Corrigendum to "Measuring inhibition of monoamine reuptake transporters by new psychoactive substances (NPS) in real-time using a high-throughput, fluorescence-based assay" [Toxicology in Vitro (2017) 60–71]

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The authors regret that incorrect IC_{50} values were listed in the article due to faulty use of the software calculating these values. In this corrigendum, changed IC_{50} values are provided in the tables (table 1, 2, 3 and supplemental table 1 and 2) in blue text. Changed IC_{50} values in the main text are indicated by bold text. These alterations did not affect data interpretation, or the conclusions drawn. The authors would like to apologise for any inconvenience caused.

Corrected Table 1. Inhibition of monoamine transporter uptake by illicit drugs, NPS and fluoxetine.

Group	Drug	IC_{50} (µM) [95% CI]		
		hDAT	hNET	hSERT
Stimulant / Entactogen / Hallucinogen	Cocaine	1.0 [0.9-1.2]	1.1 [0.8-1.4]	1.4 [1.2-1.6]
	α-PVP	0.08 [0.06-0.10]	0.07 [0.06-0.08]	> 300
	Amphetamine	3.7 [3.1-4.3]	0.5 [0.4-0.6]	> 300
	4-FA	4.8 [3.8-6.2]	0.8 [0.6-0.9]	200 [174-230]
	PMMA	40 [33-50]	4.9 [4.1-5.7]	157 [133-185]
	MDMA	13 [10-16]	2.3 [1.8-3.0]	112 [98-128]
	5-APB	4.6 [3.3-6.5]	1.0 [0.8-1.3]	30 [22-40]
	2C-B	132 [117-149]	122 [108-137]	47 [37-58]
	25I-NBOMe	53 [46-62]	11 [9.8-13]	4.0 [3.6-4.5]
	25B-NBOMe	99 [82-127]	11 [8.3-14]	4.9 [4.4-5.6]
	MXE	24 [17-34]	15 [12-20]	2.2 [1.8-2.6]
SSRI	Fluoxetine	42 [31-57]	5.8 [4.4-7.8]	0.1 [0.04-0.2]

IC_{50} values (obtained following 12 min drug exposure) are presented with 95% confidence intervals [CI] ($n=$9-29 wells, $N=$3-6 plates). Grey blocks indicate the transporter(s) at which a compound is most potent.

3. Results

3.2 *Drug-induced monoamine transporter uptake inhibition (pre-incubation with the fluorescent substrate)*

Exposure to NPS and commonly used illicit drugs concentration-dependently inhibited uptake of monoamine transporters following 12 min of exposure (Fig. 4; Table 1). Cocaine potently inhibited all three transporters with IC_{50} values of **1.0–1.4** μM. α-PVP was over ten times more potent than cocaine in inhibiting uptake of hDAT and hNET (IC_{50} **0.08 and 0.07 μM, respectively**), although α-PVP only weakly inhibited hSERT. DL-amphetamine also potently inhibited hNET and to a lesser extent hDAT, but only weakly inhibited hSERT.

Stimulants that also are entactogenic showed a somewhat higher potency for inhibiting hSERT (IC_{50} **30–200** μM) compared to α-PVP and DL-amphetamine, but most potently inhibited hNET (IC_{50} **0.8–4.9** μM) and to a lesser extent hDAT (IC_{50} **4.6–40** μM).

The hallucinogenic compounds (25B-NBOMe, 25I-NBOMe and MXE) potently inhibited hSERT (IC_{50} **2.2**–4.9 μM) and to a lesser extent hNET (IC_{50} **11–15** μM). These compounds inhibited hDAT only moderately (IC_{50} **24–99** μM). The hallucinogen 2C-B also preferentially inhibited hSERT, although with a ~10-fold higher IC_{50} compared to 25B-NBOMe and 25I-NBOMe. As expected, the selective serotonin reuptake inhibitor (SSRI) antidepressant fluoxetine potently inhibited hSERT (IC_{50} **0.1** μM), whereas IC_{50} values for hNET and hDAT were respectively ~**50**- and ~**400**-fold higher.

3.5 *Estimated drug concentration in the brain*

Almost all compounds inhibit at least one of the transporters at concentrations relevant for humans, except the NBOMe's **and 2C-B**.

Corrected Table 2. Estimated brain concentrations of commonly used illicit drugs, NPS and fluoxetine compared to their potency to inhibit monoamine transporters.

