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Use of illicit drugs, alcohol and tobacco in Spain and Portugal during the COVID-19 crisis in 2020 as measured by wastewater-based epidemiology

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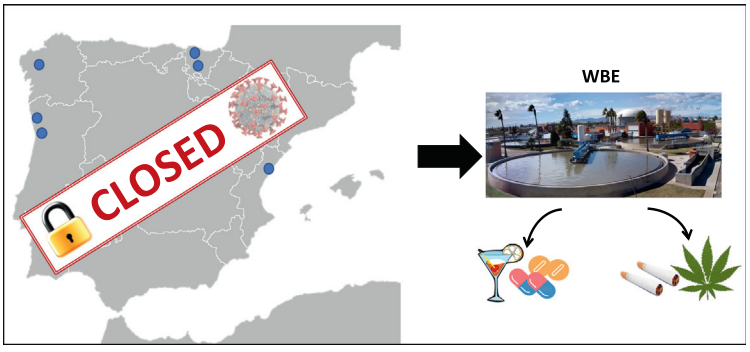
HIGHLIGHTS

- WBE was applied to study drug use in 4 Spanish and 2 Portuguese locations.
- Generally, low impact observed on substances use owing to COVID-19 restrictions
- The main exception was a notable decrease in cocaine use in Castellón (Spain).
- High consumption of amphetamine in the Basque Country
- Two MDMA (ecstasy) dumping events into the sewage network detected

GRAPHICAL ABSTRACT



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ABSTRACT

The COVID-19 pandemic spread rapidly worldwide in the year 2020, which was initially restrained by drastic mobility restrictions. In this work, we investigated the use of illicit drugs (amphetamine, methamphetamine, ecstasy, cocaine and cannabis), and licit substances of abuse (alcohol and tobacco) during the earlier months (March–July 2020) of the pandemic restrictions in four Spanish (Bilbao and its metropolitan area, Vitoria-Gasteiz, Castellón and Santiago de Compostela) and two Portuguese (Porto and Vila do Conde) locations by wastewater-based epidemiology (WBE). The results show that no methamphetamine was detected in any of the locations monitored, while amphetamine use was only detectable in the two locations from the Basque Country (Bilbao and its metropolitan area and Vitoria-

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Gasteiz), with high estimated average usage rates (700–930 mg day^{-1} 1000 inhabitant^{-1}). The remaining substances were detected in all the investigated catchment areas. In general, no remarkable changes were found in population normalized loads compared to former years, except for cocaine (i.e. its main metabolite, benzoylecgonine). For this drug, a notable decrease in use was discernible in Castellón, while its usage in Porto and Santiago de Compostela seemed to continue in a rising trend, already initiated in former years. Furthermore, two events of ecstasy (3,4-methylenedioxymethamphetamine, MDMA) dumping in the sewage network were confirmed by enantiomeric analysis, one in Santiago de Compostela just prior the lockdown and the second one in the Bilbao and its metropolitan area in July after relieving the more stringent measures. The latter could also be associated with a police intervention. The comparison of WBE with (web) survey data, which do not provide information at a local level, points towards contradictory conclusions for some of the substances, thereby highlighting the need for stable WBE networks capable of near real-time monitoring drug use.

1. Introduction

COVID-19 is an infectious illness caused by the virus SARS-CoV-2 characterized by disrupting normal immune responses (Yang et al., 2020), which has spread worldwide and has caused over 6 million deaths (Adam, 2022). Due to the rapid transmission of the virus in early 2020, most countries imposed lockdowns and perimeter closures, affecting mobility, and limiting essential activities. Subsequently, the closure of bars, pubs, clubs, restaurants etc. changed the way alcohol and tobacco were purchased, which could have affected their use. The obliged self-isolation produced a change in our lifestyle that could have had a psychological impact on human health (Brooks et al., 2020) and encouraged the use of certain substances, like alcohol or pharmaceuticals, at home (Rehm et al., 2020; Santomauro, 2021). As regards to illicit drugs, these restriction measures have had an important impact on the logistics of drugs trafficking (European Monitoring Centre for Drugs and Drug Addiction, 2020a). Despite this, access to them has not been totally affected since, new distribution strategies have been adopted to overcome the restrictions, such as the use of darknet markets (European Monitoring Centre for Drugs and Drug Addiction, 2020b).

Different surveys have been undertaken in order to assess the use of illicit and/or licit substances during the COVID-19 pandemic (Callinan et al., 2020; European Monitoring Centre for Drugs and Drug Addiction, 2020c; Observatorio Español de las Drogas y las Adicciones, 2020a). However, such methods are not, on their own, able to capture the real impact of the pandemic over drug use (Palamar and Acosta, 2020). The analysis of wastewater can give an additional and representative estimation of human consumption of licit and illicit substances during the pandemic. This methodology, known as wastewater based epidemiology (WBE), uses wastewater as an anonymized, integrated and diluted sample of urine of a particular location to obtain comprehensive results, which can be then completed with surveys results (van Wel et al., 2016). WBE has been successfully used in studying spatial and temporal differences of illicit drug use (Bijlsma et al., 2021; González-Mariño et al., 2020; Zuccato et al., 2005). Since 2010, The European Monitoring Centre for Drugs and Drugs Addiction (EMCDDA) (European Monitoring Centre for Drugs and Drug Addiction, 2021), through the Sewage Analysis Core group Europe (SCORE), is carrying out an annual monitoring of illicit drug use in many European cities (SCORE, 2021), where different consumption trends have been observed among European countries (González-Mariño et al., 2020). At Spanish level, the ESAR-Net (www.esarnet.es) network has also been established to coordinate Spanish WBE activities in close cooperation with the Spanish *Plan Nacional Sobre Drogas* and different other institutions (Bijlsma et al., 2018, 2021; Estévez-Danta et al., 2021a; López-García et al., 2020; Montes et al., 2020).

Nowadays, the scope of WBE has been extended to many applications, such as the estimation of alcohol and tobacco consumption (Castiglioni et al., 2014; López-García et al., 2020; Montes et al., 2020; Rodríguez-Álvarez et al., 2015) and the human exposure of chemicals such as plasticizers (Estévez-Danta et al., 2021b; González-Mariño et al., 2017; Lopardo et al., 2019), pesticides (Rousis et al., 2016) or flame retardants (Been et al., 2017). Recently, WBE was employed in many countries to detect SARS-CoV-2 (Bivins et al., 2020; Lundy et al., 2021). WBE has also been used to measure the impact of the COVID-19 pandemic on illicit drug and pharmaceuticals use in Australia (Bade et al., 2020, 2021), Tyrol (Austria) (Reinstadler et al., 2021), Athens (Greece) (Alygizakis et al., 2021), Central Italy (Di Marcantonio et al., 2022), and in 7 cities across Europe (Been et al., 2021).

In this work the impact of the COVID-19 pandemic in 2020 on the use of five illicit drugs (amphetamine (AMP), methamphetamine (MAMP), ecstasy (3,4-methylenedioxymethamphetamine, MDMA), cocaine (COC) and cannabis), tobacco and alcohol in four Spanish and two Portuguese locations was investigated by WBE. Wastewater samples during the initial lockdown (from March 2020) until after the most stringent measures were relieved (July 2020, herein denoted “New Normal”, see below) in order to follow the trends in use and compare it with data from former years.

2. The COVID-19 lockdown in Spain and Portugal

Fig. 1 outlines the timeline of the COVID-19 pandemic, the wastewater sampling campaign and the different levels of restrictions in the studied areas of Spain and Portugal from January to July 2020.

