Chapter 6: Supplemental materials

Non-REM sleep in major depressive disorder

Table S1

Sleep architecture statistical tests

	Dataset A	Dataset B		
	Medicated vs. controls	Unmedicated vs. controls	Unmedicated vs. medicated	Medicated vs. controls
N1[%]	**95% CI [2.50%, 8.32%], t(63.93) = 3.71, p <.001, BF_{10} = 68.92**	95% CI [-2.7%, 3.02%], t(74.14) = 0.11, p =.913, BF_{10} = 0.24	**95% CI [0.95%, 5.89%], t(37) = 2.8, p =.008, BF_{10} = 1.99**	**95% CI [0.71%, 6.43%], t(74.13) = 2.49, p =.015, BF_{10} = 3.3**
N2 [%]	95% CI [-0.53%, 8.74%], t(73.74) = 1.77, p =.082, BF_{10} = 0.89	95% CI [-5.2%, 1.39%], t(74.87) = -1.15, p =.254, BF_{10} = 0.42	**95% CI [1.03%, 6.25%], t(37) = 2.83, p =.008, BF_{10} = 1.11**	95% CI [-1.94%, 5.42%], t(69.7) = 0.94, p =.35, BF_{10} = 0.35
SWS [%]	95% CI [-7.23%, 1.19%], t(74.77) = -1.43, p =.157, BF_{10} = 0.56	95% CI [-4.99%, 2.02%], t(74.68) = 0.84, p =.402, BF_{10} = 0.32	95% CI [-3.28%, 0.32%], t(37) = 1.67, p =.103, BF_{10} = 0.32	95% CI [-6.4%, 0.47%], t(75.29) = 1.72, p =.09, BF_{10} = 0.84
Non-REM [%]	95% CI [-3.4%, 5.57%], t(68.65) = 0.48, p =.631, BF_{10} = 0.26	95% CI [-7.21%, 0.43%], t(64.83) = -1.77, p =.081, BF_{10} = 0.93	95% CI [-0.88%, 5.2%], t(37) = 1.44, p =.158, BF_{10} = 0.35	95% CI [-5.16%, 2.7%], t(63.32) = -0.62, p =.534, BF_{10} = 0.28
REM [%]	**95% CI [-7.58%, -1.14%], t(63.70) = -2.71, p = .009, BF_{10} = 5.21**	95% CI [-2.36%, 2.82%], t(75.90) = -0.18, p = .862, BF_{10} = 0.24	**95% CI [-6.88%, -2.35%], t(37) = -4.39, p < .001, BF_{10} = 31.99**	**95% CI [-7.65%, -2.23%], t(74.88) = -3.63, p = .001, BF_{10} = 54.67**
WASO [%]	95% CI [-5.55%, 0.43%], t(72.24) = 1.71, p =.092, BF_{10} = 0.82	**95% CI [0.94%, 6.07%], t(51.64) = 2.74, p =.008, BF_{10} = 6.26**	95% CI [-3.16%, 1.48%], t(37) = -0.73, p =.468, BF_{10} = 0.27	**95% CI [0.45%, 4.88%], t(57.12) = 2.41, p =.019, BF_{10} = 2.94**
TST [min]	95% CI [-9.72min, 12.62min], t(75.71) = 0.26, p =.797, BF_{10} = 0.24	95% CI [-13.74min, 6.42min], t(52.24) = -0.73, p =.47, BF_{10} = 0.3	95% CI [-8.82min, 9.88min], t(37) = 0.11, p =.91, BF_{10} = 0.24	95% CI [-9.51min, 3.25min], t(74.14) = -0.98, p =.331, BF_{10} = 0.36
Sleep onset [min]	95% CI [-7.79min, 5.82min], t(74.05) = 0.29, p =.774, BF_{10} = 0.24	95% CI [-2.17min, 18.92min], t(44.08) = 1.6, p =.117, BF_{10} = 0.74	95% CI [-13.97min, 7.74min], t(37) = 0.58, p =.564, BF_{10} = 0.27	95% CI [-0.17min, 10.7min], t(66.5) = 1.93, p =.058, BF_{10} = 1.19
SWS onset [min]	95% CI [-1.25min, 21.5min], t(65.03) = 1.78, p =.08, BF_{10} = 0.91	95% CI [-0.49min, 17.17min], t(45.53) = 1.9, p =.064, BF_{10} = 1.18	95% CI [-9.95min, 9.12min], t(36) = 0.09, p =.93, BF_{10} = 0.24	95% CI [-0.35min, 15.48min], t(46.58) = 1.92, p =.061, BF_{10} = 1.26
REM onset [min]	**95% CI [66.40min, 139.97min], t(45.48) = 5.65, p <.001, BF_{10} > 100**	95% CI [-5.82min, 37.52min], t(62.64) = 1.46, p =.149, BF_{10} = 0.6	**95% CI [36.56min, 101.67min], t(37) = 4.3, p < .001, BF_{10} > 100**	**95% CI [53.2min, 116.72min], t(48.16) = 5.38, p < .001, BF_{10} > 100**

Note. Non-REM is defined as the combination of N2 and SWS without N1. Statistical values represent a 95% percent confidence interval of the mean, a t-statisic and corresponding p-value (alpha = 0.05). In addition, Bayes factors are reported, where BF_{10} <= 1 quantifies relative evidence in favor of the null hypothesis (H0), while a BF_{10} > 1 quantifies relative evidence for the alternative hypothesis (H1). BF_{10} values can be interpreted as either anecdotal (1-3), moderate (3-10), strong (10-30), very strong (30-100) or extreme (>100) evidence for H1.

Table S1.

Sleep architecture statistical tests – cont.

	Dataset C		
	Medicated 7d vs. controls	Medicated 7d vs. Medicated 28d	Medicated 28d vs. controls
N1[%]	**95% CI [-1.38%, 6.87%], $t(42.89) = 3.03$, $p = .004$, $BF_{10} = 9.14$**	95% CI [-2.48%, 3.87%], $t(29) = 0.45$, $p = .656$, $BF_{10} = 0.28$	**95% CI [1.69%, 7.96%], $t(37.45) = 3.11$, $p = .003$, $BF_{10} = 7.95$**
N2 [%]	95% CI [-4.39%, 6.41%], $t(52.08) = 0.38$, $p = .709$, $BF_{10} = 0.28$	95% CI [-6.08%, 4.57%], $t(29) = -0.29$, $p = .775$, $BF_{10} = 0.27$	95% CI [-4.38%, 4.9%], $t(55.95) = 0.11$, $p = .911$, $BF_{10} = 0.2$
SWS [%]	95% CI [-6.48%, 2.37%], $t(54.74) = 0.93$, $p = .357$, $BF_{10} = 0.38$	95% CI [-4.4%, 5.48%], $t(29) = 0.22$, $p = .826$, $BF_{10} = 0.27$	95% CI [-6.1%, 3.07%], $t(53.7) = 0.66$, $p = .51$, $BF_{10} = 0.24$
Non-REM [%]	95% CI [-5.25%, 3.17%], $t(54.42) = -0.5$, $p = .622$, $BF_{10} = 0.29$	95% CI [-5.03%, 4.61%], $t(29) = -0.09$, $p = .928$, $BF_{10} = 0.26$	95% CI [-5.25%, 3.17%], $t(54.42) = -0.5$, $p = .622$, $BF_{10} = 0.23$
REM [%]	**95% CI [-8.59%, 1.9%], $t(46.82) = -3.16$, $p = .003$, $BF_{10} = 12.43$**	95% CI [-2.91%, 4.89%], $t(29) = -0.52$, $p = .608$, $BF_{10} = 0.29$	**95% CI [-8.59%, -1.9%], $t(46.82) = -3.16$, $p = .003$, $BF_{10} = 2.66$**
WASO [%]	95% CI [-1.48%, 5.13%], $t(55.44) = 1.1$, $p = .274$, $BF_{10} = 0.44$	95% CI [-5.04%, 1.41%], $t(29) = -1.15$, $p = .26$, $BF_{10} = 0.49$	95% CI [-1.48%, 5.13%], $t(55.44) = 1.1$, $p = .274$, $BF_{10} = 0.2$
TST [min]	95% CI [-12.3min, 6.25min], $t(51.46) = -0.66$, $p = .515$, $BF_{10} = 0.32$	95% CI [-5.34min, 9.54min], $t(29) = 0.58$, $p = .568$, $BF_{10} = 0.3$	95% CI [-12.3min, 6.25min], $t(51.46) = -0.66$, $p = .515$, $BF_{10} = 0.2$
Sleep onset [min]	**95% CI [0.23min, 12.01min], $t(44.64) = 2.09$, $p = .042$, $BF_{10} = 1.5$**	95% CI [-8.09min, 5.12min], $t(29) = 0.46$, $p = .65$, $BF_{10} = 0.28$	**95% CI [0.23min, 12.01min], $t(44.64) = 2.09$, $p = .042$, $BF_{10} = 0.57$**
SWS onset [min]	95% CI [-3.45min, 13.62min], $t(49.73) = 1.2$, $p = .237$, $BF_{10} = 0.46$	95% CI [-12.69min, 3.86min], $t(28) = 1.09$, $p = .28$, $BF_{10} = 0.42$	95% CI [-3.45min, 13.62min], $t(49.73) = 1.2$, $p = .237$, $BF_{10} = 0.21$
REM onset [min]	**95% CI [64.5min, 149.02min], $t(34.03) = 5.13$, $p < .001$, $BF_{10} > 100$**	95% CI [-64.44min, 51.03min], $t(28) = 0.23$, $p = .812$, $BF_{10} = 0.27$	**95% CI [64.5min, 149.02min], $t(34.03) = 5.13$, $p < .001$, $BF_{10} > 100$**

Note. Non-REM is defined as the combination of N2 and SWS without N1. Statistical values represent a 95% percent confidence interval of the mean, a t-statisic and corresponding p-value (alpha = 0.05). In addition, Bayes factors are reported, where $BF_{10} \le 1$ quantifies relative evidence in favor of the null hypothesis (H0), while a $BF_{10} > 1$ quantifies relative evidence for the alternative hypothesis (H1). BF_{10} values can be interpreted as either anecdotal (1-3), moderate (3-10), strong (10-30), very strong (30-100) or extreme (>100) evidence for H1.

