Supplementary Table S3. Structural and Functional Effects of Ketamine in Preclinical Models

Citation	Animal	Strain	M/F	Dose in mg/kg *Enantiomer*	Stress Model	Time of Testing (after last injection)	Structural/Functional Changes, time (dose)	Injection Method	Special Notes/Considerations
(Garcia et al., 2009)	Rat	Wistar	M	15; acute *(R,S)-ketamine*	Naïve	NS	• ↑ Body weight • = Adrenal weight	IP	
(Garcia et al., 2009)	Rat	Wistar	M	15; 7d Once Daily *(R,S)-ketamine*	Naïve	NS	• ↑ Body weight • = Adrenal weight	IP	
(Garcia et al., 2009)	Rat	Wistar	M	15; acute *(R,S)-ketamine*	CMS	NS	• ↑ Body weight • ↓ Adrenal weight (reversed CMS-induced increase)	IP	
(Garcia et al., 2009)	Rat	Wistar	M	15; 7d Once Daily *(R,S)-ketamine*	CMS	NS	• ↑ Body weight • ↓ Adrenal weight (reversed CMS-induced increase)	IP	
(Gopinath et al., 2016)	Monkey	Rhesus	F	0.345 (1min infusion) + 0.256 (53min infusion) *(R-S)-ketamine*	Naïve	1h	• ↑ Functional connectivity to the dlPFC in several (sub/)cortical regions • Hyperconnectivity in functional brain networks associated with emotional regulation, cognitive control, and motivation	IV	Consistent with human imaging studies that showed similar results.
(Li et al., 2010)	Rat	Sprague Dawley	M	10 *(R,S)-ketamine*	IES	24h	*PFC* • ↑ Spine density • ↑ Mushroom spines	IP	
(Li et al., 2011)	Rat	Sprague Dawley	M	10 *(R,S)-ketamine*	CUS	8d (Molecular)	*PFC* • ↑ Spine density	IP	
(Sarkar and Kabbaj, 2016)	Rat	Sprague Dawley	M	2.5, 5 *(R,S)-ketamine*	CSIS	1h after FST (3d)	*mPFC* • ↑ Spine density (5) • ↑ Thin spines (5) • = Mushroom spines • = Stubby spines	NS	
(Sarkar and Kabbaj, 2016)	Rat	Sprague Dawley	F	2.5, 5 *(R,S)-ketamine*	CSIS	1h after FST (3d)	*mPFC* • = Spine Density • = Thin spines • = Mushroom spines • = Stubby spines	NS	Females injected with ketamine during D1.
(Strong et al., 2017)	Rat	Sprague Dawley	M	2.5, 5; 1/wk for 7 wk *(R,S)-ketamine*	Naïve	2h after ketamine challenge (2wk)	*NAcSh (Shell)* • ↑ Spine density (2.5, 5) *NAcC (Core)* • = Spine density	IP	Males who sensitized to ketamine show an increase in spine density in the NAcSh but not NAcC
(Strong et al., 2017)	Rat	Sprague Dawley	F	2.5, 5; 1/wk for 7 wk *(R,S)-ketamine*	Naïve	2h after ketamine challenge (2wk)	*NAcSh* • ↑ Spine density (5) *NAcC* • ↑ Spine density (5)	IP	All females were tested in D1.

Citation	**Animal**	**Strain**	**M/F**	**Dose in mg/kg** ***Enantiomer***	**Stress Model**	**Time of Testing (after last injection)**	**Structural/Functional Changes, time (dose)**	**Injection Method**	**Special Notes/Considerations**
(Thelen et al., 2019)	Mouse	C57BL/6J	M	10 *(R,S)-ketamine*	Naïve	2h, 24h, 3d, 7d	*mPFC* • ↑ Spine density, 24h-7d *HC* • ↑ CA1/CA3 spine density, 24h	IP	
(Thelen et al., 2019)	Mouse	C57BL/6J	F	10 *(R,S)-ketamine*	Naïve	2h, 24h, 3d, 7d	*mPFC* • = Spine density *HC* • ↑ CA1/CA3 spine density, 24h-3d	IP	Estrus cycle not taken into account. Increase in spine density in the HC lasted longer in female mice.
(Yang et al., 2015)	Mouse	C57BL/6	M	10 *(R)-ketamine* *(S)-ketamine*	SDS	8d	*mPFC* • ↑ Spine density *HC* • ↑ CA3/DG spine density (R)-ketamine more potent in the DG than (S)-ketamine.	IP	

List of Abbreviations

Stress Model Abbreviations	Other Abbreviations
CMS: Chronic Mild Stress	(m)(dl)PFC: (medial)(dorsolateral) Prefrontal Cortex
CSDS: Chronic Social Defeat Stress	D1: Diestrus
CSIS: Chronic Social Isolation Stress	HC: Hippocampus
CUS: Chronic Unpredictable Stress	IP: Intraperitoneal
ES: Emotional/Psychological Stress	IV: Intravenous
IES: Inescapable Shock	NAcC: Nucleus Accumbens Core
LPS: Lipopolysaccharide Inflammation	NAcSh: Nucleus Accumbens Shell
SDS: Social Defeat Stress	NS: Not Specified
US: Uncontrollable Stress	PE: Proestrus

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