



Explaining variation in the premorbid adjustment of schizophrenia patients: the role of season of birth and family history[☆]

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Abstract

Several studies have shown that patients with schizophrenia are more likely to be born in the winter and early spring than at any other time of the year. Furthermore, some studies have reported that winter-born patients differ from non-winter-born patients in terms of risk factors, symptoms, sensory abnormalities and brain morphology. Associations between season of birth and premorbid adjustment (PMA), however, are still unclear.

Objective: The main purpose of this study was to determine whether winter-born and non-winter-born schizophrenia patients differ in terms of PMA and to examine how family history of schizophrenia-spectrum disorders may influence the association.

Method: Data on four PMA dimensions (attention, internalizing, externalizing and social problems) and family history were gathered from 37 schizophrenia patients (26 males and 11 females) and their mothers.

Results: Non-winter-birth and a positive family history of schizophrenia-spectrum disorders were associated with worse PMA. Results suggest that, although no significant interaction was found, season of birth and family history appear to work together in explaining distinct dimensions of PMA.

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Since the contemporary descriptions of schizophrenia by Bleuler (1911) and Kraepelin (1902), researchers have strived to uncover the origins of the illness. It is suspected that both genetic as well as non-genetic environmental factors are involved in the etiology of schizophrenia.

Season of birth is one of the most firmly established non-genetic risk factors for schizophrenia.

Many studies have consistently reported higher rates of birth in winter and early spring months among schizophrenia patients (Norris and Chowning, 1962; Pallast et al., 1994; O'Callaghan et al., 1991). Reviews conclude that the excess of schizophrenic winter births ranges between 5% and 8% (Bradbury and Miller, 1985; Torrey et al., 1997). This season of birth effect has been repeatedly observed in the Northern Hemisphere and, although less consistently, in the Southern Hemisphere (McGrath et al., 1995; Torrey et al., 1997). No season of birth effect, however, has been found for schizophrenia in equatorial regions, where there is little seasonal variation in temperatures (d'Amato et al., 1996; Parker et al., 2000).

In addition to etiological heterogeneity, schizophrenia patients may also have very different histories of premorbid adjustment (PMA). For schizophrenia, the term "premorbid" applies to the period of time prior to the onset of the first decline in functioning, that is, from birth until the onset of the prodrome. Studies have shown that schizophrenia patients tend to have a pattern of either good (normal) or poor (deteriorating) PMA (Gittelman-Klein and Klein, 1969). It has been estimated that approximately 30% of all schizophrenia patients have a history of poor PMA (Walker et al., 1996), although this estimate may only apply to patients from higher socioeconomic backgrounds. Patients with a history of poor PMA have been found to experience behavioral problems in areas such as social functioning, motor coordination and cognition before the onset of the prodromal phase of the illness (Goldberg and Schmidt, 2001; Silverstein et al., 2002; Walker et al., 1994).

To understand the heterogeneity of schizophrenia better, many investigators have attempted to categorize the illness into different subtypes, by identifying correlates of various illness dimensions. For instance, studies comparing winter-born and non-winter-born schizophrenia patients have found that those born in the winter are more likely to be females (Dassa et al., 1996), to have been born in an urban environment (O'Callaghan et al., 1995; Takei et al., 1995), to have had fewer obstetric complications (Kinney et al., 1994), to suffer from less severe negative symptoms (Kirkpatrick et al., 1998), to have enlarged cerebral ventricles (Sacchetti et al., 1992; Zipursky and Schulz,

1987) and to have a better outcome (Pulver et al., 1983). Winter-born patients are also less likely to have a family history of the illness (Kinney et al., 2000; Roy et al., 1994).

Similar subgroup comparisons have been made in relation to family history. Schizophrenia patients with a familial loading are more likely to have an earlier age at onset (Alda et al., 1996), more severe negative symptoms (Malaspina et al., 2000), worse performance on dichotic listening tasks (Malaspina et al., 1998), reduced cranial and cerebral areas without ventricular enlargement (Schwarzkopf et al., 1991) and tend to be more resistant to treatment (Silverman et al., 1987).

Finally, rather than studying subgroups of schizophrenia patients according to presumed causal factors, some studies compare patients according to premorbid adjustment. Patients with a history of poor PMA are more likely to be males (Bailer et al., 1996; Childers and Harding, 1990), to have a family history of the illness (Foerster et al., 1991), to have had an insidious onset (Bailer et al., 1996), to present with more severe negative symptoms (Addington and Addington, 1993; Bailer et al., 1996), to have the deficit syndrome (Buchanan et al., 1990), to have greater cognitive deficits (Silverstein et al., 2002) and to have a poorer outcome (Bailer et al., 1996).

