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RESEARCH ARTICLE

Temporal profile of illicit drug consumption in Guangzhou, China monitored by wastewater-based epidemiology

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Abstract

Wastewater-based epidemiology (WBE) has been widely used as a complementary method for estimating consumption of illicit drugs in the population. Temporal drug consumption estimates derived from WBE can provide important information for law enforcement and public health authorities in understanding changes in supply and demand of illicit drugs, but currently lacking in China. In this study, influent wastewater samples from a municipal sewage treatment plant in Guangzhou, China were collected for 8 weeks to investigate the temporal change in consumption of six illicit drugs in the catchment. The results indicated that methamphetamine and ketamine were the dominant illicit drugs in Guangzhou with the per capita use of 14.7–470.7 mg/day/1000 people and 64.9–673.7 mg/day/1000 people, respectively. No distinct weekly patterns were observed for illicit drug consumption in Guangzhou, indicating that drug users are likely to be regular ones. Further assessment about the impact of public holidays on the consumption behavior of drugs showed little impact for ketamine ($p = 0.689$), but higher consumptions of methamphetamine ($p = 0.003$) and cocaine ($p = 0.027$) were observed during public holidays than the control period. The considerable decrease in drug consumption observed in October 2017 compared with January and May 2017 was possibly the consequence of law enforcement action.

Keywords Ketamine · Methamphetamine · Population normalized consumption · Temporal variation · Wastewater-based epidemiology · Intervention

Introduction

The illicit drug abuse is a major threat to the public health and social security. According to the United Nations Office on Drugs and Crime, there are approximately 275 million people consuming illicit drugs at least once during 2016 globally (UNDOC 2018). In China, the number of drug users kept increasing in the past decades. By the end of 2016, there were approximately 2.5 million registered drug users in the country with 6.8% year-on-year growth mainly due to methamphetamine and ketamine uses (China Anti-Drug Network 2017). Due to the adverse effect of illicit drug consumption on health,

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social order, and economic development (Lim et al. 2012; Lai et al. 2013a, b), it is important for law enforcement agencies and public health departments to develop systematic control and harm-reduction strategies and evaluate the effects of their policies. At present, the consumption of drugs is mainly estimated by surveys of registered drug addicts and drug seizures, which can provide some insight of the consumption but cannot provide a quantitative and high-temporal-resolution profile (Du et al. 2015; Been et al. 2016).

Wastewater-based epidemiology (WBE) has been used to monitor the consumption of illicit drugs in many countries such as Europe (Zuccato et al. 2008; Thomas et al. 2012; Baker and Kasprzyk-Hordern 2013; Karolak et al. 2012), the USA (Chiaia et al. 2008), Canada (Metcalfe et al. 2010; Yargeau et al. 2014), Australia (Lai et al. 2011; Irvine et al. 2011; Tscharke et al. 2015; Lai et al. 2016b; Tscharke et al. 2016), and Korea (Kim et al. 2015). Gao et al. (2015) suggested that WBE can be used in China to effectively assess the temporal and geographical consumption profile of illicit drugs in different populations since there were more than 3000 wastewater treatment plants with diverse catchment characteristics. The first WBE study in mainland China was conducted by Khan et al. (2014) in which the use of ten illicit drugs was monitored in four large cities including Beijing, Shanghai, Guangzhou, and Shenzhen. The authors found that methamphetamine and ketamine were the most prevalent illicit drugs. A follow-up study by Du et al. (2015) also reported methamphetamine and ketamine as the major consumed illicit drugs in 18 major cities across China, including Guangzhou. They also identified higher methamphetamine consumption in north and east China than in other regions.

Some WBE studies have examined the fluctuations of drugs use during around special events. Foppe et al. (2018) found that the average per-capita consumption of amphetamine, methamphetamine, cocaine, morphine, and methadone was significantly higher on Independence Day and/or the solar eclipse observation day in USA. The consumption of cannabis, cocaine, MDMA, and methamphetamine was also found increased during Christmas and New Year in urban areas in Australia (Lai et al. 2013a). Jiang et al. (2015) documented the highest mass loads of ketamine and MDMA on surrounding aquatic environment, indicating the high drug consumption during a Youth Festival. In China, although a snapshot of the geographical consumption profile has been taken from major cities (e.g., Du et al. 2015, 2017), these studies were based on a limited number of samples in each catchment (2–4 days). Little is known regarding the temporal variation in individual catchments which can add substantial uncertainty to the geographical profile. This study aims to understand the temporal variation of illicit drug consumption in a metropolitan city (Guangzhou) of China using WBE including the period around two public holiday weeks (Chinese Spring Festival and National Day).