2.1. Spain

The first case of SARS-CoV-2 was detected on 31 January 2020 in The Canary Islands (World Health Organization, 2020a). Due to the fast expansion on the subsequent weeks, the authorities declared the state of alarm on 15 March 2020 and imposed a lockdown, where only essential activities were permitted and movement was restricted to buy groceries and other essential goods, seek medical attendance, etc. During March, cases continued to rise with a peak on 31 March 2020. In the following weeks, cases and deaths followed a decreasing pattern until 11 May 2020, when the quarantine ended. From that day on, the measures were started to be loosened (divided in three phases), allowing the gradual opening of bars, restaurants, pubs and finally the inter-regional mobility at the end of June, which was officially called “New Normal”. In Spain, wastewater sampling was performed in the period between 10 March 2020 to 14 July 2020, depending on the particular location sampled. Further details are provided in Section 3.2 and Table S1.

2.2. Portugal

The first case of SARS-Cov-2 was detected on 2 March 2020 in Porto (World Health Organization, 2020b). On 16 March 2020, schools were closed and two days later, on 18 March 2020, the Emergency State was declared, and Portugal was placed under a strict lockdown. During the consecutive weeks, new cases and deaths decreased until 2 May 2020, when the quarantine ended. The so-called state of calamity (*Estado de Calamidade*), divided in three phases started the same day, where gradually, recreative centers, activities etc. were opened until early June. From then, restrictions were withdrawn and this stage is also termed here “New Normal”, as an analogy to the Spanish definition, and since such term that has been widely used to describe past settling after a crisis, including COVID-19 crisis (Ahlstrom et al., 2020; Berwick, 2020). Wastewater samples were collected

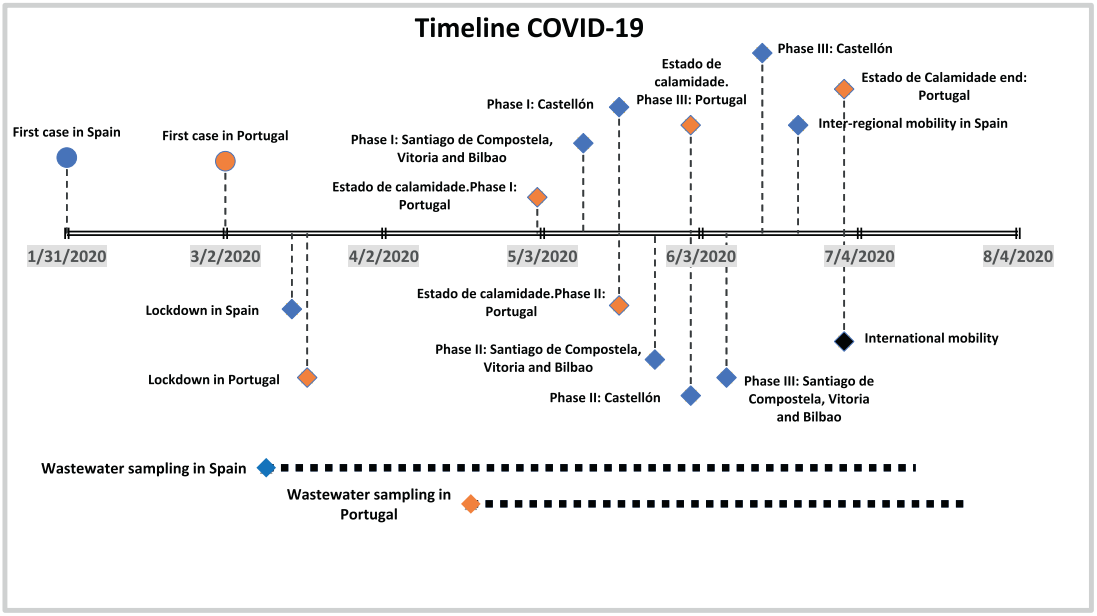

Fig. 1. Timeline summary of the COVID-19 pandemic restrictions in the period January–July 2020 in the studied areas. Dates presented as month/day/year.

from 19 April 2020 to 24 July 2020 in Portugal. Further details are provided in Section 3.2 and Table S1.

3. Material and methods

3.1. Chemicals and reagents

Individual solutions of 1 mg mL^{-1} of AMP, MAMP, MDMA, COC, benzoylecgonine (BE), 11-nor-9-carboxy-tetrahydrocannabinol (THC-COOH), cotinine (COT) and trans-3′-hydroxycotinine (OH-COT), and 0.1 mg mL^{-1} of their deuterated analogues (AMP-D_6, MAMP-D_5, MDMA-D_5, COC-D_3, BE-D_3, THC-COOH-D_9, COT-D_3 and OH-COT-D_3) used as surrogate internal standards (ISs), were supplied by Cerilliant (Round Rock, TX, USA). Sodium salts of Ethyl-Sulfate (EtS) and its deuterated analogue (EtS-D_5) were supplied by Santa Cruz Biotechnology (Santa Cruz, CA, USA). Individual solutions of 1 mg mL^{-1} of the S-(+) enantiomer of AMP, MAMP and MDMA were supplied by Merck (Darmstadt, Germany).

LC-MS grade methanol (MeOH), LC-MS grade acetic acid, LC-MS grade formic acid, ammonia (NH_3) solution in water (25%), tetrabutylammonium bromide (TBA, 99%) and β-Glucuronidase (from *Helix pomatia*, type H2) were supplied by Merck. Sodium acetate and sodium chloride were obtained from Fluka (Steinheim, Germany). Ultrapure water was obtained with a Genie Water System from RephiLe Bioscience (Boston, MA, USA).

3.2. Wastewater samples collection

Composite 24-h raw influent wastewater was sampled at the entrance of six wastewater treatment plants (WWTPs) covering four Spanish locations (Santiago de Compostela, Bilbao and its whole metropolitan area, Castellón and Vitoria-Gasteiz) and two Portuguese cities (Porto and Vila do Conde) from March to July 2020. In addition, samples from one week in 2019 were also analyzed for Santiago de Compostela, Bilbao and its metropolitan area and Castellón.

Table S1 compiles sampling dates and flow rates of each individual sample, the characteristics of the WWTPs and sampling mode. A time-proportional sampling mode was employed in all cities. Further data from 2017 and 2018 (and 2019 in the case of Porto) were obtained from the literature (Bijlsma et al., 2021; European Monitoring Centre for Drugs and Drug Addiction, 2021; González-Mariño et al., 2020; López-García et al., 2020; Montes et al., 2020).

3.3. Sample treatment and LC-MS/MS method

Analyses of illicit drugs were performed at University Jaume I (Castellón samples) or at the University of Santiago de Compostela (all remaining samples), after solid-phase extraction and LC-MS/MS analysis as described elsewhere (Bijlsma et al., 2014; González-Mariño et al., 2018). These two methods afford method limits of quantification (MQL) in the 2 (BE) – 100 (AMP) and 1.2 (MDMA) – 64 (AMP) ng L^{-1} range, respectively, and satisfactory recoveries in spiked wastewater (77–124% and 95–121%, respectively, RSD values ≤16% in both cases). Besides, both laboratories participated and satisfactorily passed the interlab study organized by the SCORE Network in 2020, which warrants good performance and comparability of the results (van Nuijs et al., 2018).

Some selected samples were also submitted to an enantiomeric analysis as described in Estévez-Danta et al. (2021a). This methodology renders MQLs in the 2–5 or 4–8 ng L^{-1} (please note that they refer to pure enantiomers) and recoveries in wastewater in the 82–116% range (RSD ≤15%) or 66–125% range (RSD ≤17%), depending on whether the SPE being used was the one from the University of Santiago de Compostela or University Jaume I, respectively, see Estévez-Danta et al. (2021a) for further details.

