

## [<sup>11</sup>C]PE2I multiple-time graphical analysis (Logan plot)

### Plasma input

Multiple-time graphical analysis for reversible ligands (Logan analysis) for regional TACs was made using program logan 1.9.1. Metabolite corrected plasma TACs were corrected for time delay, but tissue curves were not corrected for the arterial blood volume as in compartmental model fits. The seven last frames (21-63 min) were used in the fit, as suggested by Jucaité et al. (manuscript); this range was found to be appropriate in all three studies and regions (see the graphs below).

DV images calculated with program imgdv 1.2 contained numerous very high values, not only outside the brain but also inside striatal regions. Therefore the DV map cannot be used, unless dynamic image is preprocessed with filtering.

```
logan 1.9.1 (c) 2001-2004 by Turku PET Centre
Date:      2004-08-17 20:21:17
Study:     JKAR_DY
Data file:  jkaravg.dft
Plasma file: jkar_apc.delay.dat
Reference region: cer All
Data range: 21 - 63 min (N=7) lsq=c
Vb:        0 %
Data was not weighted.
```

Region		DV	Ic	r	DVR
ac	All	4.8494e+00	-2.320e+01	0.9998	9.0392e-01
	SD	5.4983e-02	1.4192e+00	.	.
cau	All	7.7837e+01	-2.276e+02	0.9813	1.4509e+01
	SD	8.3423e+00	2.8401e+01	.	.
cer	All	5.3648e+00	-2.054e+01	0.9999	1.0000e+00
	SD	3.8242e-02	9.1033e-01	.	.
dlp	All	4.6986e+00	-2.189e+01	0.9998	8.7582e-01
	SD	4.9909e-02	1.3746e+00	.	.
occ	All	5.4866e+00	-3.007e+01	0.9996	1.0227e+00
	SD	8.5030e-02	1.7718e+00	.	.
put	All	7.7792e+01	-2.045e+02	0.9909	1.4500e+01
	SD	5.7802e+00	1.8045e+01	.	.
sn	All	1.2656e+01	-4.253e+01	0.9941	2.3591e+00
	SD	7.5638e-01	5.9305e+00	.	.
tha	All	5.5800e+00	-1.934e+01	1.0000	1.0401e+00
	SD	2.8605e-02	6.2239e-01	.	.
wm	All	6.5802e+00	-6.743e+01	0.9982	1.2266e+00
	SD	2.1624e-01	3.8468e+00	.	.

```
logan 1.9.1 (c) 2001-2004 by Turku PET Centre
Date:      2004-08-17 20:21:25
Study:     JOMA_DY
Data file:  jomaavg.dft
Plasma file: joma_apc.delay.dat
Reference region: cer All
Data range: 21 - 63 min (N=7) lsq=c
Vb:        0 %
Data was not weighted.
```

Region		DV	Ic	r	DVR
ac	All	2.7454e+00	-2.326e+01	0.9997	9.1299e-01
	SD	3.4872e-02	1.6853e+00	.	.
cau	All	3.5928e+01	-1.488e+02	0.9953	1.1948e+01
	SD	1.9060e+00	1.0074e+01	.	.
cer	All	3.0071e+00	-2.194e+01	0.9999	1.0000e+00
	SD	2.7484e-02	1.2815e+00	.	.

dlp	.	All	3.1534e+00	-2.966e+01	0.9993	1.0487e+00
SD	.	.	6.3749e-02	2.6577e+00	.	.
occ	.	All	3.1983e+00	-3.016e+01	0.9975	1.0636e+00
SD	.	.	1.2424e-01	5.0173e+00	.	.
put	.	All	3.6096e+01	-1.515e+02	0.9925	1.2004e+01
SD	.	.	2.4266e+00	1.3014e+01	.	.
sn	.	All	7.6067e+00	-4.932e+01	0.9977	2.5296e+00
SD	.	.	2.8027e-01	3.8491e+00	.	.
tha	.	All	3.6006e+00	-2.229e+01	0.9996	1.1974e+00
SD	.	.	5.7756e-02	2.0368e+00	.	.
wm	.	All	3.9072e+00	-5.540e+01	0.9950	1.2993e+00
SD	.	.	2.1469e-01	5.9948e+00	.	.

logan 1.9.1 (c) 2001-2004 by Turku PET Centre  
Date: 2004-08-17 20:21:34  
Study: MAUT\_DY  
Data file: mautavg.dft  
Plasma file: maut\_apc.delay.dat  
Reference region: cer All  
Data range: 21 - 63 min (N=7) lsq=c  
Vb: 0 %  
Data was not weighted.

