Supplementary Online Content

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eTable 1. Sex-Specific Major Depression by Number of Stressful Life Events vs No Life Stressful Life Events

Source	No. of Stressful Life Events for Male Participants			No. of Stressful Life Events for Female Participants		
	1	2	≥3	1	2	≥3
Eley et al,[18] 2004	2.20 (0.99,4.90)	1.36 (0.49,3.74)	1.52 (0.41,5.54)	1.40 (0.67,2.99)	1.12 (0.44-2.80)	1.01 (0.43,2.41)
Gillespie et al,[19] 2005	1.80 (1.01-3.19)	0.60 (0.14-2.59)	2.22 (0.88-5.63)	1.35 (0.86-2.10)	1.71 (0.89-3.27)	3.34 (1.60-6.98)
Grabe et al,[20] 2005	2.13 (0.79-5.72)	6.42 (2.10-19.59)	8.66 (3.37-22.20)	5.51 (2.37-12.83)	9.09 (3.83-21.56)	14.08 (6.17-32.13)
Surtees et al,[25] 2006	1.87 (1.02-3.40)	6.48 (3.75-11.20)	8.88 (5.19-15.20)	1.80 (1.09-2.97)	2.85 (1.72-4.71)	6.66 (4.21-10.53
Wilhelm et al,[27] 2006	1.22 (0.24-6.11)	0.61 (0.09-4.02)	2.44 (0.41-14.75)	0.25 (0.06-0.95)	1.54 (0.49-4.86)	1.77 (0.48-6.56)
Taylor et al,[26] 2006	0.69 (0.13-3.75)	---	0.75 (0.11,5.11)	0.36 (0.05-2.34)	0.38 (0.06-2.54)	0.54 (0.10-2.94)
Chipman et al,[16] 2007	1.24 (0.76-2.03)	1.16 (0.67,2.00)	2.13 (1.32-3.42)	1.25 (0.82-1.90)	1.57 (0.98,2.52)	3.09 (1.99-4.78)
Cervilla et al,[15] 2007	1.56 (0.16-15.47)	5.22 (0.60-45.20)	13.85 (1.66-115.84)	0.74 (0.41-1.33)	2.03 (1.14-3.61)	2.71 (1.47-5.02)
Middeldorp et al,[29] 2007	0.40 (0.04-3.75)	0.81 (0.08-7.68)	3.63 (0.57-23.09)	0.62 (0.29-1.33)	1.56 (0.66-3.68)	0.34 (0.04-2.80)
Chorbov et al,[17] 2007	---	---	---	1.34 (0.51,3.52)	3.27 (1.05,10.19)	11.43 (2.14,61.01)
All*	**1.58 (1.21-2.08)**	**1.95 (0.88-4.32)**	**3.49 (1.87-6.51)**	**1.19 (0.80-1.75)**	**2.06 (1.42-2.98)**	**3.00 (1.73-5.21)**

*Data are odds ratio (95% confidence intervals).

eTable 2. Frequency of *S* Allele by Number of Stressful Life Events Among Those With and Without Depression