Only one known study has examined the possible relationship between season of birth and PMA. Roy et al. (1995) collected data on PMA, symptoms, neuropsychological functioning and brain morphology for 107 winter-born and 162 non-winter-born schizophrenia patients and found no differences between the 2 groups on any of the 23 variables examined. However, the authors chose a measure of PMA that only examines two dimensions of PMA (social functioning and internalizing problems) during childhood (6–12 years) and adolescence (13–21 years) and failed to systematically exclude data points occurring within the prodromal and psychotic phases. These problems may explain the investigators' inability to report an association between season of birth and premorbid behavior.

Consequently, the association between season of birth and PMA in schizophrenia is still unclear. Yet, given that patients with a family history of schizophrenia have poorer PMA and given that

winter-born patients are relatively unlikely to have a positive family history, it seems reasonable to infer that patients born in winter months would have a better PMA than those born in non-winter months, and that the association between season of birth and PMA may be confounded by a family history of the illness.

The purpose of this study was to clarify the associations among season of birth, family history and PMA. Specifically, we wished to determine whether winter-born and non-winter born schizophrenia patients differ in terms of PMA dimensions and to examine how family history may influence these associations. We hypothesized that winter-born and family history negative patients would have better PMA and that season of birth and family history would interact to explain variance in PMA, such that the worst PMA would be found in patients with a positive family history of schizophrenia spectrum-disorders born in non-winter-months. To test these hypotheses, schizophrenia patients and their mothers were interviewed about several putative risk factors for schizophrenia and about the patients' behaviors during childhood and adolescence.

1. Methods

The 37 participants in this study (26 males and 11 females) were drawn from previous studies on expressed emotion (King and Dixon, 1999; Dixon et al., 2000). Subjects for those studies represented schizophrenic outpatients from four Montreal hospitals. The current subset of patients includes those who accepted to participate in the additional assessments and agreed for their mothers to be interviewed as well. Participants met DSM-III-R criteria for schizophrenia, had neither neurological problems nor other Axis I diagnoses, were aged between 18 and 48 years (mean=31.7, S.D.=7.9), were considered stabilized and capable of giving consent by their treating psychiatrist, and were fluent in French or English. After written informed consent was obtained, subjects completed several assessments. Diagnoses were validated using the SCID for DSM-III-R (Spitzer et al., 1988), or when not possible, by chart review.

1.1. Measures

The Family Interview for Genetic Studies (FIGS, Maxwell, 1992) is a structured diagnostic instrument for establishing probable psychiatric diagnoses (depression, mania, schizophrenia, several personality disorders and alcohol/substance abuse) in relatives. Each mother, the family's primary historical informant, identified all first-, second- and third-degree relatives of the patient. She was then asked screening questions concerning these relatives, and then completed a face sheet and all relevant diagnostic checklists with the interviewer for each potentially diagnosable relative. During diagnostic rating consensus meetings, research group members made decisions about the potential psychopathology of the screened relatives: "no diagnosis", "diagnosed", "probable diagnosis" or "reported diagnosis" of a mental illness. Patients with at least one relative who was given a "diagnosed", "probable" or "reported" rating of schizophrenia or of a schizophrenia-spectrum disorder (schizoaffective disorder, paranoid or schizotypal personality disorders) were classified as family history positive. We expanded the operationalization of "family history positive" to include up to third-degree relatives as has been done by other researchers in the field (Kendler et al., 1996; Fogelson et al., 2004) who have shown elevated levels of risk in even third-degree relatives of probands (Maier et al., 2002).

Patients' age at onset of the prodrome and age at onset of first psychotic symptoms were also estimated during a consensus meeting. Consensus was derived from the "prodrome interview" (a short semi-structured interview developed by the research group), chart reviews and information provided by the mother. During the prodrome interview with the patient, the interviewer assists the patient in completing a time-line of his or her life including milestones in education, work and living circumstances. The interviewer then queries the patient about the onset of any significant personal changes or symptoms from a list inspired by the DSM-III-R prodromal symptom list. Prodrome onset was defined as any clinically significant change in DSM-III-R "prodromal" signs or symptoms, such as depression, anxiety, disturbance in sleep or attention, or non-psychotic illusions or magical thinking.

The Retrospective Child Behavior Checklist (R-CBCL, Neumann et al., 1995), comprised of 124 items

describing problem behaviors, was completed with the mother to assess PMA. We decided to use this method of assessing premorbid adjustment due to the completeness of the behavioral domains covered, relative to other scales that emphasize withdrawal and other internalizing behaviors. The questionnaire assesses eight syndrome subscales: withdrawal, somatic complaints, anxiety/depression, social problems, thought problems, attention problems, delinquency and aggression. The internalizing scale is the sum of the total scores for withdrawal, somatic complaints and anxiety/depression subscales, while the sum of scores for the aggression and delinquency subscales gives rise to the externalizing scale. For each item, the mother rated her child's behavior on a three-point scale (0=not true, 1=sometimes true or somewhat true, 2=very true or very often true) for each of five age levels (0–3, 4–7, 8–11, 12–15 and 16–18 years). For this study, we used each subject's mean score (that is, averaged across all age ranges judged to be "premorbid") on the attention, internalizing, externalizing and social problems scales. The thought problems scale was excluded from the analyses since the behaviors assessed (including "heard sounds" or "saw things that were not there") are more closely related to prodromal problems than to premorbid problems.