Analyses of EtS (ethanol biomarker) and COT and OH-COT (nicotine biomarkers) were all performed at the University of Santiago de Compostela by direct injection-LC-MS/MS, after enzymatic deconjugation of nicotine metabolites, as detailed in Rodríguez-Álvarez et al. (2014a, 2014b). These two methods provide recoveries with spiked sewage in the 92–112% range (RSD ≤7%) and MQLs in the 200–600 ng L^{-1} range.

3.4. Estimation of loads and human use

Concentrations of each particular biomarker (compiled in Table S2) were used to determine population-normalized daily loads (compiled in Table S3) of each compound in the 24 h composite wastewater samples, (Eq. (1)). Human consumption rates (presented in Table S4) were then estimated (Eq. (2)) by using the correction factor (CF) values: 2.77 (AMP), 2.3 (MAMP), 4.4 (MDMA), 3.59 (COC consumption from BE) as proposed in Gracia-Lor et al. (2016), 3.41 (nicotine consumption from COT) and 1.90 (nicotine consumption from OH-COT), whose values where then averaged for each sample as proposed in Montes et al. (2020); Rodríguez-Álvarez et al. (2014b) and 3047 (EtS) as proposed in Rodríguez-Álvarez et al. (2015). Although a recent study in Australia (Thai et al., 2021) proposed a higher CF (4000) for EtS, based on sale

statistics, that would account for in-sewer degradation, our former nationwide study (López-García et al., 2020) in Spain showed a good match of WBE data obtained with the CF 3047, compared to surveys on use or sales. Besides, the use of the same CF as previously applied in former studies in Spain warrants a better comparability of data. For THC (cannabis) calculations from THC-COOH, two CF values were used: 182 which derives only from THC-COOH and 36.4, which derives from the potential conversion of hydroxy-THC to THC-COOH, as discussed in detail in Bijlsma et al., (2021). In the case of ethanol, use was translated to L day^{-1} 1000 $inhabitant^{-1}$ by considering its density.

$$\text{Daily loads} = \text{Concentration} * \text{Flow rate} * 1000/\text{Population} \quad (1)$$

$$\text{Human use} = \text{Daily loads} * \text{CF} \quad (2)$$

3.5. Determination of enantiomeric fraction

Enantiomeric analysis was carried out for AMP and MDMA enabling the measurement of the concentration of enantiomers (C_R for the R(−)-enantiomer and C_S for S(+)-enantiomer) in randomly selected samples and those showing anomalous (too high) loads of MDMA (see Section 4.1.2). These were used to derive the enantiomeric fraction (EF), which was then employed to tentatively differentiate between licit (prescription) or illicit (abuse) consumption and direct dumping in the sewage network. In this work, EF is presented as EF_R, i.e. the ratio between the concentrations of the R(−)-enantiomer and the sum of both enantiomers (Eq. (3)).

$$EF_R = C_R/(C_R + C_S) \quad (3)$$

The obtained EF_R values are presented in Table S5.

3.6. Statistical analysis

Data were plotted with Microsoft Excel 365 and R ggplot2 package. Statistical differences ($\alpha = 0.05$) in the temporal pattern within each location and considering all the different years and lockdown phases until New Normal were assessed by a Kruskal-Wallis test, with a *post-hoc* Bonferroni correction, by using the software Statgraphics Centurion 18.

4. Results and discussion

Figs. 2–7 show the evolution of the substance divided in four phases: WBE data from previous years, lockdown period, less stringent measures (compiling all three phases) and New Normal. Moreover, a more detailed division according to the different de-escalation phases, as detailed in Section 2 and Fig. 1, and former years is shown in the Supplementary Information (Figs. S1–S6).

Table 1 compiles the most relevant WBE studies on the impact of COVID-19 on the use of drugs (Alygizakis et al., 2021; Bade et al., 2020, 2021; Been et al., 2021; Di Marcantonio et al., 2022; European Monitoring Centre for Drugs and Drug Addiction, 2020a; Reinstadler et al., 2021), whereas the most relevant international, or related to Spain and/or Portugal, reports relying on (web) surveys, and, to a minor extent, other indicators are presented in Table 2 (European Monitoring Centre for Drugs and Drug Addiction, 2020c; Global Drug Survey, 2021; Observatorio Español de las Drogas y las Adicciones, 2020a, 2020b).

4.1. Illicit drugs use

4.1.1. Amphetamine and methamphetamine

MAMP remained below the detection limits in all samples. This is consistent with former studies in Europe and Spain (Bijlsma et al., 2021; González-Mariño et al., 2020), where the WBE-derived consumption estimates were typically very low with few exceptions. In fact, in a former study where samples from 13 Spanish cities were collected during a week in Spring 2018 (Bijlsma et al., 2021), average MAMP loads were below 5 mg day^{-1} 1000 $inhabitant^{-1}$ except in Madrid (ca. 13 mg day^{-1} 1000 $inhabitant^{-1}$) and Barcelona (ca. 48 mg day^{-1} 1000 $inhabitant^{-1}$).

During 2020, AMP was detected in this study, but only in Bilbao and its metropolitan area and Vitoria-Gasteiz (estimated average consumption: 703 and 928 mg day^{-1} 1000 $inhabitant^{-1}$, respectively, Table S4), both locations belong to the Spanish region of the Basque Country, being below method detection limits in the remaining locations (Table S2). These findings confirm our former studies in the area of Bilbao, where a high consumption of AMP was observed (mean ca. 700–800 mg day^{-1} 1000 $inhabitant^{-1}$, in 2018–2019 (Bijlsma et al., 2021; Estévez-Danta et al., 2021a)), and illustrate no different trend due to COVID-19 measures (Figs. 2 and S1). The statistical analysis confirmed that there was no statistical difference (Table S6) between the different periods of the study, including former years in the case of Bilbao and its metropolitan area. Furthermore, these findings also point to the fact that AMP use is

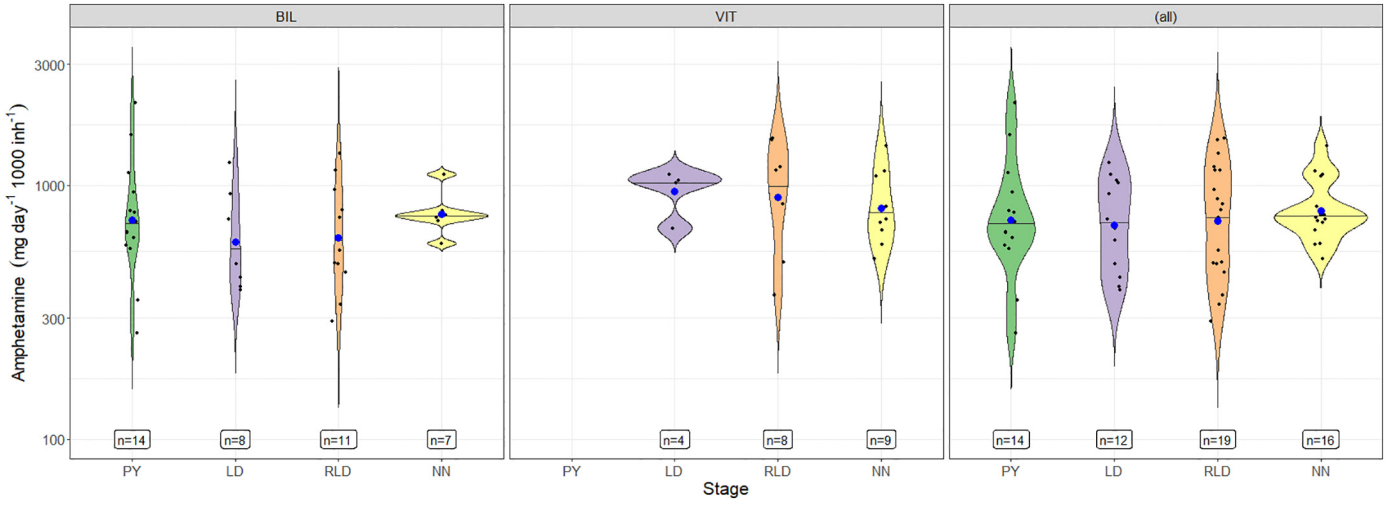

Fig. 2. Violin plots summarizing the WBE-derived consumption of AMP in Bilbao and its metropolitan area (BIL), Vitoria-Gasteiz (VIT) and both locations (all). The horizontal line and blue dots and smaller black dots represent the median, mean and individual datapoints, respectively. Coding: PY (previous years, in green), LD (lockdown, in purple), RLD (relaxed phase I-III lockdown, in orange), NN (new normal, in yellow). N.B.: logarithmic scale; AMP was below MDL in the remaining locations. Further detailed plots are presented in Fig. S1.

