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Season of Birth Effects in Autism Spectrum Disorders

Kastley Marvin

PSYC 296W- Honors Thesis

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Abstract

One factor that is investigated as a possible clue to etiological factors in Autism Spectrum Disorders (ASD) is season of birth. Season of birth effects could be the result of temperature, toxins, dietary changes, viral infections, and cultural or social factors that change seasonally (Bolton, Pickles, Harrington, Macdonald, & Rutter, 1992). A number of studies have looked for season of birth effects in ASD with no conclusive results. The current study analyzed season of birth effects in a sample of 441 children diagnosed with ASD. Analysis was also repeated after excluding prematurely born children from the data. Level of functioning and gender effects were tested by breaking the sample into a number of sub-groups. While there were no season of birth effects in the sample of all children with ASD when compared to children without ASD in either the entire sample or the non-premature sample, there were significant differences in the season of birth of low functioning children with ASD when compared with high functioning children with ASD.

Season of Birth Effects in Autism Spectrum Disorders

Autism Spectrum Disorders (ASD) are developmental disorders characterized by impairment in social interaction and impairment in communication and the presence of restricted or repetitive behavior (American Psychiatric Association, 1994). Prevalence estimates of ASD vary based on factors such as geographical region covered and diagnostic criteria, but most estimates range from 1 in 250 children to 1 in 150 children (Caronna, Milunsky, & Tager-Flusberg, 2008). Males are more likely to be affected than females. A male to female ratio from 3.4 to 1 to 6.5 to 1 is seen, depending on the site studied (Rice, 2007). The etiology of ASD is largely unknown, but recent research has focused on discovering the underlying causes. It is suspected that both genetic and environmental factors are determinants in the development of ASD (Caronna, Milunsky, & Tager-Flusberg, 2008).

One factor that has been investigated in investigating the etiology of ASD is the effect of season of birth. Season of birth refers to the quarter of the year of birth, as determined by the month in which a child is born. The number of births that occur in each month and each season varies in the general population and varies in different countries across different years (Miura, 1987). It is not yet completely understood why there are country and decade dependent variations in season of birth, but social or cultural factors influencing

reproductive behaviors is a plausible model (Miura, 1987). If the season of birth effects in the population of people with ASD are different from those of the general population, it could point to a possible etiology. Season of birth effects could be the result of temperature, toxins, dietary changes, viral infections, and cultural or social factors that change seasonally (Bolton, Pickles, Harrington, Macdonald, & Rutter, 1992).

Season of birth effects in other psychological disorders

Season of birth effects are seen in a number of other psychological disorders. A higher proportion of May, June and July births have been seen in individuals diagnosed with dyslexia (Livingston, Adam, & Bracha, 1993). In Livingston, et al.'s study of learning disorders, the risk of dyslexia was more than double in May, June and July when compared with other months of the year (Livingston, Adam, & Bracha, 1993). Polizzi, Martin and Dombrowski (2007) report that there have been consistent findings of season of birth effects for many neurologically based pathologies, namely mental retardation, multiple sclerosis and learning disabilities. Season of birth effects were seen in children receiving special education services for emotional and behavioral disorder (E/B D) when compared to expected distribution for the general population. There was a decreased incidence of September and October births and an excess of June, July and August births in the sample of children with E/B D (Polizzi, Martin, & Dombrowski, 2007). Attention deficit hyperactivity disorder (ADHD) may also have season of birth effects. An excess of September births when compared

with normal controls has been found, especially in ADHD with comorbid learning disability and ADHD with no comorbid psychiatric conditions (Mick, Biederman, & Faraone, 1996).

Schizophrenia is a disorder with the most established findings on season of birth effects. Many studies show elevated winter births in the schizophrenic population (see Bradbury & Miller, 1985 for a review). Bradbury and Miller (1985) report that 23 of the 37 studies in the Northern hemisphere, at the time of publication, showed elevated winter birthrates in samples of individuals with schizophrenia when compared to normal controls or the general population. Fouskakis, Gunnell, Rasmussen, Tynelius, Sipos, and Harrison (2004) addressed the possibility that elevated winter births and later incidence of psychosis could be confounded by a previous finding that babies born in winter months are of lower weight and shorter stature in adulthood. The authors note that there has been a consistent finding of elevated risk for "psychosis" (not defined) in babies with a low birth weight. The group found that early onset schizophrenia showed season of birth effects which were not explained by fetal growth or obstetric complications.

Season of birth findings in ASD

Season of birth effects in cases of ASD have conflicting results. Konstantareas, Hauser, Lennox, and Homatidis (1986) compared the birth months of individuals with Autistic Disorder (AD) to all live births in Ontario. There were more spring and early summer births than expected in their sample of

individuals with AD. There was also a reduction of fall and winter births in the AD sample. The effects in their data appeared to be due to the individuals who were lower functioning and/or nonverbal. The nonverbal sample showed a higher number of spring and summer births and a lower number of fall and winter births while the verbal sample did not show any effects when compared to the general population of Ontario. The sample of children with low-functioning AD showed the same pattern of season of birth as the nonverbal sample (Konstantareas, Hauser, Lennox, & Homatidis, 1986). Children who are low functioning are usually also nonverbal, which would explain the similarity in season of birth patterns in these two groups.

