Rethinking 5-HT$_{1A}$ Receptors: Emerging Modes of Inhibitory Feedback of Relevance to Emotion-Related Behavior

[1†]Stefanie C. Altieri, [4†]Alvaro L. Garcia-Garcia, [4*]E. David Leonardo, and [1,2,3*]Anne M. Andrews

[1]Semel Institute for Neuroscience & Human Behavior, Hatos Center for Neuropharmacology, David Geffen School of Medicine, [2]Department of Chemistry and Biochemistry, and [3]California NanoSystems Institute, University of California, Los Angeles, CA 90095, USA

[4]Department of Psychiatry, Division of Integrative Neuroscience, Columbia University and New York State Psychiatric Institute, New York, NY 10032, USA

[†]These authors contributed equally.

SUPPORTING MATERIAL

PAPER	BACKGROUND STRAIN	AGE	GENDER	BEHAVIOR TEST	PARAMETERS MEASURED	RESULTS	OVERALL ASSESSMENT
Heisler, L.K. et al. 1998	C57BL/6	10-14 weeks	♀ and ♂ (separate analysis)	Open Field	time/entries/distance in center of arena	↑ anxiety	↑ ANXIETY Anxiety more pronounced in males Significant heterozygous effects in open field and tail suspension
				Elevated Zero Maze	time/entries/distance open area & head dips	↑ anxiety ↓ exploratory behavior	
				Novel Object	latency/distance/entrance to quadrant of novel object & rearings	↑ anxiety	
				Tail Suspension	immobility time	↓ immobility	
Parks, C.L. et al. 1998	Swiss Webster	Adult (specific age not reported)	♀ and ♂ (separate analysis)	Open Field	crosses/time/entries in center	↑ anxiety	↑ ANXIETY Anxiety more pronounced in males
				Forced Swim	percent immobility	↓ immobility	

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Ramboz, S. et al. 1998	129 Sv CONSTITUTIVE KNOCKOUT	Adult (specific age not reported)	♀ and ♂ (separate analysis)	Open Field	time/distance in center of arena, total distance, rearings & nose pokes	↓ anxiety ↓ exploratory behavior & locomotor activity	↑ ANXIETY Anxiety more pronounced in males
				Elevated Plus Maze	time/entries into open arms, total arm entries, rearings & head dips	↑ anxiety ↓ head dips	
				Forced Swim	percent immobility	↓ immobility	
Dulawa, S.C. et al. 2000	129 Sv CONSTITUTIVE KNOCKOUT	16 18 weeks	♀	Prepulse Inhibition	Prepulse Inhibition	NC in PPI	Normal Sensorimotor gating
Gross, C. et al. 2000	129 Sv CONSTITUTIVE KNOCKOUT	Adult (specific age not reported)	♀ and ♂ (combined analysis)	Novelty Suppressed Feeding	latency to feed following 24 h food deprivation	↑ anxiety	↑ ANXIETY & FEAR RESPONSE
				Foot Shock	percent freezing	↑ freezing	

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Sarnyai, Z. et al. 2000	Swiss Webster CONSTITUTIVE KNOCKOUT	Adult (specific age not reported)	N.S.	Morris Water Maze	latency to reach hidden platform/visible platform	↑ latency to reach hidden but not visible platform	ALTERED HIPPOCAMPAL DEPENDENT LEARNING AND MEMORY
				Y Maze	entries/time in each arm, first choice novel arm	No preference for novel arms	
				Spontaneous Alternation	# arms entered and # alternations between arms of Y maze	NC in entries or alternations	
Dirks, A. et al. 2001	129 Sv CONSTITUTIVE KNOCKOUT	8 14 weeks	♂	Acoutsic Startle Reactivity	startle magnitude	NC in startle magnitude	INTACT STARTLE REACTIVITY
Gross, C. et al. 2002	mixed C57BL/6J, CBA/J, 129S6/SvEvTac CONSTITUTIVE KNOCKOUT	8 10 weeks	♀ and ♂ (combined analysis)	Open Field	distance in center & total distance in arena	↑anxiety ↓ locomotor activity	↑ ANXIETY
				Elevated Plus Maze	percent entries into open arms	↑anxiety	
				Novelty Suppressed Feeding	latency to feed following 24 h food deprivation	↑anxiety	

