Season of birth and subclinical psychosis: Systematic review and meta-analysis of new and existing data

Aldo Córdova-Palomera, Raffaella Calati, Bárbara Arias, Manuel-Ignacio Ibáñez, Jorge Moya, Generós Ortet, Benedicto Crespo-Facorro, Lourdes Fañanás

Article history:
Received 2 July 2014
Received in revised form 10 October 2014
Accepted 30 November 2014
Available online 11 December 2014

Keywords:
Season of birth
Schizotypy
Subclinical psychosis
Winter birth
General population
Seasonality

Abstract
Season of birth (SOB) has been shown to modify the risk of several health outcomes, including a number of neuropsychiatric disorders. Empirical evidence indicates that subclinical forms of psychosis in the general population share some risk factors with categorical diagnoses of psychosis. Hence, by systematically reviewing and meta-analyzing new and existing data, the current work aimed to determine whether there is evidence of an association between winter SOB and subclinical psychosis in the general population. Our meta-analytic results do not indicate an association between winter SOB and schizotypy in adult populations, although they indicate winter SOB may be a risk factor for psychotic experiences or symptoms in children around 12–15 years (OR=1.12, 95%CI:1.03–1.21). In the whole new dataset for adults (n=481, mean age=22.8 years) no association was detected in either an unadjusted model or adjusting for gender and age. Overall, our results indicate that the association between winter SOB and increased subclinical psychosis may hold in children, but does not in the broad general adult population. Nevertheless, the epidemiological and clinicopathological significance of winter SOB as a risk factor for subclinical psychosis would probably be slight due to the small effect sizes indicated by the reports available to date.
1. Introduction

Season of birth (SOB) has been shown to modify the risk of several health outcomes, including a number of neuropsychiatric disorders (Brewerton et al., 2012; Cheng et al., in press; Davies et al., 2003; Disanto et al., 2012; Dume et al., 2010). There is evidence indicating that seasonality influences fetal growth and development (Currie and Schwandt, 2013; Flouris et al., 2009; Strand et al., 2011; Watson and McDonald, 2007), which bears significance for psychiatric research.

Some mechanisms have been proposed to explain how SOB affects early neurodevelopmental trajectories, including factors such as pollution, eating patterns, vitamin D deficits, maternal infections and temperature changes (Currie et al., 2009; Eyles et al., 2013; Schwartz, 2011; Siega-Riz et al., 2004). Recent epidemiological research has indicated that seasonality exerts a strong influence on fetal features such as gestation length and birth weight, and that these may be markedly be compelled by maternal influenza and pregnancy weight gain (Currie and Schwandt, 2013). In addition, research has suggested that SOB exerts a long-lasting effect on the embryonic brain; this may persist until adulthood (Giezendanner et al., 2013; Moore et al., 2001; Pantazatos, 2013), and is probably behind the enduring effect of the factors mentioned on mental health and disease.

While the psychiatric research mentioned above focuses on clinically-defined psychotic phenotypes, there is empirical evidence that attenuated (i.e., subclinical) forms of psychosis in the general population share many but not all risk factors with categorical diagnoses of psychosis (Breetvelt et al., 2010; Kelleher and Cannon, 2011; Linscott and van Os, 2010). Remarkably, despite the psychometric, phenomenological and temporal continuity between subclinical psychotic features and psychotic disorders, population structures ranging from normality to disease are probably discontinuous, and models that support a continuum of psychosis need further evaluation (David, 2010; Lawrie et al., 2010; Linscott and van Os, 2010, 2013). Hence, more research is needed to determine the precise extent of the overlap in risk and its putative epidemiological consequences.

Even though there is broad agreement between studies that winter SOB increases the risk for some psychotic conditions, studies that evaluate this effect for subclinical psychosis in the general population provide mixed results. Therefore, by reviewing and meta-analyzing previously published reports, the current work aims to determine whether there is evidence of an association between winter SOB and subclinical psychosis. New data from an independent community sample of adults is included to increase the statistical power and to replicate previous studies.

