# Short report

# Season of birth and anorexia nervosa

Giulio Disanto, Adam E. Handel, Andrea E. Para, Sreeram V. Ramagopalan and Lahiru Handunnetthi

# Summary

Our aim was to investigate whether there is a season-of-birth effect in anorexia nervosa. In a meta-analysis, we compared the distribution of anorexia births (n = 1293) from four independent UK cohorts to that of the general UK population (n = 21914037), using both the Walter & Elwood seasonality and chi-squared tests. We found an excess of anorexia births from March to June (odds ratio (OR) = 1.15, 95% Cl 1.03–1.29, P = 0.012) and a deficit from September to October (OR = 0.8,

95% CI 0.68–0.94, P = 0.007). These results indicate that environmental risk factor(s) are operative during gestation or immediately after birth and their identification will be important for disease prevention strategies.

### **Declaration of interest**

None.

A growing body of evidence suggests a role for season of birth in determining susceptibility to a wide range of psychiatric disorders such as schizophrenia, bipolar disorder, major depression and suicidal behaviour.<sup>1,2</sup> This hypothesis has been investigated in people with anorexia nervosa and other eating disorders;<sup>3-8</sup> however, although an excess of spring births has been suggested, results are conflicting and rarely achieve statistical significance. The reasons for this conflict are at least twofold. First, seasonof-birth studies require a large number of cases to achieve sufficient statistical power to detect small differences in seasonal births between patients and controls. However, these studies only looked at a few hundred people with anorexia, resulting in less than 30% power to detect the presence of a seasonal risk factor with an odds ratio of 1.2. Second, differences in the statistical tests used may provide another explanation for conflicting results. Standard techniques such as a simple chi-squared tests (used in most of the previous studies on anorexia) are easy to perform but non-standard techniques such as harmonic and spectral analysis are more powerful and suitable for this type of investigation.<sup>9</sup> We therefore performed a meta-analysis on four UK cohorts of individuals with anorexia nervosa, making this the largest study to assess the presence of a season-of-birth effect in anorexia.

# Method

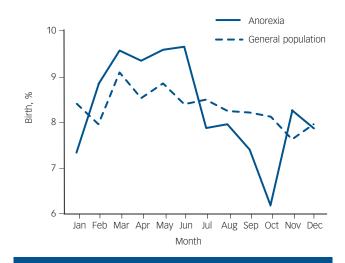
The PubMed database was searched using the search strings "anorexia nervosa AND season", "anorexia AND month" and "anorexia AND birth" to identify relevant articles. Given the potential confounding role of country-specific factors such as different social and nutritional habits, disease prevalence, birth trends and latitude, we decided to include only studies from the UK. Online Table DS1 shows the main features and findings of the studies included in the meta-analysis.

A pooled total of 1293 anorexia nervosa births were compared with those of the general population born between 1950 and 1980 (n = 21914037) obtained from the UK Office for National Statistics (www.statistics.gov.uk/). This birth interval (1950–1980) matches that of the individuals with anorexia. To assess the presence of a month-of-birth effect in anorexia nervosa, we used both the Walter & Elwood's seasonality<sup>10</sup> and chi-squared tests. With the Walter & Elwood's seasonality test it is possible to estimate within-year fluctuations with a 12-month periodicity (simple harmonic seasonal variation). Our study had a power of

80% to detect the presence of a seasonal factor with an odds ratio (OR) of 1.2.

# Results

The monthly distributions of anorexia births and general population births across the year are shown in Fig. 1. Using the Walter & Elwood's test, the birth distribution of those in the anorexia nervosa group was found to be significantly different from that of the general population (P = 0.02). To confirm these findings we performed a chi-squared analysis. Similarly, the birth distribution of those in the anorexia nervosa group significantly differed from that of the general population, being higher in the first half of the year compared with the second half (OR = 1.13, 95% CI 1.01-1.26, P=0.025). Further analyses highlighted an excess of anorexia nervosa births from March to June (OR = 1.15, 95% CI 1.03-1.29, P=0.012) and a deficit from September to October (OR = 0.8, 95% CI 0.68-0.94, P = 0.007) in comparison with the rest of the year. The peak-to-trough ratio was then evaluated comparing the periods March-June with September–October (OR = 1.31, 95% CI 1.1–1.56, P = 0.001).



**Fig. 1** Percentage distribution of births in individuals with anorexia and the general population.

404

#### Discussion

In line with the 'fetal origin of adult disease' hypothesis, formulated by David Barker, it is now acknowledged that early-life exposure to environmental factors may influence the risk of late-onset diseases.<sup>11</sup> Here we provide clear evidence in support of a season-of-birth effect in anorexia nervosa. A number of studies have shown such an effect in psychiatric disorders. Thus, the presence of similar findings in anorexia is perhaps not surprising. By using a large sample size of people with anorexia nervosa and controls and adopting both standard (chi-squared) and non-standard (Walter & Elwood) statistical approaches, we were able to confirm more confidently what other studies had previously only suggested. Consistent with our findings, an excess of anorexia and bulimia nervosa births during the spring was observed in other studies, raising the possibility that the same factor(s) could also influence susceptibility to other eating disorders. However, small sample sizes, inappropriate statistical methodologies and conflicting results did not allow any definite conclusion.<sup>8</sup> Intriguingly, a similar excess of spring births has also been observed in major depression, perhaps suggesting the presence of shared environmental risk factors acting early in life.<sup>2</sup> Also of interest is a recent study reporting an interaction between the D<sub>4</sub> dopamine receptor gene and season of birth influencing body weight regulation in women with bulimia nervosa.<sup>12</sup>

