PLOS ONE

CORRECTION

Correction: Allopregnanolone Preclinical Acute Pharmacokinetic and Pharmacodynamic Studies to Predict Tolerability and Efficacy for Alzheimer's Disease

The *PLOS ONE* Staff

In the published article Fig 3 is missing panels I-N. Please view the complete, correct, Fig 3 here.

Citation: The *PLOS ONE* Staff (2015) Correction: Allopregnanolone Preclinical Acute Pharmacokinetic and Pharmacodynamic Studies to Predict Tolerability and Efficacy for Alzheimer's Disease. PLoS ONE 10 (6): e0132210. doi:10.1371/journal.pone.0132210

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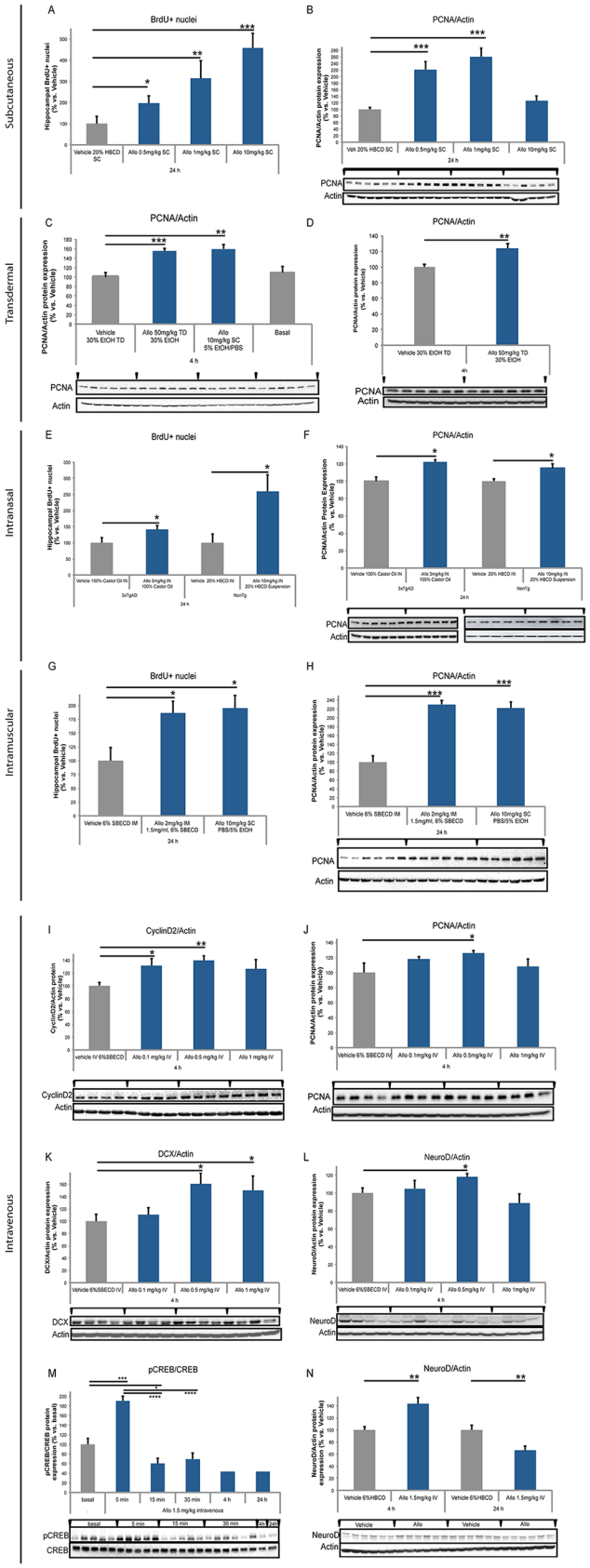
Subcutaneous
Transdermal
Intranasal
Intramuscular
Intravenous
A
BrdU+ nuclei
Hippocampal BrdU+ nuclei (% vs. Vehicle)
Vehicle 20% HBCD SC
Allo 0.5mg/kg SC
Allo 1mg/kg SC
Allo 10mg/kg SC
24 h
B
PCNA/Actin
PCNA/Actin protein expression (% vs. Vehicle)
Veh 20% HBCD SC
Allo 0.5mg/kg SC
Allo 1mg/kg SC
Allo 10mg/kg SC
24 h
PCNA
Actin
C
PCNA/Actin
PCNA/Actin protein expression (% vs. Vehicle)
Vehicle 30% EtOH TD
Allo 50mg/kg TD 30% EtOH
Allo 10mg/kg SC 5% EtOH/PBS
Basal
4 h
PCNA
Actin
D
PCNA/Actin
PCNA/Actin protein expression (% vs. Vehicle)
Vehicle 30% EtOH TD
Allo 50mg/kg TD 30% EtOH
4h
PCNA
Actin
E
BrdU+ nuclei
Hippocampal BrdU+ nuclei (% vs. Vehicle)
Vehicle 100% Castor Oil IN
Allo 3mg/kg IN 100% Castor Oil
Vehicle 20% HBCD IN
Allo 10mg/kg IN 20% HBCD Suspension