2. Materials and methods

2.1. Meta-analysis

2.1.1. Search strategy and inclusion criteria

A literature search was conducted using PubMed, The ISI Web of Science and PsycINFO to screen for studies that evaluate the association between SOB and subclinical psychosis in the general population. The string ["season of birth" OR "seasonality" OR "birth season") AND ("psychotic experiences" OR "psychotic like" OR "psychosis like" OR "subclinical psychosis" OR schizotypy OR schizophrenia), with proper syntax adjustments depending on the search engine, was applied to retrieve potentially relevant articles published before October 22nd 2013. There was no language restriction. In addition, the lists of references from the reports identified and other relevant publications were scrutinized to find further pertinent publications.

Papers were included if they: i) reported results from primary research, ii) examined the association between SOB and subclinical psychosis, iii) presented data using non-ill general population samples (or both patients and controls, but showed information for healthy subjects separately), iv) performed psychometric evaluations of individuals from the northern hemisphere, and v) considered psychotic experiences, schizotypal traits, or non-clinical psychotic symptoms as outcomes, and measures were obtained via self-rating scales. This apparently broad category of outcomes was considered in recognition of the fact that questionnaires evaluating schizotypal traits show an overlap with assessments of other psychosis-proneness traits and psychosis-spectrum symptoms in the general population (Barrantes-Vidal et al., 2013; Wang et al., 2012).

2.1.2. Data extraction

The search results were independently screened by two reviewers (ACP and RC) to identify relevant studies. A data extraction sheet was used to record important information such as the main outcome measure, psychometric scale used and number of items, definition of the seasons of the year, sample size, gender and ethnicity of participants, summary result and other comments. Also, the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement checklist (von Elm et al., 2007) was used to assess the accuracy and completeness of the observational studies reviewed. Briefly, this checklist consists of 22 items that consider six different sections of a report: 1) title and abstract, 2) introduction, 3) methods, 4) results, 5) discussion and 6) other information.

2.1.3. Data analysis

All statistical analyses were performed in R (R Development Core Team, 2011). Since not all studies provide the same effect size
measure (for example, when using continuous psychometric scales authors may report mean differences or t-statistics), odds ratios were estimated where necessary using R’s compute.es package (Del Re, 2013). The package allows statistics from one study to be converted to many other common effect size estimates; it is based on previous literature on meta-analysis methodology (Cooper et al., 2009). Along with existing findings, results from an ongoing study were included as another independent study (see below: Section 2.2).

Meta-analytic procedures were implemented with R’s metafor package (Viechtbauer, 2010), and residual heterogeneity (random effects model) was accounted for through the DerSimonian–Laird (DL) approach. For comparison, sensitivity analyses included fixed effects models for meta-analytic procedures. As there were no large differences across models, and since random effects models are especially suitable for sets of studies with non-identical methods and samples (Viechtbauer, 2010), only results obtained with random effects are shown.

Between-study differences were similarly assessed. The following indicators of heterogeneity and variability are reported: $I^2$ (estimated amount of total heterogeneity), $H^2$ (total heterogeneity/total variability), $I^2$ (total variability/sample variability) and results from Cochran’s Q-test for residual heterogeneity (Cochran, 1954), which evaluates whether the variability in effect sizes or outcomes is greater than expected based on sampling variability. Statistically significant results from the last test indicate that effects or outcomes in a meta-analysis are heterogeneous.

### 2.2. New data

#### 2.2.1. Sample description and measures

Data from a sample consisting of 561 individuals were gathered from both a university campus (Jaume I University; Castelló, Spain) and other university offices and technical schools in Barcelona, Spain, between 2005 and 2006. Recruiting was mainly conducted through advertisements in those institutions. The exclusion criteria applied were the presence of neurological conditions, medical illnesses affecting brain function, a history of head injury and a history of psychiatric treatment. These were screened via an interview based on selected items from other questionnaires (First, 1997; Maxwell, 1992). After applying the exclusion criteria and due to a lack of data about either date of birth or psychopathology for some participants, the final sample (i.e., the subset included in all analysis; hereafter “new data”) consisted of 481 subjects (46.4% male; mean age: 22.8 years, S.D.: 5.3 years). Of these individuals, 80.7% were students.

