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Corrigendum

Corrigendum to "Evaluation of TSPO PET imaging, a marker of glial activation, to study the neuroimmune footprints of morphine exposure and withdrawal" [Drug Alcohol Depend. 170 (2017) 43–50]

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This article reports the impact of morphine exposure and withdrawal on the brain kinetics of [^{18}F]DPA-714, a position emission tomography (PET) biomarker of glial activation in rats. Different normalization methods have been tested for the analysis of PET data. It has come to the attention of the authors that the values of time-activity curves reported in Figure 2 are not consistent with the selected unit for the y-axis. This led to an error in the estimation of the brain volume of distribution (V_T, Fig. 4). This corrigendum provides five corrections: to the Abstract, a sentence in the Results section, Figure 2, Figure 4, and the Graphical Abstract. The authors would like to apologize for any inconvenience caused and provide the correct values with consistent units to describe the brain kinetics of [^{18}F]DPA-714 within the article.

1. The full abstract reproduced here now has an edit to the first sentence in the results section:

Introduction: A growing area of research suggests that neuroimmunity may impact the pharmacology of opioids. Microglia is a key component of the brain immunity. Preclinical and clinical studies have demonstrated that microglial modulators may improve morphine-induced analgesia and prevent the development of tolerance and dependence. Positron emission tomography (PET) using translocator protein 18 kDa (TSPO) radioligand is a clinically validated strategy for the non- invasive detection of microglial activation. We hypothesized that TSPO PET imaging may be used to study the neuroimmune component of opioid tolerance and withdrawal.

Methods: Healthy rats (n = 6 in each group) received either saline or escalating doses of morphine (10–40 mg/kg) on five days to achieve tolerance and a withdrawal syndrome after morphine discontinuation. MicroPET imaging with [^{18}F]DPA-714 was performed 60h after morphine withdrawal. Kinetic modeling was performed to estimate [^{18}F]DPA-714 volume of distribution (V_T) in several brain regions using dynamic PET images and corresponding metabolite-corrected input functions. Immunohistochemistry (IHC) experiments on striatal brain slices were performed to assess the expression of glial markers (Iba1, GFAP and CD68) during 14 days after morphine discontinuation.

Results: The baseline binding of [^{18}F]DPA-714 to the brain ($V_T = 8.5 \pm 0.8$ mL.cm^{-3}) was not increased by morphine exposure and withdrawal ($V_T = 7.7 \pm 1.0$mL.cm^{-3}) indicating the absence of TSPO overexpression, even at the regional level. Accordingly, expression of glial markers did not increase after morphine discontinuation.

Conclusions: Morphine tolerance and withdrawal did not detectably activate microglia and had no impact on [^{18}F]DPA-714 brain kinetics in vivo.

2. Figure 2 shown here has corrected values consistent with the y-axis:

Fig. 2. [^{18}F] DPA-714 brain kinetics. Regional [^{18}F]DPA-714 time activity curves (TACs) obtained in control and morphine-treated animals are shown as a mean percentage ± SD of injected dose (% ID.cm^{-3}, n = 6) *versus* time (min) in selected brain regions.

