of recreational use of the drug (Kankaanpää et al., 2014; Thomas et al., 2012).

### 3.4. Cocaine

Cocaine is mainly excreted as the metabolite BE accounting for around 20–60% of the dose with only 1–15% excreted as unchanged cocaine (Ambre et al., 1988; Cone et al., 1998). Among the cities included in this study, both cocaine and BE were detected in samples from Oslo, Stockholm, Reykjavik and Helsinki (Fig. 2). Neither BE nor cocaine was detected in samples from Torshavn. The following discussion is based on BE loads in wastewater, representing cocaine use. Among these cities, average loads of BE were highest in Stockholm (153 mg/day/1000 people) followed by Reykjavik (136 mg/day/1000 people), Oslo (132 mg/day/1000 people) and Helsinki (16.7 mg/day/1000 people). Full

summary of calculated BE and cocaine loads can be found in Table S2 in the Supplementary information.

Stockholm had the highest average BE loads among the cities included in this study. Low BE loads from Sweden have previously been reported (48.8 mg/day/1000 people in 2011) (SCORE, 2017; Thomas et al., 2012). The number of cocaine seizures in Sweden has increased for the last ten years, reaching a peak amount in 2015 (European Monitoring Centre for Drugs and Drug Addiction, 2017e). This is in accordance with the results of this study that cocaine use is on the rise in Stockholm. However, seasonal variability and changes in the availability and purity of the drug could affect these estimates.

Average BE loads from Reykjavik in this study are comparable to what was reported in the SCORE study in March 2016 (123 mg/day/1000 people) indicating low seasonal variability of the drug (SCORE, 2017). Cocaine use in Iceland is rising according to the number of driving under the influence cases, likely in relations to the improved economic status of the country (data from the Department of Pharmacology and Toxicology, University of Iceland). Seized amounts of the drug are nevertheless low compared to amphetamine (National Police Commissioner of Iceland, 2016).

Measured average BE loads from Oslo were comparable to Reykjavik. According to the SCORE study similar BE loads from Oslo were reported in 2015 (152 mg/day/1000 people), but have decreased from a peak amount of 271 mg/day/1000 people in 2014 (SCORE, 2017). Although BE loads in wastewater from Oslo seem to be decreasing over time, the number of cocaine seizures are rising in Norway with record-breaking numbers in 2015 (European Monitoring Centre for Drugs and Drug Addiction, 2017d). This could indicate that substantial fluctuations are in the cocaine drug market in Oslo.

Helsinki had the lowest BE loads compared with other cities included in this study. The SCORE study generally showed low BE loads from Finnish cities with similar loads from Espoo (10.5 mg/day/1000 people) and Lahti (9.9 mg/day/1000 people) (SCORE, 2017). Although cocaine use is currently low in Finland, according to Kankaanpää et al. it is now rising, showing a significant increase both from 2012 to 2014 and from 2014 to 2015 (Kankaanpää et al., 2016).

Similar to MDMA, an increase in BE loads during weekends was observed in this study (Fig. 3). Changes between weekdays and weekends in BE loads from Stockholm were evident with a significant increase ( $p < 0.05$ ,  $t$ -test) by 94% during the weekend. The results from Stockholm showed high variability explained by a steep increase over the weekend and a sudden decrease during weekdays. This indicates that cocaine is largely used recreationally in Stockholm. Similar trends were observed in BE loads from Reykjavik with a significant increase ( $p < 0.05$ ,  $t$ -test) by 86% during the weekend compared with weekdays. Helsinki and Oslo showed comparable variations between weekends and weekdays with an increase in BE loads by 67% and 64%, respectively. The difference in BE loads from Helsinki between weekdays and weekends was statistically significant ( $p < 0.05$ ,  $t$ -test). Only one composite sample was collected during the weekend in Oslo and therefore statistical analysis on the significance of variations between weekdays and weekends was not possible. These trends in BE loads support known recreational use patterns of cocaine that have also been previously reported by other countries (Thomas et al., 2012).

Large amounts of cocaine that have been dumped into the sewer system can be estimated by observing the cocaine/BE ratio. According to the maximum amount of cocaine excreted unchanged (15%) versus the minimum amount excreted as the major metabolite BE (20%), the cocaine/BE ratio should be below 0.75 if the drug is excreted through urine, and was therefore not dumped (van Nuijs et al., 2009). Partial-degradation of cocaine to BE through hydrolysis during sewer transport can also affect these measurements resulting in a lower cocaine/BE ratio (Castiglioni et al., 2013). Wastewater from Helsinki was measured to have the highest average ratio (0.65), followed by Oslo (0.51), Stockholm (0.37) and Reykjavik (0.23). These results show that estimations of cocaine in wastewater in this study are from human consumption.

