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Title	Morphine self-administration alters the expression of translational machinery genes in the amygdala of male Lewis rats
Type	Article
URL	https://clok.uclan.ac.uk/27967/
DOI	https://doi.org/10.1177/0269881119836206
Date	2019
Citation	Ucha, Marcos, Coria, Santiago M, Núñez, Adrián E, Santos, Raquel, Roura-Martínez, David, Fernández-Ruiz, Javier, Higuera-Matas, Alejandro and Ambrosio, Emilio (2019) Morphine self-administration alters the expression of translational machinery genes in the amygdala of male Lewis rats. Journal of Psychopharmacology, 33 (7). pp. 882-893. ISSN 0269-8811
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https://doi.org/10.1177/0269881119836206

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Alternative analyses of the delay-discounting task with area under the curve (AUC) and normalized AUC

There is a debate in the preclinical literature on impulsivity about the best way to analyze impulsivity using delay-discounting curves (the two debated options are curve-fitting approaches or to compute the area under the delay-discounting curve). In addition to extracting the k parameter (see Methods section) we have also computed the AUC (normalized and non-normalized). When using these AUCs as input variables, the clustering approach was inadequate as it created two groups with a very unequal number of animals, even after removing two outliers (see SI Fig.1). In spite of this, the correlation obtained for *Cnr1* and the k parameter had an equivalent correlation between both the AUC (Magnard et al., 2018) and the normalized AUC (Myerson et al., 2001), with or without two identified outliers, and *Cnr1,* supporting the robustness of our results.

A)

B)

C)

D)
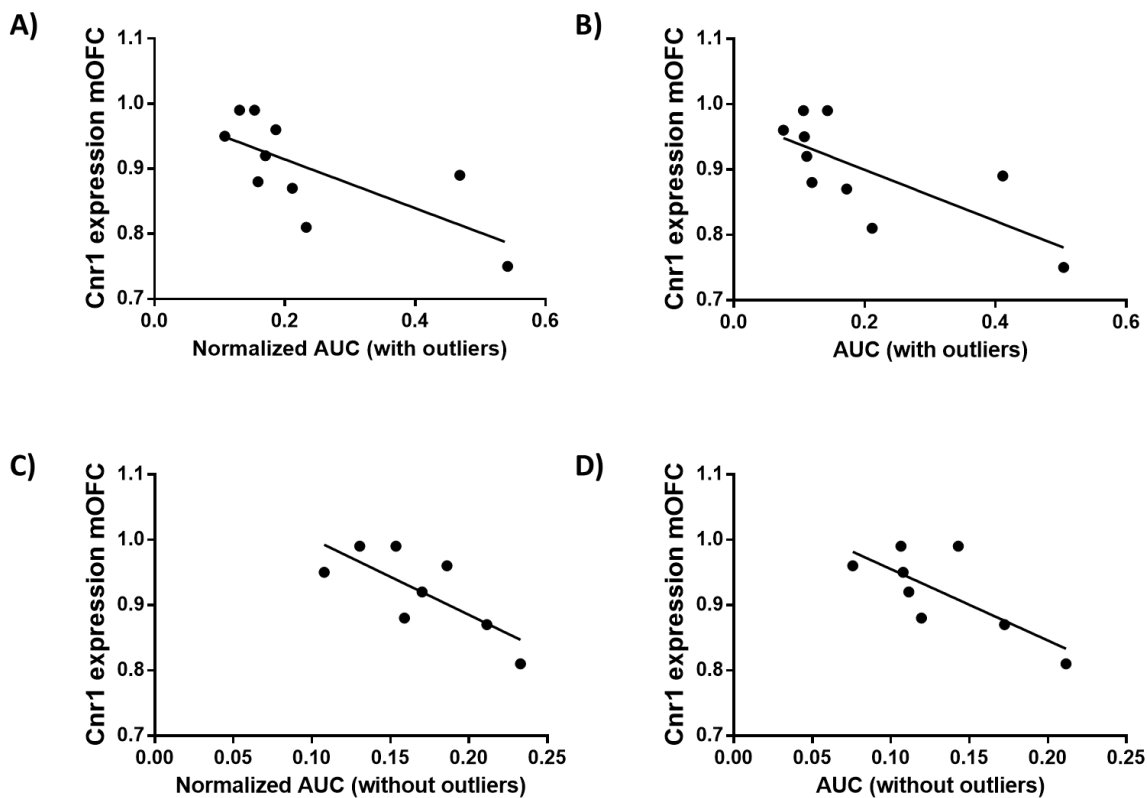
SI. Fig 1. The relationship between *Cnr1* gene expression and impulsive behavior measured (alternative analysis)

