sham titration. In both studies, on assessment day, participants completed a battery of emotional processing tasks, including facial expression recognition, emotional word categorisation and memory, emotional words/faces dot-probe and the emotion-potentiated startle. In study 1, sleep–wake actigraphy was completed for 9–16 days prior to assessment day. In study 2, sleep–wake actigraphy was completed for 7 days pre-dose and for 7 days during drug administration; assessment day was on Day 8.

**Results:** In study 1, the bipolar phenotype was associated with significantly enhanced target sensitivity for surprised faces ($F(1,58) = 4.552$, $p = 0.037$) and a trend towards enhanced target sensitivity for positive vs. negative words during emotional recognition memory ($F(1,58) = 3.495$, $p = 0.067$). Bipolar phenotype individuals also showed a trend towards increased activity during the least active 5 hours of sleep ($F(1,36) = 3.913$, $p = 0.056$) and a trend towards reduced total sleep time ($F(1,36) = 3.321$, $p = 0.077$). Study 2 revealed that quetiapine treatment was associated with a trend towards reduced target sensitivity for surprised faces ($F(1,36) = 3.875$, $p = 0.057$), a trend towards more conservative response style for angry faces ($F(1,36) = 3.434$, $p = 0.072$) and a significantly more conservative response style for positive vs. negative words during emotional recognition memory ($F(1,35) = 4.983$, $p = 0.032$). Quetiapine treatment was also associated with significantly increased total sleep time ($F(1,29) = 18.528$, $p < 0.001$) and sleep efficiency ($F(1,29) = 5.577$, $p = 0.025$), and a trend towards improved intra-daily variability ($F(1,29) = 3.109$, $p = 0.088$).

**Conclusions:** The effects of seven-day quetiapine administration opposed many of the abnormalities recorded in individuals with the bipolar phenotype, specifically greater target sensitivity for surprised faces, enhanced processing of positive vs. negative emotional words during a memory task and reduced total sleep time. The present findings suggest a number of mechanisms through which quetiapine may stabilise mood and circadian rhythms and through which its clinical effects may be mediated.

#### References

[1] Bowden CL, Grunze H, Mullen J, Brecher M, Paulsson B, Jones M, Vagero M, Svensson K (2005) A randomized, double-blind, placebo-controlled efficacy and safety study of quetiapine or lithium as monotherapy for mania in bipolar disorder. J Clin Psychiatry 66: 111–121.

[2] Calabrese JR, Keck PE, Jr., Macfadden W, Minkwitz M, Ketter TA, Weisler RH, Cutler AJ, McCoy R, Wilson E, Mullen J (2005) A randomized, double-blind, placebo-controlled trial of quetiapine in the treatment of bipolar I or II depression. Am J Psychiatry 162: 1351–1360.

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## P.2.d.032 Management of postpartum manic episode without cessation of breastfeeding: a longitudinal follow up of drug excretion into breast milk

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**Background:** Available data on excretion of second generation antipsychotics (SGAs) into breast milk is limited. We investigated breast milk excretion of two SGA, one with short: quetiapine (6 hours) and the other with a long half life: olanzapine (36 hours) at three different time zones for detecting time-dependent concentration decline [1].

**Method:** Milk samples of bipolar I manic women who was on once daily (at 23:00pm) olanzapine (15 mg/day) and quetiapine (200 mg/day) were collected at 4:00am, 8:00am, and 23:00pm for 26 days. She avoided breastfeeding between 23:00–7:00 after drug-intake. Absolute and relative infant doses were computed by trapezoidal rule estimations of the area under the daily concentration curves for each drug and by assuming 150 cc/day breastmilk intake for each of twin babies [2].

**Results:** Quetiapine had an average milk concentration of $11.7 \pm 6.4$ ng/ml (Mean$\pm$SD) at 4:00am, which decreased significantly to $5.4 \pm 3.9$ ng/ml at the second (8:00am), and $0.9 \pm 0.7$ ng/ml at the last measurement (23:00pm) just before the next drug intake ($\chi^2 = 39.5$, $p < 0.001$). The first two measurements revealed similar milk concentrations for olanzapine of $15.8 \pm 11.4$ ng/ml at 4:00am, and $15.1 \pm 13.3$ ng/ml at 8:00am; but the last measurement (23:00pm) was significantly lower at $7.8 \pm 4.7$ ng/ml $\chi^2 = 13.9$, $p = 0.001$).

The median daily milk concentration of quetiapine was computed as 2.67 ng/ml (75th percentile= 3.96 ng/ml, 25th percentile= 2.07 ng/ml). The median daily milk concentration of olanzapine was 5.39 ng/ml (75th percentile= 8.09 ng/ml, 25th percentile= 3.88 ng/ml).

Maximum absolute infant dose estimated for quetiapine was 0.37 mg/kg/day, while values at 75th and 25th percentiles of 26 days of measurements being lower at 0.15 and 0.08 mg/kg/day, respectively. Median absolute infant dose for quetiapine was also fairly low at 0.10 mg/kg/day. Maximum absolute infant dose estimated for olanzapine was 0.78 mg/kg/day, while values at 75th and 25th percentiles of 26 days of measurements being lower at 0.31 and 0.15 mg/kg/day, respectively. Median absolute infant dose for olanzapine was also fairly low at 0.21 mg/kg/day.

Relative infant doses estimated over 26 days were quite low for both drugs but especially for quetiapine (Maximum= 0.017%, 75th percentile= 0.006%, 25th percentile= 0.004%, Median= 0.005%). Maximum relative infant dose estimated for olanzapine was 0.47% (75th percentile= 0.19%, 25th percentile= 0.09%, Median= 0.13%).

**Conclusions:** A relative infant dose of 10% of weight-adjusted maternal dose is the most commonly accepted cut off for safe breastfeeding while on drug [3]. Reported relative infant doses estimated over 78 milk samples for olanzapine and quetiapine indicate that both drugs can be used safely in breastfeeding women with once daily dosing strategy. Absolute infant doses as well as time-dependent- and daily milk concentrations suggest that drug exretion into milk decreases with time throughout the day achieving lowest doses before intake of next dose. Magnitude of this decline is a reflection of drug half life with fastest decline being achieved with shorter half life drugs. For SGAs with higher excretion into milk avoiding initial hours of breast feeding may help to reduce infant exposure to drug.

#### References

[1] Schatzberg A. F., Nemeroff C. B., 2009. Textbook of Psychopharmacology 4th Edition. American Psychiatric Publishing, Washington, DC.

[2] Begg E. J., Duffull S. B., Hackett L. P.Ilett K. F., 2002. Studying Drugs in Human Milk: Time to Unify the Approach. J Hum Lact 18, 323–331.

[3] Bennet P. N., 1996. Use of Monographs on Drugs in the Drugs and Human Lactation 3rd Edition. Edited by Bennet P. N. Elsevier, Amsterdam, NL. pp 67–74.