Table S2

Overview of all sleep parameters of all three datasets (mean ± SE)

	Dataset A		Dataset B			Dataset C		
	Controls	Medicated	Controls	Unmedicated	Medicated 7d	Controls	Medicated 7d	Medicated 28d
Sleep spindles								
Density [/epoch]	2.12 ± 0.06/**2.16 ± 0.05**	**1.94 ± 0.07***	2.34 ± 0.06	2.4 ± 0.06	2.42 ± 0.06	**2.32 ± 0.07**	2.15 ± 0.1	**1.94 ± 0.11****
Count	1184 ± 43	1116 ± 63	1356 ± 46	1308 ± 58	1337 ± 56	**1354 ± 55**	1221 ± 70	**1118 ± 77***
Amplitude [µV]	31.3 ± 1.41	28.8 ± 1.41	**22.4 ± 0.85**	**25.2 ± 0.92**$^{\#}$	**25.2 ± 0.92***	33.9 ± 1.6	31.6 ± 1.65	30.9 ± 1.62
Frequency [Hz]	13.1 ± 0.07	13.2 ± 0.1	13.3 ± 0.1	13.2 ± 0.09	13.1 ± 0.09	13.3 ± 0.1	13.1 ± 0.16	13.1 ± 0.15
Duration [ms]	771 ± 8	769 ± 9	784 ± 9	800 ± 8	808 ± 8	**788 ± 10**	771 ± 9	**754 ± 10***
Slow waves								
Density [/epoch]	1.42 ± 0.06	1.48 ± 0.07	1.51 ± 0.05	1.52 ± 0.06	1.49 ± 0.07	1.48 ± 0.07	1.4 ± 0.07	1.5 ± 0.08
Count	795 ± 40	846 ± 50	879 ± 38	841 ± 53	833 ± 54	870 ± 53	805 ± 51	879 ± 62
Amplitude [µV]	**163 ± 5.25**	**136 ± 4.93*****	148 ± 4.62	146 ± 5.43	145 ± 5.57	**166 ± 6.74**	**143 ± 7.42***	**146 ± 6.77***
Frequency [Hz]	**0.84 ± 0.01**	**0.8 ± 0.01*****	0.77 ± 0.01	**0.77 ± 0.01**	**0.76 ± 0.01**$^{+}$	0.84 ± 0.01	0.81 ± 0.01	0.81 ± 0.01
Duration [ms]	**1200 ± 8**	**1260 ± 12*****	1300 ± 11	**1310 ± 11**	**1330 ± 12**$^{+}$	1200 ± 10	1240 ± 17	1230 ± 15
SW-spindles								
Count	90 ± 8	81 ± 6	106 ± 8	94 ± 9	92 ± 9	88 ± 8	80 ± 7	88 ± 9
Delay [ms]	540 ± 10	551 ± 10	556 ± 1	573 ± 9	576 ± 9	519 ± 20	492 ± 30	500 ± 23
Delay dispersion [sd]	**0.215 ± 0.006**	**0.238 ± 0.007***	**0.24 ± 0.006**	0.253 ± 0.005	**0.258 ± 0.007**$^{+}$	**0.206 ± 0.006**	**0.24 ± 0.009****	**0.235 ± 0.007***
Spindle amplitude [µV]	32.2 ± 1.17	29.5 ± 1.52	**22.7 ± 0.88**	25 ± 1.03	**25.7 ± 0.94***	33.2 ± 1.51	31.9 ± 1.62	30.8 ± 1.68
Spindle frequency [Hz]	13 ± 0.07	13.1 ± 0.1	13.3 ± 0.1	13.1 ± 0.09	13.1 ± 0.1	13.2 ± 0.12	13 ± 0.15	13 ± 0.15
Spindle duration [ms]	706 ± 10	703 ± 10	711 ± 10	719 ± 10	710 ± 10	**680 ± 10**	**710 ± 10***	**690 ± 10**$^{\#}$
SW amplitude [µV]	**164 ± 6.52**	**137 ± 5.66****	150 ± 5.53	153 ± 6.44	150 ± 6.64	**171 ± 7.05**	**143 ± 7.65***	**148 ± 6.82***
SW duration [ms]	**1210 ± 10**	**1280 ± 20****	1320 ± 10	1340 ± 10	1340 ± 10	**1190 ± 10**	**1250 ± 20****	**1240 ± 20***
Δ spindle amplitude [µV]	0.551 ± 0.292	0.213 ± 0.386	0.249 ± 0.217	-0.182 ± 0.192	-0.054 ± 0.19	-0.343 ± 0.353	0.312 ± 0.274	0.399 ± 0.207
Δ spindle frequency [Hz]	-0.068 ± 0.013	-0.07 ± 0.016	**-0.017 ± 0.013**	**-0.03 ± 0.014**	**-0.068 ± 0.017**$^{*/+}$	-0.054 ± 0.018	-0.07 ± 0.17	-0.024 ± 0.017
Δ spindle duration [ms]	-0.072 ± 0.01	-0.073 ± 0.011	**-0.083 ± 0.009**	-0.096 ± 0.011	**-0.109 ± 0.009***	**-0.113 ± 0.009**	**-0.075 ± 0.011****	**-0.079 ± 0.011***
Δ SW amplitude [µV]	6.29 ± 1.94	6.35 ± 1.82	7.3 ± 1.39	7.06 ± 1.38	9.04 ± 1.27	9.94 ± 1.82	5.81 ± 1.37	7.68 ± 1.5
Δ SW duration [ms]	0.003 ± 0.009	0.018 ± 0.012	0.028 ± 0.008	0.018 ± 0.008	0.034 ± 0.01	**-0.011 ± 0.009**	**0.016 ± 0.009***	0.003 ± 0.008

Note Non-REM is defined as the combination of N2 and SWS without N1. Epoch represents 30 seconds. Different symbols are used for indicating statistical comparisons within the datasets that are significant (highlighted in bold): differences between controls and medicated patients in Dataset A, B and C use asterisks (*, p <0.05; **, p<0.01; ***, p<0.001), between controls and unmedicated patients in Dataset B use hashes (#, p <0.05; ##, p<0.01; ###, p<0.001), and within patients for their follow-ups (i.e. Dataset B unmedicated vs. medicated 7d or Dataset C 7d medicated vs. 28d medicated patients) use pluses (+, p <0.05; ++, p<0.01; +++, p<0.001). Δ refers to difference between coupled and uncoupled spindles or slow waves (SW).