Four patients had scores that were approximately three standard deviation units above the mean on at least one of the four PMA dimension scales. The extreme scores were changed to the score in the data set closest to two standard deviation units above the mean. Even after "winsorizing" the scores of the outliers, the average PMA scores were still positively skewed. The composite scores for the four PMA dimensions were thus transformed using the log transformation (Tabachnick and Fidell, 2001). This normalized the scores for the internalizing and externalizing problems scales. The distributions of the premorbid attention and social problems scales were improved but remained slightly skewed because of the relatively large number of scores of zero. Given these improvements, the log-transformed scores were used in all analyses.

2. Results

Of the 37 schizophrenia patients in this study, 37.8% ($n=14$) were born in the winter (December

1st to March 31st) and 43% ($n=16$) had a family history of schizophrenia spectrum disorders. Participants were, on average, only moderately symptomatic: patients' total scores on the 30-item Positive and Negative Symptoms Scale (PANSS) ranged from 31 to 117 out of a possible score of 210 (mean=59.0, S.D.=18.8), while the total score on the 24-item Brief Psychiatric Rating Scale (BPRS) ranged from 33 to 55 on a possible score of 168 (mean=43.7, S.D.=9.5).

Table 1 presents the characteristics of the sample, grouped by season of birth. Overall, the winter-born and non-winter-born patients were similar with respect to age, gender, education, age at onset of prodrome, age at onset of psychotic symptoms, number of hospitalizations and severity of symptoms. The winter-born patients, however, were significantly younger than the non-winter-born patients at the time of first contact with treatment services for their psychotic symptoms [$t(35)=-2.165$, $p=0.04$]. The winter-born patients were also significantly less likely than the non-winter-born patients to have a positive family history of schizophrenia-spectrum disorders [$\chi^2(1)=-4.37$, $p=0.04$].

Generally speaking, the mothers reported few childhood behavior problems before the onset of the prodrome. Mean scores of the premorbid attention dimension scale ranged from 0 to 14.25 out of a possible score of 22 (mean=2.7, S.D.=3.1). Mean scores on the premorbid internalizing dimension scale ranged from 0 to 27.25 out of a possible score of 64 (mean=5.9, S.D.=6.7). Mean scores on the premorbid externalizing dimension scale scores ranged from 0.25 to 31.25 out of a possible score of 64 (mean=5.4, S.D.=6.7). Finally, mean scores on the premorbid social problem dimension scale ranged from 0 to 9.25 out of a possible score of 20 (mean=1.5, S.D.=1.9).

Independent t -tests were performed to determine whether the winter-born and non-winter-born patients differed in terms of PMA. As can be seen in Table 2, the non-winter-born patients had significantly higher (i.e., worse) scores on the premorbid attention problems scale [$t(35)=-2.87$, $p=0.007$] and on the internalizing problems scale [$t(35)=-2.10$, $p=0.042$] than the non-winter-born patients, but the two season of birth groups did not differ in terms of premorbid externalizing and social problems. After correcting for multiple statistical comparisons, however, only atten-

Table 1

Characteristics of the participants from full sample ($n=37$), winter-born [December–March ($n=14$)] and non-winter-born [April–November ($n=23$)] subsamples

Characteristic	Mean	S.D.
Age (years)		
Winter-born	30.4	8.6
Non-winter-born	32.6	7.5
Whole sample	31.7	7.9
Education (years)		
Winter-born	11.6	2.9
Non-winter-born	10.2	2.1
Whole sample	10.7	2.5
Age at onset of prodrome (years)		
Winter-born	17.1	3.2
Non-winter-born	16.8	6.7
Whole sample	16.9	5.6
Age at onset of psychotic symptoms (years)		
Winter-born	18.4	3.0
Non-winter-born	21.0	6.6
Whole sample	20.0	5.6
Age at first contact with treatment services (years)		
Winter-born	19.1	2.7
Non-winter-born	23.0	6.3
Whole sample	21.5	5.5
Number of hospitalisations		
Winter-born	2.2	1.5
Non-winter-born	2.0	1.7
Whole sample	2.1	1.6
Average rating on total symptom scale ^a		
Winter-born	2.1	0.5
Non-winter-born	1.8	0.6
Whole sample	1.9	0.6
% Male		
Winter-born	64.3	
Non-winter-born	73.9	
Whole sample	70.3	
% Positive family history of schizophrenia-spectrum disorders		
Winter-born ^b	21.4	
Non-winter-born ^c	56.5	
Whole sample ^d	43.2	

^a Some patients were assessed with the PANSS ($n=29$), while others were assessed using the BPRS ($n=8$). The symptom scores presented in the table represent the average rating (1–7) for either 24 (BPRS) or 30 (PANSS) items.