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Pattij, T. et al. 2002	129 Sv CONSTITUTIVE KNOCKOUT	8 weeks	♂	Elevated Plus Maze	percent open arm time, # of open arm entries	NC in anxiety	= ANXIETY
Pattij et al. 2002	129 Sv CONSTITUTIVE KNOCKOUT	12 weeks	♂	Novel Environment	locomotion, rearing, grooming, exploration, stretched approach, posture, immobility & burying behaviors	↓ time locomotion, stretched approach, rearing & burying ↓ # rearings, stretched approach, burying	↓ EXPLORATORY ACTIVITY
Groenink, L. et al. 2003	129 Sv CONSTITUTIVE KNOCKOUT	8 12 weeks	N.S.	Open Field	time/entries/distance in center of arena, total distance	NC anxiety or locomotor activity	= ANXIETY (explained as potential ceiling effect given increased anxiety of strain)
				Light Dark Test	distance/entries/percent time in light compartment, total distance	NC anxiety	
				Elevated Plus Maze	distance/entries and percent time in open arms, total distance	NC anxiety or locomotor activity	
				Fear Conditioning	percent freezing	NC freezing behavior	
Pattij, T. et al. 2003	129 Sv CONSTITUTIVE KNOCKOUT	8 weeks	♂	Operant Conditioning	autoshaping, acquisition/reversal learning, extinction	↑ autoshaping, NC acquisition/reversal learning or extinction	= REINFORCEMENT LEARNING

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Bailey, S.J. et al. 2004	Swiss Webster and C57BL/6 CONSTITUTIVE KNOCKOUT	8 20 weeks	♂	Elevated Plus Maze	percent time/entries in open arms, total arm entries	↑anxiety both strains	↑ ANXIETY & FEAR RESPONSE ↓ EXPLORATORY ACTIVITY (strain dependent)
				Open Field	percent time/entries in center of arena	↑anxiety both strains ↓ locomotor activity in B6 only	
Wolff, M. et al. 2004	129 Sv CONSTITUTIVE KNOCKOUT	12 or 88 weeks	♂	Morris Water Maze	path length to reach hidden platform	↑ path length to reach hidden platform on younger but not older mice	ALTERED AGE AND HIPPOCAMPAL DEPENDENT LEARNING AND MEMORY
Jones, M.D. & Luck,i I. 2005	129 Sv CONSTITUTIVE KNOCKOUT	12 15 weeks	♀ and ♂ (separate analysis)	Tail Suspension	immobility time	↓ immobility	↓ IMMOBILITY
Klemenhagen, K.C. et al. 2006	129 Sv CONSTITUTIVE KNOCKOUT	Adult (specific age not reported)	♂	Light Dark Test	time in light compartment and # of ambulations	↑ anxiety NC in locomotor activity	↑ ANXIETY & FEAR RESPONSE
				Novel Object	# of visits	↑ visits (session dependent)	
				Fear Conditioning	percent freezing	↑ freezing behavior	

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Tsetsenis T & Gross et al. 2007	mixed C57BL/6J, CBA/J, 129S6/SvEvTac CONSTITUTIVE KNOCKOUT	Adult (specific age not reported)	N.S.	Fear Conditioning	percent freezing	↑ freezing behavior (cue dependent)	↑ FEAR RESPONSE
Bechtholt, A.J. et al. 2008	129 Sv CONSTITUTIVE KNOCKOUT	12 24 weeks	♀ and ♂ (separate analysis)	Sucrose Consumption	Intake and preference for sucrose over water	↑ consumption and preference in females only (1% concentration)	↓ ANHEDONIA
Zanettini, C.et al. 2009	mixed C57BL/6J, CBA/J, 129S6/SvEvTac CONSTITUTIVE KNOCKOUT	12 20 weeks	♂	Open Field	time in center of arena and total distance	↑ anxiety ↓ locomotor activity	↑ ANXIETY & ↓ SOCIAL INTERACTION
				Social Approach	percent time in social side	↓ social interaction	
				Resident Intruder	social interaction with intruder mouse	NC in aggressive behavior	

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Richardson Jones J.W. et al. 2010	mixed C57Bl/6J, CBA/J, 129S6/SvEvTac POPULATION SPECIFIC KNOCKOUT	11 13 weeks	♂	Open Field	time in center of arena and total distance	NC in anxiety or locomotor activity	= ANXIETY IN MICE WITH ~30% REDUCTIONS IN 5 HT1A AUTORECEPTORS
				Light Dark Test	time in light compartment and total distance	NC in anxiety or locomotor activity	
				Forced Swim	percent mobility	↑ mobility during last minute (Trial 2)	
				Tail Suspension	percent mobility	NC in mobility	
				Novelty Suppressed Feeding	latency to feed following 24 h food deprivation and in presence of fluoxetine	↓ latency to feed following fluoxetine administration	
Richardson Jones, J.W.et al. 2011	mixed C57BL/6J, CBA/J, 129S6/SvEvTac POPULATION SPECIFIC KNOCKOUT	11 13 weeks	♂	Open Field	percent center distance and total distance	↑ anxiety in auto KO	↑ ANXIETY ONLY INAUTORECEPTOR KO ↑ IMMOBILITY ONLY IN HETERORECEPTOR KO
				Light Dark Test	percent distance/entries in light compartment and total distance	↑ anxiety and locomotor activity in auto KO	
				Forced Swim	percent mobility	↓ mobility in hetero KO	