Table S3

Overview of all sleep parameters statistics

	Dataset A	Dataset B		
	Medicated vs. controls	Unmedicated vs. controls	Unmedicated vs. medicated	Medicated vs. controls
Sleep spindles				
Density [/epoch]	**95% CI [0.4, 0.05], *t*(70.79) = -2.58, *p* = .012, BF_{10} = 1.23**	95% CI [-0.11, 0.23], *t*(75.73) = 0.73, *p* = .467, BF_{10} = 0.3	95% CI [-0.04, 0.07], *t*(37) = 0.64, *p* = .529, BF_{10} = 0.24	95% CI [-0.08, 0.24], *t*(74.58) = 0.98, *p* = .331, BF_{10} = 0.35
Count	95% CI [-219.94, 84.29], *t*(69.43) = -0.89, *p* =.377, BF_{10} = 0.33	95% CI [-196.13, 98.93], *t*(71.44) = -0.66, *p* =.513, BF_{10} = 0.28	95% CI [-54.71, 113.32], *t*(37) = 0.71, *p* =.484, BF_{10} = 0.25	95% CI [-163.68, 125.08], *t*(72.53) = -0.27, *p* =.791, BF_{10} = 0.24
Amplitude [µV]	95% CI [-6.46 µV, 1.48 µV], *t*(78) = -1.25, *p* =.215, BF_{10} = 0.47	**95% CI [0.27 µV, 5.26 µV], *t*(75.06) = 2.21, *p* =.03, BF_{10} = 1.9**	95% CI [-0.82 µV, 0.82 µV], *t*(37) < 0.001, *p* =.998, BF_{10} = 0.24	**95% CI [0.28 µV, 5.25 µV], *t*(75.12) = 2.22, *p* =.03, BF_{10} = 1.92**
Frequency [Hz]	95% CI [-0.19 Hz, 0.28 Hz], *t*(70.85) = 0.4, *p* =.69, BF_{10} = 0.25	95% CI [-0.39 Hz, 0.13 Hz], *t*(74.35) = 0.99, *p* =.327, BF_{10} = 0.36	95% CI [-0.14 Hz, 0.05 Hz], *t*(37) = 1.04, *p* =.305, BF_{10} = 0.25	95% CI [-0.45 Hz, 0.09 Hz], *t*(75.51) = 1.31, *p* =.194, BF_{10} = 0.49
Duration [ms]	95% CI [-0.03ms, 0.02ms], *t*(77.2) = -0.23, *p* =.821, BF_{10} = 0.24	95% CI [-0.01ms, 0.04s], *t*(75.96) = 1.24, *p* =.218, BF_{10} = 0.46	95% CI [0.00ms, 0.02s], *t*(37) = 1.59, *p* =.12, BF_{10} = 0.3	95% CI [-0.00ms, 0.05s], *t*(75.88) = 1.98, *p* =.051, BF_{10} = 1.25
Slow waves				
Density [/epoch]	95% CI [-0.11, 0.23], *t*(76.85) = 0.7, *p* = 0.486, BF_{10} = 0.29	95% CI [-0.18, 0.16], *t*(73.09) = 0.11, *p* = 0.916, BF_{10} = 0.24	95% CI [-0.12, 0.05], *t*(37) = 0.8, *p* = .431, BF_{10} = 0.25	95% CI [-0.2, 0.15], *t*(71.22) = 0.28, *p* = 0.782, BF_{10} = 0.24
Count	95% CI [-75.71, 178.09], *t*(74.5) = -0.8, *p* =.424, BF_{10} = 0.31	95% CI [-165.97, 91.22], *t*(67.72) = -0.58, *p* =.564, BF_{10} = 0.27	95% CI [-81.79, 64], *t*(37) = -0.25, *p* =.806, BF_{10} = 0.24	95% CI [-178.1, 85.55], *t*(66.32) = -0.7, *p* =.486, BF_{10} = 0.29
Amplitude [µV]	**95% CI [-41.38 µV, -12.69 µV], *t*(77.69) = -3.75, *p* <.001, BF_{10} = 77.42**	95% CI [-16.34 µV, -12.06 µV], *t*(67.72) = -0.3, *p* = .765, BF_{10} = 0.24	95% CI [-4.62 µV, 1.13 µV], *t*(37) = 1.23, *p* = .226, BF_{10} = 0.24	95% CI [-18.31 µV, 10.54 µV], *t*(72.71) = -0.54, *p* = .593, BF_{10} = 0.27
Frequency [Hz]	**95% CI [0.02 Hz, 0.06 Hz], *t*(72.07) = -3.77, *p* <.001, BF_{10} = 80.42**	95% CI [-0.02 Hz, 0.01 Hz], *t*(76) = -0.35, *p* =.731, BF_{10} = 0.25	**95% CI [-0.02 Hz, 0.00 Hz], *t*(37) = -2.33, *p* =.025, BF_{10} = 0.39**	95% CI [-0.03 Hz, 0.01 Hz], *t*(75.33) = -1.4, *p* =.167, BF_{10} = 0.55
Duration [ms]	**95% CI [0.03ms, 0.09ms], *t*(68.6) = -3.86, *p* <.001, BF_{10} > 100**	95% CI [0.03ms, 0.04ms], *t*(75.97) = 0.3, *p* =.765, BF_{10} = 0.24	**95% CI [0.00ms, 0.03ms], *t*(37) = 2.32, *p* =.026, BF_{10} = 0.41**	95% CI [-0.01ms, 0.06ms], *t*(75.48) = 1.39, *p* =.170, BF_{10} = 0.54
SW-spindles				
Count	95% CI [-28.53, 12.28], *t*(74.85) = -0.79, *p* =.43, BF_{10} = 0.31	95% CI [-36.15, 12.99], *t*(73.9) = -0.94, *p* =.351, BF_{10} = 0.34	95% CI [-12.59, 8.56], *t*(37) = -0.39, *p* =.702, BF_{10} = 0.24	95% CI [-38.02, 10.84], *t*(74.12) = -1.11, *p* =.271, BF_{10} = 0.4
Delay [ms]	95% CI [-0.02ms, 0.04ms], *t*(77.66) = 0.85, *p* =.395, BF_{10} = 0.32	95% CI [-0.01ms, 0.04ms], *t*(75.49) = 1.28, *p* =.204, BF_{10} = 0.47	95% CI [-0.01ms, 0.02ms], *t*(37) = 0.43, *p* =.67, BF_{10} = 0.25	95% CI [-0.01ms, 0.05ms], *t*(75.8) = 1.53, *p* =.13, BF_{10} = 0.64
Delay dispersion [sd]	**95% CI [-0.04sd, 0.00sd], *t*(77.89) = 2.46, *p* =.016, BF_{10} = 3.1**	95% CI [-0.00sd, 0.03sd], *t*(74.65) = 1.7, *p* =.093, BF_{10} = 0.8	95% CI [-0.01sd, 0.02sd], *t*(37) = 0.99, *p* =.331, BF_{10} = 0.28	**95% CI [0.00sd, 0.04sd], *t*(73.76) = 2.02, *p* =.047, BF_{10} = 1.36**
Coupled spindle amplitude [µV]	95% CI [-6.45 µV, 1.19 µV], *t*(73.39) = -1.37, *p* =.175, BF_{10} = 0.52	95% CI [-0.43 µV, 4.95 µV], *t*(73.6) = 1.67, *p* =.098, BF_{10} = 0.79	95% CI [-0.09 µV, 1.42 µV], *t*(37) = 1.78, *p* =.0.83, BF_{10} = 0.26	**95% CI [0.36 µV, 5.49 µV], *t*(75.32) = 2.27, *p* =.026, BF_{10} = 2.13**
Coupled spindle frequency [Hz]	95% CI [-0.18 Hz, 0.3 Hz], *t*(69.96) = -0.49, *p* = .624, BF_{10} = 0.24	95% CI [-0.42 Hz, 0.12 Hz], *t*(74.49) = -1.1, *p* = .273, BF_{10} = 0.29	95% CI [-0.19 Hz, 0.04 Hz], *t*(37) = -1.32, *p* = .195, BF_{10} = 0.31	95% CI [-0.51 Hz, 0.06 Hz], *t*(76) = -1.56, *p* = .123, BF_{10} = 0.24
Coupled spindle duration [ms]	95% CI [-0.03ms, 0.03ms], *t*(77.36) = -0.17, *p* = .864, BF_{10} = 0.26	95% CI [-0.01ms, 0.03ms], *t*(75.65) = 0.68, *p* = .499, BF_{10} = 0.4	95% CI [-0.02ms, 0.01ms], *t*(37) = -1.09, *p* = .282, BF_{10} = 0.27	95% CI [-0.02ms, 0.02ms], *t*(74.93) = 0.07, *p* = .942, BF_{10} = 0.67
Coupled SW amplitude [µV]	**95% CI [-45.02 µV, -10.63 µV], *t*(76.47) = -3.22, *p* =.002, BF_{10} = 17.96**	95% CI [-13.64 µV, -20.17 µV], *t*(73.67) = 0.38, *p* =.701, BF_{10} = 0.25	95% CI [-9.03 µV, -2.99 µV], *t*(37) = -1.02, *p* =.315, BF_{10} = 0.25	95% CI [-16.96 µV, -17.46 µV], *t*(73.96) = 0.03, *p* =.977, BF_{10} = 0.24
Coupled SW duration [ms]	**95% CI [0.03ms, 0.12ms], *t*(71.75) = 3.37, *p* = .001, BF_{10} = 26.7**	95% CI [-0.02ms, 0.05ms], *t*(71.95) = -0.98, *p* = .330, BF_{10} = 0.36	95% CI [-0.02ms, 0.03ms], *t*(37) = 0.46, *p* = .646, BF_{10} = 0.25	95% CI [-0.01ms, 0.06ms], *t*(73.96) = 1.36, *p* = .178, BF_{10} = 0.52
Δ coupled- uncoupled spindle amplitude [µV]	95% CI [-1.3 µV, 0.63 µV], *t*(72.69) = -0.7, *p* =.487, BF_{10} = 0.29	95% CI [-1.01 µV, 0.15 µV], *t*(72.25) = 1.49, *p* =.141, BF_{10} = 0.6	95% CI [-0.2 µV, 0.46 µV], *t*(37) = 0.79, *p* =.436, BF_{10} = 0.26	95% CI [-0.88 µV, 0.27 µV], *t*(75.12) = 1.05, *p* =.297, BF_{10} = 0.377
Δ coupled- uncoupled spindle frequency [Hz]	95% CI [-0.04 Hz, 0.04 Hz], *t*(74.18) = -0.05, *p* = 0.958, BF_{10} = 0.23	95% CI [-0.05 Hz, 0.02 Hz], *t*(74.79) = -0.69, *p* = .49, BF_{10} = 0.29	**95% CI [-0.07 Hz, -0.00 Hz], *t*(37) = 2.06, *p* = .046, BF_{10} = 0.83**	**95% CI [-0.09 Hz, -0.01 Hz], *t*(68.99) = -2.39, *p* = .02, BF_{10} = 2.75**
Δ coupled- uncoupled spindle duration [ms]	95% CI [-0.03ms, 0.03ms], *t*(76.94) = -0.07, *p* = .941, BF_{10} = 0.23	95% CI [-0.04ms, 0.01ms], *t*(73.22) = -0.93, *p* = .355, BF_{10} = 0.34	95% CI [-0.03ms, 0.00ms], *t*(37) = -1.68, *p* = .102, BF_{10} = 0.36	**95% CI [-0.05ms, 0.00ms], *t*(75.95) = -2.1, *p* = .039, BF_{10} = 1.54**
Δ coupled- uncoupled SW amplitude [µV]	95% CI [-5.24 µV, -5.35 µV], *t*(77.69) = 0.02, *p* =.984, BF_{10} = 0.23	95% CI [-4.16 µV, 3.66 µV], *t*(75.97) = 0.13, *p* =.899, BF_{10} = 0.24	95% CI [-0.79 µV, 4.77 µV], *t*(37) = 1.45, *p* =.156, BF_{10} = 0.38	95% CI [-2.02µV, 5.49 µV], *t*(75.7) = 0.92, *p* =.36, BF_{10} = 0.34
Δ coupled- uncoupled SW duration [ms]	95% CI [-0.02ms, 0.05ms], *t*(72.97) = 0.97, *p* = .336, BF_{10} = 0.35	95% CI [-0.03ms, 0.01ms], *t*(75.89) = 0.83, *p* = .409, BF_{10} = 0.32	95% CI [-0.01ms, 0.04ms], *t*(37) = 1.55, *p* = .13, BF_{10} = 0.48	95% CI [-0.02ms, 0.03ms], *t*(72.91) = 0.53, *p* = .599, BF_{10} = 0.27

Table S3

Overview of all sleep parameters statistics – cont.