Similarly, Gillberg (1990) found a higher frequency of March birthdays in his sample of individuals with AD when compared to the Swedish general population born between 1962 and 1984. The overrepresentation of March births appeared to be due to a higher percentage of boys with AD being born in March. Girls diagnosed with AD did not show any season of birth patterns different than those of the control group. Gillberg also had a group of individuals with autistic-like disorders (ALD), a group with Asperger's Syndrome, and a very small group with Childhood Disintegrative Disorder (CDD). Autistic-like disorders were defined as those that the author considered to fit most, but not all, of the criteria for a diagnosis of AD; he notes that many fit the criteria for Pervasive Developmental Disorder- Not Otherwise Specified (PDD-NOS). There were no season of birth effects for ALD or CDD and individuals with Asperger's

Syndrome tended to have birth dates in the later months of the year (Gillberg, 1990). Mouridsen, Nielsen, Rich, and Isager (1994) also found an increased incidence of March births and a decreased incidence of November births in children diagnosed with AD in a subset of their large sample when compared to the Danish general population. Males with ALD (same as defined by Gillberg, 1990) showed the opposite trend, with an increase in the later part of the year and a decrease in March/April (Mouridsen, Nielsen, Rich, & Isager, 1994).

Barak, Ring, Sulkes, Gabbay, and Elizur (1995) attempted to replicate the studies that found season of birth effects in ASD (e.g., Konstantareas et al., 1986) but with a population in a different environment than those of the previous studies, which were all carried out in the US and western Europe. The group found an increase of March and August births in their sample of individuals with AD in Israel when compared with the pattern expected from the general population of Israel (Barak, Ring, Sulkes, Gabbay, & Elizur, 1995). This study showed that the effects exist not only in western Europe and the US, but in a country with a climate and environment different from those of the countries previously studied.

In contrast, some groups have found limited season of birth effects in ASD. Stevens, Fein and Waterhouse (2000) found no effects in their sample of individuals with AD when compared with both the U.S. general population and a sample of non-ASD siblings. When the sample was divided into subgroups, however, such as gender and level of functioning, some effects were seen. For

example, there was an excess of winter births in the girls with AD. The sample of children with AD was also assessed for social functioning using the Wing (1985) system and those classified as having passive social interaction had an increased number of March and November births (Stevens, Fein, & Waterhouse, 2000).

Bolton et al. (1992) also found limited season of birth effects. Their sample of people with ASD was taken from two different sites. The sample from the National Autistic Society and the sample from the Children's Department at Maudsely Hospital showed a lower number of March through May births in children with ASD when compared with the general population and a non-ASD sibling group. The effect, however, depended on the way that the authors defined the quarters of the year. (Bolton, Pickles, Harrington, Macdonald, & Rutter, 1992). When the group changed their definition of the seasons, their season of birth effects no longer existed.

In a number of other studies no season of birth effects have been found. Kolevzon et al. (2006) examined all live births of Jews in Israel over five years diagnosed with ASD and found no significant season of birth effects. Both season (quarters of the year) and individual month analyses showed no effects (Kolevzon, et al., 2006). Landau, Cicchetti, Klin and Volkmar (1999) also found no season of birth effects. The authors chose only to address a dichotomous test of yes/no birth in August or March (the two months most often showing increased births in ASD). There was no increased incidence of March or August births in the

sample of individuals with AD when compared to a group of individuals with mental retardation not associated with AD (Landau, Cicchetti, Klin, & Volkmar, 1999). Neither gender nor level of functioning differences were seen in either of these studies.

Methodological issues in ASD season of birth research

The methodologies in the aforementioned studies vary greatly. The diagnostic criteria for inclusion in the ASD sample, the basis for comparison, the statistical methods and the definition of the seasons all differ among studies. First, earlier studies use the AD symptoms from DSM-III while more recent studies use DSM-IV criteria. Many authors choose to only include children with AD in their sample but others include any of the various ASD's, such as Asperger's Syndrome or CDD. Different inclusion criteria change the composition of the samples, which could change the season of birth effects, especially if the effects are specific to a certain subset of ASD.

Second, some studies compare the ASD sample to aggregated data on live births (e.g., Stevens, et al., 2000), while others have a clinical sample (e.g., Gillberg, 1990) or a sample of non-autistic siblings (e.g., Bolton, et al., 1992) for comparison. If the comparison samples have some season of birth effects themselves, it could result in masked or false season of birth effects in the ASD sample. Also, season of birth effects in the general population are not always constant, so even using that as a basis for comparison can result in erroneous conclusions about the effects in ASD.