Region		DV	Ic	r	DVR	
ac	.	All	4.4411e+00	-1.607e+01	0.9997	0.9867
SD	.	.	5.8655e-02	1.6234e+00	.	.
cau	.	All	3.2930e+01	-1.033e+02	0.9972	7.3164
SD	.	.	1.3427e+00	5.9011e+00	.	.
cer	.	All	4.5008e+00	-1.308e+01	1.0000	1.0000
SD	.	.	1.9375e-02	5.7853e-01	.	.
dlp	.	All	4.1049e+00	-1.685e+01	1.0000	0.9120
SD	.	.	1.4243e-02	4.3427e-01	.	.
occ	.	All	5.1629e+00	-1.938e+01	0.9999	1.1471
SD	.	.	4.2982e-02	9.8229e-01	.	.
put	.	All	3.2748e+01	-8.996e+01	0.9990	7.2760
SD	.	.	8.2020e-01	3.3367e+00	.	.
sn	.	All	9.9313e+00	-4.186e+01	0.9871	2.2066
SD	.	.	8.8158e-01	8.5166e+00	.	.
tha	.	All	6.0383e+00	-2.006e+01	0.9999	1.3416
SD	.	.	5.0173e-02	9.1164e-01	.	.
wm	.	All	5.1594e+00	-5.960e+01	0.9967	1.1463
SD	.	.	2.3091e-01	4.9416e+00	.	.

## Cerebellum input

When reference region is used as input for Logan plot analysis, a population average of reference region  $k_2$  should be used. If  $k_2$  correction is not applied, then the Logan plots reach the linearity only after about 30-40 min in striatal regions (see the figure below) and because of the few samples in that range the DVR results are not reliable (not shown); in regions with lower binding, the linearity is reached earlier.

One method to estimate  $k_2$  is to calculate it as the negative inverse of the intercept of plasma input Logan plot (Pinborg et al. 2002). These values were: 0.04869, 0.04558, 0.07645, and their average is 0.05691. When using this correction, the linearity of striatal regions was not reached any earlier (results not shown) compared to not using  $k_2$  correction at all; this was seen also by Pinborg et al. for [ $^{123}$ I]PE2I.

Instead, if  $k_2$  correction was based on the average of  $k_2/(1+k_5/k_6)$  values determined from the three-compartment model fit of cerebellum (separate values: 0.08844, 0.09716, 0.9912, and the average 0.09491 min<sup>-1</sup>), the linear phase was reached earlier for striatal regions also (see the graph below), and the same line fit range could be used as with plasma input. DVR values are listed below.

logan 1.8.1 (c) 2001-2004 by Turku PET Centre  
 Date: 2004-08-10 09:18:04  
 Study: JKAR\_DY  
 Data file: jkaravg.dft  
 Reference region: cer  
 Data range: 21 - 63 min (N=7) lsq=c refk2=0.094906  
 Vb: 0 %  
 Data was not weighted.

Region		DVR	Ic	r
ac	.	All	0.8955 -1.210e+01	1.0000
	SD	.	0.0034 4.3716e-01	.
cau	.	All	8.6171 -1.049e+02	0.9983
	SD	.	0.2746 4.5429e+00	.
dlp	.	All	0.8698 -1.074e+01	1.0000
	SD	.	0.0021 2.8673e-01	.
occ	.	All	0.9912 -1.735e+01	0.9999
	SD	.	0.0080 8.2292e-01	.
put	.	All	8.9770 -9.760e+01	0.9998
	SD	.	0.0968 1.4690e+00	.
sn	.	All	2.2339 -2.917e+01	0.9974
	SD	.	0.0892 3.4450e+00	.
tha	.	All	1.0495 -1.121e+01	0.9999
	SD	.	0.0067 7.2356e-01	.
wm	.	All	1.0645 -4.283e+01	0.9990
	SD	.	0.0261 2.2750e+00	.

logan 1.8.1 (c) 2001-2004 by Turku PET Centre  
 Date: 2004-08-10 09:18:12  
 Study: JOMA\_DY  
 Data file: jomaavg.dft  
 Reference region: cer  
 Data range: 21 - 63 min (N=7) lsq=c refk2=0.094906  
 Vb: 0 %  
 Data was not weighted.

