Supporting Information

for

Comparative modeling of the human monoamine transporters – similarities in substrate binding

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The supporting Information includes tables of the statistics for homology modeling of hSERT, hDAT and hNET in Tables S1-S3. Table S4-S6 reports the data for all poses for the induced fit docking calculations.

Table S1: Statistics from the model building of hSERT. The Molpdf which should be as low as possible is reported. Furthermore the percentage in the favorable, additionally allowed, generously allowed and disallowed regions are listed. The overall best model with χ1 of Asp98 *gauche* was chosen and is here indicated in italic and bold. The models shaded gray are the ones with χ1 of Asp98 *anti*

hSERT Model	Molpdf	Ramachandran (%)	Cavity size[1](Å^3)	Asp98 χ1 (°)
1	356	91.5/6.4/1.7/0.4	45.1	310.9
2	514	90.5/7.2/2.1/0.2	114.7	199.1
3	***310***	***89.5/8.5/1.0/1.0***	***114.2***	***58.9***
4	308	90.1/8.1/1.0/0.8	114.7	198.5
5	1985	91.1/6.8/0.4/1.7	87.0	61.0
6	597	89.5/8.3/1.2/1.0	116.2	198.9
7	2386	89.7/7.6/1.7/1.0	100.4	59.1
8	378	91.3/6.6/1.2/0.8	115.7	197.4
9	709	90.5/7.2/1.4/0.8	96.8	61.1
10	341	89.9/7.9/1.2/1.0	65.5	203.8
11	322	90.3/7.6/1.2/0.8	113.2	60.6
12	773	90.7/7.2/1.4/0.6	129.0	197.1
13	389	88.2/9.9/0.8/1.0	100.4	193.8
14	360	90.5/7.6/0.8/1.0	94.2	60.9
15	3414	89.7/7.4/1.2/1.7	88.6	62.1
16	1731	89.5/8.3/1.0/1.2	78.3	61.8
17	332	89.0/8.1/1.4/1.4	113.2	59.5
18	527	90.7/7.0/1.4/0.8	123.9	192.2
19	339	90.3/8.5/0.8/0.4	93.7	193.1
20	1794	89.3/8.7/1.4/0.6	89.1	196.2

[1] MVD molecular surface probe size 1.2 Å. 25 cavities each run

Table S2: Statistics from the model building of hDAT. The Molpdf which should be as low as possible is reported. Furthermore the percentage in the favorable, additionally allowed, generously allowed and disallowed regions are listed. The overall best model with χ1 of Asp79 *gauche* was chosen and is here indicated in italic and bold. The models shaded gray are the ones with χ1 of Asp79 *anti*

hDAT Model	Molpdf	Ramachandran (%)	Cavity size[2] (Å^3)	Asp79 χ1 (°)
1	399	91.2/6.8/1.6/0.4	85.0	310.8
2	358	90.8/7.8/1.0/0.4	103.4	58.9
3	372	90.1/7.4/1.4/1.0	109.6	62.9
4	1801	90.1/7.0/1.6/1.2	99.8	193.5
5	***396***	***90.8/7.8/0.8/0.6***	***127.5***	***59.9***
6	1869	88.9/9.0/1.4/0.6	118.8	196.5
7	374	90.8/7.8/0.8/0.6	140.3	196.7
8	377	92.6/6.2/0.8/0.4	103.9	61.9
9	724	89.1/8.2/1.8/0.8	136.7	164.6
10	2339	90.6/8.0/1.0/0.4	113.7	59.0
11	355	89.5/8.4/1.2/0.8	125.4	60.0
12	360	90.1/8.0/1.6/0.2	106.5	313.0
13	437	89.7/8.2/1.2/0.8	141.3	190.5
14	415	88.7/9.7/1.0/0.6	113.7	61.0
15	429	90.3/7.6/1.4/0.6	156.7	196.6
16	1506	89.3/8.6/1.6/0.4	131.6	59.8
17	333	92.0/5.7/1.6/0.6	167.4	197.7
18	654	90.3/6.6/2.7/0.4	155.1	196.5
19	380	91.8/6.0/1.2/1.0	131.1	194.4
20	497	89.3/8.4/1.6/0.6	113.7	314.3

