

Drivers of Locus Coeruleus Contrast

in 7T magnetization transfer magnetic resonance imaging

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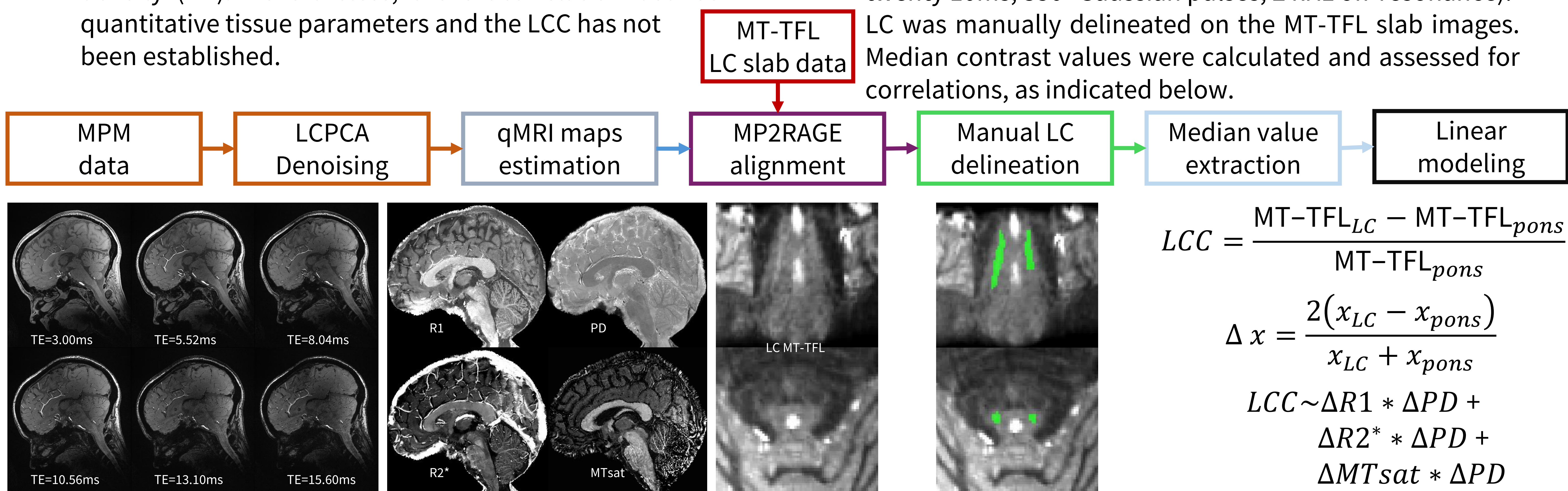
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Introduction

The integrity of the noradrenergic locus coeruleus (LC) is critical for regulating sleep, arousal, attention, cognition, memory and other integral brain functions. Non-invasive probing into the physiological state of LC can be done through magnetic resonance imaging (MRI). At ultra-high field (UHF) MRI LC is particularly prominent in the magnetization transfer (MT) based imaging techniques. LC-contrast (LCC) has been partially linked to quantitative metrics, such as R1, R2, and R2* relaxation rates, quantitative measurements of MT, and proton density (PD). Nevertheless, the exact relation between quantitative tissue parameters and the LCC has not been established.

Methods

To investigate the drivers of LCC in MT MRI, we recruited 32 healthy volunteers (16 m) from 20 to 73 years old (median of 31) for UHF (7T) MRI. We employed, first, a multiparameter mapping (MPM) protocol using 8Tx/32Rx coil with T1w, PDw, and MTw whole-brain 3D FLASH-based multi-echo sequences with isotropic resolution of 0.6mm (MT via one 4ms, 130° Gaussian pulse, 3kHz off-resonance). For LCC an MT turbo flash (MT-TFL) sequence was used in a 30mm slab with the across-slab resolution of 0.5mm and 0.4×0.4mm² in the slab plane (MT via twenty 10ms, 350° Gaussian pulses, 2 kHz off-resonance). LC was manually delineated on the MT-TFL slab images. Median contrast values were calculated and assessed for correlations, as indicated below.



$$LCC = \frac{MT-TFL_{LC} - MT-TFL_{pons}}{MT-TFL_{pons}}$$

$$\Delta x = \frac{2(x_{LC} - x_{pons})}{x_{LC} + x_{pons}}$$

$$LCC \sim \Delta R1 * \Delta PD + \Delta R2^* * \Delta PD + \Delta MTsat * \Delta PD$$

Results

The linear models showed significant dependence of LCC on $\Delta R1$ ($p < 0.0001$) and $\Delta R2^*$ ($p < 0.001$), and significant interaction between $\Delta R1$ and ΔPD ($p < 0.0001$).