	Dataset C		
	Medicated 7d vs. controls	Medicated 7d vs. medicated 28d	Medicated 28d vs. controls
		Sleep spindles	
Density [/epoch]	95% CI [-0.42, 0.08], *t*(52.67) = -1.38, *p* = .175, BF_{10} = 0.57	95% CI [-0.5, 0.08], *t*(29) = -1.45, *p* = .157, BF_{10} = 0.58	**95% CI [-0.65, -0.11], *t*(49.21) = -2.79, *p* = .007, BF_{10} = 4.4**
Count	95% CI [-311.94, 45.49], *t*(53.91) = -1.49, *p* =.141, BF_{10} = 0.66	95% CI [-293.72, 87.95], *t*(29) = -1.1, *p* =.297, BF_{10} = 0.4	**95% CI [-425.49, -46.73], *t*(51.94) = -2.5, *p* =.016, BF_{10} = 2.58**
Amplitude [µV]	95% CI [-6.86 µV, 2.33 µV], *t*(56) = -0.99, *p* =.328, BF_{10} = 0.4	95% CI [-4.13 µV, 2.59 µV], *t*(29) = -0.47, *p* =.642, BF_{10} = 0.27	95% CI [-7.59 µV, 1.52 µV], *t*(55.98) = -1.33, *p* =.187, BF_{10} = 0.44
Frequency [Hz]	95% CI [-0.56 Hz, 0.19 Hz], *t*(49.42) = -1.01, *p* =.316, BF_{10} = 0.4	95% CI [-0.46 Hz, 0.44 Hz], *t*(29) = -0.04, *p* =.965, BF_{10} = 0.26	95% CI [-0.56 Hz, 0.16 Hz], *t*(50.52) = -1.1, *p* =.278, BF_{10} = 0.34
Duration [ms]	95% CI [-0.04ms, 0.01s], *t*(55.58) = -1.27, *p* =.208, BF_{10} = 0.52	95% CI [-0.04ms, 0.01s], *t*(29) = -1.29, *p* =.207, BF_{10} = 0.5	**95% CI [-0.06ms, -0.01s], *t*(55.98) = -2.44, *p* =.018, BF_{10} = 2.42**
		Slow waves	
Density [/epoch]	95% CI [-0.28, 0.12], *t*(55.73) = 0.78, *p* = 0.437, BF_{10} = 0.34	95% CI [-0.12, 0.34], *t*(29) = 0.96, *p* = 0.347, BF_{10} = 0.41	95% CI [-0.18, 0.24], *t*(55.82) = 0.28, *p* = 0.783, BF_{10} = 0.21
Count	95% CI [-211.05, 81.05], *t*(55.71) = -0.89, *p* =.376, BF_{10} = 0.37	95% CI [-89.23, 237.96], *t*(29) = 0.93, *p* =.36, BF_{10} = 0.38	95% CI [-152.99, 171.72], *t*(55.13) = 0.12, *p* =.908, BF_{10} = 0.2
Amplitude [µV]	**95% CI [-43.38 µV, -3.23 µV], *t*(55.79) = -2.33, *p* = .024, BF_{10} = 2.38**	95% CI [15.66 µV, 22.75 µV], *t*(29) = 0.38, *p* = .709, BF_{10} = 0.28	**95% CI [-38.89 µV, -0.63 µV], *t*(55.95) = -2.07, *p* = .043, BF_{10} = 1.26**
Frequency [Hz]	95% CI [-0.05 Hz, 0.01 Hz], *t*(48.25) = -1.59, *p* =.119, BF_{10} = 0.73	95% CI [-0.03 Hz, 0.03 Hz], *t*(29) = 0.02, *p* =.981, BF_{10} = 0.26	95% CI [-0.04 Hz, 0.00 Hz], *t*(52.15) = -1.73, *p* =.089, BF_{10} = 0.73
Duration [ms]	95% CI [-0.01ms, 0.07ms], *t*(45.98) = 1.75, *p* =.087, BF_{10} = 0.92	95% CI [-0.05ms, 0.04ms], *t*(29) = -0.11, *p* =.915, BF_{10} = 0.15	95% CI [-0.00ms, 0.07ms], *t*(50.10) = 1.83, *p* =.074, BF_{10} = 0.83
		SW-spindles	
Count	95% CI [-31.17, 17.38], *t*(55.91) = -0.57, *p* =.572, BF_{10} = 0.3	95% CI [-20.5, 36.9], *t*(37) = 0.58, *p* =.564, BF_{10} = 0.3	95% CI [-26.43, 29.04], *t*(52.6) = 0.09, *p* =.925, BF_{10} = 0.2
Delay [ms]	95% CI [-0.02ms, 0.05ms], *t*(51.03) = 0.9, *p* =.374, BF_{10} = 0.37	95% CI [-0.02ms, 0.04ms], *t*(29) = -0.64, *p* =.527, BF_{10} = 0.3	95% CI [-0.03ms, 0.04ms], *t*(53.26) = 0.3, *p* =763, BF_{10} = 0.21
Delay dispersion [sd]	**95% CI [0.01sd, 0.05sd], *t*(49.61) = 3.03, *p* =.004, BF_{10} = 9.42**	95% CI [-0.03sd, 0.01sd], *t*(29) = -1.23, *p* =.228, BF_{10} = 0.39	**95% CI [0.00sd, 0.04sd], *t*(54.5) = 2.28, *p* =.026, BF_{10} = 1.76**
Coupled spindle amplitude [µV]	95% CI [-5.78 µV, 3.09 µV], *t*(55.94) = 0.61, *p* =.546, BF_{10} = 0.31	95% CI [-4.56 µV, 2.34 µV], *t*(29) = 0.66, *p* =.516, BF_{10} = 0.29	95% CI [-6.98 µV, -2.07 µV], *t*(55.75) = -1.09, *p* =.281, BF_{10} = 0.34
Coupled spindle frequency [Hz]	95% CI [-0.58 Hz, 0.17 Hz], *t*(51.27) = -1.09, *p* = 0.279, BF_{10} = 0.43	95% CI [-0.39 Hz, 0.48 Hz], *t*(29) = 0.21, *p* = .838, BF_{10} = 0.27	95% CI [-0.53 Hz, 0.21 Hz], *t*(51.6) = -0.86, *p* = .391, BF_{10} = 0.22
Coupled spindle duration [ms]	**95% CI [0.01ms, 0.04ms], *t*(54.77) = 2.53, *p* = .014, BF_{10} = 3.48**	95% CI [-0.04ms, 0.00ms], *t*(29) = -2.03, *p* = .052, BF_{10} = 1.49	95% CI [-0.01ms, 0.02ms], *t*(55.79) = 0.42, *p* = .678, BF_{10} = 0.28
Coupled SW amplitude [µV]	**95% CI [-48.21 µV, -6.52 µV], *t*(55.88) = 2.63, *p* =.011, BF_{10} = 4.29**	95% CI [-15.67 µV, 25.27 µV], *t*(29) = 0.48, *p* =.635, BF_{10} = 0.29	**95% CI [-42.21 µV, -2.91 µV], *t*(55.73) = 2.3, *p* =.025, BF_{10}= 1.88**
Coupled SW duration [ms]	**95% CI [0.02ms, 0.011ms], *t*(50.29) = 2.8, *p* = .007, BF_{10} = 5.8**	95% CI [-0.04ms, 0.02ms], *t*(29) = -0.54, *p* = .593, BF_{10} = 0.28	**95% CI [0.01ms, 0.1ms], *t*(52.54) = 2.56, *p* = .013, BF_{10}= 2.88**
Δ coupled- uncoupled spindle amplitude [µV]	95% CI [-0.24 µV, 1.55 µV], *t*(51.81) = 1.46, *p* =.149, BF_{10} = 0.66	95% CI [-0.5 µV, 0.68 µV], *t*(29) = 0.3, *p* =.764, BF_{10} = 0.27	95% CI [-0.08 µV, 1.57 µV], *t*(43.92) = 1.81, *p* =.077, BF_{10} = 0.88
Δ coupled- uncoupled spindle frequency [Hz]	95% CI [-0.07 Hz, 0.03 Hz], *t*(55.6) = 0.65, *p* = .52, BF_{10} = 5.14	95% CI [0.00 Hz, 0.09 Hz], *t*(29) = 2.01, *p* = .054, BF_{10} = 1.2	95% CI [-0.02 Hz, 0.08 Hz], *t*(55.02) = 1.2, *p* = .234, BF_{10} = 0.39
Δ coupled- uncoupled spindle duration [ms]	**95% CI [0.01ms, 0.07ms], *t*(55.31) = 2.72, *p* = .009, BF_{10} = 0.32**	95% CI [-0.03ms, 0.02ms], *t*(29) = -0.37, *p* = .712, BF_{10} = 0.27	**95% CI [0.01ms, 0.06ms], *t*(55.24) = 2.43, *p* = .018, BF_{10}= 2.32**
Δ coupled- uncoupled SW amplitude [µV]	95% CI [-8.71 µV, 0.45 µV], *t*(50.99) = 1.81, *p* =.076, BF_{10} = 1.05	95% CI [-2.31 µV, 6.04 µV], *t*(29) = 0.91, *p* =.369, BF_{10} = 0.37	95% CI [-7.01 µV, 2.47 µV], *t*(53.25) = -0.96, *p* =.341, BF_{10} = 0.31
Δ coupled- uncoupled SW duration [ms]	**95% CI [0.00ms, 0.05ms], *t*(55.84) = 2.12, *p* = .039, BF_{10} = 1.67**	95% CI [-0.03ms, 0.01ms], *t*(29) = -1.37, *p* = .181, BF_{10} = 0.43	95% CI [-0.01ms, 0.04ms], *t*(54.75) = 1.14, *p* = .26, BF_{10}= 0.36

Note. Non-REM is defined as the combination of N2 and SWS without N1. Statistical values represent a 95% percent confidence interval of the mean, a t-statisic and corresponding p-value (alpha = 0.05). In addition, Bayes factors are reported, where BF_{10} <= 1 quantifies relative evidence in favor of the null hypothesis (H0), while a BF_{10} > 1 quantifies relative evidence for the alternative hypothesis (H1). BF_{10} values can be interpreted as either anecdotal (1-3), moderate (3-10), strong (10-30), very strong (30-100) or extreme (>100) evidence for H1.