Impulsive choice was positively correlated with impulsivity measured by both measures of AUC, with or without outliers (a smaller AUC indicates a faster switch in the preference in favor of the immediate lever i.e. higher impulsivity) A) Impulsive choice (as defined by the normalized AUC, without removing outliers) was positively correlated with *Cnr1* (CB$_1$ cannabinoid receptor) gene expression in the mOFC (Kendall's $\tau=-0.584$; $p=0.02$). B) Impulsive choice (as defined by the AUC, without removing the outliers) was positively

correlated with *Cnr1* (CB$_1$ cannabinoid receptor) gene expression the mOFC (Kendall's τ-0.629=; p=0.012). C) Impulsive choice (as defined by the normalized AUC without the two outliers) was positively correlated with *Cnr1* (CB$_1$ cannabinoid receptor) gene expression the mOFC (Pearson's r=-0.747; p=0.033). D) Impulsive choice (as defined by the AUC without the outliers) was positively correlated with *Cnr1* (CB$_1$ cannabinoid receptor) gene expression in the mOFC (Pearson's r=-0.740; p=0.036).

SI Table 1. Primer sets used for RT-qPCR amplification.

Gene	Description	Forward primer	Reverse primer
Grin1	glutamate ionotropic receptor NMDA type subunit 1	AACCTGCAGAACCGCAAG	GCTTGATGAGCAGGTCTATGC
Grin2a	glutamate ionotropic receptor NMDA type subunit 2A	TGTGAAGAAATGCTGCAAGG	GAACGCTCCTCATTGATGGT
Gria1	glutamate ionotropic receptor AMPA type subunit 1	AGAGGCTGGTGGTGGTTGACT	ACCCTGGTATGGTCTCGGGA
Gria2	glutamate ionotropic receptor AMPA type subunit 2	GGCGTGTAATCCTGGACTGT	ACACCAGGGAATCGTCGTAG
Gabrg2	gamma-aminobutyric acid type A receptor gamma 2 subunit	CGGAAACCAAGCAAGGATAA	ACAGTCCTTGCCATCCAAAC
Gabrd	gamma-aminobutyric acid type A receptor delta subunit	GCTGGACCTGGAGAGCTATG	CCGAAGCTGGAAGTGTAAGC
Gabra1	gamma-aminobutyric acid type A receptor alpha 1 subunit	TTGACTGTGAGAGCCGAATG	AAACGTGACCCATCTTCTGC
Gabra2	gamma-aminobutyric acid type A receptor alpha 2 subunit	CCATGCACTTGGAGGACTT	ACTGGCCCAGCAAATCATAC
Cnr1	cannabinoid receptor 1	GTCGATCCTAGATGGCCTTGC	GTCATTCGAGCCCACGTAGAG
Dagla	diacylglycerol lipase, alpha	CTTTGCTGAATTTTTCCGTGACC	TTGTTTGCCTCATCCAGCAC
Mgll	monoacylglycerol lipase	CTACCTGCTCATGGAATC	GACACCCACGTATTTATTTC
Napepld	*N*-acyl phosphatidylethanolamine phospholipase D	AGATATGGACTCAAGAGTGAAGACTTC	TCCTCAAAGGCTTTGTCATCGG
Faah	fatty acid amide hydrolase	GTTACAGAGTGGAGAGCTGTCC	GTCTCACAGTCGGTCAGATAGG
Gapdh	glyceraldehyde-3-phosphate dehydrogenase	TCCCTGTTCTAGAGACAG	CCACTTTGTCACAAGAGA