Region		DVR	Ic	r
ac	.	All	0.9103 -1.201e+01	0.9999
	SD	.	0.0059 7.9433e-01	.
cau	.	All	8.6090 -8.275e+01	0.9994
	SD	.	0.1642 2.3666e+00	.
dlp	.	All	1.0219 -1.540e+01	0.9999
	SD	.	0.0092 1.0578e+00	.
occ	.	All	1.0346 -1.575e+01	0.9993
	SD	.	0.0205 2.2865e+00	.
put	.	All	8.5050 -8.199e+01	0.9965
	SD	.	0.3930 5.7458e+00	.
sn	.	All	2.3644 -3.387e+01	0.9990
	SD	.	0.0573 2.1654e+00	.
tha	.	All	1.1996 -1.213e+01	0.9999
	SD	.	0.0080 7.8368e-01	.
wm	.	All	1.1880 -3.707e+01	0.9977
	SD	.	0.0443 3.3994e+00	.

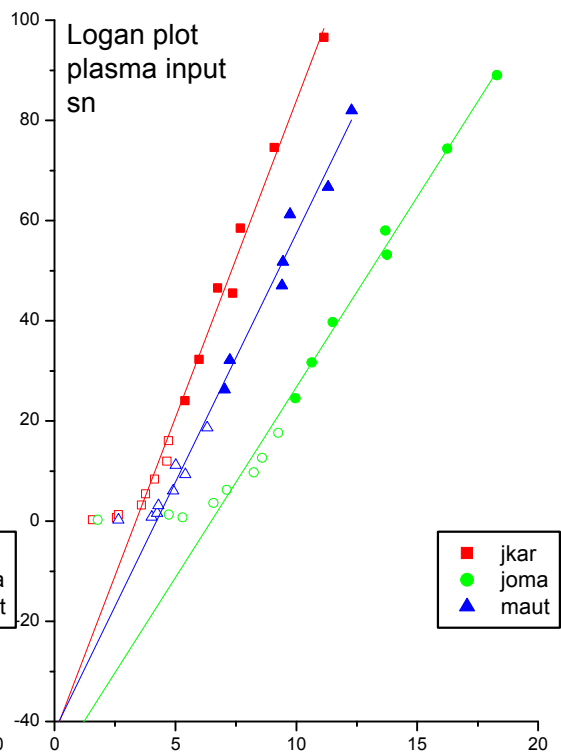
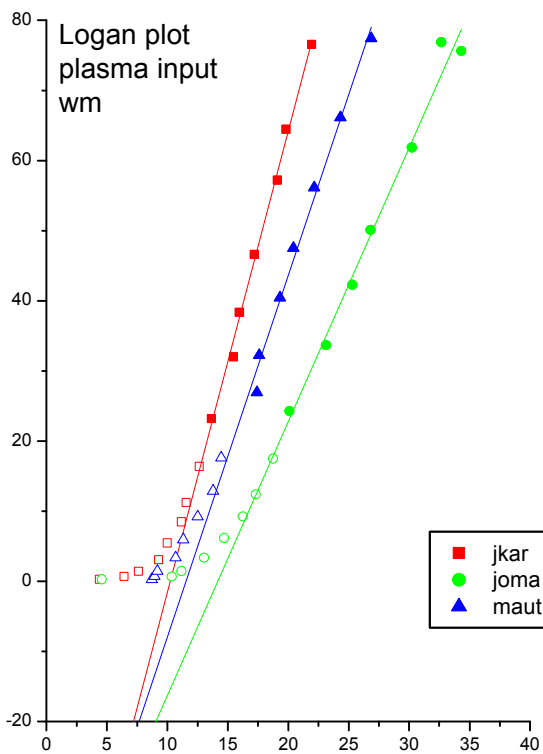
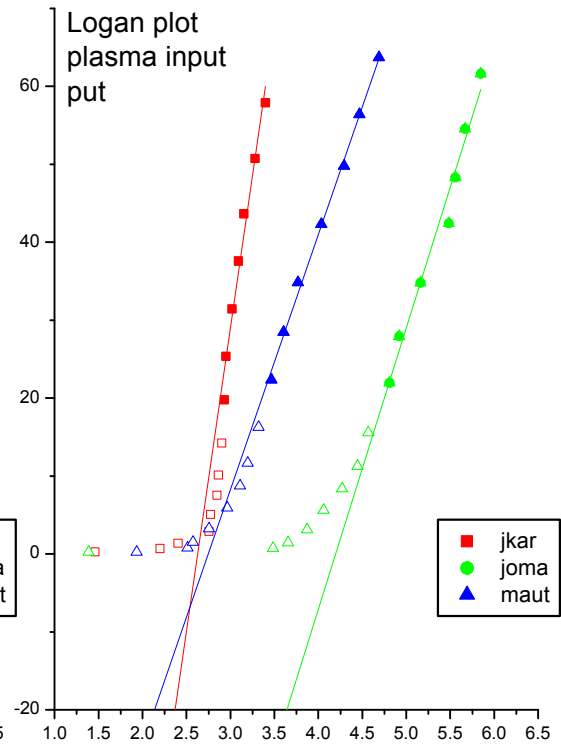
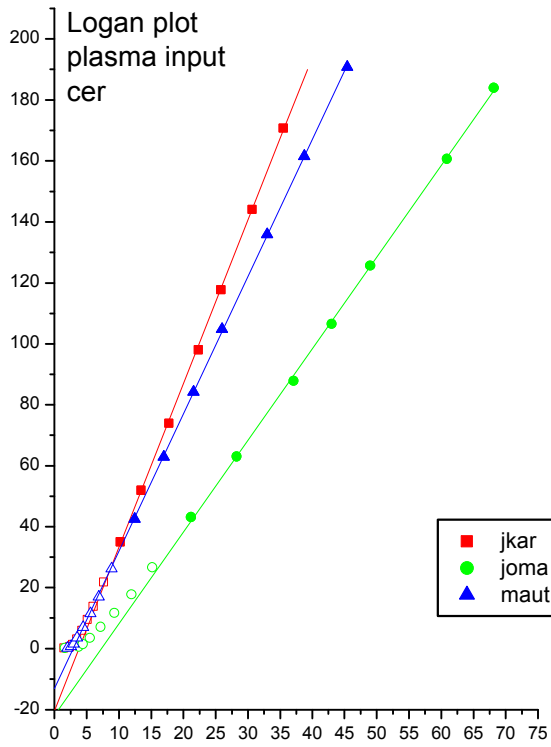
logan 1.8.1 (c) 2001-2004 by Turku PET Centre  
 Date: 2004-08-10 09:18:21  
 Study: MAUT\_DY  
 Data file: mautavg.dft  
 Reference region: cer  
 Data range: 21 - 63 min (N=7) lsq=c refk2=0.094906  
 Vb: 0 %  
 Data was not weighted.

