

Table 1.

Summary of findings on the effects of ELA on stimulant, alcohol, and opioid-seeking behaviors and relevant stress and reward circuit correlates.

Reference	Drug Class	ELA Procedure	Species	ELA Effect on Addiction-like Behavior ND = not done; Ø = no effect		Reward / Stress Circuit Correlate	Procedural Notes
				Male	Female		
Levis et al., 2019	opioid	LBN P2-9	rat	ND	↑	N/A	
Ordoñez Sanchez et al., 2021	opioid	LBN P2-9	rat	↑	Ø	transcription changes in NAc (M)	
Kalinichev et al., 2002	opioid	MS15/180 P2-14	rat	↑ (MS180 > MS15)	ND	N/A	
Matthews & Robbins, 2003	opioid	REMS360* P5-20	rat	ND	↓	N/A	* separations occurred on 10 randomly spaced occasions
Vazquez et al., 2005	opioid	MS180 P1-14	rat	↑	ND	↓ striatal endogenous opioid mRNA	
Michaels & Holtzman, 2008	opioid	24h MS P2; MS180-360* P4-12	rat	↑	Ø	N/A	* alternating 3h and 6h separations
Abad et al., 2016	opioid	MS180 P2-14	rat	↑	↑	N/A	
Mohammadian et al., 2019	opioid	MS180 P2-14	rat	↑	↑	N/A	
Bolton et al., 2018b	psychostimulant	LBN P2-9	rat	↓	ND	↑ cocaine-induced c-Fos in NAc, lateral habenula, central amygdala	
Campbell & Spear, 1999	psychostimulant	MS15 P1-12	rat	↓	↓	N/A	
Matthews et al., 1999	psychostimulant	REMS360* P5-20	rat	↓	↑	N/A	* separations occurred on 10 randomly spaced occasions
Kosten et al., 2000, 2004	psychostimulant	MS60 P2-9	rat	↑	↑	N/A	
Li et al., 2003	psychostimulant	MS15/180 P1-21	rat	ND	↓ (MS15/180)	N/A	
Brake et al., 2004	psychostimulant	MS0/15/180 P1-14	rat	↑ (MS180) ↓ (MS15)	ND	↓ striatal DAT (MS180)	
Marquardt et al., 2004	psychostimulant	MS+ P1-10	rat	↑	ND	N/A	+ additional aversive stimulus during separation
Zhang et al., 2005	psychostimulant	MS60 P2-9	rat	↑	ND	N/A	
Moffett et al., 2006	psychostimulant	MS15/180 P2-15	rat	↑ (MS180)	ND	N/A	
Vazquez et al., 2006	psychostimulant alcohol opioid	MS180 P1-14	rat	slight ↑ no effect ↑	ND	no effect of MS on VTA or striatal DAT	

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Der-Avakiann & Markou, 2010	psychostimulant	MS180 P1-14	rat	↑	ND	N/A	
Lewis et al., 2013, 2016	psychostimulant	MS15/180 P2-14	rat	↑ (MS180)	ND	↑ protective MeCP2 expression in NAc core (MS15)	
Hensleigh & Pritchard, 2014, 2015	psychostimulant	MS180 P2-8	rat	↑	Ø	MS potentiates methamphetamine-induced decrease in striatal DAT and TH expression (M)	
O'Connor et al., 2015	psychostimulant	MS180 P2-12	rat	↓	ND	N/A	
Ganguly et al., 2019	psychostimulant	MS240 P2-20	rat	↑	Ø	↓ GluA2 expression in PFC, NAc (M)	
Kikusui et al., 2005	psychostimulant	MS60 P1-13	mouse	↑ (M > F)	↑	N/A	
Gracia-Rubio et al., 2016	psychostimulant	MS240 P2-5, MS480 P6-16, weaning at P17	mouse	↓	ND	↓ striatal D2R expression	
Mitchell et al., 2018	psychostimulant	LBN P2-9	mouse	↓	ND	↓ NAc α2 subunit of GABA-A receptor mRNA	
Castro-Zavala et al., 2020a,b	psychostimulant	MS240 P2-5, MS480 P6-16, weaning at P17	mouse	↑	Ø	sex and drug experience-dependent changes of GluA1, GluA2, CREB, and pCREB expression in NAc and VTA	
Okhuarobo et al., 2020	alcohol	LBN P2-9	mouse	↑	Ø	N/A	
Huot et al., 2001	alcohol	MS15/180 P2-14	rat	↑ (MS180)	ND	↑ HPA axis reactivity (MS180)	
Ploj et al., 2003a	alcohol	MS15/360 P1-21	rat	↑ (MS360) ↓ (MS15)	ND	MS duration and alcohol-experience dependent changes in mesocorticolimbic dopamine and opioid receptor expression	
Roman et al., 2004	alcohol	MS15/360 P1-21	rat	ND	Ø	N/A	
Romano-López et al., 2012	alcohol	MS360* P2-15	rat	↑	ND	MS-induced changes in PFC, NAc, and hippocampal glutamate and GABA expression	* two daily 180-min separations
Gondré-Lewis et al., 2016	alcohol	MS180 P2-21	rat	↑	↑	↓ VTA dopamine-like neurons, ↑ amygdala neuron number & density	
Bassey & Gondré-Lewis, 2019	alcohol	MS180 P2-21	rat	↑	↑	↓ VTA, ↑ amygdala neuron number & density	
Amancio-Belmont et al., 2020	alcohol	MS180 P2-15	rat	↑	ND	↑ NAc D2R and D3R expression	
Portero-Tresserra et al., 2018	alcohol	MS240 P2-5, MS480 P6-16, weaning at P17	mouse	↑	ND	↓ PFC and striatal endocannabinoid expression	

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Kawakami et al., 2007	alcohol	MS15/180 P2-14	mouse	Ø	↑ (MS180 > MS15)	↑ basal CORT (F; MS180) ↑ EtOH CORT response (M; MS15/180)	
Cruz et al., 2008	alcohol	MS180 P1-14	mouse	↑	ND	N/A	
García-Gutiérrez et al., 2016	alcohol	12h MS P8 & P12	mouse	↑	ND	↑ NAc dopamine, opioid peptide & receptor, and CRH expression	

Table abbreviations: CORT, corticosterone; CREB, cAMP-response element binding protein; pCREB, phosphorylated CREB; CRH, corticotropin releasing hormone; D2R, dopamine receptor type 2; D3R, dopamine receptor type 3; DAT, dopamine transporter; GluA1, AMPA glutamate receptor subunit A1; GluA2, AMPA glutamate receptor subunit A2; HPA axis, hypothalamic-pituitary-adrenal axis; LBN, limited bedding and nesting; MeCP2, methyl CpG binding protein 2; MS, maternal separation; NAc, nucleus accumbens; PFC, prefrontal cortex; TH, tyrosine hydroxylase; VTA, ventral tegmental area