Materials and methods

Reagents and materials

Illicit drug standards including amphetamine (AMP), methamphetamine (METH), ketamine (KET), norketamine (NK), methylenedioxymethamphetamine (MDMA), methadone (MTD), 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), benzoylecgonine (BE) and codeine (CODE) (Table S1) and their deuterated analogs (amphetamine-d6, methamphetamine-d9, ketamine-d4, norketamine-d4, MDMA-d5, methadone-d3, EDDP-d3, benzoylecgonine-d3 and codeine-d3) were purchased from Cerilliant (USA) (purities > 99%). A native mixture standard of 1 mg/L was prepared and stored at − 20 °C. The stock solutions were diluted to 0.1–50 μg/L with pH 2 MilliQ water to obtain a calibration curve for quantification. The LC-grade acetonitrile and methanol were purchased from Merck (Germany), and hydrochloric acid was purchased from Aladdin (Shanghai, China).

Wastewater sample collection

Twenty-four-hour composite wastewater samples were collected from a municipal sewage treatment plant located in Guangzhou, China with a total treatment capacity of 250,000 m^3 per day. The samples were taken in 8 weeks across 3 months of 2017 with a total of 54 days as follows: January 01–January 10 and January 23–February 05 (including Chinese Spring Festival holiday, from January 27 to February 03), May 09–May 22, and September 27–October 12 (including National Day holiday, from October 01 to October 07). Samples were immediately acidified with 2 M hydrochloric acid to pH ≦ 2, and stored in − 20 °C freezer before analysis.

Analytical methodology

Samples were thawed at room temperature and filtered through glass fiber filters (0.45 μm, RC, Phenomenex) before spiking of 10 μL of mixed deuterated standards (1 mg/L). The solid-phase extraction was performed on HLB cartridge (Waters Oasis, 6 mL, 500 mg). Prior to extraction, HLB cartridges were activated with 6 mL of methanol and 6 mL of pH 2 Milli-Q water to drip dry under gravity. Then, 100 mL of filtered sample was loaded to the cartridge for enrichment, and then the cartridge was dried under negative pressure for 30 min, and then eluted with 3 mL of methanol twice. The eluate was combined and evaporated to ~ 0.1 mL in a gentle stream of nitrogen and reconstitute in 1 mL methanol.

The concentrations of drugs were analyzed using high-performance liquid chromatography (Nexera HPLC, Shimadzu Corp, Japan) coupled with tandem mass spectrometry (SCIEX 5500 QTRAP, Canada). The detailed instrumental analysis method in this study has been described previously (O'Brien et al. 2014; Lai et al. 2014). Gradient elution was carried out with 0.1% acetic acid methanol and 0.1% acetic acid MilliQ as the mobile phase, and separation of analytes was achieved using a Kinetix Biphenyl column (2.6 μm, 100 Å, LC Column 50 mm × 2.1 mm, Phenomenex). The multiple reaction monitoring (MRM) scanning modes were used in positive ionization mode.

QA and QC

To insure the accuracy and precision of the analysis, procedural blank samples made of Milli-Q water were used to examine the possible contamination during sample treatment. Deuterated labeled internal standards were used to compensate possible matrix effect as well as instrumental variations. In addition, matrix spiked samples were used to further evaluate the matrix effect. The SPE recoveries were from 65.1 ± 14.5% to 117.3 ± 10.2% and matrix effects were from − 3.0 ± 3.1% to 14.6 ± 6.9% for all analytes (Table S2). Six-point calibration curves (0.1–50 μg/L) were established with r > 0.9900. The procedural blank sample and quality control sample (5 μg/L) were analyzed every ten injections. No target analytes were found above the detection limits in the blank samples. In addition, the instrumental stability was reflected by the fact that the standard deviation of calculated QC sample (5 μg/L) was 4.1% to 13.2%.

Consumption estimation

Target illicit drugs

The target analytes for back calculating the drug consumption were referred to as drug target residues (DTRs). The DTRs selected in this study and their corresponding excretion factors are shown in Table 1 similarly with other studies in the literature (Du et al. 2015; Lai et al. 2016b; Thomas et al. 2012).

Drug consumption estimation

Based on the concentration profile, daily flow, and catchment population as well as the excretion of DTRs, consumption was estimated by Eq. (1) which was proposed and revised by Zuccato et al. (2005, 2008):

$$\text{Consumption of the drug}\left(\frac{\frac{\text{mg}}{\text{d}}}{1000\text{ people}}\right) = \frac{C_i \times F \times R_i}{P \times E_i} \times \frac{1}{10^3} \qquad (1)$$

Where C_i is the concentration of the target compound measured in the influent (ng/L); F—the daily flow of the sewage treatment plant (m^3/d); P—the number of people served by the wastewater treatment plant, 1000 people; R_i—the ratio of the molecular weight of the parent drug to DTR; E_i—the excretion rate of DTR (%).

