Delivery of amitriptyline by intravenous and intraperitoneal administration compared in the same animal by whole-body mass spectrometry imaging of a stable isotope labelled drug substance in mice

Supporting information

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Reproducibility of the results from Figure 3

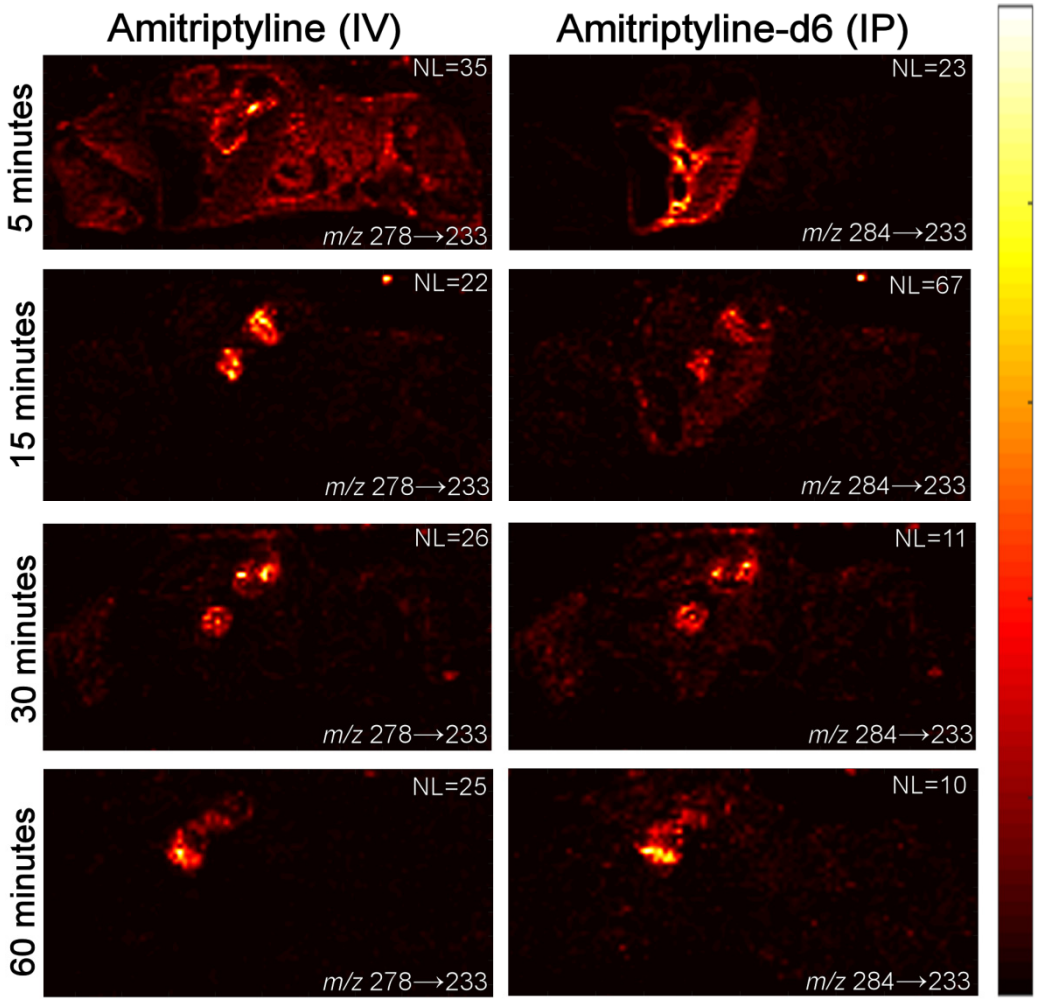

Figure S1: Replicates of the results presented in Figure 4. DESI-MS/MS images of amitriptyline and amitriptyline-d6 injected intravenously and intraperitoneally, respectively, in doses of 75 µg each (4 mg/kg). Drug substance from each of the two injections are selectively imaged with their MS/MS transitions (*m/z* 278→233 for amitriptyline and *m/z* 284→233 for amitriptyline-d6). NL is the normalization level, which indicates the absolute intensity of the brightest pixel on the color scale for the individual images.