^b $n=3$ of 14.

^c $n=13$ of 23.

^d $n=16$ of 37.

tion problems remained significant (Bonferroni adjustment $p \leq 0.0125$).

Independent t -tests were also performed to determine whether the two family history groups differed in terms of PMA. As can be noted in Table 3, patients with a positive family history of schizophrenia-spectrum disorders had significantly higher scores on the premorbid attention [$t(35)=-2.93$, $p=0.006$],

internalizing [$t(35)=-2.26$, $p=0.03$] and social problems [$t(35)=-4.13$, $p<0.001$] scales of the R-CBCL, compared to patients who did not have a family history of the illness. The groups did not differ in terms of premorbid externalizing problems. After correcting for multiple statistical comparisons, however, only attention and social problems remained significant (Bonferroni adjustment $p \leq 0.0125$).

Table 2
R-CBCL log-transformed average scores for winter-born and non-winter-born patients

	Winter-born <i>N</i> =14	Non-winter-born <i>N</i> =23	<i>t</i>	<i>df</i>	<i>p</i>
	Mean (S.D.)	Mean (S.D.)			
Attention	0.24 (0.27)	0.54 (0.32)	−2.87	35	0.007
Internalizing	0.51 (0.36)	0.76 (0.36)	−2.10	35	0.042
Externalizing	0.60 (0.28)	0.66 (0.37)	−0.49	35	0.627
Social	0.25 (0.26)	0.33 (0.28)	−0.95	35	0.351

Two-way analyses of variance (ANOVAs) were performed to determine whether there were any significant interactions between season of birth and family history in explaining variance in PMA. Sample sizes varied for the four cells combining family history and season of birth: of the 16 family history positive patients, 3 were born in the winter and 13 were born in non-winter-months; of the 21 family history negative patients, 11 were born in the winter and 10 were born in non-winter months. The two-way ANOVAs revealed that there were no significant interactions between season of birth and family history for any PMA dimension. The analyses yielded significant main effects for season of birth (attention problems) and for family history (social problems) (see Table 4 and Fig. 1). Yet, close examination of the first two graphs in Fig. 1 suggests that season of birth and family history may be working together in explaining premorbid attention and internalizing problems. We thus performed *t*-tests among the non-winter-born patients on the different premorbid adjustment dimensions and found that the non-winter-born patients who had a positive family history of schizophrenia-spectrum disorders tended to have more severe premorbid attention and internalizing problems than the non-winter born patients without a

Table 3
R-CBCL log-transformed average scores for schizophrenia patients with and without a family history of schizophrenia-spectrum disorders

	FH Positive <i>N</i> =16	FH Negative <i>N</i> =21	<i>t</i>	<i>df</i>	<i>p</i>
	Mean (S.D.)	Mean (S.D.)			
Attention	0.60 (0.29)	0.30 (0.31)	−2.93	35	0.006
Internalizing	0.82 (0.36)	0.55 (0.35)	−2.26	35	0.030
Externalizing	0.72 (0.35)	0.57 (0.32)	−1.27	35	0.213
Social	0.48 (0.20)	0.17 (0.24)	−4.13	35	<0.001

family history of schizophrenia-spectrum disorders [attention problems: $t(21)=-2.117$, $p=0.046$ ($M=0.39$, $S.D.=0.33$ for no family history group; $M=0.67$, $S.D.=0.30$ for family history positive group); internalizing problems: $t(21)=-1.68$, $p=0.107$ ($M=0.63$, $S.D.=0.39$ for no family history group; $M=0.88$, $S.D.=0.33$ for family history positive group)].

3. Discussion

Three conclusions can be drawn from this study. First, it appears that non-winter-born schizophrenia patients (born between April and November) have more severe premorbid attention and internalizing problems than winter-born patients. Second, patients with a family history of schizophrenia-spectrum disorders seem to have more severe premorbid

Table 4
Results of the two-way ANOVAs: season of birth and family history in relation to the four premorbid adjustment dimensions

	<i>F</i>	<i>df</i>	<i>p</i>
Attention problems			
Season of birth	4.71	1	0.037
Family history	2.84	1	0.101
Season×family	0.43	1	0.516
Internalizing problems			
Season of birth	2.52	1	0.122
Family history	1.50	1	0.230
Season×family	0.44	1	0.512
Externalizing problems			
Season of birth	0.11	1	0.741
Family history	0.54	1	0.466
Season×family	0.55	1	0.462
Social problems			
Season of birth	0.28	1	0.599
Family history	14.77	1	0.001
Season×family	0.51	1	0.482