References for serum concentrations: [a] Javaid et al., 1978; [b] Cone, 1995; [c] Jeffcoat et al., 1989; [d] Isenschmid et al., 1992; [e] Jenkins et al., 2002; [f] Lee et al., 2000; [g] Angrist et al., 1987; [h] Röhrich et al., 2012; [i] Eiden et al., 2013; [j] Wright and Harris, 2016; [k] de la Torre et al., 2000; [l] Vevelstad et al., 2012; [m] Elliot and Evans, 2014; [n] Adamowicz et al., 2014; [o] Adamowicz et al., 2016; [p] Ho et al., 2013; [q] Polkis et al., 2014a; [r] Laskowski et al., 2015; [s] Polkis et al., 2013; [t] Wood et al., 2012; [u] Shields et al., 2012; [v] Orsulak et al., 1988; [w] Rambourg Schepens, 1996, [x] Johansen and Hansen, 2012, [y] Holmgren et al., 2008. References for BPF calculation: [1] Brajkovic et al., 2016; [2] Bystrowska et al., 2012; [3] Rivière et al., 2000; [4] White et al., 2014; [5] Hendrickson et al., 2006; [6] Sykutera et al., 2015; [7] Hasegawa et al., 2014; [8] Mueller et al., 2009; [9] Pálenícek et al., 2011; [10] Rohanová et al., 2008; [11] Polkis et al., 2014b; [12] Horsley et al., 2016; [13] Karson et al., 1993; [14] Holladay et al., 1998; [15] Shiue et al., 1993.

4. Discussion

Paragraph 2: Importantly, inhibition of monoamine transporters was detected at concentrations relevant for human exposure. For almost all substances, the IC_{50} value for at least one of the transporters was in range of the estimated brain concentration, while **five** substances likely affect more than one transporter at estimated brain concentrations. Even the selective serotonin re-uptake inhibitor fluoxetine inhibits both hSERT (IC_{50} **0.1** μM) and hNET (IC_{50} **5.8** μM) at estimated therapeutic brain concentrations, in line with other literature (Karson et al., 1993; Renshaw et al., 1992; Komoroski et al., 1994; Strauss et al., 2002; Henry et al., 2005; Strauss and Dager, 2001).

Group	Drug	Serum concentration (μM)	Brain partitioning factor (BPF)	Estimated brain concentration (μM)	IC_{50} (μM) hDAT/hNET/ hSERT
Stimulant / Entactogen / Hallucinogen	Cocaine	0.2 - 1 [a,b,c,d,e]	4.5 - 5.5 [1,2]	0.9 - 5.5	**1.0/1.1/1.4**
	α-PVP	0.1 - 1 [i,j]	0.1 - 0.8 [6,7]	0.01 - 0.8	**0.08/0.07**/>300
	Amphetamine	0.1 - 8 [f,g,y]	8.5 - 12 [3,4,5]	0.9 - 96	**3.7/0.5**/>300
	4-FA	0.1 - 3 [h,x]	3 [15]	0.3 - 9	**4.8/0.8**/200
	PMMA	0.1 - 4 [l]	4 - 5.4 [9]	0.4 - 22	40/**4.9**/157
	MDMA	0.4 - 2 [k]	5 [8]	2 - 10	13/**2.3**/112
	5-APB	0.03 - 1 [m,n]	x	> 0.03 - 1	4.6/**1.0**/30
	2C-B	0.006 – 1.3 [o,p]	7 [10]	0.04 - 9	132/122/47
	25I-NBOMe	0.0006 - 0.007 [s]	7 [11]	0.004 - 0.05	53/11/4.0
	25B-NBOMe	0.0004 - 0.003 [q,r]	x	> 0.0004 - 0.003	99/11/4.9
	MXE	0.4 - 2 [t,u]	2.4 [12]	1 - 5	24/15/**2.2**
SSRI	Fluoxetine	0.2 - 0.4 [v,w]	20 - 23 [13,14]	4 - 9	42/**5.8**/**0.1**

Estimated brain concentrations were calculated using human serum concentrations and brain partitioning factors (BPF) found in literature. All human serum concentrations were obtained from recreational use doses (voluntary intake, driving under the influence or accidental non-fatal intoxications), except for 5-APB. Serum concentration of α-PVP is based on blood concentrations (small caps). BPFs were based on serum and brain concentrations of rat (bold) or mouse (italic) data, or human post mortem blood (underlined) or serum (strikethrough) values compared to brain concentrations. Estimated brain concentrations for 5-APB and 25B-NBOMe were based on the observation that most BPFs are > 1. Grey blocks indicate that IC_{50} values obtained using the fluorescent assay are not in the estimated brain concentration range. Bold IC_{50} values indicate values within the estimated brain concentration range.

