

ERRATUM

Daytime spikes in dopaminergic activity drive rapid mood-cycling in mice

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As the result of an editing error, the image in Figure 2e was duplicated in Figure 2f. The correct version of Figure 2 appears below. The publisher regrets the error.

Figure 2. Time-specific alterations in VTA dopaminergic activity in *ClockΔ19* mice. **(a)** Two-way analysis of variance of firing rate found a significant genotype effect ($F_{1,112} = 12.67$, $P = 0.0006$). *Post hoc* tests revealed significant differences in the firing rate of dopaminergic neurons during the first 6 h of the light cycle and the last 6 h of the dark cycle ($P < 0.05$ using Student's *t*-test; $n = 14/14/16/12$ and $14/14/17/12$ for the number of dopaminergic neurons analyzed in WT ($n = 8$) and *ClockΔ19* mice ($n = 9$), respectively). **(b)** Two-way analysis of variance of bursting rate found a significant genotype effect ($F_{1,112} = 8.6$, $P = 0.004$) with *post hoc* analyses revealing significant differences in the bursting rate of dopaminergic neurons during the first 6 h of the dark cycle ($P < 0.05$, by Student's *t*-test; $n = 14/14/16/12$ and $14/14/17/12$ for the number of dopaminergic neurons analyzed in WT and *ClockΔ19* mice, respectively). **(c)** Relative abundance of TH mRNA normalized to the expression of *Gapdh*. Two-way analysis of variance revealed a significant genotype effect ($F_{1,45} = 9.42$, $P = 0.004$) with a specific increase in TH expression at ZT4 in *ClockΔ19* mice ($P < 0.05$, $n = 3–5$ animals per genotype per time point). Diurnal variation was significant in wild-type (WT) mice (CircWave: $F_{2,27} = 10.63$, $P = 0.0004$) but not in *ClockΔ19* mutants ($P > 0.05$). **(d)** A significant main effect of time was found for total TH ($F_{3,28} = 5.34$, $P = 0.005$), with an increase in *ClockΔ19* mouse TH levels at ZT9 ($P < 0.01$). Diurnal variation was statistically significant in mutants (CircWave: $F_{2,17} = 5.15$, $P = 0.02$). **(e)** There was a significant effect of time on phosphorylated TH (ser 40) protein ($F_{3,32} = 6.50$, $P = 0.002$), with *ClockΔ19* mice exhibiting a specific increase in THser40 levels at ZT9 ($P < 0.05$, Student's *t*-test). Diurnal variation in THser40 was statistically significant in mutants (Circwave: $F_{2,17} = 7.18$, $P = 0.005$). **(f)** No differences in phosphorylated THser31 protein levels were found at any time point measured. Inset depicts average protein levels over 24 h. **(e, f)** Dopamine synthesis assay. **(g)** Dopamine synthesis was significantly increased in *ClockΔ19* mutant mice as measured by L-Dopa in the nucleus accumbens after NSD-1015 administration during the light phase, at ZT4 ($t_9 = 2.546$, $P = 0.03$). **(h)** Dopamine synthesis was unaltered in the dorsal striatum of *ClockΔ19* mutants ($P > 0.05$, $n = 5–8$ per group; dark phase = ZT16). White and dark bars below graph represent daytime and nighttime measurements, respectively.