Schizotypal personality traits were assessed using the Schizotypal Personality Questionnaire-Brief (SPQ-B) (Raine and Benishay, 1995), a brief, 32-item self-report screening instrument derived from the Schizotypal Personality Questionnaire (Raine, 1991). Items in the SPQ-B are scored “yes” or “no”, which is later translated into either the presence or the absence of a schizotypal trait. Total schizotypal scores were calculated for each subject by adding all the SPQ-B items for which he/she answered “yes”. Date of birth data was structured into winter (December 22nd–March 21st) and the rest of the year. This definition of the winter period was adopted following the conventional seasonal periodicity of annual cycles of meteorological and ecological patterns in several northern hemisphere countries, and in view of the facts that 1) all the studies included in the meta-analysis presented information suitable for comparison with the same yearly structure and 2) they and other psychiatric literature reports usually define similar periods as risk factors.

All participants were of Caucasian (Spanish) ancestry. They provided written informed consent after a detailed description of the study aims and design, approved by the local Ethics Committee.

### Table 1

Demographic and psychopathological features of the new sample of 481-individuals introduced in this manuscript.

<table>
<thead>
<tr>
<th>Group comparison*</th>
<th>Winter birth (n=119, 43% male)</th>
<th>Non-winter birth (n=362, 48% male)</th>
<th>X-squared</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Mean S.D.</td>
<td>Mean S.D.</td>
<td>p</td>
<td></td>
</tr>
<tr>
<td>Schizotypal personality featuresa</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive-perceptual</td>
<td>1.3 1.5</td>
<td>1.5 1.5</td>
<td>1.27</td>
<td>0.26</td>
</tr>
<tr>
<td>Interpersonal</td>
<td>2.5 1.9</td>
<td>2.7 2.1</td>
<td>0.7</td>
<td>0.402</td>
</tr>
<tr>
<td>Disorganized</td>
<td>3.9 3.1</td>
<td>3.9 3.3</td>
<td>0.12</td>
<td>0.727</td>
</tr>
<tr>
<td>Total schizotypy score</td>
<td>7.7 5.1</td>
<td>8 5.5</td>
<td>0.19</td>
<td>0.662</td>
</tr>
</tbody>
</table>

Fig. 1. Flowchart of study selection and inclusion of results. Seven papers were incorporated in the qualitative analysis (see Table 2), and results from six of them and the new data (i.e., a total of seven independent results) were included in the meta-analysis.

All procedures were in accordance with the Helsinki Declaration. Additional descriptive details of the sample can be found in Table 1 and elsewhere (Aguilera et al., 2009; Arias et al., 2012).

#### 2.2.2. Statistical analysis of the new data

To include the new data in the meta-analysis, raw mean differences in total SPQ scores between individuals from the winter and the rest of the year births were obtained, and unadjusted odds ratios were estimated as described above (see Section 2.1.3).

Afterwards, multivariate linear regression analysis was performed to evaluate the relationship between total schizotypal scores and SOB. Since some reports indicate that subclinical psychosis may be influenced by both gender and age (Ito et al., 2010; Miettunen and Jaaskelainen, 2010; Wigman et al., 2012), and as these variables may have accounted for the between-study heterogeneity in the previous meta-analytic section, additional analysis was performed to include them as covariates (i.e., schizotypy ~ gender + age + SOB). This was conducted using ordinary least squares in the regression tests. For comparison, permutation-based p-Values were also obtained for these linear tests. These p-Values are useful for saturated designs, non-normal data or with apparent outliers (Wheeler, 2010), and thus allowed us to lessen the probability of false positives due to some statistical artefacts. Since both ordinary least squares and permutation tests for linear regression produced similar results, only those from the former method are reported.
3. Results