Table S4

Sleep cycle durations split by non-REM and REM

Dataset	Group	Cycle	N	Duration Cycle [min] median	Duration Cycle [min] mean	Duration Cycle [min] SE	Duration Non-REM [min] median	Duration Non-REM [min] mean	Duration Non-REM [min] SE	Duration REM [min] median	Duration REM [min] mean	Duration REM [min] SE
A	Controls	1	40	87	**91.72**	4.89	70.75	**75.44**	4.85	15.75	16.29	1.37
		2	40	99	**100.76**	3.14	78.75	**80.78**	2.64	19.75	**19.99**	1.59
		3	39	114	114.51	4.71	84.5	83.38	3.4	30.5	31.13	2.9
		4	33	99	102.64	5.15	69	**71.17**	4.26	28.5	31.47	2.58
		5	15	72.5	77.73	4.8	58.5	56.1	2.66	14	21.63	4.01
		6	2	65.75	65.75	18.75	54.75	54.75	13.75	11	11	5
	Medicated	1	40	169.75	196.24/***	17.31	149.75	177.04/***	17.58	16.75	19.2	2.21
		2	37	132.5	133.73/***	7.01	92	101.08/**	5.8	26	32.65/***	2.92
		3	23	111	114.8	7.63	81	83.65	5.9	29.5	31.15	4.34
		4	11	95	96.95	6.4	56.5	57.23/*	3.6	30.5	39.73	9.03
		5	4	82.25	78.38	19.16	54.75	49.62	9.47	21	28.75	13.14
		6	3	85	78.17	10.53	55.5	55.17	7.51	24	23	11.85
B	Controls	1	40	96.25	**103.36**	6.65	84.25	**89.44**	5.76	12.75	13.93	1.9
		2	40	101.75	**108.24**	3.95	82.25	86.38	3.44	21.75	21.86	2.05
		3	40	104.75	107.03	3.65	80.25	80.6	2.85	25.25	26.43	2.43
		4	37	87.5	96.89	3.56	66.5	67.58	2.75	30	29.31	2.41
		5	17	64.5	71.53	5.84	47	48.94	4.18	17.5	22.59	3.49
		6	4	38	50.38	15.6	24.25	39.25	17.2	8.5	11.12	4.62
		7	2	27.75	27.75	8.25	19.75	19.75	0.75	8	8	7.5
	Unmedicated	1	38	102	**122.86**	10.3	87	**105.28**	9.19	17.5	17.58	1.72
		2	37	119	119.89	6.5	85.5	93.19	5.53	24.5	26.7	2.55
		3	33	102.5	105.03	4.72	76.5	79.95	4.72	24.5	25.08	1.55
		4	28	85.5	85.54	5.34	62.25	59.71	3.09	19.75	25.82	3.47
		5	14	81.5	73.54	8.05	52.5	46.46	4.78	26	27.07	4.38
		6	5	48.5	51.4	12.04	44	47.2	10.96	3.5	4.2	1.57
		7	1	25	25		18.5	18.5		6.5	6.5	
	Medicated 7d	1	38	185	192.7/***/###	16.12	169.5	172.53/***/###	15.17	16.75	20.17	2.73

		2	36	121.5	124.85/*	7.23	99	101.08	6.48	22	23.76	2.4
		3	27	112	112.87	6.74	89	89.83	4.88	18.5	23.04	3.19
		4	12	95.25	99.92	9.19	72.75	69.62	4.98	29	30.29	5.39
		5	_4_	72.5	66.62	10.37	62.5	56.12	9.97	10.25	_10.5_/**	1.34
		6	_2_	55.75	55.75	2.25	40	40	8.5	15.75	15.75	10.75
		7	_1_	48.5	48.5		44.5	44.5		4	4	
C	Controls	1	28	96.75	**97.11**	7.29	76	**79.16**	5.91	15.25	**17.95**	2.11
		2	28	98.25	**105.45**	5.16	74.25	**82.64**	4.18	20.75	22.8	2.72
		3	28	104.5	104.07	3.51	74.75	77.96	3.09	27	26.11	1.85
		4	26	105.5	102.65	3.07	71.5	72.75	2.42	29.75	29.9	2.3
		5	13	85	85.62	5.26	69	65.81	4.66	16.5	19.81	3.54
	Medicated 7d	1	30	184.25	206.73/***	20.74	164.75	186.8/***	19.94	16.75	19.93	2.7
		2	27	125.5	124.83	8.24	97	94	6.94	29.5	30.83	3.46
		3	16	119.5	123.94	9.63	82.5	90.94	8.79	31.5	33	4.3
		4	9	87	88.33/*	5.46	59	65.11	5.37	19	23.22	7.03
		5	2	64.25	64.25	45.75	30.75	30.75	13.25	33.5	33.5	32.5
		6	1	116.5	116.5		52	52		64.5	64.5	
	Medicated 28d	1	29	202	203.79/***	18.35	183	174.83/***	18.52	22.5	28.97/**	3.48
		2	27	121.5	132.44/*	8.91	96	105.11/*	7.3	26.5	27.33	3.79
		3	21	101.5	97.4	9.26	73.5	71.38	8.09	17.5	26.02	4.21
		4	10	90.5	89.7	11.54	60	62.15	9.71	21.5	27.55	7.96
		5	_4_	58.25	61.25	15.03	29	_32.25_/***	4.21	29.25	29	11.46
		6	_3_	35	62	35.84	28.5	36	13.38	6.5	26	22.57
REM suppressing medication:												
A	Controls	1	40	87	**91.72**	4.89	70.75	**75.44**	4.85	15.75	16.29	1.37
		2	40	99	**100.76**	3.14	78.75	**80.78**	2.64	19.75	**19.99**	1.59
		3	39	114	114.51	4.71	84.5	83.38	3.4	30.5	31.13	2.9
		4	33	99	102.64	5.15	69	**71.17**	4.26	28.5	31.47	2.58
		5	15	72.5	77.73	4.8	58.5	56.1	2.66	14	21.63	4.01
		6	2	65.75	65.75	18.75	54.75	54.75	13.75	11	11	5
	Medicated	1	34	186	204.62/***	18.43	155.75	187.24/***	18.59	14.75	17.38	2.27
		2	31	132.5	133.74/***	7.94	92	101.16/**	6.66	26	32.58/**	3.22
		3	18	109	116.67	9.47	82.5	85.08	7.33	31	31.58	5.15
		4	7	95	98.21	9.94	56.5	54.43/**	3.95	30.5	43.79	12.85

		5	3	65.5	65.17	19.63	56	48.33	13.27	9.5	16.83	7.84
		6	3	85	78.17	10.53	55.5	55.17	7.51	24	23	11.85
B	Controls	1	40	96.25	**103.36**	6.65	84.25	**89.44**	5.76	12.75	13.93	1.9
		2	40	101.75	108.24	3.95	82.25	86.38	3.44	21.75	21.86	2.05
		3	40	104.75	107.03	3.65	80.25	80.6	2.85	25.25	26.43	2.43
		4	37	87.5	96.89	3.56	66.5	67.58	2.75	30	29.31	2.41
		5	17	64.5	71.53	5.84	47	48.94	4.18	17.5	22.59	3.49
		6	4	38	50.38	15.6	24.25	39.25	17.2	8.5	11.12	4.62
		7	2	27.75	27.75	8.25	19.75	19.75	0.75	8	8	7.5
	Unmedicated	1	21	92.5	119.64	15.58	85	105.02	13.89	11.5	14.62	2.44
		2	20	115.75	116.95	9.01	85	91.35	6.88	23	25.6	3.82
		3	18	107	108.39	7.98	81.25	84.61	7.93	24.25	23.78	2
		4	16	84.5	81.84	6.89	61	56.78	4.82	21	25.06	3.84
		5	9	70.5	69.61	8.93	51	46.67	6.25	24	22.94	3.93
		6	3	33	43.17	17.91	32	41	17.34	2	2.17	0.73
		7	1	25	25		18.5	18.5		6.5	6.5	
	Medicated 7d	1	21	216.5	234.83/***/###	19.67	194.5	216.67/***/###	18.74	17	18.17	3.31
		2	19	125.5	126.37	11.68	99.5	101.55	10.68	22	24.82	4.1
		3	11	113.5	113	12.09	90.5	92.73	8.89	18.5	20.27	4.46
		4	2	93.75	93.75	36.75	65.5	65.5	10	28.25	28.25	26.75
		5	1	38.5	38.5		28	28		10.5	10.5	
C	Controls	1	28	96.75	**97.11**	7.29	76	**79.16**	5.91	15.25	**17.95**	2.11
		2	28	98.25	**105.45**	5.16	74.25	**82.64**	4.18	20.75	22.8	2.72
		3	28	104.5	104.07	3.51	74.75	77.96	3.09	27	26.11	1.85
		4	26	105.5	102.65	3.07	71.5	72.75	2.42	29.75	29.9	2.3
		5	13	85	85.62	5.26	69	65.81	4.66	16.5	19.81	3.54
	Medicated 7d	1	21	203.5	222.43/***	25.83	185.5	202.4/***	24.79	14.5	20.02	3.39
		2	18	127	125.39	11.53	96.5	96	9.8	26.5	29.39	4.55
		3	10	126.75	132.75	13.52	84.5	96.65	13.38	33	36.1	6.05
		4	5	91	93.4	6.76	57	61.6	6.18	30.5	31.8	11.14
		5	1	110	110		44	44		66	66	
	Medicated 28d	1	20	208.75	220.4/***	22.79	183.5	193.15/***	22.6	25	27.25/*	3.62
		2	18	126.25	136.14/*	12.05	99.5	108.97/*	10.29	27	27.17	4.55