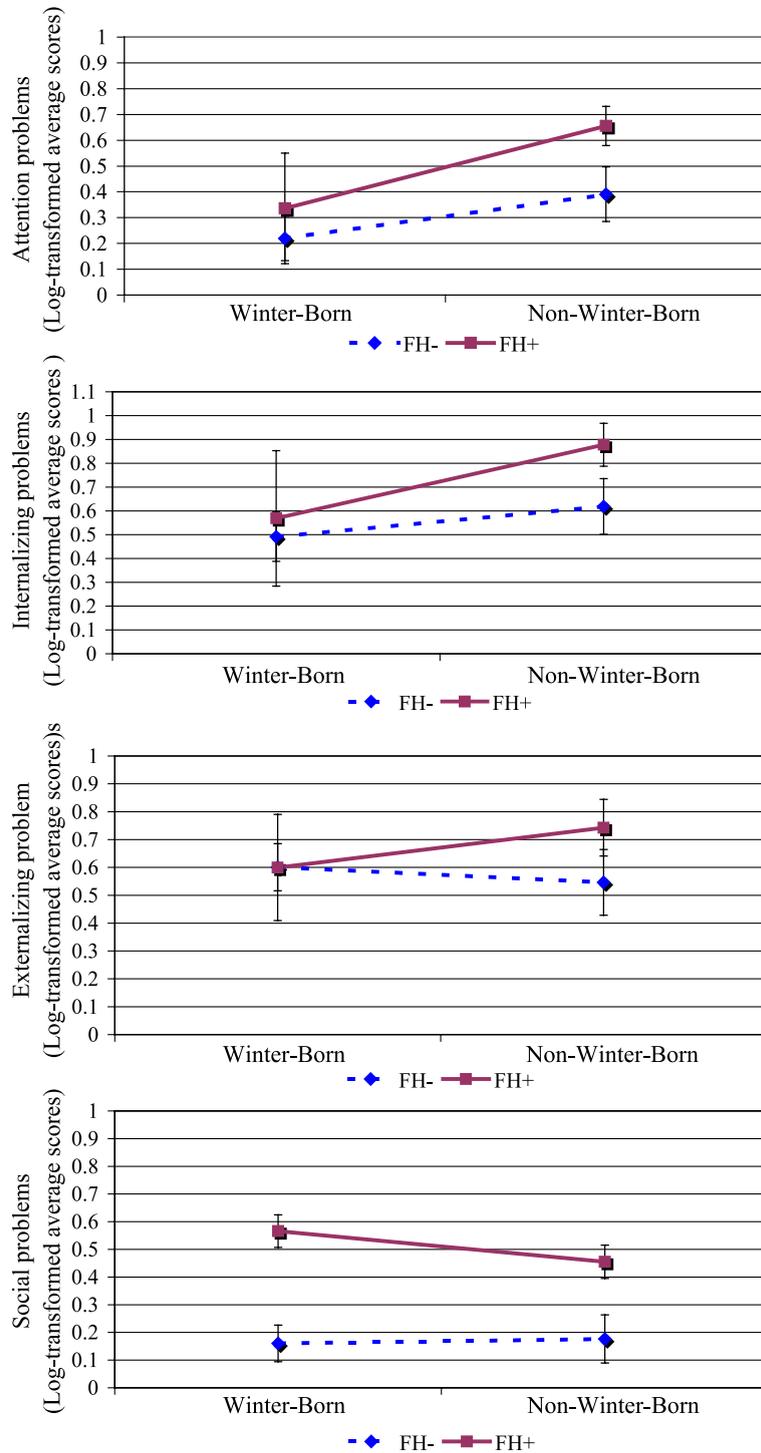


Fig. 1. Graphic representation of the two-way ANOVA: season of birth and family history in relation to the four premorbid adjustment dimensions.

attention, internalizing and social problems than patients without a family history of schizophrenia-spectrum disorders. Overlap in these results is likely due to the finding that family history positive subjects and non-winter-born subjects are largely the same individuals: one-third of the sample had both characteristics. However, season of birth retains its significant main effect on attention problems even when family history is controlled for, while family history retains its main effect on social problems even when season of birth is controlled for. Third, although we were unable to detect a statistically significant gene-environment interaction associated with PMA, season of birth (environment) and family history (genes) appear to work together in explaining premorbid attention and internalizing problems: premorbid attention and internalizing problems were greatest in the non-winter-born patients who had a positive family history of schizophrenia-spectrum disorders.