3.1. Meta-analysis

3.1.1. Eligibility-analysis

Fig. 1 depicts the search process. After applying the search strategy defined above and excluding duplicates and hits that were not scientific papers, 19 full-text papers were retrieved and assessed for eligibility. Eight studies met all inclusion criteria; description of these reports and the new data (from the independent sample characterized here) can be found in Table 2. From the nine data sources included in Table 2, an association between winter birth and subclinical psychosis is supported by three studies (Bolinskey et al., 2013; Hori et al., 2012; Tochigi et al., 2013); one study found increased risk in subjects born during summer (Kirkpatrick et al., 2008), and both the raw new data obtained here (see Section 2.2) and three other publications indicated no statistically significant association (Breetvelt et al., 2010; Cohen and Najolia, 2011; Reid and Zborowski, 2006). From the set of null studies, Reid and Zborowski (2006) report statistically significant results for the spring group (compared with all other births). Nevertheless, when combining data in their paper to arrange a winter/spring birth group, the significance of the effects is lost. It is worth noting that Kirkpatrick et al. (2008) conclude that summer births have increased risk of schizoid-like features, consistent with their previous findings in favor of a June/July excess of “deficit schizophrenia” births (Messias et al., 2004). However, this result could not be incorporated into the meta-analytic procedure due to the definition of exposure (June/July birth) and since the authors provide results from a subset of 171 high schizotypy scorers (i.e., there was no comparison with the low schizotypy scorers), wherein they evaluate the continuous psychopathological score with respect to birth season and gender. The only adjusted OR came from the study of Breetvelt et al. (2010), who account for demographical risk factors and other psychopathological traits. While adjusted and unadjusted effect sizes could be combined in meta-analysis provided they address the same relationship (Voils et al., 2011), it was not included in most of the analyses since the psychometric assessment of schizotypy implemented therein is not comparable to others.

3.1.2. Features of the studies included in the review and meta-analysis

As shown in Table 2, two studies reported empirical data from children (Polanczyk et al., 2010; Tochigi et al., 2013). Hence, they were examined separately. The other five studies reported on adult populations. Whereas the new data and two other studies (Cohen and Najolia, 2011; Hori et al., 2012) analyze relationships between schizotypal personality traits and the SPQ, the reports by Bolinskey et al. (2013) and Reid and Zborowski (2006) were based on the Chapmann Psychosis Proneness Scales (CPPS) (Chapman et al., 1978; Eckblad and Chapman, 1983; Eckblad et al., 1982). Hence, these five studies were first divided into two subsets (schizotypal personality or psychosis proneness) and later combined into a larger 5-study block for comparison. Data from all seven studies included in the meta-analysis were introduced as unadjusted effect size estimates (raw ORs).

Fig. 2 depicts the results of the accuracy and completeness assessment of the studies using the STROBE checklist. Overall, all the studies include informative abstracts and accurate explanations of their scientific background, rationale, objectives and hypotheses. Nonetheless, they exhibit some weaknesses in their discussion sections, either by not offering a cautious interpretation of results or by not discussing the external validity (generalizability) of the outcomes. Meta-analytic tests were performed afterwards to attempt to overcome such limitations of the available literature.

Notably, a cluster of 4 high-quality comprehensive studies (Bolinskey et al., 2013; Breetvelt et al., 2010; Polanczyk et al., 2010; Tochigi et al., 2013) was observed, whose minor drawbacks were mainly in the above-mentioned discussion of results. In contrast, the manuscripts by Kirkpatrick et al. (2008) and Reid and Zborowski (2006) lacked precision in a number of items that evaluate their methods (setting, description of participants, variables, data sources, bias, and study size or statistics), results and discussion. It is worth noting that neither of these two studies seemed to bias subsequent results of the meta-analysis. First, using a very particular methodological design, Kirkpatrick et al. (2008) conclude that summer SOB is a risk factor for a (non-clinical) proxy for the schizophrenia deficit syndrome (Table 2). This conclusion is derived from a new psychometric measure in which scores from the Beck Depression Inventory are subtracted from those of the Social Anhedonia Scale (i.e., anhedonia in the absence of depression). While this new measure may be problematic given the statistical correlation among psychometric scales (Lewandowski et al., 2006), the finding served as a confirmation of the authors’ previous results indicating a summer birth excess in clinically defined schizophrenia deficit syndrome (Kirkpatrick et al., 2002). That report was not included in the meta-analysis not only in view of the particular psychometric measure employed but also since its statistical approach compared SOB within a high-schizotypy group. Further research is needed to confirm this finding. Secondly, despite some methodological weaknesses, data from Reid and Zborowski (2006) indicate a very similar effect size to that found in other studies, including the new independent sample (see below). This probably suggests that raw CPPS questionnaire scores behave similarly in relation to winter SOB across studies. In fact, our meta-analytic results shown in subsequent sections do not seem to be biased by the presence or removal of this study.