Population estimation

The number of people served by the wastewater treatment plant is an indispensable parameter for back calculation, which influences the accuracy and reliability of estimation results directly (Daughton 2012; Lai et al. 2014; Zheng et al., 2019). The use of hydrochemical parameters to estimate population size, such as chemical oxygen demand (COD), biological oxygen demand (BOD), ammonia nitrogen (NH_4-N), total nitrogen (TN), and total phosphorus (TP), is also one of the commonly applied methods to estimate real-time population, which are easy to obtain since they are routinely monitored by wastewater treatment plants (van Nuijs et al. 2011a; Zheng et al. 2017). Zheng et al. (2019) have constructed a population model based on hydrochemical parameters (COD, NH_4-N, and TP) to reflect near-real consumption of METH in Jilin province in China and found a delightful accordance with the official report. Based on this model, the population can be calculated as follows:

$$\mathrm{P} = 0.53 \times \mathrm{P}_{\mathrm{NH4-N}} + 0.33 \times \mathrm{P}_{\mathrm{COD}} + 0.14 \times \mathrm{P}_{\mathrm{TP}} \qquad (2)$$

$$\mathrm{P_n} = \frac{\mathrm{C_n} \times \mathrm{F}}{\mathrm{m_n}} \times \frac{1}{10^3} \qquad (3)$$

Table 1 Selection and properties of DTRs of illicit drugs

Drugs	DTRs	Excretion rate/E_i/(%)	Molar mass ratio (parent/DTR)/R_i
METH	METH	43% (Baker et al. 2014; Du et al. 2015)	1.00
KET	NK	1.6% (Wieber et al. 1975; Baker et al. 2014)	1.06
MDMA	MDMA	20% (Baker et al. 2014)	1.00
MTD	EDDP	55% (Thai et al. 2016)	1.06
COC	BE	30% (Baker et al. 2014)	1.05
CODE	CODE	30% (Thai et al. 2016)	1.00

Where P_n is the population estimated from NH_4-N, COD or TP, 1000 people; C_n is the influent concentration of NH_4-N, COD, or TP (mg/L) (Table S3); m_n is the daily per-capita emission of NH_4-N, COD, or TP (g/day/people).

According to the manual for pollutant discharge coefficient of pollution source census (The Compilation Committee of First National Census of Pollution Sources 2011), daily per-capita emission of NH_4-N, COD, and TP in Guangzhou was estimated to be 9.46, 66, and 1.02 g/day/people, respectively. By using a dynamic population in the catchment rather than a fixed population, the associated uncertainty of the final estimates is expected to be much lower, especially for periods with large people movement such as public holidays (Daughton 2012; Castiglioni et al. 2013; Lai et al. 2014).

Statistical analysis

The independent samples *t* test was used to analyze whether the consumptions of the illicit drugs have a significant difference through the week and between public holidays and control days (SPSS Statistics 22). After performing equal variances on the original data, a two-tailed *t* test was used to check if there was a significant difference between group means with *p* values of < 0.05 used as the significance threshold level.

Results and discussions

Occurrence of illicit drugs and metabolites in wastewater samples

Influent concentrations of illicit drugs and metabolites

Nine substances were detected at concentrations of 1.1–708.8 ng/L with the frequency varied from 71% to 100% (Fig. S1). METH was detected in every sample with the average concentration of 145.6 ± 100.3 ng/L, similar to that reported in Guangzhou (2015) (189.2–215.2 ng/L) but lower than that of Shenzhen (366.4–680.8 ng/L), Qingdao (904.0–1016.0 ng/L), and Harbin (679.2–746.8 ng/L) as reported by Xu et al. (2017). The influent concentration of AMP (17.0 ± 10.3 ng/L) in this study was at the same level with Beijing (15.2–27.0 ng/L), Shanghai (22.7–25.7 ng/L), and Shenzhen (26.4–40.0 ng/L) (Xu et al. 2017; Du et al. 2015). The average concentration of KET (28.6 ± 15.6 ng/L) in Guangzhou was 2–9 times lower than that detected in the abovementioned cities but a little higher compared to that of Beijing (4.3–15.2 ng/L) (Li et al. 2014; Du et al. 2015). MDMA and NK concentrations were lower of 3.2 ± 1.9 ng/L and 8.9 ± 5.9 ng/L, respectively. CODE was detected in all samples with a concentration of 4.8 ± 2.6 ng/L. In contrast, COC was not detected in any sample although its major metabolite, BE, was quantified in 85% of samples with concentration of 1.98 ± 1.38 ng/L.