Over the last 65 years, much interest has been placed on the premorbid psychosocial functioning of schizophrenia patients (Gittelman-Klein and Klein, 1969; Offord and Cross, 1969; Wittman, 1941). Poor premorbid functioning in schizophrenia patients has been found to be related to a number of variables such as sex, obstetric complications, age at onset, family history of schizophrenia, outcome, and symptom presentation, but its relationship with season of birth was still unclear thus far. We are the first to report differences between winter-born and non-winter-born schizophrenia patients in terms of PMA dimensions. The only other known study on this topic did not find any differences in PMA between the two groups (Roy et al., 1995). This discrepancy may be due to methodological differences. In our study, the premorbid period was carefully defined as the period of time prior to the onset of the prodrome. In contrast, Roy et al. (1995) defined their premorbid period as ending one year prior to first contact with psychiatric services, or one year before the onset of florid psychotic symptoms, whichever came first. Yet, as we show in Table 1 and as other researchers have found (Malla et al., 2002), the duration of untreated psychosis as well as the length of the prodrome both tend to be longer than one year. Hence, it is quite possible that by using such a loose definition, Roy et al. included many cases that were already in their

prodromal phase, which may have inflated the number of premorbid problems noted in both seasonal groups, thereby reducing the probability of detecting group differences. Furthermore, the investigators used the Modified Premorbid Adjustment Scale (MPAS), which yields total premorbid functioning scores for two broad periods: childhood and adolescence. The adjustment problems assessed by this scale include withdrawal, peer relationships, interests, and socio-sexual adjustment, which are mostly associated with internalizing and social problems. In contrast, the R-CBCL used in the present study assesses a greater variety of childhood problems which have been identified as precursory signs of schizophrenia (Goldberg and Schmidt, 2001; Isohanni et al., 2000). It is thus possible that we were able to find a season of birth effect on PMA because we looked at specific behavior dimensions rather than a total score, in addition to systematically limiting our “premorbid” scores to age periods before the onset of each individual’s prodrome.

The finding that the family history positive group experienced more PMA problems seems to be consistent with findings from high-risk studies (Goldberg and Schmidt, 2001; Isohanni et al., 2000). There is, however, a discrepancy between our results and Roy et al.’s (1994) finding that familial and sporadic (i.e., family history negative) schizophrenia patients do not significantly differ in terms of PMA. Apart from the methodological considerations mentioned above, it is also possible that by including only individuals who had at least one first-degree relative with a diagnosis of schizophrenia into their familial category, Roy et al. actually included many familial cases in their sporadic category, reducing the variance between groups. In our sample, 50% of the 16 patients who had a positive family history were due solely to first-degree relatives whereas the other 50% were due second- and third-degree relatives.

Given that the literature suggests an association between family history and season of birth, we believed that the two independent variables might interact in explaining differences in PMA. The results of our two-way ANOVAs, however, suggest that there are no statistically significant gene-environment interactions associated with any of the PMA dimensions. Our inability to detect significant gene-environment interactions is perhaps due to our small cell sizes

(which reduced our statistical power to detect an interaction), and to the fact that dichotomizing season of birth and family history restricted the variance that could have been measured in the underlying continua.

Some methodological issues should be discussed. First, the extent to which conclusions can be drawn from this study are limited by the nature and size of our sample. Our sample of relatively high functioning schizophrenia patients was relatively homogeneous. Most subjects lived with their parents at the time of the interview, were considered stabilized by their treating psychiatrist, and reported relatively mild symptoms (either positive or negative). Our results, therefore, may not be representative of schizophrenia patients in general. Also, our PMA data were obtained from the subjects' mothers, raising the possibility that the data may have been biased by the mother's knowledge of her child's current functioning.

While these preliminary data will require replication with a larger, more representative sample, our results suggest an important role for season of birth in determining premorbid manifestations of problems: winter-born patients have better premorbid adjustment, while non-winter born have more severe premorbid problems, in the dimensions of attention and internalizing behaviors. Future studies will continue to examine possible interactions between genetic and non-genetic risk factors for schizophrenia and how they explain variance in dimensions of the illness.