Corrected Table 3. Inhibition of monoamine transporter uptake (IC$_{50}$, μM) by illicit drugs, NPS and fluoxetine compared to literature.

et al., 2013; [j] Baumann et al., 2013; [k] Rosenauer et al., 2013; [l] Simmler et al., 2013; [m] Simmler et al., 2014; [n] Marusich et al., 2014; [o] Rickli et al., 2015a; [p] Rickli et al., 2015b; [q] Rickli et al., 2015c

Group	Drug	Reported IC$_{50}$ (μM)					
		hDAT		hNET		hSERT	
		Our	*Literature*	*Our*	*Literature*	*Our*	*Literature*
Stimulant / Entactogen / Hallucinogen	Cocaine	**1.0**	0.5[e], *0.9[f]*, 0.4[i], *0.2[j,n]* 0.8[l]	**1.1**	0.3[e], *0.3[f]*, 0.2[i], *0.3[j,n]*, 0.5[l]	**1.4**	0.5[e], *2.1[f]*, 0.3[i], *0.3[j,n]*, 2.4[l]
	α-PVP	**0.08**	*0.01[n]*, 0.1[o]	**0.07**	*0.01[n]*, 0.02[o]	**>300**	*>10[n]*, >100[l]
	Amphetamine	**3.7**	*0.2[a], 0.1[j,n]*, **1.5[k]**, 1.3[l], 1.3[o]	**0.5**	*0.2[a], 0.1[j,n]*, **1.5[k]**, 0.1[l], 0.1[o]	**>300**	*3.8[a], 3.4[j,n]*, **110[k]**, >10[l], 45[o]
	4-FA	**4.8**	*0.3[a], 0.8[f]*, **10[k]**, 3.7[o]	**0.8**	*0.4[a], 0.4[f]*, **10[k]**, 0.2[o]	**200**	*2.4[a], 6.8[f]*, **95[k]**, 19[o]
	PMMA	**40**	49[m]	**4.9**	1.2[m]	**157**	1.8[m]
	MDMA	**13**	<u>**0.5[c]**</u>, *1.4[f]*, 0.2[i], *10[j]*, 17[l,m], 31[o], 17[q]	**2.3**	<u>**2.1[c]**</u>, *0.7[f]*, 0.02[i], **12[k]**, 0.5[l,m], 0.4[o], 0.36[q]	**112**	<u>1.4[c]</u>, *0.7[f]*, 0.1[i], **88[k]**, 1.4[l,m], 2.0[o], 2.4[q]
	5-APB	**4.6**	6.1[q]	**1.0**	0.2[q]	**30**	0.3[q]
	2C-B	**132**	231[p]	**122**	44[p]	**47**	18[p]
	25I-NBOMe	**53**	65[p]	**11**	10[p]	**4.0**	6.8[p]
	25B-NBOMe	**99**	117[p]	**11**	6.7[p]	**4.9**	7.1[p]
	MXE	**24**	-	**15**	-	**2.2**	-
SSRI	Fluoxetine	**42**	*5[g]*, 8[g], 15[g], 210[h]	**5.8**	0.8[g], 0.5[g], *0.2[g]*	**0.1**	0.06[g], 0.02[g], *0.01[g]*,*0.01[b]*, <u>0.05[d]</u>

All articles reported in this table used radio-labelled substrates. Potency for uptake inhibition was determined using transfected HEK293 cells (e, g, h, i, k, l, m, o, p, q), rat brain synaptosomes (a, b, f, g, j, n, italic), human platelets (c, SERT, underlined), C6 glial cells (c, DAT + NET, underlined with stripes), or JAr cells (d, underlined with dots). Almost all studies used cells in suspension, except for b,d,g,h,k and c, DAT + NET (bold).

References: [a] Marona-Lewicka et al., 1995; [b] Hyttel, 1982; [c] Cozzi et al., 1999; [d] Martel and Keating, 2003; [e] Meltzer et al., 2006; [f] Nagai et al., 2007; [g] Jørgenson et al., 2008; [h] Yoon et al., 2009; [i] Eshleman

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tiv.2019.104631.