[2] MVD molecular surface probe size 1.2 Å. 25 cavities each run

Table S3: Statistics from the model building of hNET. The Molpdf, which should be as low as possible, is reported. Furthermore the percentage in the favorable, additionally allowed, generously allowed and disallowed regions are listed. The overall best model with χ1 of Asp75 *gauche* was chosen and is here indicated in italic and bold. The models shaded gray are the ones with χ1 of Asp75 *anti*

hNET model	Molpdf	Ramachandran (%)	Cavity size[3] (Å^3)	Asp75 χ1 (°)
1	372	90.3/7.7/1.6/0.4	108.0	61.6
2	471	90.7/7.7/1.2/0.4	121.9	61.0
3	405	89.7/8.5/1.4/0.4	129.0	197.8
4	1376	89.3/7.4/.1.4/1.8	123.9	60.8
5	535	90.9/7.3/1.0/0.8	134.7	196.3
6	***444***	***89.7/8.1/1.4/0.8***	***131.6***	***59.6***
7	1145	87.7/9.9/1.6/0.8	128.5	60.7
8	500	89.9/7.7/1.6/0.8	136.7	196.8
9	634	87.9/7.5/1.8/1.0	113.2	61.7
10	359	91.1/7.5/0.8/0.6	101.9	316.9
11	1594	90.1/8.5/1.0/0.4	129.0	60.5
12	515	90.1/7.7/1.6/0.6	127.5	195.1
13	541	89.7/7.9/1.8/0.6	116.7	194.0
14	2321	90.1/8.1/1.4/0.4	113.2	61.3
15	650	90.1/6.9/2.2/0.8	146.9	199.8
16	894	89.5/8.3/1.8/0.4	103.4	57.3
17	474	90.3/7.9/1.4/0.4	121.9	61.8
18	569	90.1/7.7/1.6/0.6	105.5	57.1
19	524	90.1/7.1/1.6/1.2	127.5	61.9
20	634	89.9/8.1/1.2/0.8	127.5	59.3

[3] MVD molecular surface probe size 1.2 Å. 25 cavities each run

Table S4: Computed energies, distances and angles for all poses of 5-HT in hSERT. The mean value (Mean) and standard deviation (Stdv) are calculated