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References

- Addington, J., Addington, D., 1993. Premorbid functioning, cognitive functioning, symptoms and outcome in schizophrenia. *J. Psychiatr. Neurosci.* 18, 18–23.
- Alda, M., Ahrens, B., Lit, W., Dvorakova, M., Labelle, A., Zvolosky, P., Jones, B., 1996. Age of onset in familial and sporadic schizophrenia. *Acta Psychiatr. Scand.* 93, 447–450.
- Bailer, J., Bräuer, W., Rey, E.-R., 1996. Premorbid adjustment as predictor of outcome in schizophrenia: results of a prospective study. *Acta Psychiatr. Scand.* 93, 368–377.
- Bleuler, E., 1911. *Dementia praecox or the group of schizophrenias* (Reprinted in 1950). International University Press, New York.
- Bradbury, T.N., Miller, G.A., 1985. Season of birth in schizophrenia: a review of evidence, methodology, and etiology. *Psychol. Bull.* 98, 569–594.
- Buchanan, R.W., Kirkpatrick, B., Heinrichs, D.W., Carpenter, W.T., 1990. Clinical correlates of the deficit syndrome of schizophrenia. *Am. J. Psychiatry* 147, 290–294.
- Childers, S.E., Harding, C.M., 1990. Gender, premorbid social functioning, and long-term outcome in DSM-III schizophrenia. *Schizophr. Bull.* 16, 309–318.
- d'Amato, T., Guillaud-Bataille, J.-M., Mercier, C., Terra, J.-L., Daléry, J., 1996. No season-of-birth effect in schizophrenic patients from a tropical island in the southern hemisphere. *Psychiatry Res.* 60, 205–210.
- Dassa, D., Azorin, J.M., Ledoray, V., Sambuc, R., Giudicelli, S., 1996. Season of birth and schizophrenia: sex difference. *Prog. Neuro-psychopharmacol. Biol. Psychiatry* 20, 243–251.
- Dixon, M.J., King, S., Stip, E., Cormier, H., 2000. Continuous performance test differences among schizophrenic outpatients living in high and low expressed emotion environments. *Psychol. Med.* 30, 1141–1153.
- Foerster, A., Lewis, S.W., Owen, M.J., Murray, R.M., 1991. Low birth weight and a family history of schizophrenia predict poor premorbid functioning in psychosis. *Schizophr. Res.* 5, 13–20.
- Fogelson, D.L., Nuechterlein, K.H., Asarnow, R.F., Payne, D.L., Subotnik, K.L., 2004. Validity of the family history method for diagnosing schizophrenia, schizophrenia-related psychoses, and schizophrenia-spectrum personality disorders in first-degree relatives of schizophrenia probands. *Schizophr. Res.* 68, 309–317.
- Gittelman-Klein, R., Klein, D.F., 1969. Premorbid adjustment and prognosis in schizophrenia. *J. Psychiatr. Res.* 7, 35–53.
- Goldberg, J.O., Schmidt, L.A., 2001. Shyness, sociability, and social dysfunction in schizophrenia. *Schizophr. Res.* 48, 343–349.
- Isohanni, M., Jones, P., Kempainen, L., Croudace, T., Isohanni, I., Veijola, J., Rasanen, S., Wahlberg, K.E., Tienari, P., Rantakallio, P., 2000. Childhood and adolescent predictors of schizophrenia in the Northern Finland 1966 Birth Cohort—a descriptive life-span model. *Eur. Arch. Psychiatry Clin. Neurosci.* 250, 311–319.