Third, most studies choose to employ a chi-square analysis of birth season, comparing the affected sample to a non-affected control group. A difficulty here is that this ignores information on the order of categories (in the case of seasonality, months or groups of months) (Nonaka & Miura, 1987). This means that defining winter as beginning in December has a different effect than defining winter as starting with January. Bolton, et al. (1992) conducted all analyses twice, once with winter defined as December through February and again with winter defined as January through March. There were different results when the seasons were redefined in their samples. In fact, redefining the seasons with winter beginning in December as opposed to beginning in January eliminated any season of birth effects seen in their samples. Thus, the power of detecting seasonal effects (consecutive months with higher, or lower, than expected births), rather than month-to-month effects, is low (Nonaka & Miura, 1987). Other studies chose to fit data to a simple sinusoidal curve. However, birth cohorts of all live births do not present themselves in a simple sinusoidal fashion unless the sample size is very large, so this method can also give a false impression of season of birth effects (Nonaka & Miura, 1987). The conclusion is that chi-square, while not without limitations, is the most effective method. It is not a limitation of chi-square as a statistical tool, but rather a limitation of the organization and nature of the data used that Chi-square is not an entirely adequate statistical tool for analyzing season of birth effects.. And fourth, as explained above, results can depend on the definition of the seasons. There is

ambiguity in defining the seasons because the actual solstices, marking the beginning of a new calendar season, occur in the middle of the month. For example, the winter solstice is in the middle of December. The inclusion of December in fall or winter would seem to be arbitrary but as Bolton, et al. (1992) concluded, it can significantly affect results.

What do season of birth effects in ASD mean?

Season of birth effects in ASD could be seen for a variety of reasons. Factors that have been posited are maternal hormone levels which have been found to fluctuate seasonally, environmental toxins such as lead which may vary across seasons, dietary changes across the seasons, viral infections, and cultural or social factors such as changes in the timing of conception (Bolton, Pickles, Harrington, Macdonald, & Rutter, 1992). Exposure to some of these factors during pregnancy could possibly affect critical brain development of the embryo and subsequently lead to pathology in the child. Bolton, et al. (1992) points out, however, that season of birth effects could be a by-product of another underlying cause such as pre-, peri- or neo- natal complications, mental handicap, or congenital abnormalities, which are all thought to be related to season of birth on their own.

Fatemi, et al. (2005; 2008) found a possible animal model of ASD that is based on maternal viral infection of mice at various stages of prenatal development. Infection of a mouse with influenza virus during the late first trimester of pregnancy had effects on prenatal brain development by affecting

the regulation of genes critical for brain development (Fatemi, Pearce, Brooks, & Sidwell, 2005). Infection during the late second trimester also led to abnormal regulation of genes previously associated with ASD as well as abnormal brain development in areas that have been implicated in ASD by various neuroimaging techniques (Fatemi, et al., 2008).

Konstantareas and colleagues (1986) suggest that viral infections or nutritional deficiencies may have an adverse effect on “highly vulnerable” fetuses. They explain “highly vulnerable” fetuses to be a subgroup of fetuses whose gestational period includes the late fall and/or winter months. The criteria for inclusion in this subgroup are not defined as such. To explain the decreased number of winter and fall births in individuals with AD, the authors hypothesize that most of these highly vulnerable fetuses scheduled to be born in these months succumb to environmental factors, such as viral infection or nutritional deficiencies, and die prior to delivery. Therefore, there would be fewer of these children to be diagnosed with ASD (Konstantareas, Hauser, Lennox, & Homatidis, 1986). Others have hypothesized similar mechanisms of season of birth effects that are not necessarily specific to ASD. Viral infections, which themselves occur in a seasonal trend, could cause: the loss of embryos and result in a decreased number of births in a season, damage to embryos resulting in an increase in abnormal fetuses in a season, damage to system functioning in the embryo also resulting in an increase in abnormal fetuses in a season, or an impaired immune

system response resulting in an increase in fetuses with a hypersensitivity to certain environmental agents after birth (Miura, 1987).

It has been suggested that there is at least a partial genetic contribution to the development of ASD and there has been a considerable amount of research to identify the specific genetic or chromosomal abnormalities that may contribute to the development of ASD (Caronna, Milunsky, & Tager-Flusberg, 2008). Specifically, regions in 17q, 19p (McCauley, et al., 2005), and 7q (Skaar, et al., 2005) and a number of growth factor genes (Toyoda, et al., 2007) have been identified as possible locations of anomaly. Identifying genetic contributions to development of ASD could answer many questions about the etiology of the disorder and vice versa. Season of birth effects also reportedly exist in some chromosomal abnormalities. For instance, in Down's syndrome there is a peak of births in July to September and January to March (Kanai & Nakamura, 1987). There also may be a season of birth effect in the mothers of children with Down's syndrome- in other words, potential carriers of a chromosomal abnormality (Kanai & Nakamura, 1987). Season of birth effects have also been seen in both Klinefelter's and Turner's syndromes, which are both sex chromosome abnormalities (Kanai & Nakamura, 1987). If ASD shows season of birth effects similar to those of chromosomal abnormalities, it could suggest the role of a chromosome anomaly in the diagnosis of ASD (this has yet to be determined, however).

