Supplemental Information

CCR5 Is a Therapeutic Target for Recovery

after Stroke and Traumatic Brain Injury

Mary T. Joy, Einor Ben Assayag, Dalia Shabashov-Stone, Sigal Liraz-Zaltsman, Jose Mazzitelli, Marcela Arenas, Nora Abduljawad, Efrat Kliper, Amos D. Korczyn, Nikita S. Thareja, Efrat L. Kesner, Miou Zhou, Shan Huang, Tawnie K. Silva, Noomi Katz, Natan M. Bornstein, Alcino J. Silva, Esther Shohami, and S. Thomas Carmichael

Number of patients	Non-carriers	CCR5-Δ32 heterozygosity	CCR5-Δ32 homozygosity
446 at admission	375 (84.1%)	67 (15%)	4 (0.9%)
396 at 1-year follow-up	328 (82.8%)	64 (16.2%)	4 (1%)

Table S1. Related to Table 1: Genotype data for patient cohorts

	CCR5-Δ32 non-carriers	CCR5-Δ32 carriers	p
N	328	68	
Age, years (SD)	66.7 (9.5)	66.8 (9)	0.093
Male Gender, n (%)	215 (65.5)	37 (54.5)	0.025
Education, years (SD)	13.1 (3.5)	14.9 (4.3)	<0.001
Body-mass index, kg/m^2 (SD)	26.9 (4.2)	27.9 (3.8)	0.064
Ethnicity, Ashkenazi, n (%)	189 (57.6)	61 (89.7)	<0.001
Admission Systolic blood pressure, mmHg (SD)	146.4 (22.8)	151.7 (25.4)	0.087
Current smokers, n (%)	125 (38.1)	30 (44.1)	0.339
Diabetes mellitus, n (%)	83 (25.3)	21 (30.9)	0.329
Dyslipidemia, n (%)	172 (52.4)	37 (54.4)	0.772
Hypertension, n (%)	189 (57.6)	41 (60.3)	0.666
Ischemic heart disease, n (%)	52 (15.9)	12 (17.6)	0.713
Framingham Risk Score for Stroke	11.2 (5.5)	12.4 (6)	0.155
APOE ε4 allele, n (%)	62 (18.9)	8 (11.8)	0.166
Admission NIHSS, (SD)	2.9 (3)	2.0 (0.3)	0.006
Brain MRI parameters			
Not performed MRI	69 (21)	12 (17.6)	0.528
New lesion in MRI, n (%)	157 (60.6)	36 (64.3)	0.749
Infarct type			
Cortical infarct, n (%)	54 (20.8)	18 (32.1)	0.081
Sub-cortical infarct, n (%)	72 (27.8)	12 (21.4)	0.194
Subtentorial infarct, n (%)	28 (10.8)	5 (0.09)	0.571
Ischemic lesions volume, mm^3 (SD)	4119.9 (9945.5)	7382.7 (13969.7)	0.286

Table S2. Related to Table 1: Baseline characteristics at admission

	Model 1			Model 2		
Cognitive domain	β	SE	p	β	SE	p
Global cognitive score (Neurotrax)	0.100	1.761	0.057	-0.270	1.548	**0.029**
Memory score (Neurotrax)	0.108	2.197	**0.040**	0.113	2.123	**0.026**
Executive function score (Neurotrax)	0.046	1.753	0.386	0.049	1.691	0.342
Visuo-spatial score (Neurotrax)	-0.019	2.467	0.722	0.002	2.352	0.973
Verbal function score	0.117	3.141	**0.027**	0.128	3.136	**0.015**
Attention score (Neurotrax)	0.115	1.957	**0.027**	0.103	1.923	**0.045**
MoCA score (Neurotrax)	0.108	0.517	**0.036**	0.084	0.462	0.070

Table S3. Related to Table 1: CCR5-Δ32 allele in relation to cognitive domains 1 year post-stroke/TIA, unadjusted (model 1) and adjusted for age, gender and education (model 2). TIA, transient ischemic attack; MoCA, Montreal Cognitive Assessment. Significant results are shown in bold ($p < 0.05$).