Cluster	Method	Scorings Function	Emodel (kcal/mol)	GlideScore (kcal/mol)	Distance Asp98(Oδ)-N^+(Å)
5HT-0	IFD	SPXP	-58.9	-8.1	2.66
5HT-0	IFD	SPXP	-59.3	-7.9	2.75
5HT-0	IFD	SPXP	-54.0	-7.5	2.63
5HT-0	IFD	SPXP	-56.2	-6.6	3.03
5HT-0	IFD	SPXP	-55.4	-6.3	3.07
Mean			**-59.3**	**-8.1**	**2.63**
Stdv			**2.3**	**0.8**	**0.21**
5HT-1	IFD	SPXP	-45.1	-8.2	2.49
5HT-1	IFD	SPXP	-64.5	-8.1	2.96
5HT-1	IFD	SPXP	-57.7	-7.9	2.85
5HT-1	IFD	SPXP	-69.6	-7.9	2.97
5HT-1	IFD	SPXP	-59.1	-7.9	2.75
5HT-1	IFD	SPXP	-61.4	-7.9	2.80
5HT-1	IFD	SPXP	-67.4	-7.8	2.93
5HT-1	IFD	SPXP	-57.1	-7.6	2.55
5HT-1	IFD	SPXP	-56.8	-7.6	4.11
5HT-1	IFD	SPXP	-68.7	-7.6	4.63
5HT-1	IFD	SPXP	-58.5	-7.5	4.81
5HT-1	IFD	SPXP	-62.7	-7.5	3.09
5HT-1	IFD	SPXP	-54.1	-7.5	2.82
5HT-1	IFD	SPXP	-63.5	-7.4	4.01
5HT-1	IFD	SPXP	-57.2	-7.4	3.25
5HT-1	IFD	SPXP	-63.9	-7.3	2.99
5HT-1	IFD	SPXP	-57.9	-7.2	3.06
5HT-1	IFD	SPXP	-46.9	-7.1	4.72
5HT-1	IFD	SPXP	-53.0	-7.1	3.03
5HT-1	IFD	SPXP	-62.2	-6.9	3.16
5HT-1	IFD	SPXP	-59.1	-6.9	3.02
5HT-1	IFD	SPXP	-57.2	-6.9	3.30
5HT-1	IFD	SPXP	-60.6	-6.9	4.56
5HT-1	IFD	SPXP	-53.3	-6.8	4.34
5HT-1	IFD	SPXP	-51.1	-6.8	2.88
5HT-1	IFD	SPXP	-55.0	-6.5	4.52
5HT-1	IFD	SPXP	-42.6	-6.3	4.04
5HT-1	IFD	SPXP	-58.3	-6.2	3.26
5HT-1	IFD	SPXP	-52.3	-6.2	5.98
5HT-1	IFD	SPXP	-50.9	-6.1	3.33
5HT-1	IFD	SPXP	-55.5	-5.5	4.94
5HT-1	IFD	SPXP	-49.7	-5.0	5.04
Mean			**-57.3**	**-7.1**	**3.60**
Stdv			**6.5**	**0.7**	**0.90**
5HT-2	IFD	SPXP	-62.8	-8.8	2.59
5HT-2	IFD	SPXP	-64.1	-8.4	3.22
5HT-2	IFD	SPXP	-56.4	-8.1	2.51
5HT-2	IFD	SPXP	-63.8	-7.9	3.11
5HT-2	IFD	SPXP	-61.7	-7.7	2.97
5HT-2	IFD	SPXP	-56.2	-7.7	2.90

5HT-2	IFD	SPXP	-68.5	-7.6	2.79
5HT-2	IFD	SPXP	-61.0	-7.6	2.55
5HT-2	IFD	SPXP	-57.8	-7.6	2.93
5HT-2	IFD	SPXP	-52.3	-7.6	3.23
5HT-2	IFD	SPXP	-62.7	-7.5	2.89
5HT-2	IFD	SPXP	-61.3	-7.5	3.19
5HT-2	IFD	SPXP	-44.4	-7.4	2.77
5HT-2	IFD	SPXP	-56.3	-7.4	2.92
5HT-2	IFD	SPXP	-54.2	-7.3	2.83
5HT-2	IFD	SPXP	-53.5	-7.3	2.82
5HT-2	IFD	SPXP	-63.9	-7.2	2.78
5HT-2	IFD	SPXP	-61.2	-7.0	2.41
5HT-2	IFD	SPXP	-53.1	-6.3	4.32
5HT-2	IFD	SPXP	-63.9	-6.3	3.30
5HT-2	IFD	SPXP	-50.1	-6.1	4.36
5HT-2	IFD	SPXP	-62.6	-5.2	2.85
Mean			**-58.7**	**-7.3**	**3.01**
Stdv			**5.8**	**0.8**	**0.49**
5HT-3	IFD	SPXP	-64.9	-8.1	2.80
5HT-3	IFD	SPXP	-57.7	-7.7	3.84
5HT-3	IFD	SPXP	-56.9	-7.7	4.03
5HT-3	IFD	SPXP	-58.0	-6.7	3.99
5HT-3	IFD	SPXP	-54.7	-6.2	3.46
Mean			**-58.4**	**-7.3**	**3.62**
Stdv			**3.9**	**0.8**	**0.51**

Table S5: Computed energies, distances and angles for all poses of DA in hDAT. The mean value (mean) and standard deviation (stdv) is calculated