In summary, there was no evident relationship between the STROBE quality assessment and the effect size derived from each report.

3.1.3. Association between winter birth and subclinical psychosis: meta-analysis results

Fig. 3 shows forest plots of two meta-analyses performed. Data from children suggest there is an association between winter/spring SOB and psychotic symptoms or experiences in the general population, though the effect size is relatively small (OR = 1.12, 95% CI: 1.03–1.21, p = 0.009; t²: 0; I²: 0%; H²: 1, Q = 0.53, p = 0.469). Publication bias did not seem to be an issue in this case since there was both a positive and a null result. It is worth noting that, despite providing a null result, inclusion of the study by Polanczyk et al. (2010) in the child meta-analysis did increase the overall effect size and narrow the confidence intervals, and Cochran’s Q-test indicated no statistically significant between-study sampling heterogeneity. Furthermore, since the report is based on a population with a mean age of 12 years, and Tochigi et al. (2013) also report estimates for the youngest half of their sample (whose mean age should also be around 12 years), additional meta-analysis was performed to compare these two 12-year-old samples (Supplementary Fig. 1). Remarkably, an increase in effect size was observed, and indexes of heterogeneity were smaller (i.e., samples were more homogeneous) in the former case (OR = 1.15, 95% CI: 1.03–1.29, p = 0.014; t²: 0; I²: 0%; H²: 1, Q = 0.33, p = 0.563).