Concentration ratios between illicit drugs and metabolites

As demonstrated in Fig. S1, the concentrations between illicit drugs and corresponding metabolites appeared to similar fluctuation patterns over the sampling period, indicating that most if not all of metabolites detected originated from the use of parent drugs. The concentration ratios between AMP and METH were 0.12 ± 0.03 in January and 0.05 ± 0.03 in May (Fig. 1a), close to 0.05–0.10 reported by Li et al. in 2014. In October, the concentration of AMP below the detection limit may attribute to a significant decrease in the concentration of METH in the influent. The similar result was also found by Li et al. in 2014. The ratios of influent concentration of NK to KET in 3 months were 0.43 ± 0.06, 0.23 ± 0.03, and 0.20 ± 0.03, respectively (Fig. 1b). The concentration of EDDP in

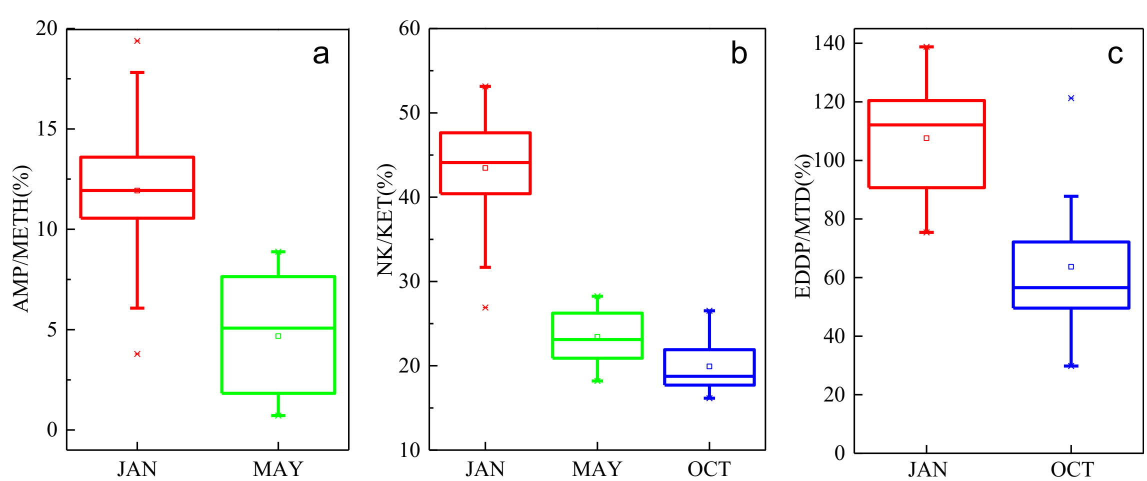

Fig. 1 Concentration ratios between illicit drugs and metabolites. **a** AMP/METH. **b** NK/KET. **c** EDDP/MTD

January was slightly higher than that of MTD with the concentration ratio of them was 1.07 ± 0.18. However, by October, the ratio of the two dropped to 0.64 ± 0.23 (Fig. 1c).

It should be noted that the concentration ratios varied in different months while higher ratio was observed in January than May and October. We speculate several possible explanations for this observation. Firstly, the deliberate dumping of illicit drugs to sewers from drug addicts or illegal drug factories forced by drug enforcements may occur during sampling periods since a series of drug busts were successively launched in Guangzhou from 2017 (Guangzhou Municipal Public Security Bureau 2018). It could possibly result in the increased drugs in sewage, leading to lower concentration ratios (metabolites/parent drug). Similar surmise was also proposed by Causanilles et al. (2016) and van Nuijs et al. (2011b). Secondly, the wastewater temperature would have an effect on the transformation of some drugs during its residence in sewers. During the sampling campaigns, the average temperatures in Guangzhou were 8–24 °C in January, 23–33 °C in May, and 25–34 °C in October, respectively. Sometimes, a difference of several degrees would affect the transformation behaviors of drugs. For example, COC showed only 7% decrease after 24 h at 4 °C in wastewater (Gonzalez-Marino et al. 2010). However, when the temperature rose to 20 °C, 40% reduction could be observed after 12 h (van Nuijs et al. 2012). For MTD, the transformation rates varied from − 20% to + 9% as the wastewater temperature rose from 4 °C to 20 °C (Gonzalez-Marino et al. 2010; van Nuijs et al. 2012). But, with regard to some stable analytes, such as BE and EDDP with no or little degradation in wastewater, the impact of temperature could be negligible (van Nuijs et al. 2012; McCall et al. 2016). These results suggested that both parameters should be taken into account when explaining the concentration ratio of drugs and metabolites.