Depression Status	No. of Participants	No. of Stressful Life Events								β (SE)*
		0		1		2		≥3		
		No. of Participants	Allele Frequency (SE)†	No. of Participants	Allele Frequency (SE)†	No. of Participants	Allele Frequency (SE)†	No. of Participants	Allele Frequency (SE)†	
Caspi et al,10 2003‡										
Without	713	237	0.454 (0.023)	184	0.424 (0.026)	137	0.426 (0.030)	155	0.458 (0.028)	−0.011 (0.047)
With	133	26	0.442 (0.069)	27	0.333 (0.064)	24	0.354 (0.069)	55	0.609 (0.047)	0.290 (0.108)‖
δ§			−0.011 (0.073)		−0.091 (0.069)		−0.072 (0.075)		0.152 (0.055)‖	0.301 (0.118)‖
Eley et al,18 2004										
Without	241	69	0.572 (0.042)	34	0.515 (0.061)	21	0.643 (0.074)	117	0.618 (0.034)	0.080 (0.115)
With	187	74	0.554 (0.041)	61	0.516 (0.045)	27	0.500 (0.068)	25	0.560 (0.070)	−0.022 (0.100)
δ§			−0.018 (0.059)		0.002 (0.076)		−0.143 (0.100)		−0.058 (0.109)	−0.102 (0.152)
Gillespie et al,19 2005										
Without	2071	1373	0.427 (0.009)	477	0.416 (0.016)	142	0.465 (0.030)	79	0.386 (0.039)	−0.008 (0.040)
With	182	100	0.450 (0.035)	52	0.490 (0.049)	14	0.393 (0.092)	16	0.531 (0.088)	0.064 (0.111)
δ§			0.023 (0.036)		0.074 (0.052)		−0.072 (0.097)		0.145 (0.096)	0.072 (0.118)
Grabe et al,20 2005										
Without	838	327	0.376 (0.019)	255	0.406 (0.022)	113	0.385 (0.032)	143	0.444 (0.029)	0.078 (0.045)
With	161	14	0.536 (0.094)	42	0.452 (0.054)	36	0.375 (0.057)	69	0.362 (0.041)	−0.213 (0.112)
δ§			0.160 (0.096)		0.046 (0.058)		−0.010 (0.066)		−0.082 (0.050)	−0.291 (0.121)‖
Surtees et al,25 2006										
Without	3762	1657	0.436 (0.009)	1043	0.412 (0.011)	586	0.430 (0.014)	476	0.410 (0.016)	−0.029 (0.022)
With	298	50	0.490 (0.050)	59	0.398 (0.045)	76	0.408 (0.040)	113	0.403 (0.033)	−0.088 (0.075)
δ§			0.054 (0.051)		−0.014 (0.046)		−0.022 (0.042)		−0.007 (0.036)	−0.059 (0.078)
Wilhelm et al,27 2006										
Without	74	24	0.583 (0.071)	25	0.420 (0.070)	16	0.250 (0.077)	9	0.500 (0.118)	−0.303 (0.170)
With	53	17	0.441 (0.085)	8	0.313 (0.116)	15	0.467 (0.091)	13	0.615 (0.095)	0.232 (.168)
δ§			−0.142 (0.111)		−0.108 (0.135)		0.217 (0.119)		0.115 (0.152)	0.535 (0.239)‖
Taylor et al,26 2006										
Without	90	22	0.568 (0.075)	27	0.500 (0.068)	19	0.421 (0.080)	22	0.500 (0.075)	−0.109 (0.135)
With	20	8	0.438 (0.124)	5	0.700 (0.145)	2	1.000 (−−−)	5	0.600 (0.155)	0.311 (0.280)
δ§			−0.131 (0.145)		0.200 (0.160)		0.579 (0.263)‖		0.100 (0.172)	0.420 (0.311)
Chipman et al,16 2007										
Without	1508	581	0.431 (0.015)	421	0.426 (0.017)	267	0.446 (0.022)	239	0.448 (0.023)	0.025 (0.034)
With	336	94	0.383 (0.035)	85	0.471 (0.038)	59	0.466 (0.046)	98	0.480 (0.036)	0.116 (0.066)
δ§			−0.048 (0.038)		0.044 (0.042)		0.020 (0.051)		0.032 (0.042)	0.091 (0.074)
Cervilla et al,15 2007										
Without	598	162	0.485 (0.028)	236	0.483 (0.023)	124	0.488 (0.032)	76	0.500 (0.041)	0.018 (0.059)
With	137	28	0.500 (0.067)	29	0.690 (0.061)	41	0.537 (0.055)	39	0.372 (0.055)	−0.242 (0.112)‖
δ§			0.015 (0.072)		0.207 (0.065)‖		0.049 (0.064)		−0.128 (0.068)	−0.260 (0.127)‖
Middeldorp et al,29 2007										
Without	309	154	0.458 (0.028)	97	0.392 (0.035)	40	0.350 (0.053)	18	0.361 (0.080)	−0.186 (0.094)‖
With	58	32	0.422 (0.062)	12	0.583 (0.101)	11	0.455 (0.106)	3	0.333 (0.192)	0.028 (0.198)

δ§			−0.036 (0.068)		0.192 (0.107)		0.105 (0.112)		−0.028 (0.208)	0.214 (0.219)
Chorbov et al,17 2007										
Without	81	49	0.429 (0.050)	22	0.432 (0.075)	8	0.500 (0.125)	2	0.500 (0.250)	0.102 (0.205)
With	39	15	0.367 (0.088)	9	0.278 (0.106)	8	0.500 (0.125)	7	0.214 (0.110)	−0.083 (0.212)
δ§			−0.062 (0.101)		−0.154 (0.129)		0.000 (0.177)		−0.286 (0.273)	−0.185 (0.295)
Kim et al,30 2007										
Without	635	193	0.671 (0.024)	245	0.696 (0.021)	155	0.735 (0.025)	42	0.643 (0.052)	0.061 (0.068)
With	97	13	0.615 (0.095)	36	0.708 (0.054)	29	0.759 (0.056)	19	0.763 (0.069)	0.231 (0.171)
δ§			−0.056 (0.098)		0.012 (0.057)		0.023 (0.062)		0.120 (0.087)	0.170 (0.184)
All										
Without	10 891									−0.003 (0.014)
With	1701									−0.004 (0.034)
δ§			−0.004 (0.018)		0.045 (0.020)§		0.009 (0.022)		−0.006 (0.021)	−0.001 (0.037)

*From logistic regression analysis of frequency of *S* alleles on number of stressful life events.