		3	13	92.5	91.12	14.03	60	65.19	12.07	17	25.92	6.21
		4	6	102.5	98.08	16.29	67.5	70.5	14.19	20.75	27.58	12.23
		5	2	40.75	40.75	12.75	28.75	28.75	2.25	12	12	10.5
		6	2	26.5	26.5	8.5	23	23	5.5	3.5	3.5	3
REM non-suppressing medication:												
A	Controls	1	40	87	91.72	4.89	70.75	75.44	4.85	15.75	16.29	1.37
		2	40	99	**100.76**	3.14	78.75	80.78	2.64	19.75	19.99	1.59
		3	39	114	114.51	4.71	84.5	83.38	3.4	30.5	31.13	2.9
		4	33	99	102.64	5.15	69	71.17	4.26	28.5	31.47	2.58
		5	15	72.5	77.73	4.8	58.5	56.1	2.66	14	21.63	4.01
		6	2	65.75	65.75	18.75	54.75	54.75	13.75	11	11	5
	Medicated	1	13	124.5	163.04	34.59	107	141.85	34.94	18	21.19	3.92
		2	11	126	126.64/*	9.91	92	95.41	8.25	25	31.23	4.96
		3	10	119	115.4	11.55	76.25	85.5	9.87	24.75	29.9	5.03
		4	7	95	95.57	3.63	56.5	59.71	4	38	35.86	7.01
		5	2	108.5	108.5	9.5	60	60	6.5	48.5	48.5	16
		6	1	92	92		68	68		24	24	
B	Controls	1	40	96.25	103.36	6.65	84.25	89.44	5.76	12.75	13.93	1.9
		2	40	101.75	108.24	3.95	82.25	86.38	3.44	21.75	21.86	2.05
		3	40	104.75	107.03	3.65	80.25	80.6	2.85	25.25	26.43	2.43
		4	37	87.5	96.89	3.56	66.5	67.58	2.75	30	29.31	2.41
		5	17	64.5	71.53	5.84	47	48.94	4.18	17.5	22.59	3.49
		6	4	38	50.38	15.6	24.25	39.25	17.2	8.5	11.12	4.62
		7	2	27.75	27.75	8.25	19.75	19.75	0.75	8	8	7.5
	Unmedicated	1	17	104	126.82	13.1	88.5	105.59	11.76	19.5	21.24/*	2.15
		2	17	119	123.35	9.59	87.5	95.35	9.13	29	28	3.35
		3	15	102.5	101	4.13	74	74.37	4.07	26	26.63	2.43
		4	12	86	90.46	8.57	68	63.62	3.18	17.75	26.83	6.47
		5	5	88	80.6	16.85	54	46.1	8.19	39.5	34.5	9.86
		6	2	63.75	63.75	15.25	56.5	56.5	12.5	7.25	7.25	2.75
	Medicated 7d	1	17	133	140.65	20.95	124	118	17.65	16.5	22.65	4.57
		2	17	120.5	123.15	8.37	97	100.56	7.16	24.5	22.59	2.32
		3	16	110	112.78	8.13	87.5	87.84	5.72	19.25	24.94	4.47
		4	10	95.25	101.15	9.64	72.75	70.45	5.81	29	30.7	5.16

		5	*3*	81.5	76	6.26	69	65.5/*	4.8	10	*10.5/***	1.89
		6	2	55.75	55.75	2.25	40	40	8.5	15.75	15.75	10.75
		7	1	48.5	48.5		44.5	44.5		4	4	
C	Controls	1	28	96.75	**97.11**	7.29	76	79.16	5.91	15.25	17.95	2.11
		2	28	98.25	105.45	5.16	74.25	82.64	4.18	20.75	22.8	2.72
		3	28	104.5	104.07	3.51	74.75	77.96	3.09	27	26.11	1.85
		4	26	105.5	102.65	3.07	71.5	72.75	2.42	29.75	29.9	2.3
		5	13	85	85.62	5.26	69	65.81	4.66	16.5	19.81	3.54
	Medicated 7d	1	9	139	170.11	32.7	119.5	150.39	31.39	18.5	19.72	4.54
		2	9	120.5	123.72	9.85	98	90	7.67	34.5	33.72	5.21
		3	6	107.75	109.25	11.15	82.25	81.42	7.22	26.5	27.83	5.43
		4	4	77.5	82	8.88	62.25	69.5	9.91	8.5	*12.5/**	4.51
		5	1	18.5	18.5		17.5	17.5		1	1	
		6	1	116.5	116.5		52	52		64.5	64.5	
	Medicated 28d	1	9	152.5	**166.89/***	28.44	105	134.11	29.51	21.5	32.78	8.04
		2	9	119	125.06	12.08	92	97.39	7.59	26.5	27.67	7.2
		3	8	103.75	107.62	8.42	74.25	81.44	7.85	24.25	26.19	5.08
		4	4	86.5	77.12	15.76	53.25	49.62	10.83	21.5	27.5	10.07
		5	2	81.75	81.75	18.75	35.75	35.75	8.75	46	46	10
		6	1	133	133		62	62		71	71	

Note. Sleep cycle durations median, mean and standard error (SE) split by non-REM and REM parts defined according to Feinberg & Floyd (1979). Note that the number of available sleep cycles (N) drop sharply after 3rd or 4th cycle. Medicated patients in all datasets have extended first and second sleep cycles. This effect seemed to be driven by extension of non-REM periods of the sleep cycle. REM sleep was extended after prolonged sleep cycles, suggesting higher REM pressure, in the long-term medication groups (i.e. Dataset A Medication, Dataset C Medicated 28d). Effects seemed to be driven by patients that received REM suppressing medication as above effects were lessened under medication not known to suppress REM. Different symbols are used for indicating statistical comparisons (two-tailed paired and unpaired two sample *t*-tests with assumptions for unequal variance) within the datasets that are significant (highlighted in bold, red higher, blue lower): differences to Controls use asterisks (*, *p* <.05; **, *p*<.01; ***, *p*<.001), within patients for their follow-ups (Dataset B Unmedicated vs. Medicated 7d; Dataset C Medicated 7d vs. Medicated 28d) use hashes (###, *p*<.001). Note that some statistics were run on very low <10 sleep cycles in one of the groups and were thus not interpreted.

SW-spindle coupled parameters results

Here, we checked for differences between patients and controls on the *coupled* spindle (amplitude, duration, frequency) and SW (amplitude, duration) properties and we explored if the differential scores between coupled and uncoupled spindle and SW properties differed per group in all datasets. For an overview of all reported values all datasets see supplemental Table S2 and for all statistical comparisons and details, see supplemental Table S3.

In Dataset A, MDD patients, compared to controls, showed lower amplitude ($t(76.47) = -3.22$, $p = .002$) as well as longer duration of SW that coupled with a spindles ($t(71.75) = 3.37$, $p = .001$).

In Dataset B, medicated MDD patients, compared to controls, showed higher spindle amplitude of those spindles that coupled with a SW ($t(75.32) = 2.27$, $p = .026$). In addition, medicated patients compared to controls, showed a larger difference in spindle frequency ($t(68.99) = -2.39$, $p = .02$) as well as spindle duration ($t(75.95) = -2.1$, $p = .039$) between coupled and uncoupled spindles.

In Dataset C, 7-day medicated MDD patients, compared to controls, showed longer spindle duration of those spindles that coupled with a SW, ($t(54.77) = 2.53$, $p = .014$), as well as lower amplitude and longer duration of SW that coupled with a spindles, ($t(55.88) = -2.63$, $p = .011$; $t(50.29) = 2.8$, $p = .007$, resp.). Patients after 28 days of medication compared to 7 days of medication showed a shorter spindle duration in the coupled spindles, ($t(57.53) = 2.05$, $p = .045$). Similarly, 28-day medicated MDD patients, compared to controls, lower amplitude and longer duration of SW that coupled with a spindles, ($t(55.73) = -2.3$, $p = .025$; $t(52.54) = 2.56$, $p = .013$, resp.). 7-day medicated MDD patients, compared to controls, showed a smaller difference in spindle duration between coupled and uncoupled spindles, ($t(55.31) = 2.72$, $p = .009$). In addition, 7-day medicated patients compared to 28-day medicated patients showed a larger difference in SW duration between coupled and uncoupled SW ($t(55.84) = 2.12$, $p = .039$). Similarly, 28-day medicated MDD patients, compared to controls, showed also a smaller difference in spindle duration between coupled and uncoupled spindles, ($t(55.24) = -2.43$, $p = .02$).

Medication

In all datasets, when medicated, the MDD patients were prescribed a great variety of antidepressant medication classes and most took a combination of different types. In addition, some took benzodiazepines and GABA-ergic drugs (typically hypnotics), which are known to influence sleep (Brunner et al., 1991). Given the variety of drugs, no analysis on the specific type of medication on any of the outcome measurements of interest were performed on the specific datasets. However, medication data was available for 103 patients after combining the three datasets (all the patients in medicated state were pooled together, for Dataset C the patients after 7 days of medication were taken).

Medication types were pooled together into 5 main antidepressant classes: selective serotonin reuptake inhibitors (SSRIs, n = 32), serotonin-norepinephrine reuptake inhibitors (SNRIs, n = 34), tricyclic antidepressants (TCAs, n = 33), hypnotics (n = 11), or an alternative drugs (n = 47). Spindle count was descriptively higher in patients taking hypnotics, but this did not reach significance (p =.1) and SW amplitude was decreased (b = -25.05, t(101) = -2.35, p = .021). Since hypnotics were only prescribed in Dataset A and C, which included older patients, we added age as a moderating predictor in the regression model as age is known to decrease SW amplitude (Dubé et al., 2015). The interaction effect between the hypnotic and age on SW amplitude was not significant, suggesting age was not a strong mediator of the SW amplitude decreases on hypnotics (p = 0.12). As expected SW amplitude was reduced with age (main effect, b = -1.37, t(99) = -6.38, p < .001). Lastly, TCAs prescription was associated with a decrease in SW amplitude as well, (b = -16.46, t(101) = -2.33, p = .022) and age was no moderator on this association (p = 0.9).

In addition, we explored the influence of the three most common prescribed specific medication drugs in our combined sample. These were venlafaxine (SSNRI, n = 24), mirtazapine (NaSSA, n= 19) and trimipramine (TCA, n = 18). Of these drugs, only venlafaxine showed significant influences, namely decreased spindle density (b = -0.23, t(108) = -2.08, p = .039) as well as, expectedly, decreased the time spent in REM sleep (b = -6.82, t(108) = -4.16, p < .001).