The metabolite coca-ethylene is produced after the co-consumption of cocaine and ethanol (Rodríguez-Álvarez et al., 2015). Coca-ethylene accounts for 0.7% of a cocaine dose but is less active than cocaine (Baselt, 2014). Coca-ethylene was analyzed in wastewater samples from Oslo, Reykjavik, Stockholm and Torshavn. Coca-ethylene was detected in samples from all the cities mentioned above, except Torshavn, with very low loads in all instances (Fig. 2). Total average loads indicate that co-consumption of cocaine and ethanol was comparable in Oslo (4.2 mg/day/1000 people), Reykjavik (3.9 mg/day/1000 people) and Stockholm (3.6 mg/day/1000 people). Coca-ethylene was not analyzed in samples from Helsinki. Full summary of calculated coca-ethylene loads can be found in Table S2 in the Supplementary information. Comparison between BE and coca-ethylene detected in samples from these three cities showed similar geographical trends. Coca-ethylene loads in wastewater from Oslo, Reykjavik and Stockholm increased extensively during the weekend, causing high variability of results. The co-consumption of ethanol and cocaine can therefore be related to recreational use of a combination of these substances.

#### 4. Conclusions

By using WBE, a reliable comparison between five capitals in the Nordic countries has been achieved. For the first time, information on stimulant drugs in wastewater is available from Torshavn, indicating very little stimulant drug abuse in the Faroe Islands. The results support previous findings indicating a high prevalence of amphetamines in northern Europe compared with cocaine. Clear variations between days in MDMA and BE loads support reports of the rising recreational use of ecstasy and cocaine. Temporal and geographical changes were observed that further add to current information on illicit drug use in the Nordic countries. This study enables a comparison with previously published studies in the field of WBE and illicit drug use in other European countries.

#### Acknowledgements

We wish to acknowledge support by COST (European Cooperation in Science and Technology) [Grant number ES1307], as well as the Icelandic Research Fund [Grant number 163049-051] and the University of Iceland Research Fund [Grant number HI17060092]. We want to acknowledge Rakul Mortensen from the Environmental Agency, Torshavn, Faroe Islands, for assisting with sampling in Sersjantvíkin WTP and Pia Ryrfors and colleagues at Vestfjorden Avløpselskap (VEAS), Oslo, Norway, for sample collection and provision of flow data. Finally, we acknowledge Birgir Tómas Arnar from Verkís and Íris Þórarinsdóttir from Veitur, Reykjavik Iceland, assisting with sample collection and for providing flow data.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.scitotenv.2018.01.274>.

#### References

- Ambre, J., Ruo, T.I., Nelson, J., Belknap, S., 1988. Urinary excretion of cocaine, benzoylecgonine, and ecgonine methyl ester in humans. *J. Anal. Toxicol.* 12 (6), 301–306.
- Baker, D.R., Očenášková, V., Kvalalova, M., Kasprzyk-Hordern, B., 2012. Drugs of abuse in wastewater and suspended particulate matter – further developments in sewage epidemiology. *Environ. Int.* 48:28–38. <https://doi.org/10.1016/j.envint.2012.06.014>.
- Baker, D.R., Barron, L., Kasprzyk-Hordern, B., 2014. Illicit and pharmaceutical drug consumption estimated via wastewater analysis. Part A: chemical analysis and drug use estimates. *Sci. Total Environ.* 487:629–641. <https://doi.org/10.1016/j.scitotenv.2013.11.107>.
- Baselt, R.C., 2014. *Disposition of Toxic Drugs and Chemicals in Man*. 10th. ed. Biomedical publications, Seal Beach, California.
- Baz-Lomba, J.A., Salvatore, S., Gracia-Lor, E., Bade, R., Castiglioni, S., Castrignanò, E., et al., 2016. Comparison of pharmaceutical, illicit drug, alcohol, nicotine and caffeine levels