Reproducibility of the results from Figure 4

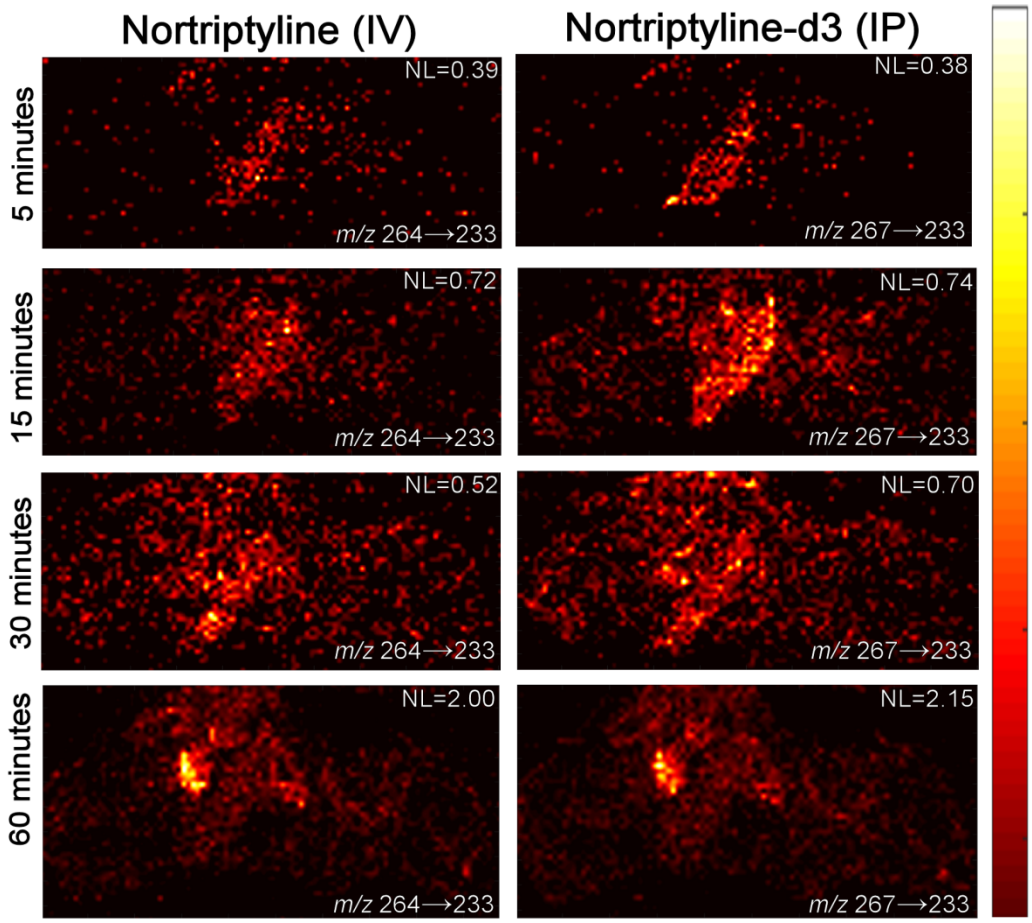

Figure S2: Replicates of the results presented in Figure 5. DESI-MS/MS images of the metabolites nortriptyline and nortriptyline-d3 from neighboring sections to the sections which are imaged in the Figure S1. Metabolites from each of the two injections are selectively imaged with their MS/MS transitions (*m/z* 264→233 for nortriptyline and *m/z* 267→233 for nortriptyline-d3). NL is the normalization level, which indicates the absolute intensity of the brightest pixel on the color scale for the individual images.

Analysis of a blank sample – a non-dosed mouse

A mouse which had not been exposed to amitriptyline was cryo-sectioned and imaged using the same MS/MS settings as were used in Figure 4 and 5.

MS/MS images of all four analytes were made in one single MSI experiment using the Displaced Dual-mode method with a pixel size of 600 µm.

None of the four compounds had any significant interferences with endogenous compounds from the mouse. For amitriptyline, the MS/MS transition appeared constantly in the background, also outside tissue, but at levels much lower than in Figure 4. The intensity levels appear in Figure S3 on the color scales to the right of the images; in Figures 4, 5, S1 and S2, the maximum intensity is specified by the NL value (Normalization Level).