Variation of real-time population

During the monitoring periods, the population served by the wastewater treatment plant was estimated to be 416,000–681,000 (Fig. S2). Such a fluctuation is logical since the catchment population is dynamic due to various factors, such as official holidays, events, and regional mobility (van Nuijs et al. 2011a). A 33% population decrease during the week of the Spring Festival was observed, while the population kept relatively stable during the week of National Day and control period. This population fluctuation is highly consistent with the decrease in water supply volume (30%) in Guangzhou during the same time (Lin et al. 2019). This can be explained by the large population movements during the Spring Festival for two-way migration since Guangzhou is an urban hub with many migrant workers, with the population mobility of up to 42% (Guangzhou Statistics Bureau 2016). A similar result was previously found by Been et al. (2014), which indicated the movement of people in and out of the metropolitan area of Lausanne, mainly related to the absence and arrival of university students. Van Nuijs et al. (2011a) also calculated the number of serving inhabitants based on the concentration of COD, BOD, TP, and NH_4-N as the real-time population of a wastewater treatment plant in Brussels, Belgium, and found a great population fluctuation during the entire sampling campaign.

Daily consumptions of illicit drugs

METH use

The per-capita consumption of METH in this study was estimated to 149 ± 101 mg/day/1000 people (Fig. 2), similar to that reported in Hong Kong (190 ± 11 mg/day/1000 people) (Lai et al. 2013b), Dalian (206 mg/day/1000 people) (Wang et al. 2019), and Beijing (220–377 mg/day/1000 people) (Xu et al. 2017), but a little lower than that of Shenzhen (313–587 mg/day/1000 people) (Xu et al. 2017). A distinct difference in METH use existed between January, May, and October with the highest per-capita consumption of 231 ± 69 mg/day/1000 people in May, about 8 times higher than in October (30 ± 10 mg/d/1000 people) (Fig. 2). It may be related to a series of law enforcement anti-narcotics operations such as "Thunder's Anti-drug," "Hurricane Action," and "100-day tough fighting" in Guangzhou, destroying several large-scale transnational channels of METH trafficking. As a result, the price of METH in October was four times higher than in January (Guangzhou Municipal Public Security Bureau 2018), which could lead to the significant drop in the consumption (Fig. 2). A decrease of METH use was also reported in Dalian, China and attributed to strict crack-down on illicit drugs in the area (Wang et al. 2019). These findings again prove that WBE is a useful tool to evaluate the effects of intervention activities related to drug control.

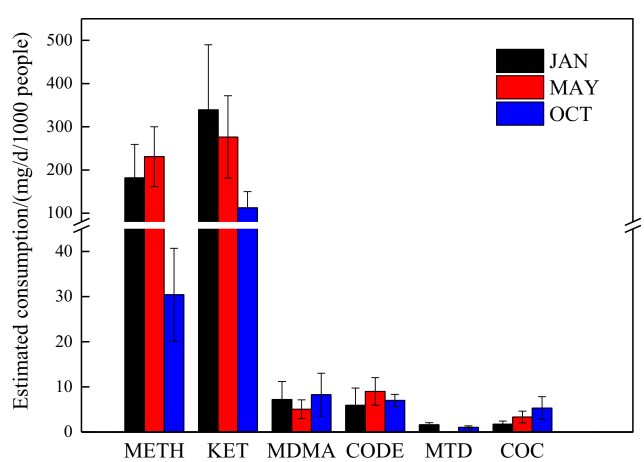

Fig. 2 Estimated consumptions of illicit drugs in different months

Table 2 Comparison of illicit drugs consumption in different regions (mg/day/1000people) =

Location	METH	KET	MDMA	MTD	COC	CODE	References
Guangzhou, China	14.7–470.7	64.9–673.7	1.7–18.4	0.6–2.6	0.9–9.5	1.8–18.0	This study
Shenzhen, China	312.9–587.0	43.7	n.r	n.r	n.r	n.r	Du et al. (2015), Xu et al. (2017)
Beijing, China	219.7–376.5	2.2	n.r	n.r	n.r	n.r	
Dalian, China	206	n.r	n.r	n.r	n.r	n.r	Wang et al. (2019)
Hong Kong, China	180–200	1400–1600	N/A	n.r	160–180	n.r	Lai et al. (2013a, b)
South Africa	181.9–1184.8	n.r	n.r	n.r	155.8–533.0	n.r	Archer et al. (2018)
Canada	135	53.3	40	n.r	1570	n.r	Metcalfe et al. (2010), Yargeau et al. (2014)
Australia	340–1200	n.r	18–230	40	15–440	1960	Lai et al. (2016a), Thai et al. (2016)
United Kingdom	13.3–29.8	n.r	80.1–392	84	1023–1767	565	Baker et al. (2014)
France	n.r	n.r	5–41	n.r	110–130	n.r	Nefau et al. (2013)
USA	1740 ± 1190	n.r	n.r	131 ± 81.9	938 ± 706	140 ± 127	Skees et al. (2018)