†Frequency of S Allele = Proportion of individuals who are SS plus one-half the proportion who are SL.

‡Estimated from Figure 3 (Caspi et al[10]) assuming Hardy Weinberg proportions.

§Difference in frequency of *S* alleles between those with and without depression by number of stressful life events.

‖$P<.05$.

eTable 3. Sex-Specific Frequency of *5-HTTLPR S* Allele for Participants With and Without Depression and Allele Frequency Difference (Delta) by Number of SLEs, and Logistic Regression of Allele Frequency on Number of SLEs (β) (* $P<.05$)

	Male Sex					Female Sex				
	No. of Stressful Life Events				β (SE)	No. of Stressful Life Events				β (SE)
STUDY	**0**	**1**	**2**	**≥3**		**0**	**1**	**2**	**≥3**	
Eley et al,[18] 2004										
Without	0.600 (0.055)	0.526 (0.081)	0.583 (0.101)	0.667 (0.136)	0.020 (0.169)	0.534 (0.065)	0.500 (0.091)	0.444 (0.106)	0.591 (0.105)	0.144 (0.160)
With	0.636 (0.073)	0.543 (0.073)	0.611 (0.115)	0.700 (0.145)	0.025 (0.203)	0.519 (0.049)	0.500 (0.057)	0.444 (0.083)	0.525 (0.079)	−0.027 (0.116)
δ§	0.036 (0.091)	0.017 (0.109)	0.028 (0.153)	0.033 (0.199)	0.005 (0.264)	−0.015 (0.082)	0.000 (0.108)	−0.278 (0.134)*	−0.066 (0.131)	−0.171 (0.198)
Gillespie et al,[19] 2005										
Without	0.412 (0.016)	0.414 (0.027)	0.510 (0.051)	0.397 (0.055)	0.046 (0.063)	0.435 (0.012)	0.417 (0.020)	0.441 (0.036)	0.375 (0.054)	−0.043 (0.052)
With	0.424 (0.061)	0.548 (0.077)	0.500 (0.250)	0.500 (0.144)	0.154 (0.195)	0.463 (0.043)	0.452 (0.063)	0.375 (0.099)	0.550 (0.111)	0.020 (0.136)
δ§	0.012 (0.063)	0.133 (0.081)	−0.010 (0.255)	0.103 (0.155)	0.108 (0.205)	0.028 (0.045)	0.034 (0.066)	−0.066 (0.105)	0.175 (0.124)	0.063 (0.146)
Grabe et al,[20] 2005										
Without	0.377 (0.032)	0.437 (0.038)	0.381 (0.075)	0.446 (0.058)	0.085 (0.085)	0.376 (0.024)	0.390 (0.027)	0.386 (0.036)	0.443 (0.034)	0.080 (0.054)
With	0.571 (0.132)	0.318 (0.099)	0.250 (0.108)	0.316 (0.075)	−0.265 (0.197)	0.500 (0.134)	0.500 (0.064)	0.411 (0.066)	0.380 (0.049)	−0.212 (0.138)
δ§	0.194 (0.136)	−0.119 (0.106)	−0.131 (0.132)	−0.130 (0.095)	−0.350 (0.215)	0.124 (0.136)	0.110 (0.069)	0.025 (0.075)	−0.063 (0.059)	−0.292 (0.148)*
Surtees et al,[25] 2006										
Without	0.439 (0.011)	0.412 (0.015)	0.432 (0.021)	0.417 (0.023)	−0.029 (0.031)	0.431 (0.013)	0.412 (0.016)	0.429 (0.020)	0.403 (0.022)	−0.028 (0.032)
With	0.476 (0.077)	0.413 (0.073)	0.397 (0.055)	0.378 (0.051)	−0.122 (0.128)	0.500 (0.066)	0.389 (0.057)	0.419 (0.057)	0.419 (0.042)	−0.065 (0.097)
δ§	0.037 (0.078)	0.001 (0.074)	−0.034 (0.059)	−0.039 (0.056)	−0.093 (0.122)	0.069 (0.067)	−0.024 (0.060)	−0.010 (0.061)	0.016 (0.048)	−0.037 (0.102)
Wilhelm et al,[27] 2006										
Without	0.591 (0.105)	0.500 (0.144)	0.417 (0.142)	0.667 (0.192)	−0.075 (0.264)	0.577 (0.097)	0.395 (0.079)	0.150 (0.080)	0.417 (0.142)	−0.443 (0.230)
With	0.333 (0.136)	0.375 (0.171)	0.750 (0.217)	0.750 (0.153)	0.658 (0.322)*	0.500 (0.107)	0.250 (0.153)	0.423 (0.097)	0.556 (0.117)	0.067 (0.203)