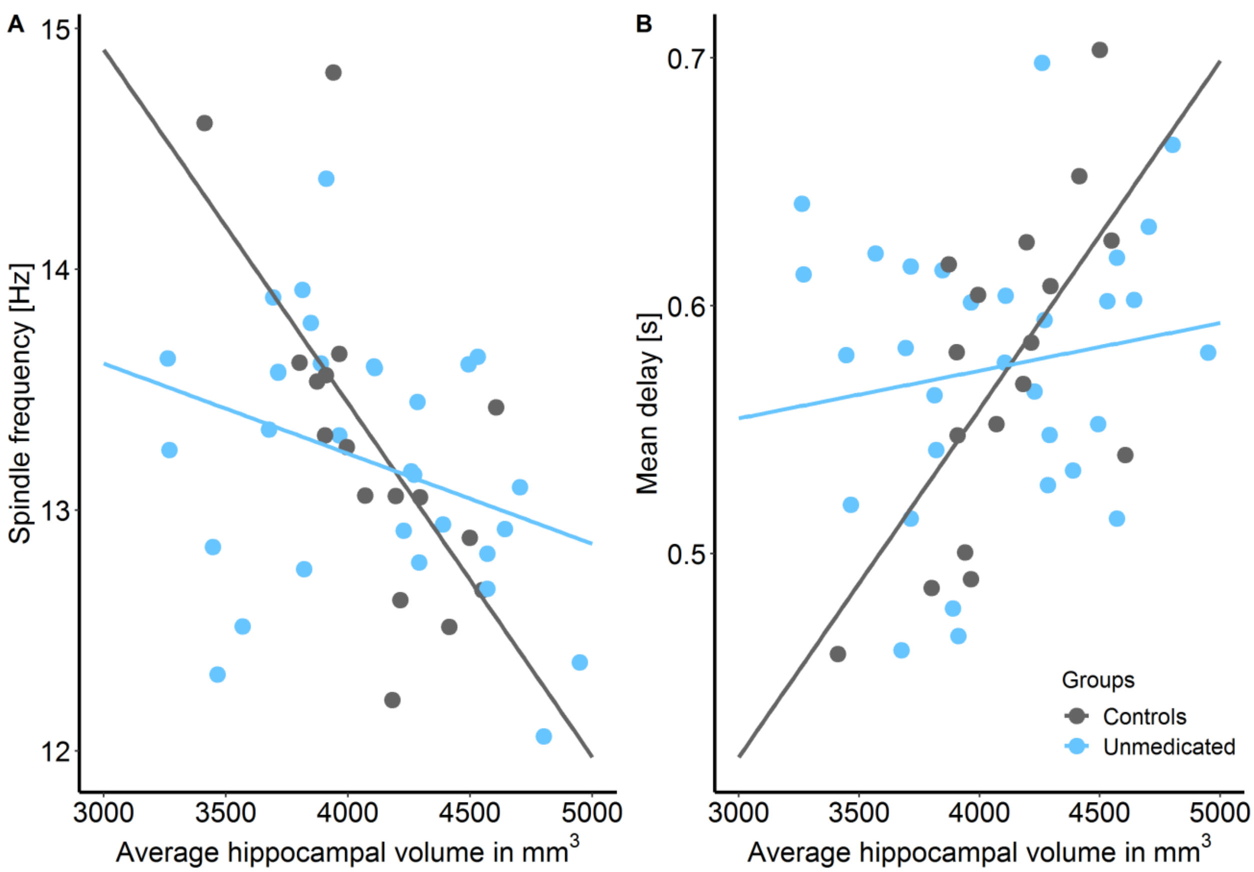
Hippocampal volume

In Dataset B, high-resolution structural magnetic resonance (MR) scans were acquired using a T1-weighted fast RF-spoiled gradient (FSPGR) sequence with the following parameters: TR = 6.18 ms; TE = 2.26 ms; flip angle = 12°; FOV = 256 mm; voxel resolution = 1 mm isotropic. MDD patients were in unmedicated state at the time of the MR scan. Data was available for 17 controls and 31 unmedicated patients. Data was available for 31 unmedicated patients and 17 controls. Subcortical structure segmentation was performed using the fsl (FMRIB Software Library) FIRST function. Next, volumetric analysis of the hippocampus was performed using fslstats based on standard labeling of the structures.

Given the previous mentioned literature on hippocampal size reductions in MDD, we wanted to explore if we could replicate these findings in our sample and correlate hippocampal size with overnight consolidation performance. Neither left or right, nor the average hippocampal volume (in mm^3) differed between the unmedicated MDD patients and controls (p > 0.5). An interaction between group and average hippocampal size on spindle frequency was found (b = 0.00, t(44) = 2.36, p = .023), suggesting a stronger negative correlation between hippocampal volume and spindle frequency in controls (*r* = -0.67, *p* = 0.003) than in patients (*r* = -0.32, *p* = 0.076). In addition, an interaction between group and average hippocampal size on delay between SW and spindles was found, (*b* = 0.00, *t*(44) = 2.48, *p* = .017). Here, controls show a moderate correlation between delay and hippocampal size (*r* = 0.67, *p* = 0.004), whereas patients do less so (*r* = 0.16, *p* = 0.4). See figure S1. Other sleep parameters nor overnight consolidation performance were correlated with hippocampal volume in either of the groups.

Figure S1

Hippocampal volume in Dataset B.



Note. (A). Hippocampal volume was stronger negatively correlated with spindle frequency in controls than in MDD patients. (B). Hippocampal volume was stronger correlated with mean delay between spindles and SW in controls than in MDD patients.

Results on combined data

Here, we combined the three datasets by pooling all controls (*n* = 108) and all the patients in medicated state (*n* = 108). The patients after 7 days of medication were taken for Dataset C. All the main analysis were repeated on the combined data.

Sleep architecture. When combining the three datasets, the MDD patients spent a higher proportion in S1 sleep (ΔM = 4.33%, 95% CI [2.61%, 6.06%], t(198.29) = -4.96, p <.001) spent less time in SWS, ΔM = -2.8, 95% CI [-5.11, -0.49], t(208.86) = 2.39, p = .018. As expected, less proportion of sleep was spent in REM sleep (ΔM = -4.79%, 95% CI [-6.55%, 3.02%], t(189.75) = 5.35, p < .001) and patients took longer time to reach it compared to controls (ΔM = 97.58 min, 95% CI [76.95 min, 118.2 min], t(130.02) = 9.36, p <.001). Lastly, patients had less SWS (ΔM = -2.8 %, 95% CI [-5.11. %, -0.49 %], t(208.86) = -2.39, p = .018) and a later onset of SWS (ΔM = 7.85 min, 95% CI [2.36 min, 13.34 min], t(167.21)= -2.82, p = .005). See Table S5 for all results.

Sleep spindles. In the combined datasets, no group differences in spindle density nor in duration nor in amplitude were found. See Table S5 for all results.

Slow waves. Compared to controls, the medicated MDD patients had SW with lower SW amplitude (ΔM= -17.53 μV, 95% CI [-26.66 μV, -8.4 μV], *t*(213.28) = -3.78, *p* <.001), longer duration, (ΔM=0.04 s, 95% CI [0.01 s, 0.06 s], *t*(210.25) = 3.23, *p* = .001) and lower frequency, (ΔM= - 0.02 Hz 95% CI [-0.01 Hz, -0.04 Hz], *t*(211.22) = -3.17, *p* =.002). See Table S5 for all results.

SW-spindles. In the combined data, there were no group differences on the SW-spindle counts or differences in the mean spindle delay to SW of the coupling. MDD patients showed a greater delay dispersion – or spread around the mean, than controls (ΔM = 0.02 SD, 95% CI [0.01 SD, 0.03 SD], t(211.33) = 3.98, p <.001). See Table S5 for all results.

Table S5

Sleep parameters of all three datasets combined (mean ± SE).

	Combined datasets	
	Controls	Medicated
	Sleep architecture	
N1[%]	**10.8 ± 0.523**	**15.1 ± 0.699*****
N2[%]	46.6 ± 0.79	49 ± 1.04
SWS[%]	**17 ± 0.76**	**14.2 ± 0.891****
Non-REM[%]	63.6 ± 0.7	63.3 ± 1
REM [%]	**17.9 ± 0.507**	**13.1 ± 0.737****
WASO [%]	7.45 ± 0.619	7.99 ± 0.57
TST [min]	466 ± 2.04	465 ± 1.76
Sleep onset [min]	21 ± 1.26	24.4 ± 1.39
SWS onset [min]	**19.7 ± 1.36**	**27.6 ± 2.42****
REM onset [min]	**81 ± 3.27**	**179 ± 9.9*****
	Sleep spindles	
Density [/epoch]	2.25 ± 0.039	2.16 ± 0.046
Count	1292 ± 28.4	1223 ± 36.9
Amplitude [μV]	28.7 ± 0.871	28.3 ± 0.799
Frequency [Hz]	13.2 ± 0.05	13.1 ± 0.06
Duration [s]	0.78 ± 0.005	0.783 ± 0.005
	Slow waves	
Density [/epoch]	1.47 ± 0.035	1.46 ± 0.039
Count	845 ± 24.5	830 ± 29.8
Amplitude [μV]	**158 ± 3.18**	**141 ± 3.37*****
Frequency [Hz]	**0.811 ± 0.01**	**0.789 ± 0.01****
Duration [s]	**1.24 ± 0.008**	**1.27 ± 0.009****
	SW-spindles	
Count	96.1 ± 4.72	86.1 ± 4.7
Mean delay [s]	0.551 ± 0.006	0.567 ± 0.006
Delay dispersion [sd]	**0.221 ± 0.004**	**0.244 ± 0.004*****

Note. Controls (n = 108), Medicated patients (n = 108). Differences between controls and medicated patients in use the following: **, p<.01; ***, p<.001.

Behavioral results

When Dataset A and B (medicated sample) were combined on their behavioral data (80 controls, 78 patients), there was a small effect at baseline after removal of one outlier, where MDD patients tapped less sequences correct than controls (ΔM = -1.29, 95% CI [-2.53, 0.05], $t(145.48) = 2.06$, $p = .042$). No differences in training effect were found (p = 0.23). However, MDD patients showed worse overnight consolidation than healthy controls after removal of 2 outliers (ΔM = -0.17, 95% CI [-0.25, -0.08], $t(122) = 3.94$, $p < .001$).