However, season of birth effects in ASD also point to an environmental factor in development of the disorder. An environmental factor may interact with some biological factor (i.e., genetic contribution) to ultimately lead to an ASD diagnosis (Landau, Cicchetti, Klin, & Volkmar, 1999). Lee, et al. (2008) found that season of birth effects exist in multiple births concordant for ASD, as well as in singleton births. Both singleton births and concordant multiple births showed season of birth effects when compared to the general population of singleton and multiple births, respectively. There were peaks in ASD multiple births in March, June and October. The contribution of genetics to ASD diagnosis has been determined from twin studies on the heritability of ASD (Caronna, Milunsky, & Tager-Flusberg, 2008). So, while concordant multiple births indicates a heritability factor in ASD, season of birth effects in this same population provides evidence for an environmental factor in ASD (Lee, Newschaffer, Lessler, Lee, Shah, & Zimmerman, 2008).

The present study

Based on previous findings on season of birth effects in ASD, it would seem that if we were to see any effects in the current data, there would be an overrepresentation of March and/or August births. We used a chi-square test, and did both a month-by-month comparison as well as a season-by-season comparison to address the lack of an adequate statistical tool to test for season of birth effects. We also used a heterogeneous control group composed of

children with a variety of diagnoses as well as some typically developing children to be more representative of the general population.

None of the studies mentioned previously bring up the possibility that premature birth may affect their results. It could be expected, however, that if a child is born premature the season of their birth would be altered. In Lee, et al.'s (2008) study there were peaks in singleton ASD births in April, July and October, roughly 2 to 4 weeks later than the multiple births. Because multiple births often have a slightly shorter gestation period, the date of conceptions could be similar, in which case the timing of gestation would be the same. The issue with prematurity is one that is not usually addressed, but the different peaks in multiple births and single births that may be the result of the multiples being born prematurely indicates that it is a factor that should be considered further. Also, prematurity itself may be confounded with other factors that may lead to a diagnosis of ASD (such as pregnancy complications) or show season of birth effects on their own. Therefore, we carried out analyses on the sample of children with ASD twice: once with all individuals and again with only those who were not born prematurely.

Methods

The present study aimed to analyze season of birth effects in a sample of individuals with ASD. The children were part of a larger, on-going study to develop and test a screening tool, the Modified Checklist for Autism in Toddlers (M-CHAT), for the early detection of ASD. Sixteen to thirty month old infants are

screened using the M-CHAT. Infants are screened either by their primary health care provider at a well-child visit or by an early intervention agency. Younger siblings are also screened between 16 and 30 months if they have an older sibling with ASD. Children who screen positive by the criteria of the M-CHAT are then given a full developmental evaluation resulting in a diagnosis using the following instruments:

Mullen Scales of Early Learning (Mullen, 1989) measures a child's ability in the domains of gross motor, fine motor, receptive language, expressive language and visual problem solving. Only the scores for visual problem solving and expressive language were used in this study.

Vineland Adaptive Behavior Scales (Sparrow, Balla & Cicchetti, 1984) is a parent interview that is used to measure a child's level of adaptive functioning in communication, socialization, daily living and motor skills. Composite scores and scores on expressive language were used in this study.

The Autism Diagnostic Observation Schedule-Generic (ADOS) (Lord, Rutter, DiLavore, & Risi, 1999) is a semi-structured interview that is used to diagnose a child with AD, PDD-NOS or as non-autistic. The module assesses communication, social interactions, social relatedness, play and imagination. Diagnosis is made by exceeding cut-off scores in the domains of communication, socialization and combined social and communication.

The Autism Diagnostic Interview- Revised (ADI-R) (Lord, et al., 1994) is a semi-structured parent interview that is used to aid in diagnosis of children as either

having AD or being non-autistic based on an algorithm considering DSM-IV criteria. The interview evaluates a child's communication abilities, social development, play, and restricted, repetitive or stereotyped behaviors.

The Childhood Autism Rating Scale (CARS) (Schopler, Reichler, & Renner, 1988) measures the presence and severity of AD. A child is classified as either Mild-Moderate autism (total score 30-36.5), Severe autism (total score above 37), or non-autistic (total score 15-36) based on parent report and clinician observation in the areas of communication, socialization, sensory sensitivity and emotional responsiveness.

Clinical best estimate diagnosis as per DSM-IV (APA, 1994) Clinicians, using all of the available information from other instruments, behavior observation, and parent report, filled out a "DSM-IV checklist" for recording symptoms of ASD. The DSM-IV criteria for AD and PDD-NOS were used to determine the final best estimate diagnosis.

See Robins, Fein, Barton and Green (2001) and Ventola, et al. (2007) for a more detailed description of the methods.