To understand the drug use in different regions, the drug use levels in Guangzhou and abroad are presented in Table 2 based on this study and previous literature published. It can be seen that the consumption of METH was generally in the same order of magnitude as that of many other countries such as South Africa (Archer et al. 2018), Canada (Yargeau et al. 2014), the USA (Skees et al. 2018), and Australia (Lai et al. 2016a) indicating the widespread METH use.

KET use

A significantly higher KET consumption (256 ± 148 mg/d/1000 people) was estimated in Guangzhou in comparison with Beijing (2.2 mg/day/1000 people), Wuhan (61.9 mg/day/1000 people), and Shanghai (9.1 mg/day/1000 people), which is in accordance with the fact that KET use in south China is much greater than in north China (Du et al. 2015). Moreover, the highest consumption was also observed for KET among the six drugs monitored in this study (Fig. 2). This observation is in good agreement with the China Food And Drug Administration (2017) which indicated that "K powder" ranked in the top five of abused drugs in China with the consumption rapidly increasing (China Food And Drug Administration 2017). Similarly with METH, the consumption of KET in October was the lowest among the 3 months, which may also be concerned with the government's anti-drug operations. Compared with other countries where KET abuse was rarely reported (Table 2), a much higher KET consumption was obtained in Guangzhou. The result observed here is consistent with the fact that KET was mainly prevalent in East and South-East Asia, especially in mainland China, Hong Kong, and Taiwan where ketamine seizures were more than doubled, from 6 tons to more than 12 tons in 2014 (Feng et al. 2016; Han et al. 2016; UNDOC 2016). In Hong Kong, which borders with Guangzhou, the consumption of KET was higher than that in Guangzhou at 1400–1600 mg/day/1000 people. Nonetheless, a similar use pattern of drugs was observed between two regions where KET was the predominant drug followed by METH (Lai et al. 2013b).

MDMA use

The consumption of MDMA varied from 1.7 to 18.4 mg/day/1000 people with a mean of 7.0 ± 4.0 mg/day/1000 people (Fig. 2), similar to the result observed in Hong Kong (< 10 mg/day/1000 people) (Lai et al. 2013b). The average abuse estimated during this study is lower than those reported in Canada (40 mg/day/1000 people) (Metcalfe et al. 2010), Australia (18–230 mg/day/1000 people) (Lai et al. 2016a) and the UK (80.1–392 mg/d/1000 people) (Baker et al. 2014) (Table 2). Such geographical difference in MDMA consumption is well documented by a survey report. According to the World Drug Report (2016), the seizures of "ecstasy" tablets containing little or no MDMA were reported in South-East and East Asia, while in Europe, diversified compositions of "ecstasy" tablets with a high dose of MDMA or in powder form of high purity (UNDOC 2016) were reported. So, it stands to reason that the abuse of MDMA is lower in China than in European countries.

COC use

The calculated consumption of COC during 3 months was 1.7 ± 0.7 mg/day/1000 people, 3.3 ± 1.3 mg/day/1000 people and 5.3 ± 2.5 mg/day/1000 people, respectively (Fig. 2). The maximum consumption in Guangzhou was less than 5% of that measured in Hong Kong (170 ± 11 mg/day/1000 people) (Lai et al. 2013b), and two orders of magnitude lower than the consumption of the UK (Baker et al. 2014), Canada (Metcalfe et al. 2010; Yargeau et al. 2014), and USA (Skees et al. 2018) (Table 2). This finding demonstrated that cocaine is not a popular illicit drug in Guangzhou. This is consistent with findings from other studies in different cities of mainland China (Khan et al. 2014). The regional difference in COC use has also been reported by UNDOC (2016) as heavy COC consumption was mainly concentrated in USA and Europe while it was weak for Asia.