Table S6

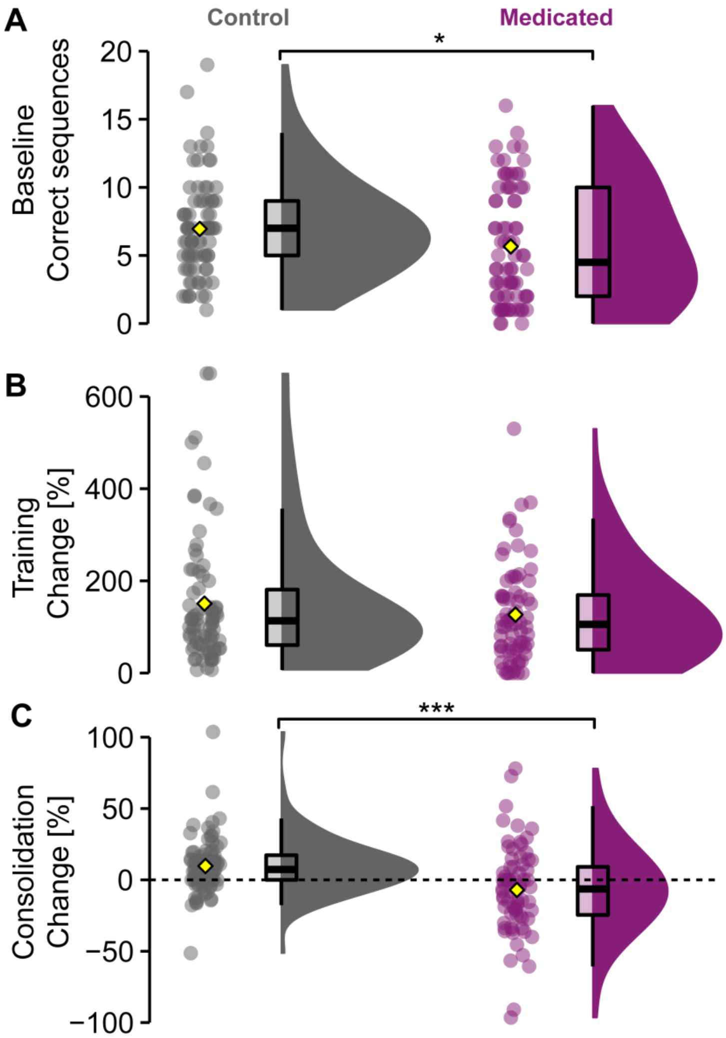
Behavioral results of finger tapping test of Dataset A and Dataset B combined

	Controls (comb)	Medicated (comb)
Baseline	6.95 ± 0.395 (1 rm)	5.66 ± 0.488 *
Training	1.51 ± 0.158 (2 rm)	1.27 ± 0.126 (1 m)
Consolidation	0.097 ± 0.023	-0.07 ± 0.036 ***(2 rm)

Note. Results are reported after removal of outliers 3sd from the overall mean Differences between controls and medicated patients in use the following: *, p <0.05; ***, p<0.001. 1/2 rm = one/two outlier(s) more than 3sd from the mean removed

Figure S2

Behavioral results of finger tapping test of Dataset A and Dataset B combined



Note. (A). Amount of correctly tapped sequences of first 30-second run. Medicated patients tap less sequences correct than Controls. (B) Percentage change score between the first run and the mean of the last three runs. (C) Percentage change score between the mean of three test runs after sleep in the morning and the mean of the last three training runs before sleep. Medicated patients perform worse after sleep than Controls. Data depicted like in Figures in the main text. Significances for two-group comparisons in asterisks (*, *p*<.05; ***, *p*<.001).

Sleep parameters related to overnight consolidation performance

When combining datasets A and B, an interaction effect between group (medicated MDD x controls) and spindle density on overnight consolidation re-emerged (after removal of two outliers: $b = 0.26$, 95% CI $[0.03, 0.49]$, $t(148) = 2.22$, $p = .028$) which suggests a stronger association between spindle density and consolidation for patients (*r* = 0.31) than for controls (*r* = 0.04). No such interactions were found on SW parameters. In contrast, the significant interactions between the SW-spindle parameters in Dataset A could not be replicated in the combined dataset.

Table S7

Medication of patients

Participant	Dataset	Medication type
1	Dataset A	Sertraline
2	Dataset A	Mirtazapine
3	Dataset A	Venlafaxine, Quetiapine
4	Dataset A	Amitriptyline, Amlodipine
5	Dataset A	*Medication type unknown*
6	Dataset A	Mirtazapine, Trimipramine, Sertraline
7	Dataset A	Mirtazapine, Venlafaxine, Lorazepam
8	Dataset A	Venlafaxine, Olanzapine, Ramipril, Propranolol
9	Dataset A	*Medication type unknown*
10	Dataset A	*Medication type unknown*
11	Dataset A	Duloxetine, Amitriptyline, Escitalopram
12	Dataset A	Escitalopram, Trimipramine
13	Dataset A	Venlafaxine
14	Dataset A	Quetiapine, Amitrityline, Lorazepam
15	Dataset A	Mirtazapine
16	Dataset A	Duloxetine, Trimipramine, Lithium, Lorazepam, L-Thyroxin
17	Dataset A	Citalopram, Amitriptyline, Zopiclon, Bisohexal, Atorvastatin, L-Thyroxin
18	Dataset A	Mirtazapine
19	Dataset A	Sertraline, Zopiclon, Bisohexal, Atorvastatin, L-Thyroxin
20	Dataset A	*Medication type unknown*
21	Dataset A	Quetiapine, Escitalopram, Venlafaxine, Lamotrigine, Olanzapin
22	Dataset A	Lithium, Venlafaxine, Escitalopram, Pregabalin
23	Dataset A	Escitalopram, Lorazepam, Pantoprazol, L-Thyroxin

24	Dataset A	*Medication type unknown*
25	Dataset A	Trimipramine, Sulpiride, Lithium
26	Dataset A	Quetiapine, Escitalopram, L-Thyroxin
27	Dataset A	Trimipramine, Escitalopram, Lamotrigin
28	Dataset A	Venlafaxine, Escitalopram, Mirtazapine, Thyronajod
29	Dataset A	Citalopram, Trimipramine, Lamotrigin
30	Dataset A	Quetiapine, Mirtazapine, Venlafaxine, Metroprolol, Enahexal
31	Dataset A	*Medication type unknown*
32	Dataset A	Doxepine
33	Dataset A	Duloxetine, Pregabaline, Enahexal, Metohexal, Pantoprazol
34	Dataset A	Mirtazapine, Trimipramine, Sertraline
35	Dataset A	Clomipramine
36	Dataset A	Mirtazapine
37	Dataset A	*Medication type unknown*
38	Dataset A	Mirtazapine, Duloxetine
39	Dataset A	Venlafaxine, Lorazepam, Zopiclon
40	Dataset A	Trimipramine, Sertraline
1	Dataset B	Citalopram
2	Dataset B	Duloxetine
3	Dataset B	Venlafaxine
4	Dataset B	Citalopram
5	Dataset B	Venlafaxine
6	Dataset B	Venlafaxine
7	Dataset B	Trimipramine
8	Dataset B	Citalopram
9	Dataset B	Bupropion
10	Dataset B	Citalopram
11	Dataset B	Citalopram
12	Dataset B	Citalopram
13	Dataset B	Escitalopram
14	Dataset B	Escitalopram

15	Dataset B	Amitriptyline
16	Dataset B	Paroxetine
17	Dataset B	Trimipramine
18	Dataset B	Duloxetine
19	Dataset B	Amitriptylineoxide
20	Dataset B	Venlafaxine
21	Dataset B	Escitalopram
22	Dataset B	Trimipramine
23	Dataset B	Mirtazapine
24	Dataset B	Escitalopram
25	Dataset B	Escitalopram
26	Dataset B	Mirtazapine
27	Dataset B	Trimipramine
28	Dataset B	Mirtazapine
29	Dataset B	Trimipramine
30	Dataset B	Trimipramine
31	Dataset B	Bupropion
32	Dataset B	Trimipramine
33	Dataset B	Sertraline
34	Dataset B	Bupropion
35	Dataset B	Bupropion
36	Dataset B	Mirtazapine
37	Dataset B	Bupropion
38	Dataset B	Bupropion
39	Dataset B	Bupropion
40	Dataset B	Mirtazapine
1	Dataset C	Mirtazapine
2	Dataset C	Venlafaxine
3	Dataset C	Reboxetine
4	Dataset C	Venlafaxine
5	Dataset C	Venlafaxine

6	Dataset C	Venlafaxine
7	Dataset C	Cymbalta, Elontril
8	Dataset C	Duloxetine, Trimipramine
9	Dataset C	Equilibrine, Stangyl, Tavor
10	Dataset C	Sertraline, Lamotrigine, Olanzapine
11	Dataset C	Doxepine
12	Dataset C	Elontril
13	Dataset C	Trimipramine
14	Dataset C	Venlafaxine
15	Dataset C	Venlafaxine
16	Dataset C	Venlafaxine, Trimipramine, Quetiapine
17	Dataset C	Citalopram
18	Dataset C	Amitriptyline, Amitriptylinoxid
19	Dataset C	Venlafaxine
20	Dataset C	Equilibrine, Movicol
21	Dataset C	Stangyl
22	Dataset C	Mirtazapine
23	Dataset C	Paroxetine, Anafranil, Seroquel, Musaril, Piroxicam, ASS, Allopurinol, Sortis
24	Dataset C	Elontril, Trevilor, Lithium
25	Dataset C	Trimipramine, Saroten
26	Dataset C	Duloxetine, Lorazepam, Lthyron, Trazodon
27	Dataset C	Venlafaxine, Mirtazapine, LTG, Lorazepam, Thyronajod
28	Dataset C	Venlafaxine, Mirtazapine, Lorazepam, Gabapentin
29	Dataset C	Elontril, Zyprexa
30	Dataset C	Venlafaxine