The sample of children with ASD for the present study (n=278; males=220, females= 58) was taken from those who received a diagnosis of Autistic Disorder (n=178), PDD-NOS (n=93) or other spectrum disorders (n=7) during the M-CHAT study described above. Those who did not receive a diagnosis of ASD (n=163; males=129, females=34) were used for comparison. The non-ASD group consisted of children diagnosed with Developmental Language Disorder (n=25),

Mental Retardation/ Global Developmental Delay (n=88), in addition to children who received no specific diagnosis (n=27), who were typically developing (n=15), and who were given another diagnosis not specified in the examined records (n=8). There were a total of 441 children who had diagnosis and date of birth information available. They had birthdates from January 1996 to February 2006 and evaluations were carried out from 1998 to 2007; the mean age at the time of evaluation was 2.19 years (SD=0.39 years). There was ethnicity information available for 327 of the 441 children, the majority of the sample was Caucasian (n=263). Other ethnicities represented were Hispanic/ Latino (n=18), African American (n=18), Asian or Pacific Islander (n=11), Native Hawaiian (n=1), Biracial (n=11), Native American (n=1), other (n=4).

A Pearson Chi-Square test was used to determine any season of birth effects in our samples. The Pearson Chi-Square test calculates an expected value and compares it with the observed value. Analysis was conducted using both month of birth and season of birth as variables for the entire sample, and then only season of birth was used in the various sub-samples to increase the power of the tests given the relatively small sample sizes. For purposes of determining season of birth, the year was divided into quarters (seasons). Winter was defined as January through March, spring was defined as April through June, summer was defined as July through September, and fall was defined as October through December.

Analyses were first carried out on the entire sample (n=441), comparing children diagnosed with ASD (n=278) to those without ASD (n=163). Then the sample of children diagnosed with ASD was divided into sub-groups to see if certain subsets of the heterogeneous diagnosis of ASD exhibit season of birth effects. Analyses were repeated with boys vs. girls, low functioning (see below for a description) compared with high functioning, and non-verbal (see below for a description) compared with verbal.

Sections of the Mullen Scales of Early Learning and the Vineland Adaptive Behavior Scales were used to divide the sample of children with ASD into various sub-samples. The cutoffs for level of functioning and language abilities were taken as the median of the sample of individuals with ASD to prevent discrepancies in sample size. However, for the Mullen Visual Reception (VR) test a cutoff of 30 was used for the Mullen VR scores; 30 is minus 2 standard deviations from the mean score of the test (mean=30, SD=10). The median score for the sample was too low to classify the high functioning group as truly high functioning. The Mullen VR measures nonverbal problem solving skills, and the score was also used to assess level of functioning. Mullen VR data were available for 202 children. The VR high functioning group was defined as children who scored above 30 (n=75) and the VR low functioning group was defined as children who scored 30 or below (n=127). The Vineland Adaptive Behavior Composite (ABC) scores were also used to divide the sample into a high functioning and low functioning group. Data were available for 234

children, 122 of whom were classified as low functioning (score 66 or below) and 112 of whom were classified as high functioning (score above 66).

The sample of children with ASD was also divided into non-verbal and verbal sub-samples, using two different methods. The Mullen Expressive (EXP) raw scores and the Vineland Expressive (EXP) raw scores were used. Mullen EXP scores were available for 205 children, 106 of whom had a score of 12 or below and were classified as non-verbal, and 99 of whom had a score above 12 and were classified as verbal. We had Vineland EXP scores for 232 children. The verbal sub-sample was defined as those with a score above 6 (n=108), while the non-verbal sub-sample was defined as those with a score of 6 or below (n=124).

It was hypothesized that premature birth may affect season of birth effects by changing the season of birth. For example, if a child were due to be born in January but was actually born in December, their season of birth, as we defined, would be changed from winter to fall. Based upon the current hypotheses as to why season of birth effects may exist, it is the timing of the gestation of the fetus that is important, not necessarily the month or season of birth per se. Prematurity affects the timing of the gestation, so a child born prematurely in December had a slightly different gestational period than a child born at full-term in December. Thus, we repeated the season of birth analysis on a reduced sample of children who were not born prematurely (n=102; ASD=68, non-ASD=34). Those children who were born more than two weeks prematurely, or for whom we did not have prematurity data, were excluded from the data

set. The analysis was carried out in the same way as with the entire sample, except only season of birth was used as a variable. The sample was too small for an analysis with more than 4 categories, as with month of birth. The non-premature sample was not divided into the sub-samples, such as male/female or high functioning/low functioning because the sample sizes were too small for chi-square analysis.

Results

Data were analyzed using Pearson's Chi-square goodness-of-fit, using month of birth and season of birth as independent variables in comparison of ASD to non-ASD groups, and using season of birth as the independent variable for the remainder of the analyses to conserve power. In the comparison of children with ASD and without ASD ($\chi^2(1,11)=12.411$, $p=ns$) chi-square was not significant at the $p<.05$ level when comparing the months of birth between the two groups. Chi-square was also not significant when comparing season of birth of children with ASD and children without ASD ($\chi^2(1,3)=1.699$, $p=ns$). Further, the percent of children with ASD in each season is close to 25% indicating no large excess of births in one season. Please refer to Tables 1 and 2 for the number and percentage of children born in each month and season.