Cluster	Method	Scorings Function	Emodel (kcal/mol)	GlideScore (kcal/mol)	Distance Asp79(Oδ)-N^+(Å)
DA-0	IFD	SPXP	-46.4	-8.9	2.89
DA-0	IFD	SPXP	-47.0	-8.9	2.67
DA-0	IFD	SPXP	-39.8	-8.3	2.80
DA-0	IFD	SPXP	-46.3	-8.3	2.51
DA-0	IFD	SPXP	-51.0	-8.1	2.85
DA-0	IFD	SPXP	-44.6	-8.1	2.68
DA-0	IFD	SPXP	-33.3	-7.7	2.83
DA-0	IFD	SPXP	-50.8	-7.4	2.94
DA-0	IFD	SPXP	-52.7	-7.3	2.89
Mean			**-45.8**	**-8.1**	**2.78**
Stdv			**6.1**	**0.6**	**0.14**
DA-1	IFD	SPXP	-43.2	-9.2	2.64
DA-1	IFD	SPXP	-47.2	-8.9	2.92
DA-1	IFD	SPXP	-50.7	-8.8	2.77
DA-1	IFD	SPXP	-55.1	-8.7	2.61
DA-1	IFD	SPXP	-46.1	-8.7	2.73
DA-1	IFD	SPXP	-51.9	-8.7	2.68
DA-1	IFD	SPXP	-50.4	-8.7	2.76
DA-1	IFD	SPXP	-54.7	-8.7	2.78
DA-1	IFD	SPXP	-48.4	-8.6	2.75
DA-1	IFD	SPXP	-52.7	-8.6	2.70
DA-1	IFD	SPXP	-47.8	-8.6	2.68
DA-1	IFD	SPXP	-51.3	-8.6	2.69
DA-1	IFD	SPXP	-47.1	-8.5	2.70
DA-1	IFD	SPXP	-51.3	-8.5	2.76
DA-1	IFD	SPXP	-45.5	-8.5	2.59
DA-1	IFD	SPXP	-43.4	-8.4	2.71
DA-1	IFD	SPXP	-50.3	-8.4	2.65
DA-1	IFD	SPXP	-46.0	-8.4	3.18
DA-1	IFD	SPXP	-50.1	-8.4	2.74
DA-1	IFD	SPXP	-53.5	-8.4	2.37
DA-1	IFD	SPXP	-45.1	-8.4	2.58
DA-1	IFD	SPXP	-50.0	-8.3	2.57
DA-1	IFD	SPXP	-51.9	-8.3	2.74
DA-1	IFD	SPXP	-48.7	-8.3	2.66
DA-1	IFD	SPXP	-49.2	-8.3	2.67
DA-1	IFD	SPXP	-47.8	-8.2	3.21
DA-1	IFD	SPXP	-51.0	-8.2	2.78
DA-1	IFD	SPXP	-51.5	-8.2	2.60
DA-1	IFD	SPXP	-54.3	-8.1	2.87
DA-1	IFD	SPXP	-48.5	-8.1	3.08
DA-1	IFD	SPXP	-50.5	-8.1	2.64
DA-1	IFD	SPXP	-52.5	-8.1	2.59
DA-1	IFD	SPXP	-46.8	-8.0	2.51
DA-1	IFD	SPXP	-47.7	-7.9	2.63
DA-1	IFD	SPXP	-45.8	-7.9	2.80
DA-1	IFD	SPXP	-45.8	-7.8	2.54
DA-1	IFD	SPXP	-52.0	-7.7	2.87