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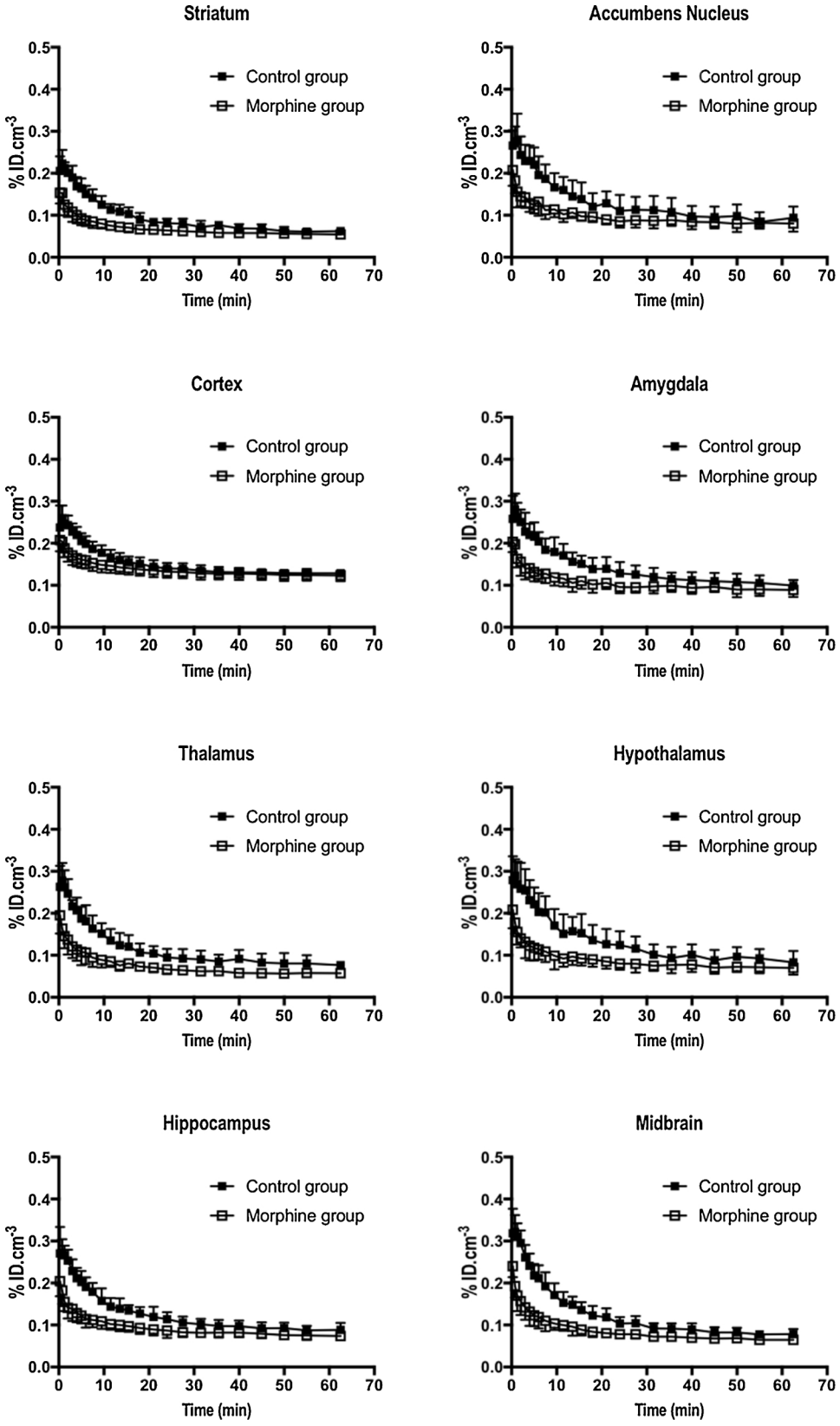
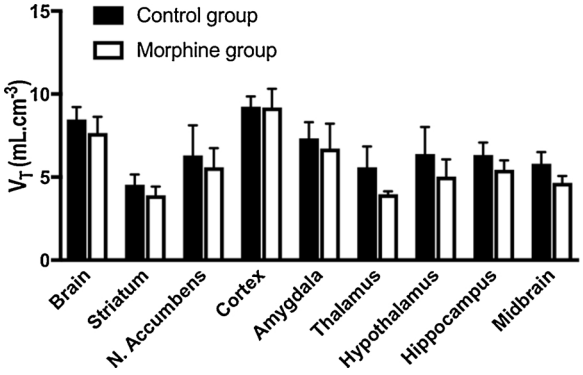

Striatum
Accumbens Nucleus
Cortex
Amygdala
Thalamus
Hypothalamus
Hippocampus
Midbrain
Control group
Morphine group
% ID.cm-3
Time (min)
0.0
0.1
0.2
0.3
0.4
0.5
0
10
20
30
40
50
60
70

3. Figure 4 shown here now has corrected values consistent with the y-axis:

Fig. 4. [^{18}F] DPA-714 volume of distribution in selected brain regions. Kinetic modelling of the regional brain kinetics [^{18}F]DPA-714 was performed for each animal using the Logan Plot analysis and the corresponding mean parent [^{18}F]DPA-714 plasma kinetics as an input function. Reported data are means of the total volume of distribution (V_T, mL. cm^{-3}) in the whole brain (brain), striatum, nucleus accumbens (N. Accumbens, Amygdala, Hippocampus, hypothalamus, thalamus, Midbrain and cortex in both the control (black column) and morphine (white column) groups (n = 6 in each group). Data are presented as mean ± SD for each region. Differences in regional V_Ts were shown not statistically significant.



4. In section 3.1 of the paper (a part of the Results section), the sixth sentence should read:

Differences in estimated [^{18}F]DPA-714 volume of distribution (V_T) in the brain of control (V_T = 8.5 ± 0.8 mL.cm^{-3}) and the morphine-treated animals (V_T = 7.7 ± 1.0 mL.cm^{-3}) were not statistically significant.

5. The Graphical Abstract should also be corrected as it incorporates Figure 4 from the paper, which has corrected values consistent with the y-axis.