The observed dependences (Fig.1,A) were on the order of 0.45 ± 0.10 p.u._{LCC}/p.u. _{$\Delta R1$} in $\Delta R1$ with an interaction term of -0.030 ± 0.006 p.u._{LCC}/p.u. _{$\Delta R1$} p.u. _{ΔPD} (Fig.1,C, and Fig.2), and $\Delta R2^*$ term of -0.20 ± 0.05 p.u._{LCC}/p.u. _{$\Delta R2^*$} (Fig.1,B). No significant relation with the $\Delta MTsat$ metric (Fig.1,D) was observed ($p > 0.50$) despite the LC-contrast being driven primarily by MT-weighting.

Figure 2: The estimated model LCC response to combined changes in $\Delta R1$ and ΔPD

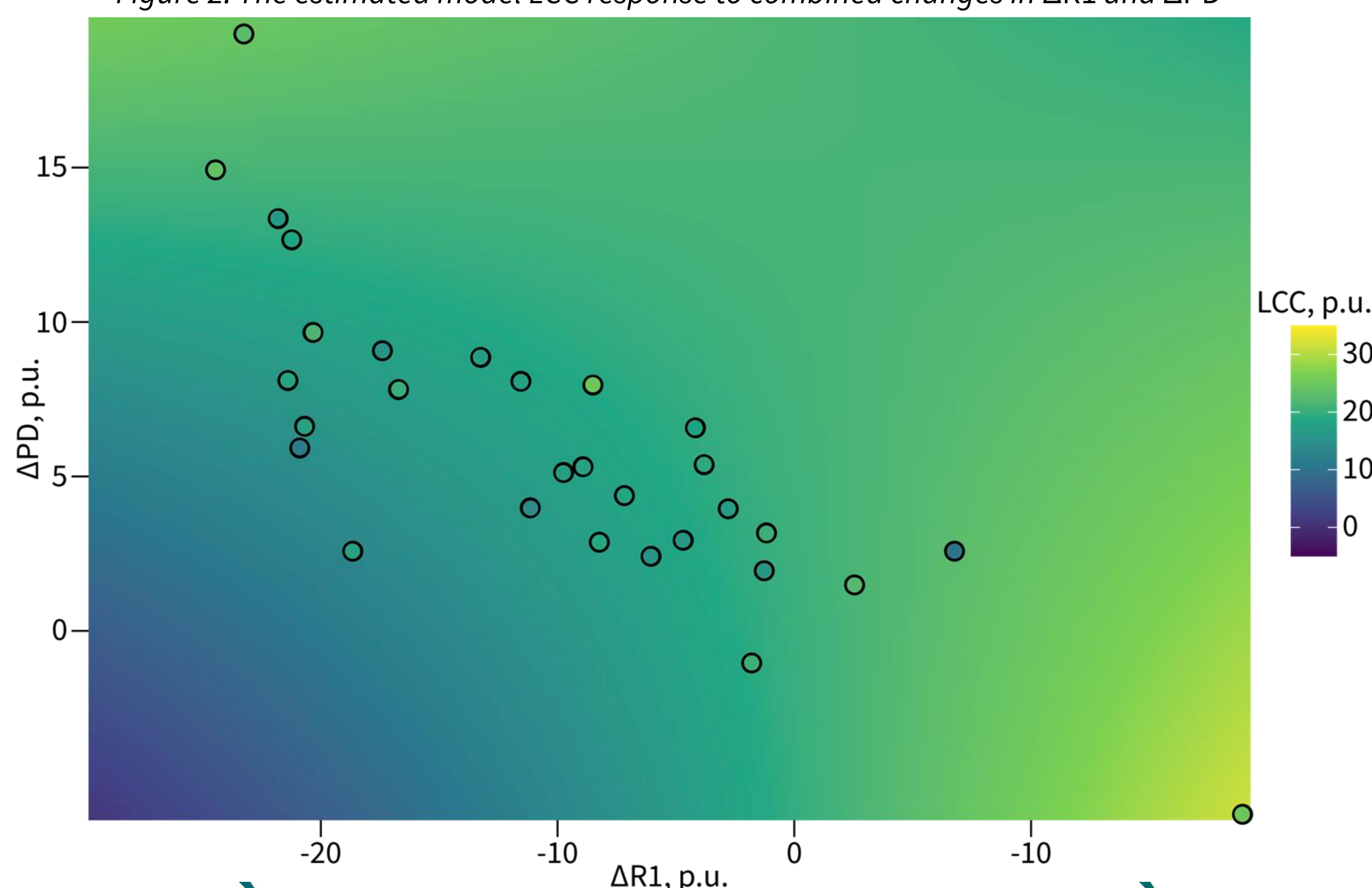