CODE use

The consumption of CODE in January, May, and October 2017 was 5.9 ± 3.8 mg/day/1000 people, 9.0 ± 3.0 mg/day/1000 people, and 7.0 ± 1.3 mg/day/1000 people respectively (Fig. 2). Unlike METH and KET, the consumption decrease is not as much in October compared with January and May, and this indicates that the law enforcement activities significantly affect the consumption of METH and KET, but not CODE. It also means that the level of CODE abuse was probably low in the monitored catchment although the China National Drug Abuse Monitoring Annual Report (2016) has showed that oral liquid preparation containing codeine compound has been officially listed as the second category of psychotropic drug management since 2015. The abuse rate of CODE, reported at 0.3% in 2017 compared to 0.2% in 2015 (China Food And Drug Administration 2017) was in fact too low to be measured by WBE.

MTD use

The per-capita consumptions of MTD in January and October were 1.6 ± 0.5 mg/day/1000 people and 1.5 ± 0.3 mg/day/1000 people, respectively (Fig. 2). This observation was in a comparable level with the observation in 2012 with the average consumption of MTD about 1.7 mg/day/1000 people, which was calculated in conjunction with the excretion rate of the EDDP (55%) and the reported influent load of EDDP of 0.9 mg/day/1000 people in Guangzhou (Khan et al. 2014). This result between the 2 years revealed that MTD used in China is under strict supervision for analgesic and opioid-dependence detoxification treatment since 2004 (Sun et al. 2015; INCB 2017). Compared with developed countries, the usage amount of MTD among Guangzhou residents was about 60 times lower than the values reported in the UK (113 mg/day/1000 people) (Baker et al. 2014), Croatia (148 mg/day/1000 people) (Terzic et al. 2010), and Belgium (138 mg/day/1000 people) (van Nuijs et al. 2011a) (Table 2).

Temporal patterns of illicit drugs use

Variation of illicit drugs use between holidays and control periods

A significantly higher consumption of METH was observed during the Spring Festival week compared with the control period Fig. 3a ($p = 0.003$). Lai et al. (2013a, b) also observed that a higher consumption of METH was during the New Year holiday in an urban area of Australia. However, during the National Day week, the consumption of METH was comparable to control weeks. The level of KET use during the public holiday periods did not show a statistically significant difference from those in control periods ($p = 0.235$ for Spring Festival, $p = 0.689$ for National day). A similar pattern was also found in the use of CODE ($p = 0.138$ for Spring Festival, $p = 0.925$ for National day). MDMA, known as a party drug, was observed with higher mean consumption (+ 37%) during National Day holidays ($p = 0.045$). Interestingly, the level of MTD use increased (+ 42%) during the Spring Festival holiday ($p = 0.003$) but decreased (− 28%) in National Day period ($p = 0.034$). It could be speculated that MTD may also be used in groups to enhance the festive atmosphere during the New Year period due to its addiction and narcotic properties. However, during the National Day, some regular methadone maintenance treatment patients may go out to visit friends or travel in the 7-day holiday, resulting in

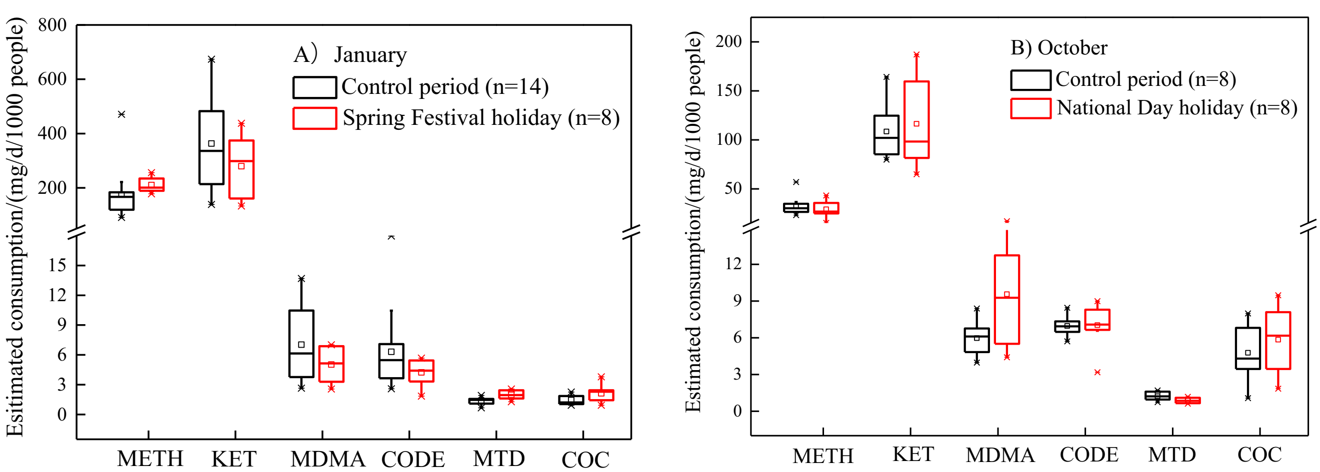

Fig. 3 Estimated consumption of illicit drugs during major holidays and control periods. **a** January. **b** October

reduced usage of MTD. Higher consumption of COC was also observed during the holiday period which increased by 47% during the Spring Festival ($p = 0.027$), known for its "party and dance" character.