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Bortolozzi, A. et al. 2012	C57BL/6 POPULATION SPECIFIC MODELS	10 15 weeks	♂	Elevated Plus Maze	percent time/entries into open arms	↑ anxiety in KO restored in C-1A siRNA	↑ ANXIETY IN KO THAT IS RESTORED IN MICE WHERE C 1A siRNA IS INFUSED INTO THE DORSAL RAPHE ↓ IMMOBILITY IN BOTH MODELS
				Tail Suspension	immobility time	↓ immobility in KO and C	
				Forced Swim	immobility time	↓ immobility in C	
Ferres Coy, A. et al. 2012	C57BL/6 POPULATION SPECIFIC MODELS	9 12 weeks	♂	Elevated Plus Maze	percent time/entries into open arms	↑ anxiety in KO restored in C-1A siRNA	↑ ANXIETY IN KO THAT IS RESTORED IN MICE WHERE C 1A siRNA IS INFUSED INTO THE DORSAL RAPHE ↓ IMMOBILITY IN BOTH MODELS
				Tail Suspension	immobility time	↓ immobility in KO and C	
				Forced Swim	immobility time	↓ immobility in C	

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Iacono, L.L. & Gross, C. 2008	mixed C57BL/6J, CBA/J, 129S6/SvEvTac PHARMACOLOGIC INHIBITION	14 16 weeks	♂	Open Field	time/distance in center & total distance in arena	↑ anxiety	↑ ANXIETY IN WILDTYPE MICE TREATED WAY100635 VIA OSMOTIC MINIPUMP FROM P13 P34 (0.15 mg/h per kg body weight)
				Elevated Plus Maze	time/entries into open arms	= anxiety	
				Novelty Suppressed Feeding	latency to feed following 24 h food deprivation	↑ anxiety	
Vinkers, C.H. et al. 2010	Swiss Webster PHARMACOLOGIC INHIBITION	P7, P12, P21	♂	Elevated Plus Maze	percent open arm entries & total arm entries	↑ anxiety	↑ ANXIETY AND USVs IN 5 HT1A KO MICE AND MICE TREATED WITH WAY100365 FROM P0 P21
				Open Field	# entries, percent distance and time spent in center of arena	↑ anxiety and ↓ locomotor activity	
				Ultrasonic Volcalizations	# of ultrasonic vocalizations (USVs)	↑ USVs	
Kusserow, H. et al. 2004	NMRI outbred OVEREXPRESSION	15 22 weeks	♀ and ♂ (separate analysis)	Elevated Plus Maze	time/entries in open/closed arms, total arm entries, rearings & head dips	↓ anxiety and ↑ locomotor activity	↓ ANXIETY & ↑ LOCOMOTOR ACTIVTIY
				Open Field	entries/time spent in center of arena, total distance & rearings	↑ locomotor activity (male only) and = anxiety	

PAPER	BACKGROUND STRAIN	AGE	GENDER	BEHAVIOR TEST	PARAMETERS MEASURED	RESULTS	OVERALL ASSESSMENT
Bert, B. et al. 2005	NMRI outbred OVEREXPRESSION	12 13 weeks	♀ and ♂ (separate analysis)	Hole Board Morris Water Maze	# nose pokes & distance traveled latency & path length to find hidden platform	NC in spatial habituation ↑ latency & path length	ALTERED HIPPOCAMPAL DEPENDENT LEARNING AND MEMORY IN MICE WITH TRANSIENT OVEREXPRESSION
Bert, B. et al. 2006	NMRI outbred OVEREXPRESSION	18 weeks	♀ and ♂ (separate analysis)	Open Field	rearings & total distance in arena	↓ locomotor activity & exploration	= ANXIETY & ↓ LOCOMOTOR AND EXPLORATORY BEHAVIORS IN MICE PERMANENTLY OVEREXPRESSION Changes more prominent in males
				Elevated Plus Maze	time/entries into open arms, closed/total arm entries, rearings & head dips	= anxiety and locomotor activity	
Gunther, L. et al. 2011	NMRI outbred OVEREXPRESSION	12 14 weeks	♀ and ♂ (separate analysis)	Forced Swim	Immobility Time	↓ immobility	↓ IMMOBILITY

Supplemental Table 1. Behavior phenotypes of animal models of altered 5-HT_{1A} receptor expression. Information pertaining to models of 5-HT_{1A} knockout, overexpression, and pharmacological inhibition is summarized. The outcome of these manipulations on tests of emotion-related behavior, including anxiety and depression parameters, as well as learning and memory, is detailed.

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