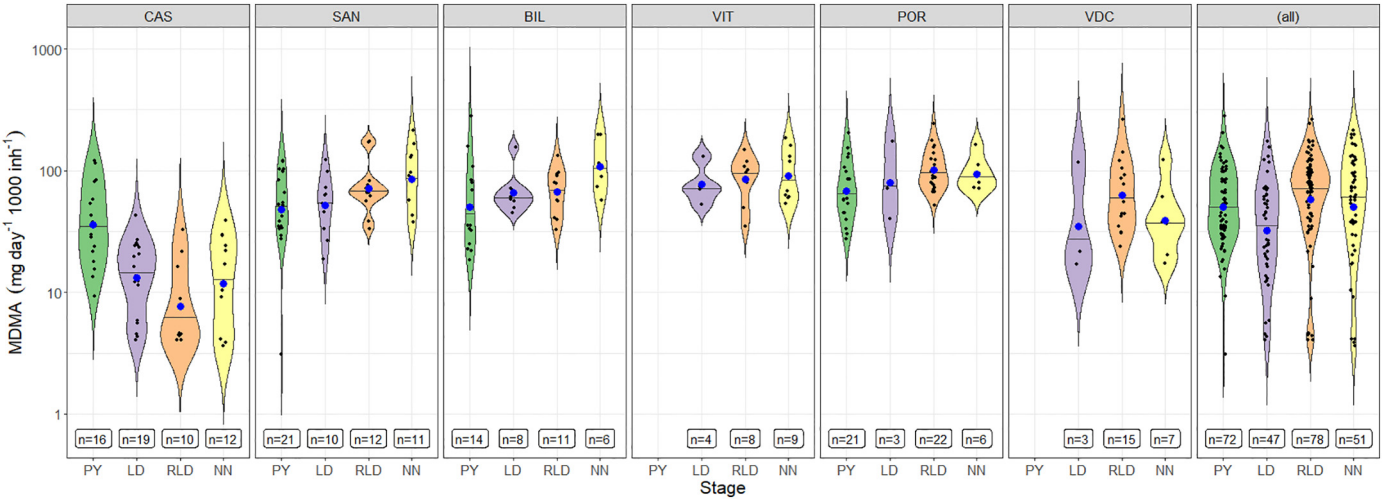

Fig. 3. Violin plots summarizing the WBE-derived consumption of MDMA in Castellón (CAS), Santiago de Compostela (SAN), Bilbao and its metropolitan area (BIL), Vitoria-Gasteiz (VIT), Porto (POR) and Vila do Conde (VDC) and all locations (all). The horizontal line and blue dots and smaller black dots represent the median, mean and individual datapoints, respectively. Coding: PY (previous years, in green), LD (lockdown, in purple), RLD (relaxed phase I-III lockdown, in orange), NN (new normal, in yellow). N.B.: logarithmic scale. Further detailed plots are presented in Fig. S2.

not a local issue in Bilbao and its metropolitan area, but a regional behaviour, which will position the consumption of AMP in the Basque Country at levels close to those found in central Europe, e.g. Belgium, The Netherlands and some parts of Germany (González-Mariño et al., 2020). Data from this region agree with general-population surveys (GPS), as regards the fact that AMP consumption is higher in this region as compared to the rest of Spain, but WBE estimations indicate that such difference is larger to what GPS report, as already discussed in former studies (Bijlsma et al., 2021; Estévez-Danta et al., 2021a). Besides, the enantiomeric analysis confirmed a slight enrichment of R(−)-AMP in the wastewater of both locations, with EF_R values higher than 0.5 (Table S5). This is coherent with data from former years in the area of Bilbao and pointing to illicit consumption, taking into account also prescription figures of related pharmaceuticals, which in these two locations would represent less than 1% of AMP loads in wastewater (Estévez-Danta et al., 2021a). On the other hand, this enantiomeric method is more sensitive (MQL for AMP isomers is 5–8 ng L^{-1}) that the regular one. Thus, EF_R values could be calculated for all samples subject to this method except those from Castellón and one of the samples from Santiago de Compostela. Furthermore, EF_R values were more variable, particularly in Santiago de Compostela, which may indicate that prescription of pharmaceuticals may be a source of amphetamine in this location (Estévez-Danta et al., 2021a), although concentrations remain low (ca. 5–10 ng L^{-1}).

Other WBE studies (Alygizakis et al., 2021; Been et al., 2021; European Monitoring Centre for Drugs and Drug Addiction, 2020a; Reinstadler et al., 2021) compiled in Table 1 show a mixed picture, with cities exhibiting divergent trends as compared to the pre-COVID-19 era. Besides, the EMCDDA report on the impact of COVID-19 (European Monitoring Centre for Drugs and Drug Addiction, 2020a) which includes WBE data from 29 locations in Europe indicates that AMP consumption was recovered (or even increased) when the lockdown measures were eased. All these WBE data do not agree, however, with web-surveys (Table 2), particularly for Spain (Observatorio Español de las Drogas y las Adicciones, 2020a), which seem to point towards a decrease in AMP use. Yet, the Global Drug Survey (which does not include Spanish nor Portuguese data (Global Drug Survey, 2021)), pointed towards a certain level of substitution of AMP by MAMP