DA-1	IFD	SPXP	-49.2	-7.7	2.68
DA-1	IFD	SPXP	-50.0	-7.6	2.95
DA-1	IFD	SPXP	-48.0	-7.5	3.38
DA-1	IFD	SPXP	-44.4	-7.3	2.71
DA-1	IFD	SPXP	-51.8	-7.1	3.01
Mean			**-49.3**	**-8.3**	**2.75**
Stdv			**3.0**	**0.4**	**0.20**
DA-2	IFD	SPXP	-45.5	-9.2	2.59
DA-2	IFD	SPXP	-50.0	-9.1	2.64
DA-2	IFD	SPXP	-49.9	-9.1	2.65
DA-2	IFD	SPXP	-49.6	-9.0	2.96
DA-2	IFD	SPXP	-51.5	-9.0	2.48
DA-2	IFD	SPXP	-56.4	-8.9	2.87
DA-2	IFD	SPXP	-43.4	-8.8	2.98
DA-2	IFD	SPXP	-54.2	-8.3	2.58
DA-2	IFD	SPXP	-48.2	-8.1	3.07
DA-2	IFD	SPXP	-52.9	-8.0	3.00
DA-2	IFD	SPXP	-51.2	-7.9	2.82
Mean			**-50.3**	**-8.7**	**2.79**
Stdv			**3.7**	**0.5**	**0.20**
DA-3	IFD	SPXP	-55.3	-9.2	2.74
DA-3	IFD	SPXP	-56.7	-9.1	2.81
DA-3	IFD	SPXP	-46.8	-9.0	2.80
DA-3	IFD	SPXP	-54.2	-9.0	2.77
DA-3	IFD	SPXP	-57.8	-8.6	2.98
DA-3	IFD	SPXP	-50.5	-8.4	2.88
DA-3	IFD	SPXP	-58.0	-8.1	3.09
DA-3	IFD	SPXP	-42.6	-8.1	2.86
DA-3	IFD	SPXP	-50.8	-7.7	2.96
DA-3	IFD	SPXP	-47.5	-7.6	2.88
DA-3	IFD	SPXP	-56.0	-7.6	3.14
DA-3	IFD	SPXP	-48.4	-7.6	3.73
Mean			**-52.1**	**-8.3**	**2.97**
Stdv			**5.0**	**0.6**	**0.27**

Table S6: Computed energies, distances and angles for all poses of NE in hNET. The mean value (mean) and standard deviation (stdv) is calculated

Cluster	Method	Scorings Function	Emodel (kcal/mol)	GlideScore (kcal/mol)	Distance Asp75(Oδ)-N^+(Å)
NE-0	IFD	SPXP	-48.3	-9.2	2.81
NE-0	IFD	SPXP	-52.6	-8.5	2.69
NE-0	IFD	SPXP	-58.3	-8.2	2.84
NE-0	IFD	SPXP	-59.4	-7.5	2.61
NE-0	IFD	SPXP	-51.0	-6.9	4.68
NE-0	IFD	SPXP	-54.1	-6.9	2.69
Mean			**-53.9**	**-7.9**	**3.05**
Stdv			**4.2**	**0.9**	**0.80**
NE-1	IFD	SPXP	-61.0	-9.9	2.64
NE-1	IFD	SPXP	-60.9	-9.5	2.85
NE-1	IFD	SPXP	-61.5	-9.4	2.70
NE-1	IFD	SPXP	-54.8	-9.4	2.91
NE-1	IFD	SPXP	-55.1	-9.3	2.74
NE-1	IFD	SPXP	-58.2	-9.0	2.66
NE-1	IFD	SPXP	-60.2	-9.0	2.60
NE-1	IFD	SPXP	-56.9	-8.9	2.70
NE-1	IFD	SPXP	-58.8	-8.9	2.74
NE-1	IFD	SPXP	-52.6	-8.8	2.77
NE-1	IFD	SPXP	-59.0	-8.6	2.94
NE-1	IFD	SPXP	-63.1	-8.3	2.70
NE-1	IFD	SPXP	-58.7	-8.3	2.57
NE-1	IFD	SPXP	-61.1	-8.3	2.71
NE-1	IFD	SPXP	-54.5	-8.2	2.98
NE-1	IFD	SPXP	-67.9	-8.2	2.50
NE-1	IFD	SPXP	-59.6	-8.1	2.56
NE-1	IFD	SPXP	-68.1	-7.9	2.67
NE-1	IFD	SPXP	-60.4	-7.9	3.07
NE-1	IFD	SPXP	-68.9	-7.9	2.57
NE-1	IFD	SPXP	-56.4	-7.8	2.61
NE-1	IFD	SPXP	-59.1	-7.8	2.57
NE-1	IFD	SPXP	-55.9	-7.7	2.66
NE-1	IFD	SPXP	-56.7	-7.6	2.58
NE-1	IFD	SPXP	-57.1	-7.6	3.50
NE-1	IFD	SPXP	-58.2	-7.1	3.22
Mean			**-59.4**	**-8.4**	**2.76**
Stdv			**4.1**	**0.7**	**0.23**
NE-2	IFD	SPXP	-60.1	-9.8	2.72
NE-2	IFD	SPXP	-62.3	-9.8	2.66
NE-2	IFD	SPXP	-64.0	-9.4	2.74
NE-2	IFD	SPXP	-57.8	-9.2	2.67
NE-2	IFD	SPXP	-60.3	-9.2	2.74
NE-2	IFD	SPXP	-62.5	-9.2	2.54
NE-2	IFD	SPXP	-60.2	-9.0	2.58
NE-2	IFD	SPXP	-58.1	-9.0	2.61
NE-2	IFD	SPXP	-62.3	-9.0	2.50
NE-2	IFD	SPXP	-61.0	-9.0	2.70
NE-2	IFD	SPXP	-59.6	-9.0	2.51