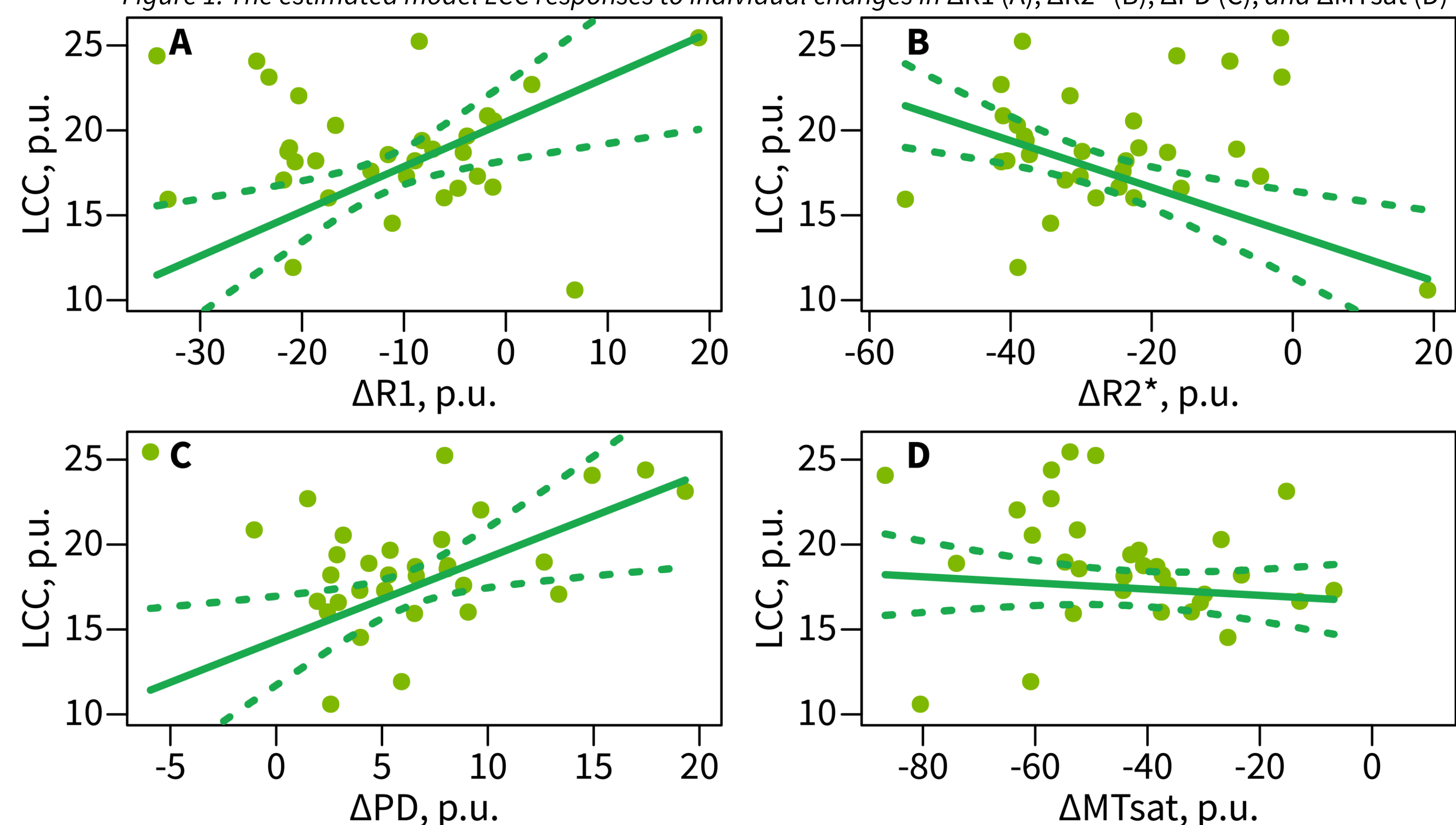


Figure 1: The estimated model LCC responses to individual changes in $\Delta R1$ (A), $\Delta R2^*$ (B), ΔPD (C), and $\Delta MTsat$ (D)



Discussion

Neuromelanin and iron, considered to be the primary drivers for the LCC, can result in the $\Delta R1$ and $\Delta R2^*$ dependence, while the ΔPD influence is not directly rooted in the neuromelanin content. The lack of dependence on $\Delta MTsat$ is potentially due to different MT approaches in the MPM and MT-TFL sequences, thus suggesting LCC being driven by a mixture of contrast mechanisms.