- in wastewater with sale, seizure and consumption data for 8 European cities. *BMC Public Health* 16 (1):1035. <https://doi.org/10.1186/s12889-016-3686-5>.
- Baz-Lomba, J.A., Löve, A.S.C., Reid, M.J., Ólafsdóttir, K., Thomas, K.V., 2018. A high-throughput solid-phase microextraction and post-loop mixing large volume injection method for water samples. *J. Chromatogr. A* 1531:32–38. <https://doi.org/10.1016/j.chroma.2017.11.051>.
- Been, F., Bijlsma, L., Benaglia, L., Berset, J.-D., Botero-Coy, A.M., Castiglioni, S., et al., 2016. Assessing geographical differences in illicit drug consumption - a comparison of results from epidemiological and wastewater data in Germany and Switzerland. *Drug Alcohol Depend.* 161:189–199. <https://doi.org/10.1016/j.drugalcdep.2016.02.002>.
- Bramness, J.G., Reid, M.J., Solvik, K.F., Vindenes, V., 2015. Recent trends in the availability and use of amphetamine and methamphetamine in Norway. *Forensic Sci. Int.* 246: 92–97. <https://doi.org/10.1016/j.forsciint.2014.11.010>.
- Castiglioni, S., Bijlsma, L., Covaci, A., Emke, E., Hernandez, F., Reid, M., et al., 2013. Evaluation of uncertainties associated with the determination of community drug use through the measurement of sewage drug biomarkers. *Environ. Sci. Technol.* 47 (3):1452–1460. <https://doi.org/10.1021/es302722f>.
- Castiglioni, S., Thomas, K.V., Kasprzyk-Hordern, B., Vandam, L., Griffiths, P., 2014. Testing wastewater to detect illicit drugs: state of the art, potential and research needs. *Sci. Total Environ.* 487:613–620. <https://doi.org/10.1016/j.scitotenv.2013.10.034>.
- Causanilles, A., Baz-Lomba, J.A., Burgard, D.A., Emke, E., González-Mariño, I., Krizman-Matic, I., et al., 2017. Improving wastewater - based epidemiology to estimate cannabis use: focus on the initial aspects of the analytical procedure. *Anal. Chim. Acta* 988 (Supplement C):27–33. <https://doi.org/10.1016/j.aca.2017.08.011>.
- Cone, E.J., Tsadik, A., Oyler, J., Darwin, W.D., 1998. Cocaine metabolism and urinary excretion after different routes of administration. *Ther. Drug Monit.* 20 (5), 556–560.
- European Monitoring Centre for Drugs and Drug Addiction, 2016a. *ESPAD Report 2015 - Results from the European School Survey Project on Alcohol and Other Drugs*. Publications Office of the European Union, Luxembourg.
- European Monitoring Centre for Drugs and Drug Addiction, 2016b. *European Drug Report 2016 - Trends and Developments*. Publications Office of the European Union, Luxembourg.
- European Monitoring Centre for Drugs and Drug Addiction, 2017a. *Denmark, Country Drug Report 2017*. Publications Office of the European Union, Luxembourg.
- European Monitoring Centre for Drugs and Drug Addiction, 2017b. *European Drug Report 2017 - Trends and Developments*. Publications Office of the European Union, Luxembourg.
- European Monitoring Centre for Drugs and Drug Addiction, 2017c. *Finland, Country Drug Report 2017*. Publications Office of the European Union, Luxembourg.
- European Monitoring Centre for Drugs and Drug Addiction, 2017d. *Norway, Country Drug Report 2017*. Publications Office of the European Union, Luxembourg.
- European Monitoring Centre for Drugs and Drug Addiction, 2017e. *Sweden, Country Drug Report 2017*. Publications Office of the European Union, Luxembourg.
- Griffiths, P., Mravcik, V., Lopez, D., Klempova, D., 2008. Quite a lot of smoke but very limited fire—the use of methamphetamine in Europe. *Drug Alcohol Rev.* 27 (3):236–242. <https://doi.org/10.1080/09595230801932588>.
- Kankaanpää, A., Ariniemi, K., Heinonen, M., Kuoppasalmi, K., Gunnar, T., 2014. Use of illicit stimulant drugs in Finland: a wastewater study in ten major cities. *Sci. Total Environ.* 487:696–702. <https://doi.org/10.1016/j.scitotenv.2013.11.095>.