3xTgAD
Non Tg
24 h
F
PCNA/Actin
PCNA/Actin Protein Expression (% vs. Vehicle)
Vehicle 100% Castor Oil IN
Allo 3mg/kg IN 100% Castor Oil
Vehicle 20% HBCD IN
Allo 10mg/kg IN 20% HBCD Suspenson
3xTgAD
Non Tg
24 h
PCNA
Actin
G
BrdU+ nuclei
Hippocampal BrdU+ nuclei (% vs. Vehicle)
Vehicle 6% SBECD IM
Allo 2mg/kg IM 1.5mg/ml, 6% SBECD
Allo 10mg/kg SC PBS/5% EtOH
24 h
H
PCNA/Actin
PCNA/Actin protein expression (% vs. Vehicle)
Vehicle 6% SBECD IM
Allo 2mg/kg IM 1.5mg/ml, 6% SBECD
Allo 10mg/kg SC PBS/5% EtOH
24 h
PCNA
Actin
I
CyclinD2/Actin
CyclinD2/Actin protein (% vs. Vehicle)
vehicle IV 6%SBECD
Allo 0.1 mg/kg IV
Allo 0.5 mg/kg IV
Allo 1 mg/kg IV
4 h
CyclinD2
Actin
J
PCNA/Actin
PCNA/Actin protein expression (% vs. Vehicle)
Vehicle 6% SBECD IV
Allo 0.1mg/kg IV
Allo 0.5mg/kg IV
Allo 1mg/kg IV
4 h
PCNA
Actin
K
DCX/Actin
DCX/Actin protein expression (% vs. Vehicle)
Vehicle 6%SBECD IV
Allo 0.1 mg/kg IV
Allo 0.5 mg/kg IV
Allo 1 mg/kg IV
4 h
DCX
Actin
L
NeuroD/Actin
NeuroD/Actin protein expression (% vs. Vehicle)
Vehicle 6%SBECD IV
Allo 0.1mg/kg IV
Allo 0.5mg/kg IV
Allo 1mg/kg IV
4 h
NeuroD
Actin
M
pCREB/CREB
pCREB/CREB protein expression (% vs. Vehicle)
basal
5 min
15 min
30 min
4 h
24 h
Allo 1.5 mg/kg intravenous
pCREB
CREB
N
NeuroD/Actin
NeuroD/Actin protein expression (% vs. Vehicle)
Vehicle 6%HBCD
Allo 1.5mg/kg IV
Vehicle 6%HBCD
Allo 1.5mg/kg IV
4 h
24 h
Vehicle
Allo
Vehicle
Allo
NeuroD
Actin