- Kendler, K.S., O'Neill, F.A., Burke, J., Murphy, B., Duke, F., Straub, R.E., et al., 1996. Irish study of high-density schizophrenia families: field methods and power to detect linkage. *Am. J. Med. Genet.* 67, 179–190.
- King, S., Dixon, M.J., 1999. Expressed emotion and relapse in young schizophrenia outpatients. *Schizophr. Bull.* 25, 377–386.
- Kinney, D.K., Jacobsen, B., Jansson, L., Faber, B., Tramer, S.J., Suozzo, M., 2000. Winter birth and biological family history in adopted schizophrenics. *Schizophr. Res.* 44, 95–103.
- Kinney, D.K., Levy, D.L., Yurgelun-Todd, D.A., Medoff, D., LaJonchere, C.M., Radford-Paregol, M., 1994. Season of birth and obstetrical complications in schizophrenics. *J. Psychiatr. Res.* 28, 499–504.
- Kirkpatrick, B., Ram, R., Amador, X.F., Buchanan, R.W., McGlashan, T., Tohen, M., Bromet, E., 1998. Summer birth and the deficit syndrome in schizophrenia. *Am. J. Psychiatry* 155, 1221–1226.
- Kraepelin, E., 1902. *Dementia Praecox*. Macmillan, New York.
- Maier, W., Lichtermann, D., Franke, P., Heun, R., Falkai, P., Reietschel, M., 2002. The dichotomy of schizophrenia and affective disorders in extended pedigrees. *Schizophr. Res.* 57, 259–266.
- Malaspina, D., Friedman, J.H., Kaufmann, C., Bruder, G., Amador, X., Strauss, D., Clark, S., Yale, S., Lukens, E., Thorning, H., Goetz, R., Gorman, J., 1998. Psychobiological heterogeneity of familial and sporadic schizophrenia. *Biol. Psychiatry* 43, 489–496.
- Malaspina, D., Goetz, R.R., Yale, S., Berman, A., Friedman, J.H., Treméau, F., Printz, D., Amador, X., Johnson, J., Brown, A., Gorman, J.M., 2000. Relation of familial schizophrenia to negative symptoms but not to the deficit syndrome. *Am. J. Psychiatry* 157, 994–1003.
- Malla, A.K., Norman, R.M., Manchanda, R., Ahmed, M.R., Scholten, D., Harricharan, R., Cottese, L., Takhar, J., 2002. One year outcome in first episode psychosis: influence of DUP and other predictors. *Schizophr. Res.* 54, 231–242.
- Maxwell, M.E., 1992. *Manual for the FIGS*. National Institute for Mental Health, Clinical Neurogenetics Branch, Washington, D.C.
- McGrath, J., Welham, J., Pemberton, M., 1995. Month of birth, hemisphere of birth and schizophrenia. *Br. J. Psychiatry* 167, 783–785.
- Neumann, C.S., Grimes, K., Walker, E.F., Baum, K., 1995. Developmental pathways to schizophrenia: behavioral subtypes. *J. Abnorm. Psychology* 104, 558–566.
- Norris, A.S., Chowning, J.R., 1962. Season of birth and mental illness. *Arch. Gen. Psychiatry* 7, 206–212.
- O'Callaghan, E., Cotter, D., Colgan, K., Larkin, C., Walsh, D., Waddington, J.L., 1995. Confinement of winter birth excess in schizophrenia to the urban-born and its gender specificity. *Br. J. Psychiatry* 166, 51–54.
- O'Callaghan, E., Gibson, T., Colohan, H.A., Walshe, D., Buckley, P., Larkin, C., Waddington, J.L., 1991. Season of birth in schizophrenia: evidence for confinement of an excess of winter births to patients without a family history of mental disorder. *Br. J. Psychiatry* 158, 764–769.
- Offord, D., Cross, L., 1969. Behavioral antecedents of adult schizophrenia. *Arch. Gen. Psychiatry* 21, 267–283.
- Pallast, E.G.M., Jongbloet, P.H., Straatman, H.M., Zielhuis, G.A., 1994. Excess seasonality of births among patients with schizophrenia and seasonal ovopathy. *Schizophr. Bull.* 20, 269–276.
- Parker, G., Mahendran, Seng Koh, E., Machin, D., 2000. Season of birth in schizophrenia: no latitude at the equator. *Br. J. Psychiatry* 176, 68–71.
- Pulver, A.E., Stewart, W., Carpenter, W.T., Childs, B., 1983. Risk factors in schizophrenia: season of birth in Maryland, USA. *Br. J. Psychiatry* 143, 389–396.
- Roy, M.-A., Flaum, M., Andreasen, N., 1995. No difference found between winter and non-winter born schizophrenic cases. *Schizophr. Res.* 17, 241–248.
- Roy, M.-A., Flaum, M., Gupta, S., Jaramillo, L., Andreasen, N.C., 1994. Epidemiological and clinical findings in familial vs sporadic schizophrenia. *Acta Psychiatr. Scand.* 89, 324–328.
- Sacchetti, E., Calzeroni, A., Vita, A., Terzi, A., Pollastro, F., Cazzullo, C.L., 1992. The brain damage hypothesis of the seasonality of births in schizophrenia and major affective disorders: evidence from computerized tomography. *Br. J. Psychiatry* 160, 390–397.
- Schwarzkopf, S.B., Nasrallah, H.A., Olson, S.C., Bogerts, B., McLaughlin, J.A., Mitra, T., 1991. Family history and brain morphology in schizophrenia: an MRI study. *Psychiatry Res.* 40, 49–60.
- Silverman, J.M., Mohs, R.C., Davidson, M., Losonczy, M.F., Keefe, R.S., Breitner, J.C., Sorokin, J.E., Davis, K.L., 1987. Familial schizophrenia and treatment response. *Am. J. Psychiatry* 144, 1271–1276.
- Silverstein, M.L., Mavrolefros, G., Close, D., 2002. Premorbid adjustment and neuropsychological performance in schizophrenia. *Schizophr. Bull.* 28, 157–165.
- Tabachnick, B.G., Fidell, L.S., 2001. *Using Multivariate Statistics*, (4th Edition). Allyn & Bacon, Boston, MA.
- Takei, N., Sham, P.C., O'Callaghan, E., Glover, G., Murray, R.M., 1995. Schizophrenia: increased risk associated with winter and city birth—a case control study in 12 regions within England and Wales. *J. Epidemiol. Community Health* 49, 106–107.
- Torrey, E.F., Miller, J., Rawlings, R., Yolken, R.H., 1997. Seasonality of births in schizophrenia and bipolar disorder: a review of the literature. *Schizophr. Res.* 28, 1–38.
- Walker, E.F., Neumann, C.C., Baum, K.M., Davis, D.M., DiFurio, D., Bergman, A., 1996. The developmental pathways to schizophrenia: potential moderating effects of stress. *Dev. Psychopathol.* 8, 647–665.
- Walker, E.F., Savoie, T., Davis, D., 1994. Neuromotor precursors of schizophrenia. *Schizophr. Bull.* 20, 441–452.
- Wittman, P., 1941. A scale for measuring prognosis in schizophrenic patients. *Elgin Pap.* 4, 20–33.
- Zipursky, R.B., Schulz, S.C., 1987. Seasonality of birth and CT findings in schizophrenia. *Biol. Psychiatry* 22, 1288–1292.