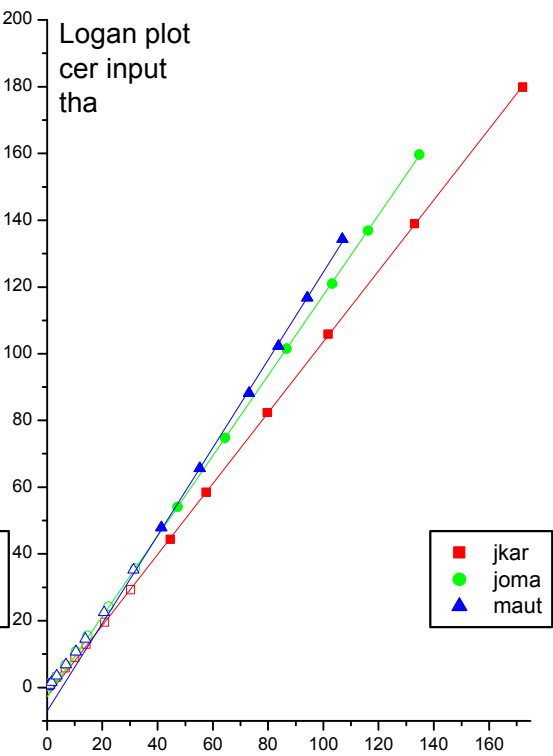
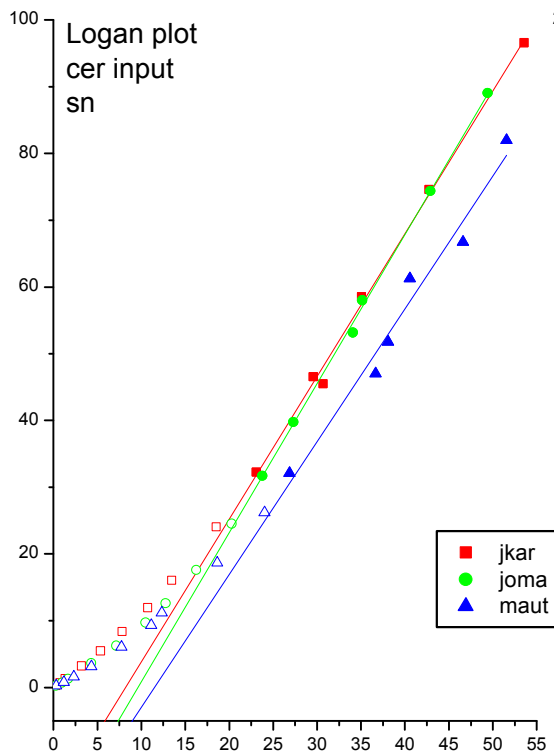
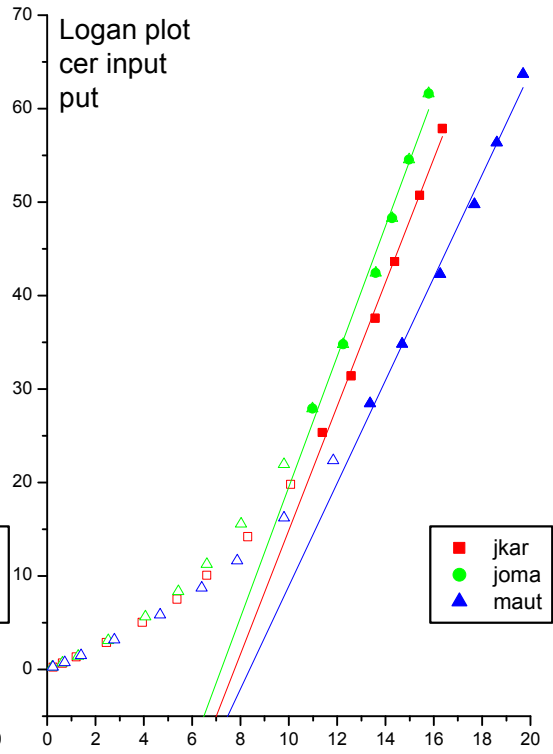
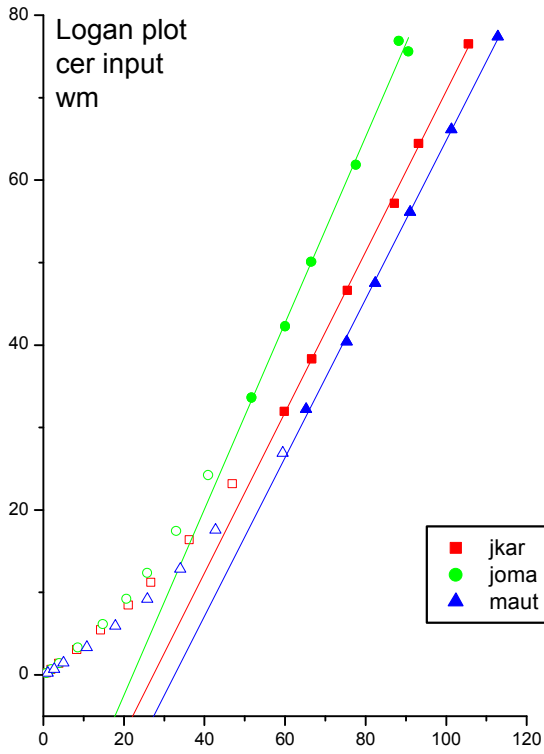
Region		DVR	Ic	r
ac	.	All	0.9852 -1.348e+01	0.9998
	SD	.	0.0109 1.3343e+00	.
cau	.	All	6.6538 -8.710e+01	0.9978
	SD	.	0.2424 4.6861e+00	.
dlp	.	All	0.9070 -1.372e+01	1.0000
	SD	.	0.0049 6.6416e-01	.
occ	.	All	1.1362 -1.593e+01	0.9998
	SD	.	0.0132 1.3344e+00	.
put	.	All	6.7031 -7.663e+01	0.9989
	SD	.	0.1726 3.0892e+00	.
sn	.	All	2.1428 -3.705e+01	0.9885
	SD	.	0.1792 7.6282e+00	.
tha	.	All	1.3314 -1.709e+01	0.9997

	SD	.	.	0.0165	1.3268e+00	.
wm	.	All	.	1.1019	-5.292e+01	0.9989
	SD	.	.	0.0289	2.7268e+00	.

## Conclusions from the Logan plot analysis

The DV and DVR values from plasma input Logan analysis are lower than from compartment model fits. DVR values from reference region Logan analysis are even lower, and most importantly, the difference between the subjects is then minimal. This suggests that most of the large intersubject variance seen in plasma input methods are caused by measurement inaccuracy, not by true binding differences.





$$k'_2 = 0.094906 \text{ (cerebellum } k_2 / (1 + k_5/k_6))$$

