

Supplementary Materials

**Mechanisms of imidazoline I₂ receptor agonist-induced antinociception in rats:
involvement of monoaminergic neurotransmission**

Justin N. Siemian¹, Kaixuan Wang¹, Yanan Zhang², Jun-Xu Li¹

Table S1. Pharmacological properties of drugs used in this study.

Drug	Property
2-BFI	Selective I ₂ receptor agonist
CR4056	Selective I ₂ receptor agonist
Fluoxetine	Selective SERT inhibitor
Desipramine	Selective NET inhibitor
Imipramine	Combined SERT/NET inhibitor
GBR12909	Selective DAT inhibitor
pCPA	5-HT synthesis inhibitor
Fenfluramine	5-HT releasing agent
DSP-4	Neurotoxin selective for noradrenergic neurons
WAY100635	Selective 5-HT _{1A} receptor antagonist
MDL100907	Selective 5-HT _{2A} receptor antagonist
SB242084	Selective 5-HT _{2C} receptor antagonist
WB4101	Selective α_1 -adrenergic receptor antagonist
Yohimbine	Selective α_2 -adrenergic receptor antagonist
SCH23390	Selective D1 receptor antagonist
Raclopride	Selective D2 receptor antagonist

Table S2. Group mean PWTs (in g) for the effects of 2-BFI alone and in combination with monoaminergic reuptake inhibitors or before and after monoamine depletion on CCI-induced mechanical nociception.

2-BFI (mg/kg)	V	1.0	1.78	3.2	5.6	10	17.8
Fluoxetine							
0	4.3			6.3	10.5	22.3	
3.2	5.0		5.7	10.3	19.7		
10	5.3	6.3	10.3	20.5			
Desipramine							
0	5.2			7.2	10.8	21.6	
3.2	5.6		7.2	12.2	22.8		
10	6.0	6.4	10.8	20.6			
GBR12909							
0	5.0			7.0	11.8	22.3	
10	5.2			7.2	13.0	23.8	
pCPA/FEN							
Pre	5.7			6.7	10.7	21.5	
Post	6.3				6.7	7.3	9.2
DSP-4							
Pre	6.3			8.2	13.0	22.3	
Post	6.7				7.7	9.2	13.2

Table S3. Group mean PWTs (in g) for the effects of 2-BFI alone and in combination with monoaminergic receptor antagonists on CCI-induced mechanical nociception.

2-BFI (mg/kg)	V	3.2	5.6	10	17.8	32
WAY100635						
0	6.0	7.0	10.7	20.7		
0.01	4.7	5.0	8.3	20.5		
0.032		4.7	6.8	8.7	17.0	
0.1			5.0	5.3	16.7	23.0
MDL100907						
0	4.4	6.8	13.4	23.8		
0.01	4.0	6.0	13.4	23.8		
0.032		4.4	6.4	9.6	21.6	
0.1			4.8	9.4	13.4	23.8
SB242084						
0	6.3	6.7	14.5	21.5		
0.32	5.7	6.3	12.5	24.2		
1	4.7	9.0	12.8	24.2		
WB4101						
0	6.0	6.4	8.8	18.4		
0.32	5.2	6.8	10.6	20.6		
1		4.8	5.2	9.4	20.6	
3.2			4.8	5.6	10.2	23.8
Yohimbine						
0	6.0	7.3	10.3	24.2		
1	8.0	9.0	13.5	24.2		
3.2	7.3	8.7	14.0	22.3		
SCH23390						
0	6.0	7.5	14.3	20.7		
0.032	5.3	6.3	14.8	21.2		
0.1	5.3	7.5	16.3	21.5		
Raclopride						
0	6.0	6.8	13.4	22.4		
0.32	7.6	9.8	15.2	23.8		
1	6.8	10.6	16.2	26.0		

Table S4. Group mean PWTs (in g) for the effects of CR4056 alone and in combination with monoaminergic receptor antagonists on CCI-induced mechanical nociception.

CR4056 mg/kg)	V	5.6	10	17.8	32	56
WAY100635						
0	5.0	7.3	14.2	24.2		
0.01	4.3	6.7	11.3	22.3		
0.032		5.0	6.7	9.5	24.2	
0.1			5.3	7.0	10.7	23.3
MDL100907						
0	5.6	7.2	17.0	21.6		
0.01	5.2	6.0	10.2	20.6		
0.032		4.8	6.0	9.2	19.6	
0.1			4.8	6.4	9.2	18.4
SB242084						
0	5.7	7.5	15.5	21.5		
0.32	5.7	7.8	13.7	23.3		
1	5.3	6.8	12.2	21.5		
WB4101						
0	5.3	7.3	12.7	21.5		
0.32	6.0	6.0	11.5	21.5		
1		4.7	5.3	9.7	20.7	
3.2			5.0	5.7	8.8	21.5
Yohimbine						
0	7.2	7.2	12.6	21.6		
1	6.8	8.4	14.8	22.8		
3.2	7.2	8.4	14.0	23.8		
SCH23390						
0	6.4	8.6	13.8	23.8		
0.032	7.2	9.4	15.0	21.6		
0.1	6.0	9.8	13.4	23.8		
Raclopride						
0	7.6	7.6	12.6	22.8		
0.32	7.2	8.0	12.4	21.6		
1	5.6	9.2	18.4	23.8		

Table S5. Group mean PWTs (in g) for the effects of 2-BFI alone and in combination with monoaminergic receptor antagonists on CFA-induced mechanical nociception.

2-BFI (mg/kg)	V	3.2	5.6	10	17.8	32
WAY100635						
0	4.7	5.7	7.0	19.7		
0.01	4.7	5.0	7.7	19.7		
0.032		4.7	5.0	7.7	18.7	
0.1			4.3	5.7	6.7	23.3
MDL100907						
0	4.3	6.3	7.7	18.8		
0.01	4.0	4.3	7.3	18.8		
0.032		4.3	5.3	8.3	18.8	
0.1			4.0	4.7	7.7	21.5
SB242084						
0	4.3	4.7	7.3	19.7		
0.32	4.3	5.0	6.3	19.7		
1	4.0	4.7	6.0	18.8		
WB4101						
0	4.7	5.0	7.0	20.0		
0.32	4.0	4.0	6.7	18.8		
1		4.7	6.0	11.0	22.3	
3.2			4.8	5.6	10.2	23.8
Yohimbine						
0	5.6	8.0	9.6	21.6		
1	4.8	7.2	11.2	21.6		
3.2	5.2	6.4	8.8	21.6		
SCH23390						
0	5.0	7.0	9.0	20.5		
0.032	5.3	6.3	14.8	21.2		
0.1	5.0	6.3	8.3	19.7		
Raclopride						
0	4.7	6.7	8.0	21.5		
0.32	5.0	7.3	8.3	17.8		
1	4.3	6.3	9.8	20.5		