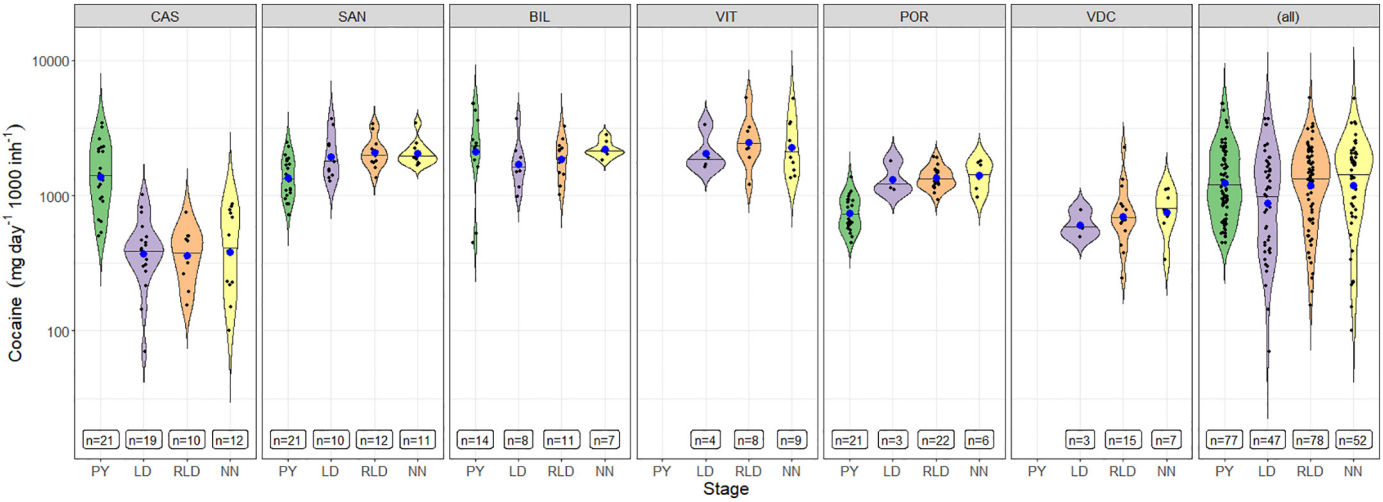

Fig. 4. Violin plots summarizing the WBE-derived consumption of Cocaine in Castellón (CAS), Santiago de Compostela (SAN), Bilbao and its metropolitan area (BIL), Vitoria-Gasteiz (VIT), Porto (POR) and Vila do Conde (VDC) and all locations (all). The horizontal line and blue dots and smaller black dots represent the median, mean and individual datapoints, respectively. Coding: PY (previous years, in green), LD (lockdown, in purple), RLD (relaxed phase I-III lockdown, in orange), NN (new normal, in yellow). N.B.: logarithmic scale. Further detailed plots are presented in Fig. S3.

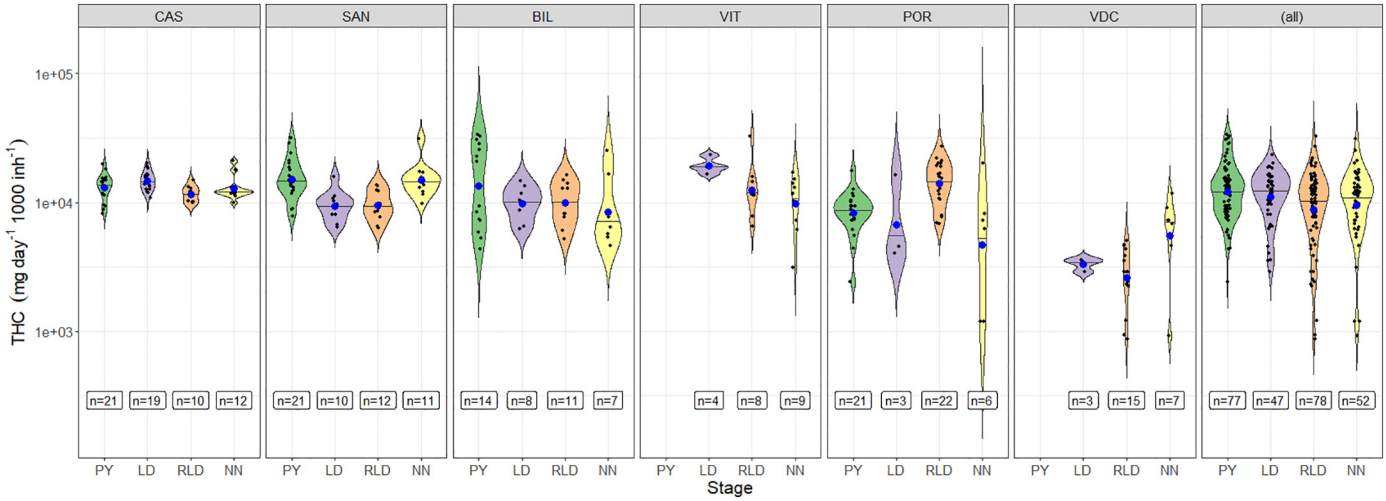

Fig. 5. Violin plots summarizing the WBE-derived consumption of THC (recalculated from TH-COOH with a CF of 182) in Castellón (CAS), Santiago de Compostela (SAN), Bilbao and its metropolitan area (BIL), Vitoria-Gasteiz (VIT), Porto (POR) and Vila do Conde (VDC) and all locations (all). The horizontal line and blue dots and smaller black dots represent the median, mean and individual datapoints, respectively. Coding: PY (previous years, in green), LD (lockdown, in purple), RLD (relaxed phase I-III lockdown, in orange), NN (new normal, in yellow). N.B.: logarithmic scale. Further detailed plots are presented in Fig. S4.

during lockdown, which was also observed in a WBE study in Innsbruck (Austria) (Reinstadler et al., 2021). However, this trend was not observed in this study.

4.1.2. MDMA

MDMA was detected in the six studied cities. The excretion loads of MDMA in 2020 ranged from 0.8 to 60 mg day^{-1} 1000 inhabitant^{-1} (Table S3), with two notable exceptions: Santiago de Compostela on March 12 (i.e. 3 days prior the lockdown) and Bilbao and its metropolitan area on July 9 (i.e. New Normal), which resulted into calculated loads of 309 and 306 mg day^{-1} 1000 inhabitant^{-1}, respectively. Hence, these two (together with other randomly selected) samples were subjected to enantiomeric analysis. A slight enrichment of R(−)-MDMA was found in the wastewater, with EF_R in the 0.54–0.72 range, except these two samples, whose EF_R was 0.48 (Santiago de Compostela) and 0.51 (Bilbao) (Table S5). This shift into EF_R towards a racemic mixture combined with higher loads suggest a disposal of MDMA in the sewer network (Estévez-Danta et al., 2021a; Vazquez-Roig et al., 2014), similarly to that reported by Emke et al. in The Netherlands (Emke et al., 2014). Given this observation, these two events were not considered for calculating average loads (Table S3) nor for consumption back-calculation (Table S4). In the case of the metropolitan area of Bilbao the finding was also consistent with media reports (e.g. (EITB.EUS, 2020; El Diario Vasco, 2020)) from July 2020 reporting a police action taking place on the previous day where a drug trafficking organization was dismantled. No media news were found related to the case of Santiago de Compostela, but it happened a few days before the lockdown was in place, when many people were moving to their hometowns/weekend settles and police was expected to control mobility.

Considering the loads on those two days related to disposal events and average loads in wastewater in Santiago de Compostela and Bilbao and its metropolitan area under normal circumstances (Table S3), we could calculate the disposed amount, which would translate into 39 and 247 g of pure MDMA in the event in Santiago de Compostela and Bilbao and its metropolitan area, respectively. This would correspond to either 204 tablets or 47.6 g of MDMA crystal (Santiago de Compostela) and either 1372 tablets