- Kankaanpää, A., Ariniemi, K., Heinonen, M., Kuoppasalmi, K., Gunnar, T., 2016. Current trends in Finnish drug abuse: wastewater based epidemiology combined with other national indicators. *Sci. Total Environ.* 568:864–874. <https://doi.org/10.1016/j.scitotenv.2016.06.060>.
- Mackul'ak, T., Škubák, J., Grabic, R., Ryba, J., Birošová, L., Fedorova, G., et al., 2014. National study of illicit drug use in Slovakia based on wastewater analysis. *Sci. Total Environ.* 494–495:158–165. <https://doi.org/10.1016/j.scitotenv.2014.06.089>.
- National Police Commissioner of Iceland, 2016. *Afrotatölfræði 2016 - Bráðingbörgatölur. Reykjavík (In Icelandic)*.
- Ort, C., van Nuijs, A.L.N., Berset, J.-D., Bijlsma, L., Castiglioni, S., Covaci, A., et al., 2014. Spatial differences and temporal changes in illicit drug use in Europe quantified by wastewater analysis. *Addiction* 109 (8):1338–1352. <https://doi.org/10.1111/add.12570>.
- Östman, M., Fick, J., Näsström, E., Lindberg, R.H., 2014. A snapshot of illicit drug use in Sweden acquired through sewage water analysis. *Sci. Total Environ.* 472:862–871. <https://doi.org/10.1016/j.scitotenv.2013.11.081>.
- Rodríguez-Álvarez, T., Racamonde, I., González-Mariño, I., Borsotti, A., Rodil, R., Rodríguez, I., et al., 2015. Alcohol and cocaine co-consumption in two European cities assessed by wastewater analysis. *Sci. Total Environ.* 536:91–98. <https://doi.org/10.1016/j.scitotenv.2015.07.016>.
- SCORE, 2017. *Wastewater Monitoring Data 2011–2016 Sewage Analysis CORe Group Europe, COST Action ES1307*. <http://score-cost.eu/monitoring2016/> Accessed: 2017-04-02. (Archived by WebCite® at). <http://www.webcitation.org/6pQSupjAk>.
- Terzić, S., Senta, I., Ahel, M., 2010. Illicit drugs in wastewater of the city of Zagreb (Croatia) - estimation of drug abuse in a transition country. *Environ. Pollut.* 158 (8): 2686–2693. <https://doi.org/10.1016/j.envpol.2010.04.020>.
- Thomas, K.V., Bijlsma, L., Castiglioni, S., Covaci, A., Emke, E., Grabic, R., et al., 2012. Comparing illicit drug use in 19 European cities through sewage analysis. *Sci. Total Environ.* 432:432–439. <https://doi.org/10.1016/j.scitotenv.2012.06.069>.
- Thomas, K.V., Amador, A., Baz-Lomba, J.A., Reid, M., 2017. Use of mobile device data to better estimate dynamic population size for wastewater-based epidemiology. *Environ. Sci. Technol.* 51 (19):11363–11370. <https://doi.org/10.1021/acs.est.7b02538>.
- United Nations Office on Drugs and Crime, 2016. *World Drug Report 2016*. United Nations publication, Vienna.
- van Nuijs, A.L.N., Pecceu, B., Theunis, L., Dubois, N., Charlier, C., Jorens, P.G., et al., 2009. Can cocaine use be evaluated through analysis of wastewater? A nation-wide approach conducted in Belgium. *Addiction* 104 (5):734–741. <https://doi.org/10.1111/j.1360-0443.2009.02523.x>.
- van Nuijs, A.L.N., Mougel, J.-F., Tarcomnicu, I., Bervoets, L., Blust, R., Jorens, P.G., et al., 2011. Sewage epidemiology - a real-time approach to estimate the consumption of illicit drugs in Brussels, Belgium. *Environ. Int.* 37 (3):612–621. <https://doi.org/10.1016/j.envint.2010.12.006>.
- van Nuijs, A.L.N., Lai, F.Y., Been, F., Andres-Costa, M.J., Barron, L., Baz Lomba, J.A., et al., 2018. Six years of inter-laboratory exercises for the analysis of illicit drugs and metabolites in wastewater: development of a quality control system. *Trends Anal. Chem.* (submitted manuscript).
- Zuccato, E., Chiabrando, C., Castiglioni, S., Calamari, D., Bagnati, R., Schiarea, S., et al., 2005. Cocaine in surface waters: a new evidence-based tool to monitor community drug abuse. *Environ. Health* 4:14–20. <https://doi.org/10.1186/1476-069X-4-14>.
- Zuccato, E., Castiglioni, S., Tettamanti, M., Olandese, R., Bagnati, R., Melis, M., et al., 2011. Changes in illicit drug consumption patterns in 2009 detected by wastewater analysis. *Drug Alcohol Depend.* 118 (2–3):464–469. <https://doi.org/10.1016/j.drugalcdep.2011.05.007>.