In the children who were not born more than 2 weeks premature only season of birth was included in the Chi-square. Month of birth was not analyzed because the number of children in each category was too low to show any reliable effects. The difference in season of birth between non-premature

children diagnosed with ASD and non-premature children not diagnosed with ASD was not significant ($\chi^2(1,3)=0.354, p=ns$). Table 2 includes the number and percentage of non-premature children born in each season. As in the entire sample, the percentage of non-premature children with ASD born in each season is close to 25%.

For the remainder of the analyses, only the children in the entire sample diagnosed with ASD were included. Males and females showed no significant differences in season of birth ($\chi^2(1,3)=1.045, p=ns$). Both males and females with ASD had an even distribution of births across the four seasons (see Table 3). The children with ASD that had Mullen and/ or Vineland scores available were split into low functioning and high functioning groups and verbal and non-verbal groups. When Mullen VR scores were used to define high functioning ASD and low functioning ASD, the difference in season of birth between the high functioning children with ASD and low functioning children with ASD was significant ($\chi^2(1,3)=8.249, p=0.041$). There were a higher percentage of high functioning children with ASD in spring and a higher percentage of low functioning children with ASD in summer. No other sample divisions yielded any significant differences in season of birth. Table 3 contains the number of births in each season for the different sub-groups.

Discussion

This study was designed to investigate season of birth effects in ASD. Many groups have found such effects in samples of children with ASD (e.g.,

Konstantareas, Hauser, Lennox, & Homatidis, 1986), while many other groups have not found any significant effects (e.g., Landau, Cicchetti, Klin & Volkmar, 1999). Some groups have found effects only in a limited sub-sample of their data (e.g., Stevens, Fein & Waterhouse, 2000). It is important to explore season of birth effects because they present the possibility of discovering an (the) etiology of ASD. It was hypothesized that if any season of birth effects were seen in the sample there would be an increase in March and/or August births in the entire sample of children with ASD and that effects in children born prematurely would be different than those of the entire sample.

The present study

The findings of the present study suggest the possibility of season of birth effects in ASD. While there were no season of birth effects in the entire sample of children with ASD when compared with the children not diagnosed with ASD, there were season of birth effects in a sub-group of the entire sample of all children diagnosed with ASD. Specifically, when Mullen VR scores were used to define level of functioning there was an increase in spring births in the group of high functioning children with ASD in the entire sample when compared with the low functioning children with ASD, who showed an increase in summer births. An increase in the number of low functioning children with ASD born in summer, specifically the early summer months, was also found by Konstantareas and colleagues (1986). Difference in season of birth in high versus low functioning children is consistent with the possibility that different etiological factors might be

involved in these two different groups of ASD; this idea could be followed up with genetic studies and family history studies.

When the Vineland ABC score was used to define level of functioning in children with ASD there were no significant differences in season of birth of the entire sample of low functioning children with ASD compared with the high functioning children with ASD. However, there were an increased number of births in the spring in the high functioning groups of all children with ASD and an increased number of summer births in the low functioning groups, regardless of the test used to define level of functioning. Significance, though, was reached only when the Mullen VR was used. There may be season of birth effects when Mullen VR is used as opposed to when Vineland ABC is used because of the nature of the tests. The Mullen is an observation based test while the Vineland is based on parent report. This difference could account for the difference in significant effects. Parent report may not be entirely accurate, probably in the direction of more children being classified as high functioning (i.e., parents overestimate child's abilities) which could mask the season of birth effects. Another factor that may have influenced the significance of season of birth effects in these sub-groups was the choice of score cutoffs. The choice of score cutoffs for high functioning and low functioning as determined by both of these tests was different which may have changed the composition of each the high functioning and low functioning groups in the case of each test. The cutoff for the Mullen VR was 30 which is minus 2 standard deviations from the mean score

(the typical definition of impairment) while the cutoff for the Vineland ABC was 66 which was the median for our sample.

Lee, et al. (2008) included children diagnosed with any ASD and found peaks in spring, summer and fall in singleton ASD births. While the current findings were in a very selective population, spring and summer peaks were also seen. In fact, only one study has showed any increase in winter ASD births and it was restricted to girls with AD (Stevens, Fein, & Waterhouse, 2000). Most studies show fewer winter births in children with AD. Konstantareas, et al. (1986) and others have hypothesized about the vulnerability of children to be born in the winter and fall months. It is possible that more fetuses to be born at these times succumb to viral infection or some other external factor, and die in utero and thus are never able to be diagnosed with ASD (Konstantareas, Hauser, Lennox, & Homatidis, 1986). It is impossible to tell exactly why the season of birth effects observed in the present study exist, but viral infection in utero is a plausible hypothesis.