Weekly profile of drug use

In this study, we did not observe a significant difference in consumption of all target drugs between weekend and weekdays although there was certain variation within the week. For example, a higher level of METH and KET consumption can be seen on Saturday but not on Sunday (Fig. 4). This was similar to the finding of a WBE study in Hong Kong where no apparent intra-week variations were found in KET, METH, and COC use (Lai et al. 2013a, b). It is probably due to regular users being dominant in the catchment. MTD consumption remained relatively stable throughout the week, which is in good agreement with the results in England (Baker et al. 2014) and Belgium (van Nuijs et al. 2011b). Party drugs such as COC and MDMA also had no significant consumption increase over the weekend ($p = 0.720$, 0.393). Such findings are in contrast with other studies in Europe, Australia, and South Africa, where consumption of COC and MDMA showed a significant upward trend over the weekend (Thomas et al. 2012; Lai et al. 2014; Archer et al. 2018). The result was similar for CODE with no weekend increase (Fig. 4).

Limitations

While our study is among the first WBE studies in China to investigate the temporal pattern of illicit drug use, there are a few limitations that should be noted for better interpretation of the results. Firstly, as shown in Eq. (2), the use of excretion rate of target drug and estimated population served by sewage treatment plant would bring a certain degree of uncertainty to back-estimation. As is well known, the metabolization varies between individuals (Leimanis et al. 2012). A certain metabolism rate used could lead to some impacts on the calculation although the excretion percentage is selected based on a large number of literatures (Baker et al. 2014; Thai et al. 2016). Besides, we have attempted to use a validated method to estimate the number of people contributing to a wastewater sample for better estimation of per-capita illicit drug use; however, the variation was large and that could influence the accuracy of the final estimates. So, cautions should be taken in the overestimation or underestimation of drug consumption brought by these two parameters. Secondly, this study monitored drug use across 8 weeks at different times of the year with 2 weeks of national holidays. This could reduce the power of statistical tests to compare the level of use between weekdays and weekend because of the limited number of days and the seasonal variation as reported by Li et al. (2014).

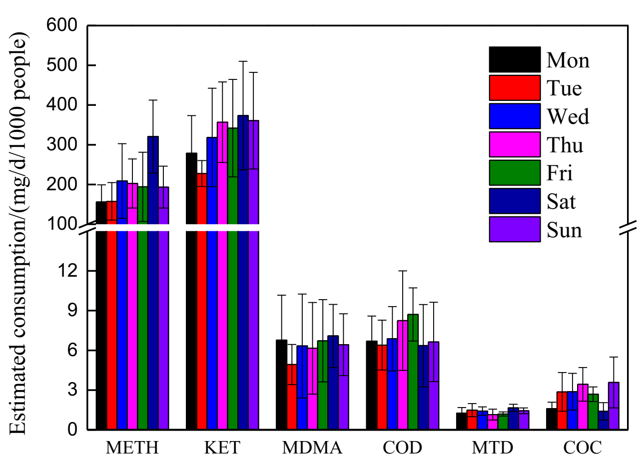

Fig. 4 Weekly pattern in drugs consumption (public holidays excluded) (mg/day/1000 people), including METH, KET, MDMA, CODE (weekdays, $n = 27$; weekend, $n = 9$), MTD (weekdays, $n = 19$; weekend, $n = 6$), and COC (weekdays, $n = 22$; weekend, $n = 6$)

Conclusions

This study revealed the temporal consumption profiles of six illicit drugs in Guangzhou monitored by WBE for 8 weeks including 2 weeks of public holiday in 2017. We found that METH and KET were the predominant illicit drugs in Guangzhou. A sharp decline of METH and KET consumption was observed in October, possibly due to the impact of law enforcement efforts. Increase in weekend consumption was little compared with weekdays, which is different from observations in Western countries. Drug consumption during public holidays were higher for METH, MDMA, and COC than in control periods while the consumption of KET remained steady, which indicated the high variability of the drug scene in China.

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Compliance with ethical standards

Ethics statement This paper is our original work.

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