It is important to understand that the season-of-birth effect can be considered as a marker of several environmental agents influencing disease risk. The excess of spring births could be the consequence of environmental factor(s) acting at any time from conception to the first postnatal months. Thus, the identification of the relevant factors remains a challenging goal. However, seasonal changes in temperature, sunlight exposure and consequent vitamin D levels, maternal nutrition and infections are all strong candidate factors. Intriguingly, vitamin D levels have been shown to be associated with psychiatric disorders.<sup>13</sup> Although the presence of low vitamin D levels in people with psychiatric illness may be the consequence of reverse causation, further support for a role for vitamin D comes from functional studies showing that it is also involved in neuroprotection and brain development.<sup>14,15</sup>

To conclude, using the largest cohort of people with anorexia to date, we demonstrated that susceptibility to anorexia nervosa is significantly influenced by the season of birth, with higher rates in those individuals born in the spring and lower ones in those born in the autumn. Future studies with even larger sample sizes in different populations and at different latitudes are needed to confirm these findings. Identification of the relevant seasonal risk factors will undoubtedly be important for future disease prevention strategies.

# Funding

This work was supported by the Wellcome Trust (075491/Z/04).

Giulio Disanto, MD, Adam E. Handel, BMBCh, Andrea E. Para, MSc, Wellcome Trust Centre for Human Genetics, University of Oxford and Department of Clinical Neurology, University of Oxford, John Radcliffe Hospital, Oxford; Sreeram V. Ramagopalan, DPhil, Wellcome Trust Centre for Human Genetics, University of Oxford, Department of Clinical Neurology, University of Oxford, John Radcliffe Hospital, Oxford and Blizard Institute of Cell and Molecular Science, Queen Mary University of London, Barts and The London School of Medicine and Dentistry, London; Lahiru Handunnetthi, DPhil, Wellcome Trust Centre for Human Genetics, University of Oxford and Department of Clinical Neurology, University of Oxford, John Radcliffe Hospital, Oxford, UK

**Correspondence**: Lahiru Handunnetthi, The Wellcome Trust Centre for Human Genetics, Roosevelt Drive, Headington, Oxford OX3 7BN, UK. Email: lahiruh@well.ox.ac.uk

First received 15 Aug 2010, final revision 27 Oct 2010, accepted 9 Dec 2010

## References

- 1 Davies G, Welham J, Chant D, Torrey EF, McGrath J. A systematic review and meta-analysis of Northern Hemisphere season of birth studies in schizophrenia. *Schizophr Bull* 2003; 29: 587–93.
- 2 Torrey EF, Rawlings RR, Ennis JM, Merrill DD, Flores DS. Birth seasonality in bipolar disorder, schizophrenia, schizoaffective disorder and stillbirths. *Schizophr Res* 1996; 21: 141–9.
- 3 Rezaul I, Persaud R, Takei N, Treasure J. Season of birth and eating disorders. Int J Eat Disord 1996; 19: 53–61.
- 4 Eagles JM, Andrew JE, Johnston MI, Easton EA, Millar HR. Season of birth in females with anorexia nervosa in Northeast Scotland. *Int J Eat Disord* 2001; 30: 167–75.
- 5 Button E, Aldridge S. Season of birth and eating disorders: patterns across diagnoses in a specialized eating disorders service. Int J Eat Disord 2007; 40: 468–71.
- 6 Watkins B, Willoughby K, Waller G, Serpell L, Lask B. Pattern of birth in anorexia nervosa. I: early-onset cases in the United Kingdom. Int J Eat Disord 2002; 32: 11–7.
- **7** Waller G, Watkins B, Potterton C, Niederman M, Sellings J, Willoughby K, et al. Pattern of birth in adults with anorexia nervosa. *J Nerv Ment Dis* 2002; **190**: 752–6.
- 8 Winje E, Willoughby K, Lask B. Season of birth bias in eating disorders fact or fiction? Int J Eat Disord 2008; 41: 479–90.
- 9 Hakko H. Seasonal Variation of Suicides and Homicides in Finland: With Special Attention to Statistical Techniques used in Seasonality Studies. University of Oulu, 2000.
- 10 Walter S, Elwood J. A test for seasonality of events with a variable population at risk. *Br J Prev Soc Med* 1975; 29: 18–21.
- 11 Langley-Evans SC, McMullen S. Developmental origins of adult disease. *Med Princ Pract* 2010; 19: 87–98.
- 12 Levitan R, Kaplan A, Davis C, Lam R, Kennedy J. A season-of-birth/DRD4 interaction predicts maximal body mass index in women with bulimia nervosa. *Neuropsychopharmacology* 2010; 35: 1729–33.
- 13 Kinney DK, Teixeira P, Hsu D, Napoleon SC, Crowley DJ, Miller A, et al. Relation of schizophrenia prevalence to latitude, climate, fish consumption, infant mortality, and skin color: a role for prenatal vitamin d deficiency and infections? *Schizophr Bull* 2009; 35: 582–95.
- 14 Fernandes de Abreu DA, Eyles D, Feron F. Vitamin D, a neuroimmunomodulator: implications for neurodegenerative and autoimmune diseases. *Psychoneuroendocrinology* 2009; **34** (suppl 1): S265–77.
- 15 Eyles DW, Feron F, Cui X, Kesby JP, Harms LH, Ko P, et al. Developmental vitamin D deficiency causes abnormal brain development. *Psychoneuroendocrinology* 2009; 34 (suppl 1): S247–57.

