Supplementary Material

Estimation of Human Brain Fluid Clearance Using Intrathecal Imaging Contrast Agents

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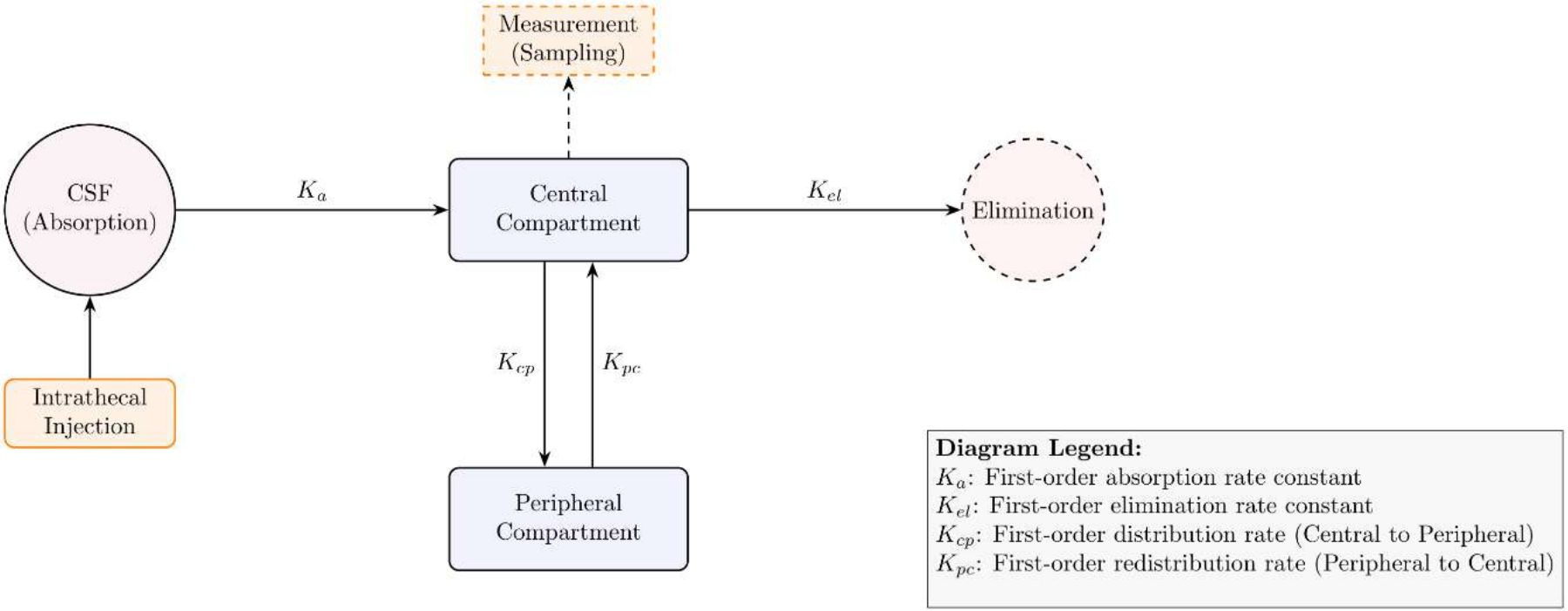
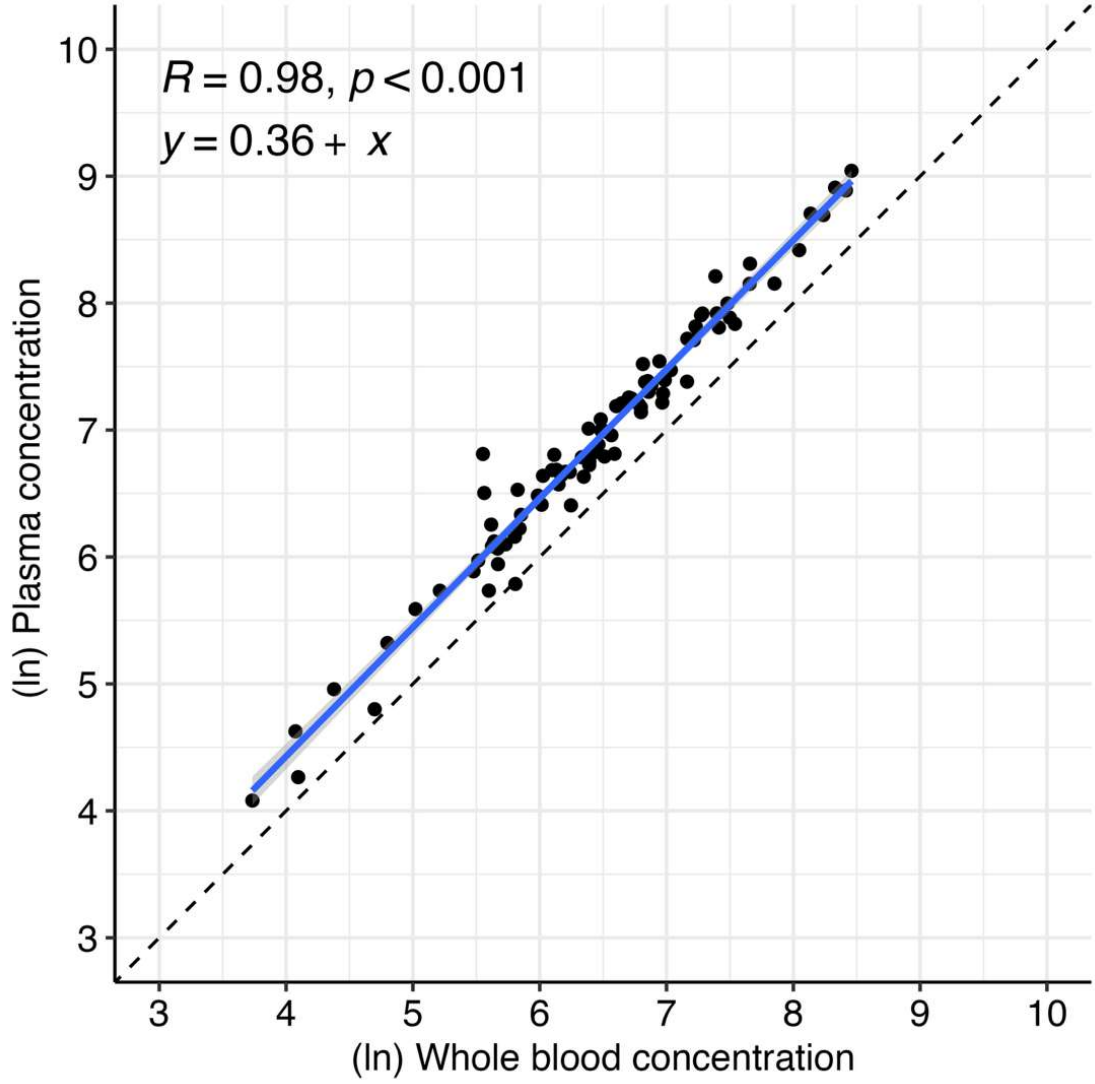
Supplementary Figure 1