Data for adults did not support statistically significant associations (OR = 1.22, 95% CI: 0.87–1.7, p = 0.256; t²: 0.09, I²: 66.44%, H²: 2.98, Q = 11.92, p = 0.018 (Fig. 3), with no evidence of publication bias (test for funnel plot asymmetry: z = 1.82, p = 0.069).
Table 2
Summary of data considered for review and meta-analysis. All odds ratios (OR) shown were included in posterior procedures; statistics and descriptives from Kirkpatrick et al. (2008) are informative here but not suitable for direct comparison and inclusion in the meta-analysis.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Main outcome*</th>
<th>n</th>
<th>Country of origin</th>
<th>Gender (% male)</th>
<th>Mean age (S.D.) years</th>
<th>Ethnicity</th>
<th>Scale; # of items</th>
<th>Winter definition</th>
<th>Result OR (95% CI, p)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>New data</strong></td>
<td>Schizotypal traits</td>
<td>481</td>
<td>Spain</td>
<td>46.4</td>
<td>22.78 (5.31)</td>
<td>Caucasian</td>
<td>Schizotypal Personality Questionnaire-Brief (SPQ-B); 32 items</td>
<td>Dec. 22–Mar. 21</td>
<td>OR = 0.89 (95% CI = 0.61–1.29, p = 0.526) Winter: no differential risk</td>
<td></td>
</tr>
<tr>
<td><strong>Tochigi et al. (2013)</strong></td>
<td>Psychotic-Like Experiences (PLEs)</td>
<td>17702</td>
<td>Japan</td>
<td>49.4</td>
<td>15.2 (1.7)</td>
<td>Japanese</td>
<td>Items from the Diagnostic Interview Schedule for Children (DISC-C); 4 items</td>
<td>Nov.–Mar.</td>
<td>OR = 1.11 (95% CI = 1.02–1.21, p = 0.016) Winter: increased risk</td>
<td></td>
</tr>
<tr>
<td><strong>Bolinskey et al. (2013)</strong></td>
<td>Psychometric schizotypy</td>
<td>84</td>
<td>USA</td>
<td>16.7</td>
<td>18.77 (1.02)</td>
<td>Mixed (Caucasian, African-American, Hispanic)</td>
<td>Chapman psychosis proneness scales (CPSS); 105 items</td>
<td>Dec. through mid-Mar. (“winter/early spring”)</td>
<td>OR = 3.69 (95% CI = 1.24–11.01, p = 0.009) Winter: increased risk</td>
<td></td>
</tr>
<tr>
<td><strong>Hori et al. (2012)</strong></td>
<td>Schizotypal traits</td>
<td>451</td>
<td>Japan</td>
<td>24.8</td>
<td>45.2 (15.2)</td>
<td>Japanese</td>
<td>Schizotypal Personality Questionnaire (SPQ); 74 items</td>
<td>Dec., Jan. and Feb. (“Japanese winter”)</td>
<td>OR = 1.72 (95% CI = 1.19–2.48, p = 0.004) Winter: increased risk</td>
<td></td>
</tr>
<tr>
<td><strong>Cohen and Najola (2011)</strong></td>
<td>Schizotypal traits</td>
<td>3485</td>
<td>USA</td>
<td>36.2</td>
<td>19.28 (2.26)</td>
<td>Mixed (Caucasian, African-American, Hispanic and “other”)</td>
<td>Different versions of the Schizotypal Personality Questionnaire (SPQ); on average, 42 items answered by each individual</td>
<td>Dec. 22–Mar. 21</td>
<td>OR = 1.06 (95% CI = 0.76–1.5, p = 0.735) Winter: no differential risk</td>
<td></td>
</tr>
<tr>
<td><strong>Polanczyk et al. (2010)</strong></td>
<td>Psychotic symptoms</td>
<td>2127</td>
<td>UK</td>
<td>49</td>
<td>12 (0)</td>
<td>Caucasian</td>
<td>Items from dunedin study and avon longitudinal study of parents and children interview protocols; 7 items</td>
<td>Not mentioned in article</td>
<td>OR = 1.28 (95% CI = 0.88–1.87, p = 0.196) Winter: no differential risk Twin sample (statistical adjustment of responses to study each co-twin individually).</td>
<td></td>
</tr>
<tr>
<td><strong>Breitvelt et al. (2010)</strong></td>
<td>Non-clinical psychotic symptoms</td>
<td>4894</td>
<td>The Netherlands</td>
<td>44.9</td>
<td>39 (12.6)</td>
<td>Mixed (Dutch, Western European, and a few from Surinam, Morocco and Turkey)</td>
<td>Dutch version of the symptom check list (SCQ-90-R); 4 items</td>
<td>Jan., Feb. and Mar.</td>
<td>OR adjusted for demographical risk factors.</td>
<td></td>
</tr>
<tr>
<td><strong>Kirkpatrick et al. (2008)</strong></td>
<td>Schizoid-like features: “proxy for the deficit syndrome”</td>
<td>426</td>
<td>USA</td>
<td>28</td>
<td>20.1 (3.5)</td>
<td>Mixed (Caucasian, African-American, Asian/Pacific, Hispanic and “other”)</td>
<td>Combined measure: chapman psychosis proneness scales (CPSS) and Beck Depression Inventory (BDI); 105 (CPSS) plus 21 (BDI)</td>
<td>“Summer” was defined as Jun–July, and tests were about “Summer” versus other months</td>
<td>OR adjusted for demographical risk factors.</td>
<td></td>
</tr>
</tbody>
</table>

A. Córdova-Palomera et al. / Psychiatry Research 225 (2015) 227–235
Complementary analyses were performed to explore these data, assorted by psychometric scale. Nevertheless, no associations were detected either when evaluating schizotypal personality traits (OR=1.17, 95% CI: 0.8–1.71, p\textsubscript{OR}=0.408; r²: 0.08, I²: 69.63%, H²: 3.29, Q=6.59, p\textsubscript{Q}=0.037) or when assessing psychosis proneness (OR=1.69, 95% CI: 0.45–6.36, p\textsubscript{OR}=0.439; r²: 0.76, I²: 81.04%, H²: 5.28, Q=5.28, p\textsubscript{Q}=0.022) (Supplementary Fig. 2).

3.2. Further results using new data

In the previous meta-analysis, mean differences in raw SPQ scores were used to compute ORs from the new data. This allowed comparison with other effect size estimates which were mostly also unadjusted. Hence, additional tests using linear regression models were performed to evaluate whether adjusting for gender and age (two important sources of heterogeneity in the former results, which indeed influence measures of subclinical psychosis) could provide additional insight.