	CCR5-Δ32 non-carriers	CCR5-Δ32 carriers	p
Functional scores 3 months post-stroke			
N	314	52	
SIS (strength) (SD)	76.7 (27.9)	85.1 (23.7)	0.024
SIS (hand function) (SD)	81.1 (28.3)	87.3 (20.1)	0.061
SIS (ADL) (SD)	84.4 (22.1)	92.4 (14.9)	0.001
SIS (mobility) (SD)	79 (23.9)	85.3 (18.7)	0.034
SIS (communication) (SD)	92.6 (15.6)	96.7 (6.2)	0.001
SIS (emotion) (SD)	78.3 (24)	82.2 (20.3)	0.277
SIS (participation) (SD)	72.5 (30.8)	81.8 (24.9)	0.019
SIS-16 (physical)	80.1 (23.3)	86.2 (21.2)	0.081
SIS (memory and thinking) (SD)	85.9 (19.5)	92.2 (16)	0.013
FIM (total) (SD)	119.8 (12)	122.4 (735)	0.042
RNL (indoor mobility)	1.2 (0.6)	1.0 (0.2)	0.025
RNL (community mobility)	1.9 (1.4)	1.6 (1.2)	0.174
RNL (distance mobility)	2.1 (1.5)	1.6 (1.2)	0.047
RNL (daily living/self-care)	1.2 (1.3)	1.7 (1.1)	0.197
RNL (productivity)	2.1 (1.4)	1.9 (1.4)	0.411
RNL (recreation activities)	2.7 (1.6)	2.0 (1.3)	0.004
RNL (social activities)	2.0 (1.3)	1.6 (1)	0.031
RNL (family roles)	1.8 (1.2)	1.7 (1.1)	0.709
RNL (personal relationship)	1.4 (0.8)	1.5 (0.8)	0.475
RNL (presentation of self to others)	1.5 (0.9)	1.5 (0.9)	0.904
RNL (general coping skills)	1.9 (1.2)	1.7 (1.1)	0.215
RNL Total score (SD)	17.0 (12.1)	14.3 (11.1)	0.136
SIS (memory and thinking) (SD)	31.9 (4.9)	32.6 (3.0)	0.114
Functional scores 6 months post-stroke			
N	338	63	
SIS (strength) (SD)	17.1 (4.3)	18.1 (2.8)	0.013
SIS (hand function) (SD)	22 (5.7)	23.9 (2.9)	<0.001
SIS (ADL) (SD)	45.7 (8.6)	48.2 (4.8)	0.002
SIS (mobility) (SD)	39.1 (7.8)	41.1 (5.2)	0.011
SIS (communication) (SD)	33.5 (3.2)	33.7 (1.9)	0.776
SIS (emotion) (SD)	31.2 (4.6)	31.3 (2.4)	0.428
SIS (participation) (SD)	35.6 (7.5)	38.3 (3.5)	<0.001
SIS-16 (physical)	80.9 (21.5)	87.5 (15.0)	0.004
SIS (memory and thinking) (SD)	31.9 (4.9)	32.6 (3.0)	0.114
RNL (indoor mobility)	1.3 (0.8)	1.0 (0.2)	<0.001
RNL (community mobility)	1.6)1.2)	1.4 (1.1)	0.227
RNL (distance mobility)	1.7 (1.3)	1.4 (1.0)	0.056
RNL (daily living/self-care)	1.6 (1.1)	1.5 (0.9)	0.525
RNL (productivity)	1.7 (1.2)	1.5 (1)	0.167
RNL (recreation activities)	2.6 (1.7)	2.2 (1.6)	0.118
RNL (social activities)	1.8 (1.2)	1.4 (0.8)	0.002