Fig 3. Subcutaneous Allo increased BrdU incorporation and PCNA protein expression in male mouse AD model. A. In 5-month-old 3xTgAD mouse hippocampus, BrdU+ nuclei increased significantly in 24 h after a single subcutaneous (SC) dose of Allo 0.5, 1, or 10 mg/kg. B. In 5-month-old 3xTgAD mouse hippocampus, protein expression of ~29 kDa PCNA increased significantly at 24 h after SC Allo 0.5 and 1 mg/kg doses whereas 10 mg/kg dose trended towards increase but did not reach significance. Transdermal and subcutaneous Allo increased PCNA protein expression in male mouse AD model. C. In 5-month-old 3xTgAD mouse hippocampus, protein expression of PCNA increased significantly at 4 h after transdermal (TD) Allo 50 mg/kg and SC Allo 10 mg/kg doses. D. In 15-month-old nonTg mouse hippocampus, protein expression of PCNA increased significantly at 4 h after TD Allo 50 mg/kg dose. E. In 5-month-old 3xTAD and 15-month-old nonTg mouse hippocampus, BrdU+ nuclei increased significantly in 24 h after intranasal (IN) dose of Allo 3 mg/kg 100% Castor Oil and Allo 10 mg/kg 20% HBCD suspension doses. F. In 5-month-old 3xTgAD and 15-month-old nonTg mouse hippocampus, protein expression of PCNA increased significantly at 24 h after IN Allo 3 mg/kg 100% Castor Oil and Allo 10 mg/kg 20% HBCD suspension doses. Intramuscular Allo-induced increase in cell cycle marker in male mouse AD model. G. In 5-month-old 3xTgAD mouse hippocampus, BrdU+ nuclei increased significantly in 24 h after a single intramuscular (IM) dose of Allo 2 mg/kg and SC Allo 10 mg/kg dose. H. In 5-month-old 3xTgAD mouse hippocampus, protein expression of PCNA increased significantly at 24 h post-IM Allo 2 mg/kg dose and SC Allo 10 mg/kg dose. Intravenous Allo-induced increase in cell cycle and neurodifferentiation markers in male mouse AD model. I. In 5-month-old 3xTgAD mouse hippocampus, protein expression of 30 kDa cyclinD2 increased significantly at 4 h post-intravenous (IV) Allo 0.1 and 0.5 mg/kg dose whereas 1 mg/kg dose trended towards increase but did not reach significance. J. In 5-month-old 3xTgAD mouse hippocampus, protein expression of PCNA increased significantly at 4 h after IV Allo 0.5 mg/kg dose whereas 0.1 and 1 mg/kg dose did not reach significance. K. In 5-month-old 3xTgAD mouse hippocampus, protein expression of ~40 kDa doublecortin (DCX) increased significantly at 4 h after IV Allo 0.5 and 1 mg/kg doses. L. In 5-month-old 3xTgAD mouse hippocampus, protein expression of 49 kDa NeuroD increased significantly at 4 h after IV Allo 0.5 mg/kg, whereas 0.1 and 1 mg doses did not reach significance. Intravenous Allo-induced rapid transient increase in CREB phosphorylation in male mouse aging model. M. In 15-month-old nonTg mouse hippocampus, protein expression of 43 kDa serine 133 phosphorylated CREB (pCREB) increased significantly 5 min after IV Allo 1.5 mg/kg dose. N. In 15-month-old nonTg mouse hippocampus, protein expression of 49 kDa NeuroD1 (NeuroD) increased significantly at 4 h then decreased at 24 h after intravenous Allo 1.5 mg/kg dose. * $p<0.05$, ** $p<0.01$, *** $p<0.001$, **** $p<0.0001$, $n = 4–6$, bars represent mean value ± SEM.

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Reference

1. Irwin RW, Solinsky CM, Loya CM, Salituro FG, Rodgers KE, Bauer G, et al. (2015) Allopregnanolone Preclinical Acute Pharmacokinetic and Pharmacodynamic Studies to Predict Tolerability and Efficacy for Alzheimer's Disease. PLoS ONE 10(6): e0128313. doi:10.1371/journal.pone.0128313 PMID: 26039057