Season of birth effects are probably seen because of something that happens to the embryo during gestation, such as a viral infection or nutritional deficiency. Thus, it is the period and timing of gestation that should really be considered, not season of birth, per se. As Fatemi, et al. (2005; 2008) showed in mice, maternal infection during pregnancy can have deleterious effects on the embryo and result in developmental pathology. It was not the timing of the birth of the mouse that resulted in the abnormal behavioral phenotype; it was the

timing of the viral infection in the mother (Fatemi, et al., 2005; Fatemi, et al., 2008).

Prematurity indicates an altered gestation period, which could alter any season of birth effects seen. There are no known studies that have accounted for prematurity and repeated analyses with just those participants who were not born prematurely or controlled for prematurity in some other way. While there were no significant differences in season of birth in our non-premature sample, an increase of pre-term deliveries in the summer months has been previously reported (Nakamura & Uno, 1987). This finding indicates that prematurity may exhibit season of birth effects on its own signifying that prematurity should be considered and controlled for in other season of birth studies.

Methodological Issues

There is a great inconsistency of findings in the literature on season of birth effects in ASD, so it should not be surprising that the results of the present study are not entirely consistent with the findings of other studies. A possible reason for such inconsistency is the methodological differences in the studies. Diagnostic criteria and inclusion of subjects vary greatly among studies. Earlier studies used the criteria for diagnosis in DSM-III, whereas more recent studies use criteria from DSM-IV. The criteria for diagnosis vary greatly between the two versions of the DSM which has changed the types of children who receive an ASD diagnosis. The diagnoses in the present study result from scores on standardized diagnostic tests and clinical best judgment using DSM-IV criteria. The findings from studies

employing other means of diagnosis cannot be generalized to the subjects in this study, and vice versa. A child diagnosed with ASD by DSM-IV criteria may not have been diagnosed with ASD by DSM-III criteria, thus the composition of the samples is likely different in each case. Likewise, some authors choose to include children with any ASD, whereas others examine the effects only in children with AD, this difference also alters the composition of the clinical sample. To adequately compare the findings of studies, both the clinical sample and the comparison samples should be consistent among the studies.

Another methodological issue among studies is the way in which season of birth effects are analyzed. Chi-square goodness-of-fit test is used in many studies, but others use different types of curvilinear fit tests. Each of these statistical analyses has its limitations when dealing with season of birth effects, as mentioned previously. Another limitation comes when studies employing the different methods are compared. The two types of analyses examine two completely different things in the data. Chi-square compares expected values to observed values based on the samples being compared while curvilinear analyses attempt to fit month of birth data to some type of curvilinear function. The findings of the present study may have been different had a different statistical test been used.

Inconsistency in season of birth effects findings could also stem from the definition of the seasons used in studies. It has been shown that the way in which the months of the year are divided into seasons impacts the findings of season

of birth effects in ASD (Bolton, Pickles, Harrington, Macdonald, & Rutter, 1992). The seasons were defined with winter starting in January in the present study. It is possible to define winter starting in December, however, and if that had been done our findings may have been different. Likewise, the findings of other groups may be different, or even cease to be seen, if their definitions of the seasons were changed.

Limitations of the present study

There were limitations of this study, so the findings should be interpreted with caution. While there were significant findings, they were restricted to selected sub-groups of the entire sample. Season of birth effects were limited to level of functioning groups, and even then only when defined by Mullen VR, which measures nonverbal problem solving. They cannot be generalized to the population of ASD as a whole, and should not be taken to indicate season of birth effects in ASD. Another limitation of this study was the small sample sizes.

All of the sub-groups had very small samples. These small samples may not be representative of the population of people with ASD. It has also been seen that the typical pattern of season of birth effects in the general population are not seen until samples are very large (Nonaka & Miura, 1987). Therefore, the season of birth effects in our small samples may not be accurate and/or season of birth effects may not have been seen in other samples because the sample was too small for them to appear. To conserve power with the small samples, in all of the sub-samples of data only season of birth was examined. Month of birth

alone was ignored because there were too many empty categories for the results to be meaningful. The inclusion of only season of birth, however, makes detailed analysis difficult. We can only conclude what group of three months showed an increased number of births, not if one particular month is responsible for the seasonal increase as is shown in many other studies (e.g., Konstantareas, Hauser, Lennox, & Homatidis, 1986).

The control groups used for comparison are another limitation of this study. In the entire sample of all children the control group was those children who were not diagnosed with ASD. This sample was heterogeneous in the diagnoses, or lack thereof, the children received. While this made for a more representative sample, it also may have masked season of birth effects in ASD. The diagnoses that made up the control sample may exhibit season of birth effects of their own that would change the basis for comparison of increases or decreases in the number of births of children with ASD. In the other sub-samples analyzed the control population was another sub-sample. For example, the low functioning ASD and high functioning ASD groups were compared to each other as opposed to a more neutral control group that had no specific diagnosis. In other words, groups were compared within the diagnosis of ASD and not to the general population or some other control. Because the comparison groups in these cases also were diagnosed with ASD they may have had season of birth effects compared to the general population, but not to other children with ASD.