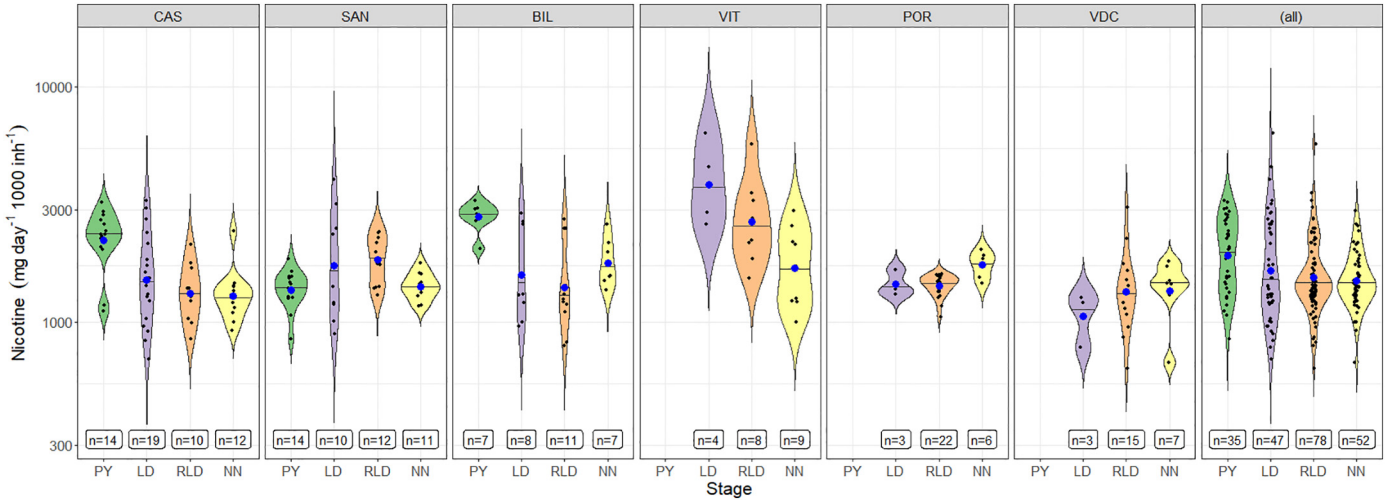

Fig. 6. Violin plots summarizing the WBE-derived consumption of nicotine in Castellón (CAS), Santiago de Compostela (SAN), Bilbao and its metropolitan area (BIL), Vitoria-Gasteiz (VIT), Porto (POR) and Vila do Conde (VDC) and all locations (all). The horizontal line and blue dots and smaller black dots represent the median, mean and individual datapoints, respectively. Coding: PY (previous years, in green), LD (lockdown, in purple), RLD (relaxed phase I-III lockdown, in orange), NN (new normal, in yellow). N.B.: logarithmic scale. Further detailed plots are presented in Fig. S5.

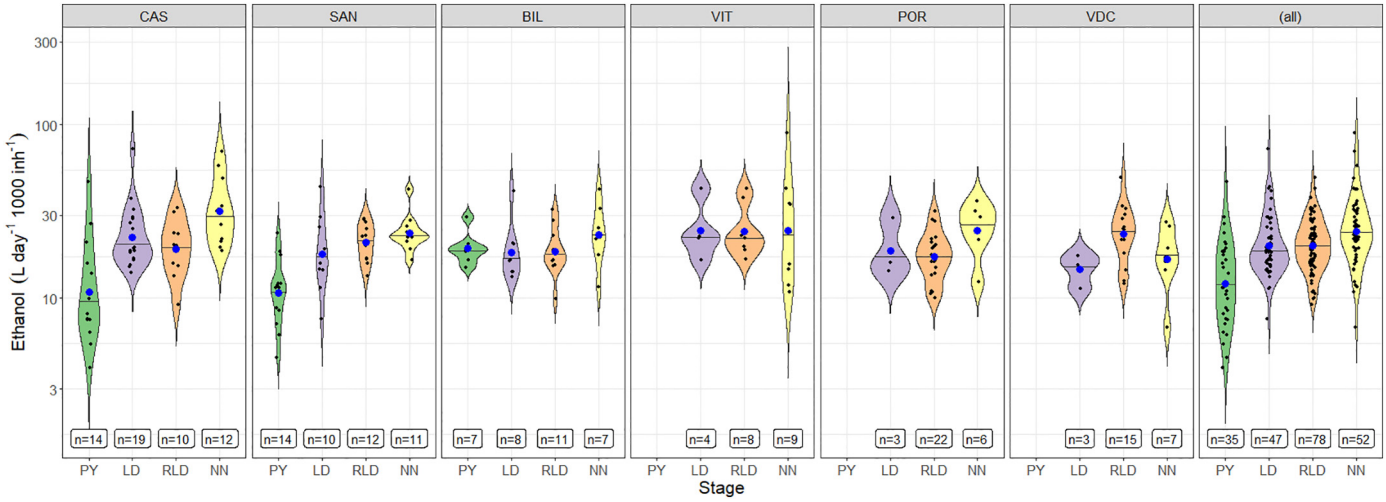

Fig. 7. Violin plots summarizing the WBE-derived consumption of ethanol in Castellón (CAS), Santiago de Compostela (SAN), Bilbao and its metropolitan area (BIL), Vitoria-Gasteiz (VIT), Porto (POR) and Vila do Conde (VDC) and all locations (all). The horizontal line and blue dots and smaller black dots represent the median, mean and individual datapoints, respectively. Coding: PY (previous years, in green), LD (lockdown, in purple), RLD (relaxed phase I-III lockdown, in orange), NN (new normal, in yellow). N.B.: logarithmic scale. Further detailed plots are presented in Fig. S6.

or 305 g of MDMA crystal (Bilbao and its metropolitan area), considering an average content of 180 mg tablet^{-1} of MDMA and 81% purity of MDMA crystal (Bijlsma et al., 2021). These figures could be, however, underestimated, since they assume that all MDMA was dissolved in the transit from the disposal site to the WWTP where water was collected, but this may not be true.

The extrapolated MDMA consumption (after excluding the two direct disposal events) is summarized in Fig. 3 (further details into Fig. S2 and Table S4). The highest consumption levels were found in Porto (mean: 105 mg day^{-1} 1000 inhabitant^{-1}) while the lowest consumption was determined in Castellón (mean: 15 mg day^{-1} 1000 inhabitant^{-1}), less than a third of 2019 use in this city (mean: 54 mg day^{-1} 1000 inhabitant^{-1})

Table 1
Compilation of WBE studies on the impact of COVID-19 on substances of abuse, which include data from before COVID-19.

Reference	(Reinstadler et al., 2021)	(Been et al., 2021)	(Alygizakis et al., 2021)	(Di Marcantonio et al., 2022)	(European Monitoring Centre for Drugs and Drug Addiction, 2020a)	(Bade et al., 2021)	(Bade et al., 2020)
Geographical scope	Austria (Innsbruck, ca. 175,000 inhabitants)	Europe (7 cities from 4 countries)	Greece (Athens, ca. 4 million inhabitants)	Italy (2 WWTPs from the center of the country, ca. 800,000 inhabitants)	EMCDDA report, including WBE from several European cities	Australia (20 locations, ca. 47% Australian population)	Australia (Adelaide area, ca. 1.1 million inhabitants)
Temporal scope	Lockdown (March–April 2020)	Lockdown (1 week in March–April 2020)	Lockdown (2 weeks in March–April 2020)	Lockdown-"New Normal" (23 samples in total in March–December 2020)	Lockdown (LD) and "New normal" (NN)	Lockdown (1 week in April 2020) and "New Normal" (1 week in June 2020)	Lockdown (1 week in April 2020)
Amphetamine	Slight decrease	Did not change (3 locations) Decrease (1 location)	Increase	–	Did not change (13 cities LD, 11 NN) Decrease (11 LD, 5 NN) Increase (5 LD, 13 NN)	–	–
MDMA	Decrease	Did not change (4 locations) Decrease (2 locations)	Decrease	–	Did not change (9 cities LD, 11 NN) Decrease (23 LD, 14 NN) Increase (7 LD, 12 NN)	Did not change (7 states) Decrease (1 states)	–
Cocaine	Did not change	Did not change (2 locations) Increase (1 location) Decrease (4 locations)	Increase	Increase	Did not change (5 cities LD, 13 NN) Decrease (18 LD, 1 NN) Increase (7 LD, 14 NN)	Did not change (6 states) Decrease (2 states)	–
Cannabis	Did not change	Did not change (4 locations)	Did not change	–	Did not change (8 cities LD, 6 NN) Decrease (4 LD, 4 NN) Increase (4 LD, 7 NN)	Did not change (1 state) Increase (7 states)	–
Tobacco	Did not change	–	Decrease	–	–	–	–
Alcohol	Decrease	–	–	–	Did not change (6 NN) Decrease (4 NN) Increase (6 NN)	Did not change (5 states) Decrease (3 states)	Decrease

(European Monitoring Centre for Drugs and Drug Addiction, 2019) (Table S4). No statistical difference was appreciated in MDMA consumption in Bilbao and its metropolitan area, Santiago de Compostela, Vitoria-Gasteiz and Vila do Conde in the studied period (Table S6, see also Fig. S2 and Fig. 3), which includes former years only in the two first locations. Conversely, this was not the case of Castellón and Porto (Table S6). However, the *post-hoc* test detected only significant differences in Castellón between 2019 (when consumption was at its maximum in this location, particularly during the weekend) and Phase I; and, in Porto, between 2017 (lowest measured consumption in that location, without observable weekend peak) and Phase III (Fig. S2). Therefore, and considering the overall picture presented in Fig. 3, we may conclude that overall, MDMA consumption remained stable in the considered period.