RNL (family roles)	1.5 (1.0(	1.4 (0.9)	0.500
RNL (personal relationship)	1.4 (0.8)	1.3 (0.6)	0.444
RNL (presentation of self to others)	1.4 (0.9)	1.4 (0.9)	0.917
RNL (general coping skills)	1.8 (1.2)	1.4 (0.8)	0.007
RNL Total score (SD)	18.2 (8.1)	15.9 (6.6)	0.067
DEX (subjective) (SD)	10 (9.6)	7.4 (6.4)	0.012
DEX (family/caregiver) (SD)	16.5 (13.0)	16 (7)	0.944
Functional scores 1 year post-stroke			
N	328	68	
SIS (strength) (SD)	17.2 (4.1)	18.5 (3.1)	0.004
SIS (hand function) (SD)	22.2 (5.6)	23.9 (3.2)	0.001
SIS (ADL) (SD)	46.3 (8.6)	47.5 (6.0)	0.178
SIS (mobility) (SD)	40.1 (6.8)	41.2 (5.4)	0.224
SIS (communication) (SD)	33.5 (3.0)	34.1 (1.9)	0.069
SIS (emotion) (SD)	31.4 (3.4)	32 (3.9)	0.205
SIS (participation) (SD)	36.4 (7.1)	38.6 (3.6)	0.001
SIS-16 (physical)	82.5 (20.5)	89.9 (15.0)	0.001
SIS (memory and thinking) (SD)	27.7 (4.9)	28.8 (1.8)	0.003
RNL (indoor mobility)	1.2 (0.6)	1.2 (0.5)	0.750
RNL (community mobility)	1.4 (1.0)	1.3 (0.7)	0.207
RNL (distance mobility)	1.5 (1.1)	1.5 (1.1)	0.768
RNL (daily living/self-care)	1.6 (1.1)	1.5 (0.8)	0.325
RNL (productivity)	1.6 (1.2)	1.4 (0.9)	0.117
RNL (recreation activities)	2.5 (1.6)	2.0 (1.4)	0.019
RNL (social activities)	1.7 (1.2)	1.3 (0.8)	0.004
RNL (family roles)	1.5 (1.1)	1.3 (0.8)	0.149
RNL (personal relationship)	1.4 (0.9)	1.3 (0.7)	0.300
RNL (presentation of self to others)	1.4 (0.9)	1.4 (0.9)	0.872
RNL (general coping skills)	1.6 (1.1)	1.5 (0.9)	0.350
RNL Total score (SD)	17.1 (7.7)	15.6 (6.6)	0.206
DEX (subjective) (SD)	10.3 (10.5)	7 (8.1)	0.012
DEX (family/caregiver) (SD)	19.1 (15.3)	12.1 (15.1)	0.249
Functional scores 2 years post-stroke			
N	285	49	
SIS (strength) (SD)	17.2 (4.1)	17.3 ((4.5)	0.887
SIS (hand function) (SD)	22.3 (5.3)	22.5 (5.5)	0.785
SIS (ADL) (SD)	46.9 (7.0)	47.1 (7.5)	0.808
SIS (mobility) (SD)	39.8 (6.6)	40.9 (6.7)	0.256
SIS (communication) (SD)	33.7 (2.5)	33.5 (2.2)	0.486
SIS (emotion) (SD)	30.9 (3.7)	31.4 (4.1)	0.402
SIS (participation) (SD)	36.4 (7.3)	38.6 (3.6)	0.703
SIS-16 (physical)	83.5 (19.9)	87.7 (17.6)	0.168
SIS (memory and thinking) (SD)	31.4 (5.2)	32.3 (3.7)	0.148
RNL (indoor mobility)	1.1 (0.5)	1.1 (0.5)	0.749
RNL (community mobility)	1.4 (1.0)	1.5 (1.0)	0.840

RNL (distance mobility)	1.5 (1.2)	1.6 (1.3)	0.832
RNL (daily living/self-care)	1.5 (1.0)	1.5 (1.0)	0.729
RNL (productivity)	1.6 (1.1)	1.7 (1.3)	0.613
RNL (recreation activities)	2.4 (1.6)	2.1 (1.5)	0.214
RNL (social activities)	1.7 (1.2)	1.4 (0.9)	0.020
RNL (family roles)	1.4 (1.0)	1.1 (0.4)	<0.001
RNL (personal relationship)	1.4 (0.8)	1.2 (0.7)	0.277
RNL (presentation of self to others)	1.3 (0.8)	1.2 (0.6)	0.582
RNL (general coping skills)	1.6 (1.0)	1.4 (0.8)	0.075
RNL Total score (SD)	17.0 (7.5)	15.6 (6.6)	0.423

Table S4. Related to Table 1: Functional outcomes in CCR5-Δ32 carriers vs non-carriers. SD, standard deviation; SIS, stroke impact scale; DEX, BADS Dysexecutive Questionnaire; RNL, Reintegration to Normal Living Index. Entries are mean (SD) or n and %, as indicated. Significant results are shown in bold (p<0.05).