This choice of comparison groups may have obscured season of birth effects in our samples and reduced significance.

Future Implications

Despite the limitations of the present study, it provides many avenues for future research in season of birth effects in ASD. If the present study were to be repeated, we would use a more neutral control group in the analyses. It is unclear whether this change would affect the results, but at the least it would provide a cleaner point of comparison. Sample sizes should be increased as well, especially for those children not born prematurely, to increase power and perhaps uncover different season of birth effects. We would also repeat analyses after defining the seasons as winter beginning in December. If the season of birth effects seen persist even when the seasons are redefined it would increase the likelihood that they are not an artifact of the lack of adequate statistical tests for season of birth effects.

In addition to revisions of the present study, more studies on season of birth effects should be done. In future studies, prematurity of birth should be considered and either controlled for by testing for month or season of conception effects (i.e., what month or season the child was conceived in) or excluding children born prematurely from the data. Likewise, other factors often considered to be confounded with ASD that have been shown to exhibit season of birth effects on their own, such as peri-natal complications, should be controlled. Controlling for these factors would address the possibility that season

of birth effects in ASD are the by-product of season of birth effects in some other factor associated with ASD.

A related direction of study that is important to consider is uncovering why season of birth effects exist in ASD. Fatemi, et al. (2005; 2008) started to deal with the topic, with some success; however much more needs to be done. Season of birth effects could exist for a wide variety of reasons ranging from viral infection to nutritional deficiencies or even cultural factors (Bolton, Pickles, Harrington, Macdonald, & Rutter, 1992). Research on whether any of these things do in fact contribute to the development of ASD or if they even exhibit seasonal differences (and thus could possibly contribute to season of birth effects) could help discover the etiology of these complex disorders.

Overall, there is still much research that needs to be done to determine the etiology of ASD. Season of birth effects research begins to get at some of the possible factors that may contribute to the development of ASD. However, season of birth research on its own will not result in the answers to the etiology of ASD question. Season of birth research combined with other areas could resolve many issues in our knowledge of ASD.

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	All ASD	All Not ASD	Total
January	18 (6.5%)	15 (9.2%)	33 (7.5%)
February	22 (7.9 %)	8 (4.9%)	30 (6.8%)
March	27 (9.7%)	17 (10.4%)	44 (10.0%)
April	15 (5.4%)	10 (6.1%)	25 (5.7%)

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Table 1

Number and Percentage of Children Born in Each Month

May	25 (9.0%)	15 (9.2%)	40 (9.1%)			
June	26 (9.4%)	6 (3.7%)	32 (7.3%)			
July	27 (9.7%)	15 (9.2%)	42 (9.5%)			
August	All ASD	All Not ASD	All Total	Non-Premature ASD	Non-Premature Not ASD	Non-Premature Total
September			(9.8%)			
October			(8.6%)			
November	29 (10.4%)	14 (8.6%)	43 (9.8%)			
December	20 (7.2%)	21 (12.9%)	41 (9.3%)			

Table 2

Number and Percentage of Children Born in each Season

Winter	67 (24.1%)	40 (24.5%)	107 (24.3%)	19 (27.9%)	8 (23.5%)	27 (26.5%)
Spring	66 (23.7%)	31 (19.0%)	97 (22.0%)	18 (26.5%)	9 (26.5%)	27 (26.5%)
Summer	73 (26.3%)	43 (26.4%)	116 (26.3%)	15 (22.1%)	9 (26.5%)	24 (23.5%)
Fall	72 (25.9%)	49 (30.1%)	121 (27.4%)	16 (23.5%)	8 (23.5%)	24 (23.5%)

Table 3

Season of Birth of Children with ASD in Each Sub-Sample

	Winter	Spring	Summer	Fall
Gender				
Male	55 (25.0%)	53 (24.1%)	55 (25.0%)	57 (25.9%)
Female	12 (20.7%)	13 (22.4%)	18 (31.0%)	15 (25.9%)
Mullen VR				
High Functioning*	21 (28.0%)	25 (33.3%)	13 (17.3%)	16 (21.3%)
Low Functioning*	30 (23.6%)	24 (18.9%)	39 (30.7%)	34 (26.8%)
Vineland ABC				
High Functioning	26 (23.2%)	35 (31.3%)	22 (19.6%)	29 (25.9%)
Low Functioning	27 (22.1%)	24 (19.7%)	37 (30.3%)	34 (27.9%)
Mullen EXP				
Verbal	31 (31.3%)	25 (25.3%)	20 (20.2%)	23 (23.2%)
Non-verbal	20 (18.9%)	25 (23.6%)	33 (31.1%)	28 (26.4%)
Vineland EXP				
Verbal	30 (27.8%)	21 (19.4%)	31 (28.7%)	26 (24.1%)
Non Verbal	31 (25.0%)	36 (29.0%)	28 (22.6%)	29 (23.4%)