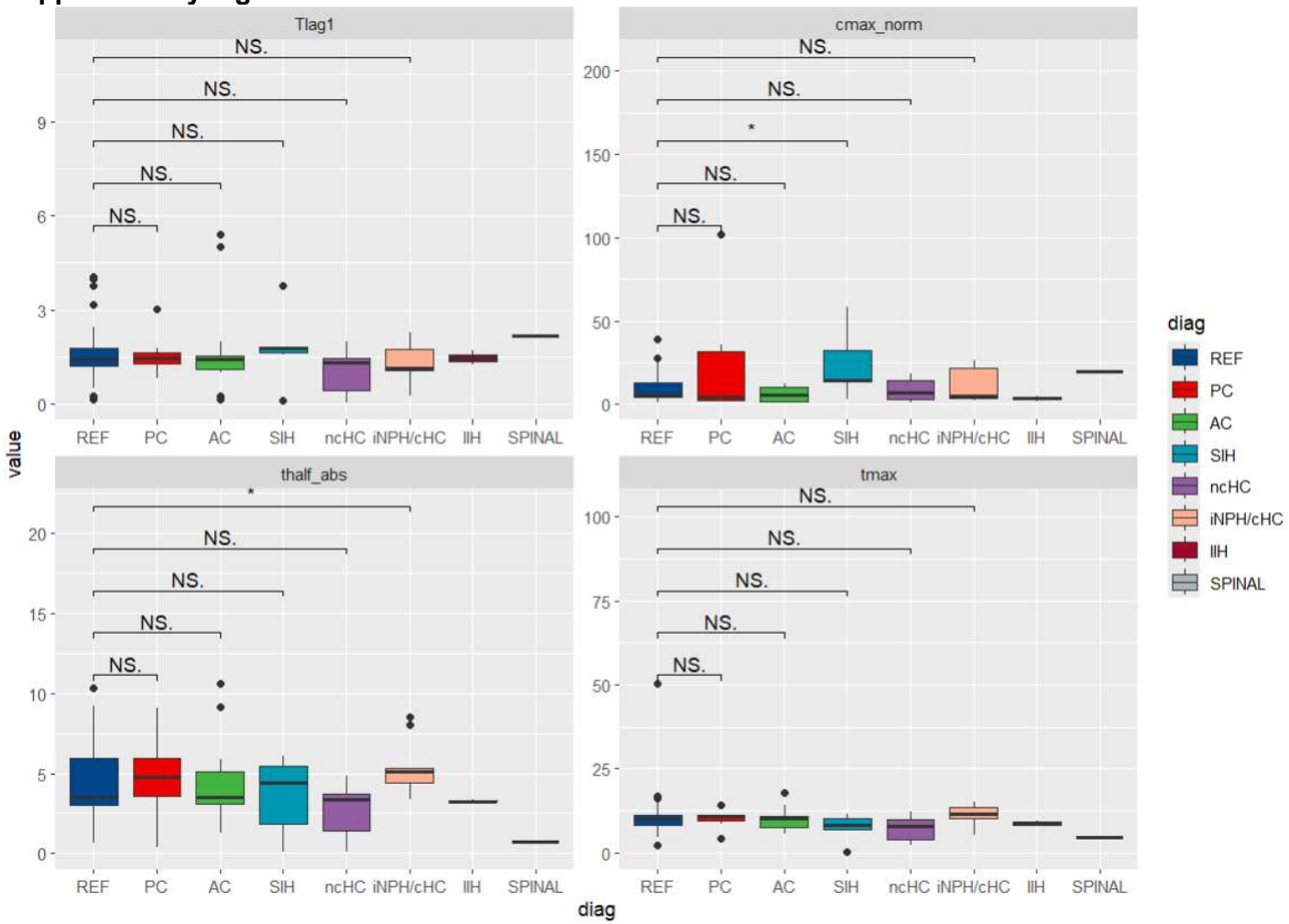
Structural overview of the population pharmacokinetic model, demonstrating absorption from cerebrospinal fluid (CSF) following intrathecal injection, from which first-order absorption is mediated by the transfer rate constant Ka. Distribution is assumed to be to a single peripheral compartment, with distribution and redistribution rate coefficients Kcp and Kpc, respectively. Elimination is assumed from the central compartment only, and to be of first-order, described by the elimination rate constant Ke.