δ§	−0.258 (0.172)	−0.125 (0.224)	0.333 (0.259)	0.083 (0.246)	0.733 (0.416)	−0.077 (0.144)	−0.145 (0.172)	0.273 (0.126)*	0.139 (0.184)	0.510 (0.307)
Taylor et al,[26] 2006 δ§										
Without	0.542 (0.102)	0.423 (0.097)	0.333 (0.136)	0.563 (0.124)	−0.021 (0.206)	0.600 (0.110)	0.571 (0.094)	0.462 (0.098)	0.464 (0.094)	−0.209 (0.185)
With	0.375 (0.171)	0.667 (0.192)	–––––	0.750 (0.217)	0.563 (0.447)	0.500 (0.177)	0.750 (0.217)	10.000 (–––)	0.500 (0.204)	0.120 (0.364)
δ§	−0.167 (0.199)	0.244 (0.215)	–––––	0.188 (0.250)	0.584 (0.520)	−0.100 (0.208)	0.179 (0.236)	0.538 (0.279)	0.036 (0.225)	0.329 (0.408)
Chipman et al,[16] 2007										
Without	0.426 (0.022)	0.441 (0.026)	0.445 (0.030)	0.445 (0.030)	0.027 (0.047)	0.436 (0.020)	0.415 (0.023)	0.447 (0.031)	0.451 (0.035)	0.023 (0.049)
With	0.350 (0.053)	0.457 (0.060)	0.333 (0.068)	0.534 (0.053)	0.202 (0.101)*	0.407 (0.047)	0.480 (0.050)	0.557 (0.059)	0.435 (0.048)	0.053 (0.087)
δ§	−0.076 (0.058)	0.017 (0.065)	−0.112 (0.074)	0.089 (0.061)	0.175 (0.111)	−0.028 (0.051)	0.065 (0.055)	0.111 (0.067)	−0.016 (,059)	0.030 (0.100)
Cervilla et al,[15] 2007										
Without	0.513 (0.056)	0.448 (0.040)	0.467 (0.052)	0.442 (0.069)	−0.07 (0.108)	0.475 (0.032)	0.500 (0.028)	0.500 (0.040)	0.530 (0.050)	0.063 (0.072)
With	1.000 (–––)	1.000 (–––)	0.417 (0.142)	0.389 (0.115)	−10.18 (0.494)*	0.481 (0.068)	0.654 (0.066)	0.557 (0.059)	0.367 (0.062)	−0.179 (0.199)
δ§	0.487 (0.358)	0.552 (0.208)*	−0.051 (0.152)	−0.053 (0.134)	−10.12 (0.506)*	0.006 (0.075)	0.154 (0.072)*	0.057 (0.072)	−0.163 (0.080)	−0.242 (0.212)
Middeldorp et al,[29] 2007										
Without	0.422 (0.046)	0.458 (0.059)	0.306 (0.077)	0.375 (0.121)	−0.126 (0.143)	0.479 (0.036)	0.352 (0.043)	0.386 (0.073)	0.350 (0.107)	−0.230 (0.124)
With	0.500 (0.177)	0.500 (0.353)	0.500 (0.353)	0.250 (0.217)	−0.305 (0.414)	0.411 (0.066)	0.591 (0.105)	0.450 (0.111)	0.500 (0.354)	0.148 (0.234)
δ§	0.078 (0.182)	0.042 (0.358)	0.194 (0.362)	−0.125 (0.248)	−0.179 (0.438)	−0.068 (0.075)	0.238 (0.113)*	0.064 (0.133)	0.150 (0.369)	0.378 (0.265)
Chorbov et al,[17]										

2007										
Without	–––	–––	–––	–––	–––	0.429 (0.050)	0.432 (0.075)	0.500 (0.125)	0.500 (0.250)	0.102 (0.205)
With	–––	–––	–––	–––	–––	0.367 (0.088)	0.278 (0.106)	0.500 (0.125)	0.214 (0.110)	−0.083 (0.212)
δ§	–––	–––	–––	–––	–––	−0.062 (0.101)	−0.154 (0.129)	0.000 (0.177)	−0.286 (0.273)	−0.185 (0.295)
All										
Without	–––	–––	–––	–––	**−0.004 (0.022)**	–––	–––	–––	–––	**−0.006 (0.020)**
With	–––	–––	–––	–––	**0.041 (0.061)**	–––	–––	–––	–––	**−0.025 (0.044)**
δ§	**−0.006 (0.032)**	**0.038 (0.035)**	**−0.050 (0.039)**	**0.002 (0.034)**	**0.045 (0.065)**	**0.000 (,023)**	**0.055 (0.026)***	**0.037 (0.029)**	**−0.023 (0.027)**	**−0.019 (0.048)**

§δ represents the difference in frequency of *S* allele or regression coefficients.