As expected from the literature, higher schizotypy scores were found to be associated with both male gender and younger age (β\textsubscript{gender}=1.91, β\textsubscript{age}=-3.95, p\textsubscript{gender}<10\textsuperscript{-4}; β\textsubscript{age}=-4.15, p\textsubscript{age}<10\textsuperscript{-4}). Nevertheless, there was no association with winter SOB in the same regression test (β\textsubscript{winter}=-0.36, p\textsubscript{winter}=0.521; adjusted R² for the whole test=0.055). The significance of these results did not change when including individuals with a previous history of psychiatric treatment.

4. Discussion

The present study aims to determine whether there is enough evidence to support the association between psychometrically-assessed subclinical psychosis and winter SOB, by evaluating previous results and new data. A total of nine independent results were included in a qualitative and systematic review, and seven of them were statistically assessed by means of meta-analytic procedures. New data was explored to control for potentially confounding demographic variables.

4.1. Interpretation of meta-analysis results and literature review

The meta-analysis results indicate that an association between winter SOB and childhood (~12–15 years old) psychotic symptoms/experiences is sustained by the current empirical evidence, though the effect size is relatively small (OR=1.12, 95% CI: 1.03–1.21, p=0.009). In the broad adult population, there was no association between SOB and subclinical psychosis, either when using an extensive definition of psychosis or when carefully separating reports according to their psychometrical approach to the assessment of psychopathology (i.e., independently examining schizotypal personality and psychosis proneness). It is noteworthy that the reports included in the meta-analysis of child psychotic symptoms/experiences display large sampling homogeneity, suggesting reliability of the winter SOB-psychosis relationship in child samples. However, currently available reports for adults may lack homogeneity. It is likewise worth noting that all these outcomes are based on unadjusted effect size estimates.

An important topic raised by these meta-analysis results is the contrast in the relationship between SOB and psychopathological profiles across ages: while winter SOB seems to increase the risk of psychotic symptoms in children, this may not be the case in adults. It is worth noting that lower schizotypal scores are typically found with increasing age in adults, as shown in the literature (Badcock and Drągović, 2006) and confirmed by the new community sample used here. One could speculate that, since the effect size of winter SOB on child subclinical psychosis is small, the continuous and

---

<table>
<thead>
<tr>
<th>Authors</th>
<th>Main outcome</th>
<th>Scale: # of items</th>
<th>Ethnicity</th>
<th>Gender</th>
<th>Mean (SD) years</th>
<th>Country</th>
<th>Main result</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reid and Zbroinski (2006)</td>
<td>Winter SOB</td>
<td>65 items</td>
<td>Mixed (White, Black, Hispanic, Asian, American-Indian and &quot;other&quot;)</td>
<td>Male</td>
<td>24.6</td>
<td>USA</td>
<td>OR=0.94, 95% CI=0.62–1.41, p=0.766</td>
<td>Winter/Spring births associated with higher risk than other seasons. Seasonality results were obtained by analyzing a 171-individual high-schizotypy group. Winter/Spring births associated with higher risk than other seasons. Winter/Spring births associated with higher risk than other seasons. Winter/Spring births associated with higher risk than other seasons.</td>
</tr>
</tbody>
</table>
perhaps stronger influence of age may render SOB effects practically undetectable in adults.

As in all meta-analysis, the feasibility of results largely depends on the quality of the incorporated data. Although publication bias does not seem to be present in the studies included here (all null results were derived from reports emphasizing further positive findings), there was large study heterogeneity, ostensibly derived from differences in gender and age distributions, number of ethnic groups included and length of psychometric instruments used. It is worth noting that all previous reports openly supporting a winter SOB-subclinical psychosis association (Bolinskey et al., 2013; Hori et al., 2012; Tochigi et al., 2013) are derived from populations with large heterogeneity for such study attributes.

4.2. Analysis of new data

Further analysis was performed with data from an independent adult sample, to evaluate the effect of the two aforementioned potentially confounding variables in the relationship between SOB and subclinical psychosis. Inclusion of this sample helped increase the statistical power in the meta-analysis and also allowed us to replicate prior studies. This new data came from individuals with no previous history of psychiatric drug consumption (another infrequently controlled variable in prior reports), though the results did not change when treated individuals were included in the analysis. Winter SOB was not associated with subclinical psychosis, either in a univariate model or adjusting for gender and age. Results from this independent sample were in agreement with a number of previously published reports for adult populations, and sensitivity analysis suggested its inclusion improved the meta-analysis.