Interestingly, these findings contrast both with on-line surveys and expert information (Table 2), which indicate an overall decrease in MDMA consumption during the lockdown. However, the conclusions from other WBE studies (Table 1) differ from location to location, but the overall trend during the lockdown was also towards a decrease or no change in MDMA consumption as compared to former years in the studied areas. However, consumption seemed to recover in those places after lockdown relaxation in Europe (European Monitoring Centre for Drugs and Drug Addiction, 2020a).

4.1.3. Cocaine

Both cocaine and its metabolite, benzoylecgonine were detected in all samples (Table S2). The ratio of cocaine to benzoylecgonine was calculated as it may indicate a direct disposal event when above 1 (Bijlsma et al., 2012; Postigo et al., 2010). In this study, the ratio was ≤ 0.8 in all samples, with averages ranging from 0.2 (Vila do Conde) to 0.6 (Bilbao and its metropolitan area). Also, in the dates and locations of the two MDMA dumping events (see Section 4.1.2), this ratio was calculated to be 0.3 (Santiago de Compostela) and 0.7 (Bilbao and its metropolitan area), without a spike in cocaine concentration nor ratio being observed. Altogether, this data points to the fact that no significant cocaine dumping occurred in 2020.

The average calculated consumption of cocaine from benzoylecgonine, summarized in Fig. 4 (further detailed in Fig. S3 and Table S4), was similar to that found in former years (mean between 783 and 2503 mg day^{-1} 1000 $inhabitant^{-1}$) (González-Mariño et al., 2020), except for Castellón, where the consumption was lower (mean: 437 mg day^{-1} 1000 $inhabitant^{-1}$), as compared to mean values in 2017–2019 (mean: 1064–2565 mg day^{-1} 1000 $inhabitant^{-1}$). No statistical differences among the different time-periods considered were found in Vitoria-Gasteiz or Vila do Conde, where data from former years were not available, neither for Bilbao and its metropolitan area (Table S6), where data were available for one week in 2018 and 2019. However, statistical differences were observed in Santiago de Compostela, Castellón and Porto (Table S6). The post-hoc test could not detect any statistical pairwise differences among periods in Santiago de Compostela, however, the data plotted in Figs. 4 and S3 points towards a sustained trend of increasing use of cocaine, which was not disrupted by COVID-19 mobility restrictions. As regards Castellón, differences between 2017 and the lockdown period and between 2019 (when measured cocaine consumption was at its highest level) and all sample subsets from 2020 confirm the observable decline in cocaine consumption in this location (Fig. S3, Fig. 4, Table S6). Conversely, in Porto, pairwise statistical differences were obtained among 2017 and the relaxed lockdown period (Phases I–III), and between 2018 and Phase III (Table S6), but in this case the trend observed is completely the opposite to Castellón and similar to Santiago de Compostela, i.e. a trend of sustained increase in cocaine consumption along the years, which could not be impaired by the COVID-19 restrictions (Fig. S3 and Fig. 4).

Although survey data seem to indicate that cocaine consumption decreased during the lockdown (Table 2) and even after the lockdown (from a Spanish phone survey) (Observatorio Español de las Drogas y las Adicciones, 2020b), WBE data from other publications (Table 1) show a

Table 2
Main reports based on (web) surveys on the impact of COVID-19 on substances of abuse.

Reference	(Global Drug Survey, 2021)	(European Monitoring Centre for Drugs and Drug Addiction, 2020c)	(Observatorio Español de las Drogas y las Adicciones, 2020a)	(Observatorio Español de las Drogas y las Adicciones, 2020b)
Overall description	Global Drug Survey Special Edition on COVID-19. Web survey of ca. 55,000 responders being reported	EMCDDA European Web Survey on Drugs (EWSD) with 10,600 responders	Spanish OEDA report based on a subset of the EMCDDA EWSD, by considering only the 991 Spanish responders, other web surveys and sources	Spanish OEDA telephonic survey with 8780 responders. Only the responders in the 15–64 years range (7886) are considered here[b]
Geographical scope	11 countries with over 1000 responders (not including Spain nor Portugal)	Europe (including Spain and Portugal)	Spain	Spain
Temporal scope	May–June 2020	Lockdown-relaxed lockdown	Lockdown-relaxed lockdown	March–December 2020
Amphetamine	Change in frequency: 35% decrease; 45% did not change; 20% increase	Overall decrease[a]	Change in amount: 40% decrease; 52% did not change; 8% increased[a]	–
MDMA	Change in frequency: 42% decrease; 46% did not change; 13% increase	Overall decrease	Change in amount: 40% decrease; 55% did not change; 5% increased	–
Cocaine	Change in frequency: 39% decrease; 41% did not change; 21% increase	Overall decrease	Change in amount: 49% decrease; 46% did not change; 5% increased	0.3% initiated or increased consumption; 0.4% did not change; 0.9% decreased or stopped consumption
Cannabis	Change in frequency: 22% decrease; 39% did not change; 39% increase	Non-conclusive (mixed picture)	Change in amount: 31% decrease; 43% did not change; 26% increased	2.2% initiated or increased consumption; 2.8% did not change; 3.5% decreased or stopped consumption
Tobacco	–	–	10.8% increased; 73.5% did not change; 12.7% decreased or stopped consumption	6.9% initiated or increased consumption; 15.3% did not change; 8.1% decreased or stopped consumption
Alcohol	Change in amount: 21% decrease; 42% did not change; 36% increase Change in frequency: 25% decrease; 32% did not change; 43% increase	Overall increase	Overall decrease	5.5% initiated or increased consumption; 30.1% did not change; 28.7% decreased or stopped consumption

[a] Amphetamine and methamphetamine are grouped under the term "amphetamines" in the EWSD (and Spanish subset).
[b] Please note that responders not consuming a substance either before nor after COVID-19 are not included in this summary, leading to sum of % lower than 100%.

mixed picture, highly dependent on the specific location that was investigated. Besides, again the EMCDDA study points towards a recovery of cocaine consumption during lockdown relaxation (European Monitoring Centre for Drugs and Drug Addiction, 2020a). As regards the findings of this study showing a particularly different profile (decrease of cocaine use in Castellón only) may be associated to local distribution or stock problems due to restriction that where more easily circumvented in the remaining locations.

4.1.4. Cannabis

Cannabis use was detected in all cities in the form of its main metabolite, THC-COOH. Consumption levels were estimated with two different correction factors (see Section 3.4), but for simplicity only the calculations with CF 182 are presented into Fig. 5 (and Fig. S4), while calculations with CF 36.4 are presented into Table S4. Given that several uncertainties exit around this compound, as detailed elsewhere (Bijlsma et al., 2021; Causanilles et al., 2017), discussion will focus on temporal trends rather than spatial trends and use estimates. In this context, the statistical analysis confirmed the existence of temporal statistically differences in all investigated locations, except Vila do Conde (Table S6). In the case of Bilbao and its metropolitan area, the statistical difference is due to the higher loads of THC measured in 2018 respective subsequent periods (Fig. S4, Table S6). Similarly, in Castellón and Santiago de Compostela the differences are due to the relatively higher cannabis use estimated in 2019, whereas in Vitoria-Gasteiz differences are found between lockdown and New Normal, and in Porto there is no difference being statistically significant in the pairwise post-hoc test, but a sort of trend towards more consumption during the post-lockdown can be observed (Table S6, Fig. S4).