For nortriptyline-D3 there seem to be an extremely weak potential interference around the cecum and colon on the mouse, but this is at levels similar to what is found outside the tissue (and at levels which are much lower than in Figure 4), and the pattern of potential interference appears to play no role for the imaged nortriptyline-D3 distributions in Figure 5.

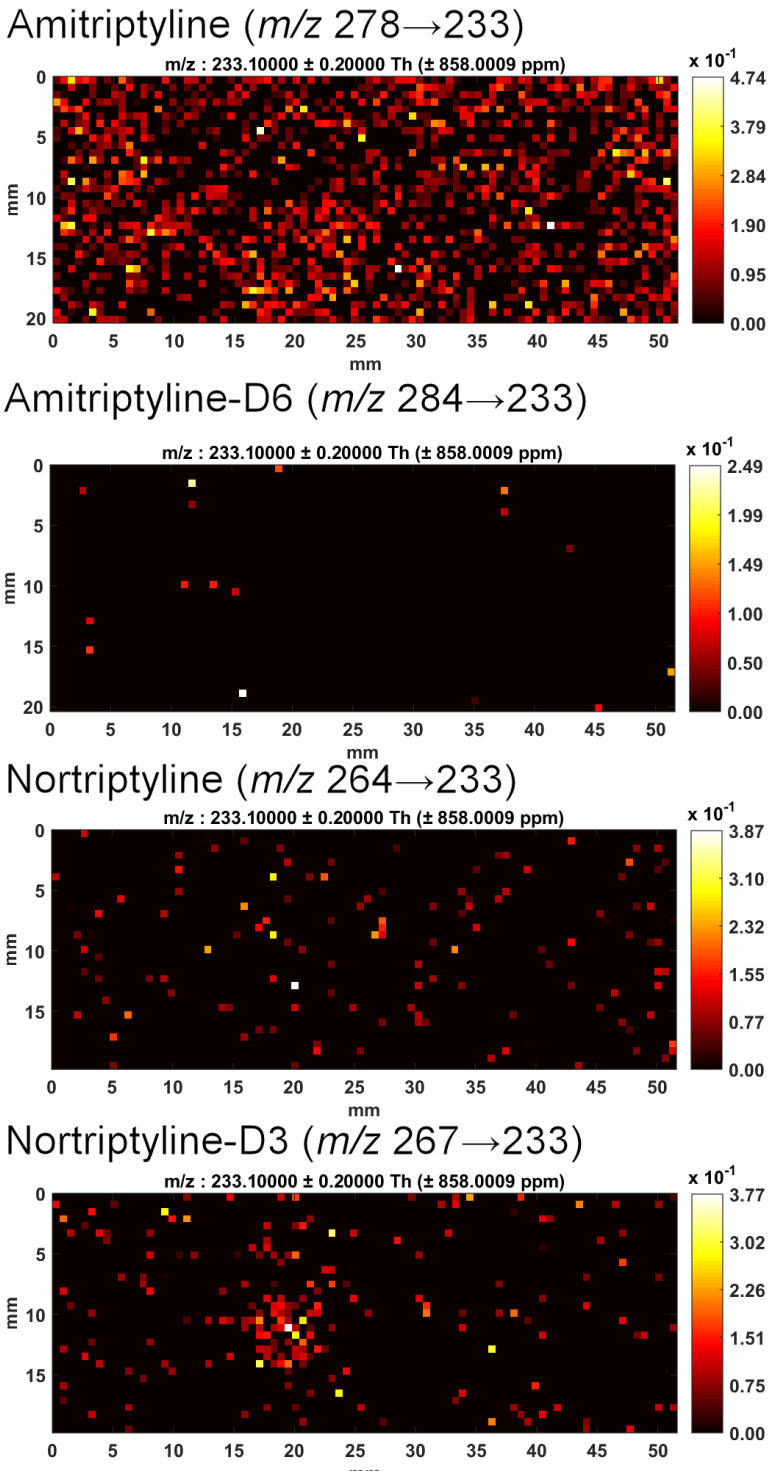

Figure S3.