4.3. Further issues and future directions

Some limitations of the current study and supplementary recommendations for subsequent research warrant mention. The limitations include the definition of seasonal exposure (winter SOB in the northern hemisphere), which was conventionally adopted due to its high rate of recurrence in research reports. Nevertheless, since SOB may be a proxy of prenatal insults occurring during developmental windows prior to birth, further contrast between seasons may lead to distinct outcomes. For instance, Reid and Zborowski (2006) report an association between winter/spring when compared to summer/fall births. However, such an association was driven by spring births, and comparison of winter versus other seasons led to the inclusion of data from their report as a non-significant odds ratio.

Recent epidemiological evidence provided by Currie and Schwandt (2013) is relevant in this context. They conclude that May conception (i.e., birth around mid-February) increases the risk of a short gestation and low birth weight, which is probably mediated by influenza exposure. Therefore, assessment of populations conceived during this
narrow window may help identify at-risk individuals. Also, those authors indicate that conception during summer may lead to high pregnancy weight gain, which is often reflected as high birth weight. Inclusion of individuals conceived in this season may possibly bias some results in epidemiological research.

The small number of reports may also affect meta-analysis results. Two points must be discussed in this regard. First, in the meta-analysis of children, combining studies gave optimal homo-
some results in epidemiological research. Inclusion of individuals conceived in this season may possibly bias the narrow window may help identify at-risk individuals. Also, those authors enthusiastically invited to address this topic, only mild effects could be expected on the basis of the current results. Hence, the clinico-pathological significance of winter SOB on later subclinical psychotic outcomes may not be severe and the epidemiological relevance would probably be small.

Contributors

Study design: Aldo Córdova-Palomera, Raffaella Calati, Bárbara Arias, and Lourdes Fañanás.

Collection of new data (including sample recruitment and psychometric evaluations): Bárbara Arias, Manuel-Ignacio Ibáñez, Jorge Moya, Generós Ortet, and Lourdes Fañanás.

Data management and statistical analyses: Aldo Córdova-Palomera and Raffaella Calati.

Writing of the manuscript: Aldo Córdova-Palomera, Raffaella Calati, Bárbara Arias, Manuel-Ignacio Ibáñez, Jorge Moya, Generós Ortet, Benedicto Crespo-Facorro, and Lourdes Fañanás.

Role of funding source

Funding sources had no further role in study design, analysis and interpretation of the data, writing, or decision to submit the manuscript for publication. Authors are responsible for statements and assertions, which do not constitute the views of the funding sources.

Conflict of interest

Authors have no conflict of interest to declare.

Acknowledgment

This work received support from projects funded by the Spanish Ministry of Science and Innovation (Grant numbers SAF2008-05674-C03-00 and 03, PNSD2008-1090, PNSD2009-1019 and IT2009-0016), the Institute of Health Carlos III (CIBERSAM, research group 08), the Comissionat per a Universitats i Recerca, DIUE, Generalitat de Catalunya, Spain (Grant number 2014SGR1636), Fundació Caixa Castelló-Bancaixa (Grant numbers P1-1B2010-40 and P1-1B2011-47) and the Ministerio dell’Istruzione, dell’Università e della Ricerca, Italy (IT107CB8DC). ACP was funded by CONACYT, Mexico (Grant number 310762). Authors are indebted to Prof. Dr. Alessandro Serretti for critical reading of the manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2014.11.072.

References


Bolinsky, P.K., Iati, C.A., Hunter, H.K., Novi, J.H., 2013. Season of birth, mixed-
handness, and psychiatric schizophrenia: preliminary results from a prospec-


Davies, G., Welham, J., Chant, D., Torrey, E.F., McGrath, J., 2003. A systematic review and meta-analysis of Northern Hemisphere season of birth studies in schizo-

Del Re, A., 2013. compute.es: Compute effect sizes.


Dome, P., Kapitány, B., Ignitó, G., Rihmer, Z., 2010. Season of birth is signi-


Eckblad, M., Chapman, I.J., Chapman, J.P., Mishlove, M., 1982. The revised social

environment, adult brain function and the links between low levels of vitamin D and neuropsychiatric disease. Frontiers in Neuroendocrinology 34, 47–64.