Altogether, there is no clear trend on cannabis consumption (Fig. 5). Moreover, in this case, findings are in line with other WBE studies showing no change in cannabis consumption or even an increase (Table 1), which also agree with (on-line) surveys (Table 2) where a remarkable change in cannabis consumption is not very clear.

4.2. Alcohol and tobacco

4.2.1. Nicotine

Nicotine consumption is presented in Fig. 6 (detailed in Table S4 and Fig. S5) as the average estimation from its two metabolites (Montes et al., 2020; Rodríguez-Álvarez et al., 2014b). In this case, data from previous years were only available for Castellón, Santiago de Compostela and Bilbao and its metropolitan area and for a limited number of years. Although the presence of nicotine metabolites in wastewater may also be due to smoking cessation products or e-cigarettes, besides tobacco smoking, these other sources are expected to be rather small in the case of Spain, as discussed in Montes et al. (2020).

Vitoria-Gasteiz stands out with 2-fold consumption compared to the other cities sampled in 2020 (mean: 2654 mg day^{-1} 1000 $inhabitant^{-1}$ vs. 1391–1674 mg day^{-1} 1000 $inhabitant^{-1}$ in the other cities). The higher usage rate in this location may partially be due to the higher variability and should be confirmed in future studies. Considering 0.8 mg of nicotine being absorbed per cigarette (Montes et al., 2020; Rodríguez-Álvarez et al., 2014b; St. Charles et al., 2010), that would represent and average of 1.7–3.1 cigarettes day^{-1} $inhabitant^{-1}$, depending on the location sampled.

All locations showed statistical differences among periods, with the exception of Vila do Conde (Table S6). In Castellón and Bilbao and its metropolitan area, this was attributed to a higher consumption in 2018 as compared to some of the periods in 2020 (Table S6), suggesting a slight decreasing trend (Figs. 6 and S5). In Santiago de Compostela, the differences were due to the low measured consumption during the 5 pre-lockdown days sampled as compared to Phases I and II of lockdown relaxation (Table S6, Fig. S5), while in Vitoria-Gasteiz there was significant lower consumption in New Normal as compared to lockdown, and in Porto, the trend was towards an increase from Phase I towards New Normal (Table S6, Fig. S5).

The only two WBE studies considering tobacco (Table 1) show contradictory conclusions (Alygizakis et al., 2021; Reinstadler et al., 2021). Thus, overall, the picture is not conclusive, but points towards a minor impact of COVID-19 on tobacco. Although there was a significant decrease in tobacco sales in April and June 2020 respecting the same period of the former year (Fig. S7), surveys (Table 2) indicate only a marginal impact towards a small decrease in consumption of tobacco (Observatorio Español de las Drogas y las Adicciones, 2020a, 2020b).

4.3. Alcohol

Average ethanol consumption in 2020 ranged from 20 (Porto) to 28 (Vitoria-Gasteiz) L day^{-1} 1000 $inhabitant^{-1}$ (Table S4 and Figs. 7 and S6), similarly to a former study which considered Santiago de Compostela, Bilbao and its metropolitan area and Castellón, performed in 2018 (López-García et al., 2020). Statistical differences were obtained only in Castellón and Santiago de Compostela, which in the post-hoc test could be attributed to the lowest measured consumption in 2018 as compared to lockdown and New Normal in Castellón, and when comparing Phase I and New Normal in Santiago (Table S6), overall pointing to a trend of increased consumption in the 3 years, sustained despite the COVID-19 mobility restrictions. In Bilbao and its metropolitan area consumption of ethanol in 2018 and 2020 remained stable (Kruskal-Wallis p-value: 0.59, no data available from 2019) and in general, the consumption did not change during the lockdown till the New Normal was reached (Figs. 7 and S6).

Other WBE studies (Table 1) either point towards a stable alcohol consumption or decrease, which may also recovered after the strict lockdown period (European Monitoring Centre for Drugs and Drug Addiction, 2020a). As regards to global and Spanish survey reports, divergent results were shown (Table 2), pointing towards an increase or decrease at Global or Spanish level, respectively. Other publications considering surveys at Spanish level also point towards an overall decline in alcohol consumption (Kilian et al., 2021; Villanueva-Blasco et al., 2021a, 2021b), but at the cost of an increase in risky-consumption (Villanueva-Blasco et al., 2021a). Yet, the data from the panel (survey) of domestic consumption of foods in Spain (which includes alcoholic drinks) show a dramatic increase of alcoholic drinks being sold in supermarkets and similar shops (Fig. S8). This increase in alcohol being taken home does, however, not necessary translate in an increased consumption, since alcohol consumption at bars, restaurants, etc. was seriously impaired by restrictions, and WBE studies in Australia seem to confirm this (Bade et al., 2020, 2021).

5. Concluding remarks

In this work, we have studied the use of illicit drugs, alcohol and tobacco by WBE during the initial months (March–July 2020) of the pandemic in six locations in Spain and Portugal. The overall picture obtained points towards low impact of the COVID-19 mobility restrictions, particularly after relieving the more stringent measures. The only remarkable exception was the decline of cocaine consumption in Castellón. Other WBE published studies showed very inconsistent conclusions, highly dependent on the locations under study. Conversely, web-surveys seem to point towards a clear reduction of consumption of AMP, MDMA and COC, but not so comprehensible for the remaining substances. Yet, the Spanish statistics on mortality related to poisoning due to drugs of abuse, registered 974 vs. 796 deaths in 2020 and 2019, respectively (being 2020 the second highest registry in the period between 2011 and 2020) (Instituto Nacional de Estadística, 2020). This data may be associated with an increase in problematic use and/or saturation of emergency services but may also indicate that the decline on consumption did not take place.

Although the results of this study need to be interpreted with caution, they stress the importance and need for a stable WBE network for drug use monitoring that can provide rapid near real-time data to inform policy interventions in a pandemic context, as it has become a common practice for COVID-19 monitoring itself.

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CRediT authorship contribution statement

Andrea Estévez-Danta: Investigation, Methodology, Formal analysis, Visualization, Writing – original draft; **Lubertus Bijlsma:** Investigation, Resources, Methodology, Writing – review & editing; **Ricardo Capela:** Investigation, Writing – review & editing; **Rafael Cela:** Resources, Funding acquisition, Writing – review & editing; **Alberto Celma:** Investigation, Writing – review & editing; **Félix Hernández:** Resources, Funding acquisition, Writing – review & editing; **Unax Lertxundi:** Investigation, Writing – review & editing; **João Matias:** Formal analysis, Writing – review & editing; **Rosa Montes:** Methodology, Supervision, Writing – review & editing; **Gorka Orive:** Resources, Funding acquisition, Writing – review & editing; **Ailette Prieto:** Resources, Writing – review & editing; **Miguel M. Santos:** Investigation, Funding acquisition, Writing – review & editing; **Rosario Rodil:** Resources, Supervision, Funding acquisition, Formal analysis, Writing – review & editing; **José Benito Quintana:** Conceptualization, Resources, Visualization, Supervision, Funding acquisition, Writing – review & editing.

Availability of data

All relevant data generated or analyzed during this study are included in the supplementary information.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2022.155697.

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