Supplementary Figure 2



Interpolation of plasma iodixanol concentration from whole blood. Linear regression of whole blood to plasma iodixanol (μM). The dashed line represents the unity line, and the blue line represents the regression line. The equation in log-space is y = 0.36 + x, while the equation in regular space is y = $e^{0.3633}$ * $x^{1.0165}$.

Supplementary Figure 3



Comparison of brain fluid indices between patient categories. No significant differences were shown except for significantly higher C_{max} in SIH subjects as compared to REF individuals ($P<0.05$; Wilcoxon test).

Supplementary Table 1. Correlations between intrathecal contrast enhancement in different compartments at CT

	Intrathecal contrast enhancement at CT (Hounsfield units) Cisterna magna		
	2 hrs	4 hrs	24 hrs
Sylvian fissure			
2 hrs	R=0.70, P<0.001		
4 hrs (n= 49)		R =0.76, P<0.001	
24 hrs (n= 49)			R =0.75, P<0.001
Vertex			
2 hrs	R=0.19, P=0.195		
4 hrs		R=0.20, P=0.176	
24 hrs (n= 49)			R=0.31, P=0.030

Data presented as Pearson correlation coefficient with significance levels (only statistically significant correlations are shown).

Supplementary Table 2. Correlations between intrathecal contrast enhancement in different compartments at MRI

	Intrathecal contrast enhancement at MRI (% normalized T1 signal change) Cisterna magna					
	1 hr	3 hr	4 hr	6 hr	24 hr	48 hr
Sylvian fissure						
1 hr	R=0.35, P=0.023					
3 hrs		R=0.39, P=0.011				
4 hrs			R=0.44, P=0.005			
6 hrs				R=0.43, P=0.005		
24 hrs					R=0.63, P<0.001	
48 hrs						R=0.71, P<0.001
Vertex						
1 hr	R=-0.06, P=0.711					
3 hrs		R=0.09, P=0.56				
4 hrs			R=0.13, P=0.411			
6 hrs				R=0.16, P=0.322		
24 hrs					R=0.28, P=0.059	
48 hrs						R=0.30, P=0.047

Data presented as Pearson correlation coefficient with significance levels (only statistically significant correlations are shown).