NE-2	IFD	SPXP	-57.3	-8.9	2.74
NE-2	IFD	SPXP	-57.0	-8.9	2.68
NE-2	IFD	SPXP	-56.8	-8.9	2.72
NE-2	IFD	SPXP	-62.1	-8.9	2.84
NE-2	IFD	SPXP	-54.4	-8.7	2.99
NE-2	IFD	SPXP	-59.0	-8.7	2.73
NE-2	IFD	SPXP	-59.1	-8.7	2.72
NE-2	IFD	SPXP	-58.0	-8.7	3.04
NE-2	IFD	SPXP	-59.3	-8.6	2.54
NE-2	IFD	SPXP	-55.9	-8.6	2.72
NE-2	IFD	SPXP	-60.7	-8.6	2.48
NE-2	IFD	SPXP	-65.9	-8.5	2.70
NE-2	IFD	SPXP	-57.3	-8.5	2.58
NE-2	IFD	SPXP	-50.6	-8.5	2.83
NE-2	IFD	SPXP	-59.5	-8.5	3.03
NE-2	IFD	SPXP	-43.8	-8.4	2.68
NE-2	IFD	SPXP	-58.4	-8.4	2.65
NE-2	IFD	SPXP	-66.0	-8.3	2.74
NE-2	IFD	SPXP	-66.9	-8.3	2.70
NE-2	IFD	SPXP	-68.1	-8.3	2.62
NE-2	IFD	SPXP	-64.8	-8.2	2.74
NE-2	IFD	SPXP	-60.7	-8.2	4.10
NE-2	IFD	SPXP	-55.0	-8.2	2.69
NE-2	IFD	SPXP	-55.1	-8.1	2.55
NE-2	IFD	SPXP	-60.3	-8.0	2.64
NE-2	IFD	SPXP	-50.0	-7.9	3.24
NE-2	IFD	SPXP	-62.4	-7.9	2.85
NE-2	IFD	SPXP	-52.8	-7.8	2.67
NE-2	IFD	SPXP	-48.4	-6.9	3.16
Mean			**-58.8**	**-8.6**	**2.76**
Stdv			**5.0**	**0.6**	**0.27**
NE-3	IFD	SPXP	-56.3	-8.8	2.91
NE-3	IFD	SPXP	-51.1	-8.6	3.28
NE-3	IFD	SPXP	-55.9	-8.3	2.81
NE-3	IFD	SPXP	-65.6	-7.4	2.80
NE-3	IFD	SPXP	-46.6	-6.8	2.86
NE-3	IFD	SPXP	-57.2	-6.6	2.80
Mean			**-55.5**	**-7.7**	**2.91**
Stdv			**6.4**	**1.0**	**0.18**