

Seasonality of Birth in Alzheimer's Disease

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Abstract

The previous research provided a suggestive but inconclusive perspective regarding Alzheimer's patients having an excess of births in the early months of the year. The date of birth from 1906 to 1923 for 1,359 cases was collected from the Alzheimer's Disease Research Centers of California database. The general population's monthly distributions from 1906 to 1923 were also obtained. When the present distribution of Alzheimer's disease and control cases were combined with those from three previous studies, there was a disproportionate number of Alzheimer's cases in the first three months of the year. The present findings were related to nutritional factors and to research that has demonstrated a disproportionate number of early month births in other disorders such as schizophrenia and Down syndrome. It was suggested that infection and nutritional variables could account for the present findings.

Introduction

The purpose of the present study was to determine if there is a monthly distribution of births of Alzheimer's disease patients that differs from the monthly distribution of births within the general population of persons of comparable age. This research is in the context of the previous research on seasonality of birth in Alzheimer's disease not yielding a clear perspective. Philpot, Rottenstien, Burns and Der,¹ using the records of 239 patients with Alzheimer's disease, found an excess of births in the first quarter of the year in comparison to general population London births. Vezina et al.² with 399 cases of Alzheimer's disease in Quebec reported a

deficit of Alzheimer's disease births in May. However, the importance of their significant findings is questionable since a test of significance was done with each of the 12 months. One out of the 12 analyses providing significance at the .05 level does not warrant highly confident inferences. Vitiello et al.³ found no seasonality variation in the births of 150 Alzheimer's patients in comparison to the births of normal Americans. Henderson et al.⁴ found no seasonality of births in 170 Australians in comparison to 170 matched control normal persons. A major weakness in all four of these studies was that the N was much too small. In schizophrenia, the disorder with seasonal distribution of births most heavily researched and documented, the excess in seasonality of births is only a few percent in comparison to the general population births. It would appear that the N needed to detect a statistically significant difference is in the thousands rather than the hundreds.

Method

The monthly distribution of Alzheimer's disease in California was compared with the monthly distributions of general population births in California from 1906 to 1923. California was chosen because it has an extensive Alzheimer's disease data collection program. The general population distribution was obtained from the California Department of Health Services Office of Health Information and Research Vital Statistics Section.⁵ The dates of birth for 1,359 Alzheimer's cases were included in the study. This data was collected from the Alzheimer's Disease Research Centers of California database. All cases listed as "probable Alzheimer's disease" and "Alzheimer's disease" (verified by autopsy) were employed. "Possible Alzheimer's disease"

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cases were excluded. In addition, persons under the age of 65 at the time of diagnosis were excluded because it appears that etiological factors for persons with early-onset Alzheimer's may not be identical to that of the more typical presentation of the disease after age 65.⁵ A reason the early-onset cases were the ones not chosen for inclusion is their relatively small number would have provided insufficient power for the research design. The monthly distributions were recorded on a year-by-year basis for these 29 years because of the possibility that the general population pattern of births changed during that time period.

Results

Table 1 (below) displays the obtained and expected distribution of births of persons who later developed Alzheimer's disease in California. The 12 months were divided into four 3 month periods as was done in three previous seasonality of birth studies χ^2 (2, N = 1359) = 0.26, NS. In order to support or refute the finding of Philpot et al.¹ who reported a significant excess of Alzheimer's births in the first three months, the present data were combined with that of the four pre-

vious studies as indicated by Table 2 (p. 164). For the Henderson et al.⁴ study in the Southern hemisphere, July was regarded as the first month of the year. There was a 10.8% greater than expected number in the first three months in comparison to the other nine months, χ^2 (1, N=2393) =9.51, $p < .01$.

It was observed in the California distribution that there was a disproportionate number of births in the first 4 months, χ^2 (1, N = 1359) = 3.90, $p < .05$. Three of the previous season of birth studies did not provide the distribution of obtained and expected births for the individual months. The study of Vezina et al.² provided their monthly distribution. When the Vezina et al. trimester distribution was combined with the present trimester distribution, an acceptable level of statistical significance was not obtained, χ^2 (1, N= 1758) = 3.75, $p < .10$.

Discussion

The excess findings of Alzheimer's births in the first quarter of the year replicates and strengthens previously reported findings. Although the composite perspective provided by the present and previous studies does not permit inferences about

Table 1: Distribution of births for alzheimer's patients versus normative birth rates in California for 1906–1923.

Month	AD Births	Expected Births
January	123	113
February	110	103
March	104	113
April	133	107
May	112	113
June	101	112
July	113	117
August	114	119
September	117	116
October	123	117
November	94	112
December	115	117

relative importance of each of the 12 months of the year, there is now strong reason to believe that there is an excess of births in the early months. Both the credibility and importance of the present findings gain stature when they are viewed in conjunction with research that has demonstrated that other diseases have a disproportionate number of births in the early months of the year. A great deal of research on seasonality of birth in schizophrenia has been published over several decades. Moore, et al.⁶ stated, "the 8% excess of winter births among patients with schizophrenia remains one of the best established findings of psychiatric epidemiology." The broadly conceptualized "harmful influences hypothesis" of McNeil, Raff, and Cromwell⁷ contends that there are harmful effects surrounding birth or during gestation, such as infection or nutritional variables. Templer and Veleber⁸ found that

schizophrenic persons with presumably a lesser genetic predisposition, namely paranoid schizophrenics, had greater seasonality of birth than did catatonic and hebephrenic schizophrenics. And, a decreasing seasonality of schizophrenia in Missouri from 1900 to 1960 was said by Templer and Austin⁹ to reflect increasing technology and protection from the elements. Narita, Sasaki, Akaho, and Okazaki¹⁰ found a high incidence of human leukocyte antigen (HLA)-DRI in Japanese persons with schizophrenia. They reported that the schizophrenic patients with such tended to be born in February and March. These researchers suggested an interaction between (HLA)-DRI and winter births.

A disproportionate number of bipolar patients are born in the winter and early spring months.⁶ Possibly related to the above finding with bipolar patients is the study of Chotai and Asberg¹¹ who found

Table 2: Comparison of individual birth quarters using composite data from previous and current studies.

Annual Quarters		1st Quarter	2nd Quarter	3rd Quarter	4th Quarter
Present Study	Observed	337	346	344	332
	Expected	329	332	352	346
Vitiello et al.	Observed	71	81	72	49
	Expected	56	88	64	56
Philpot et al.	Observed	75	51	60	52
	Expected	59	61	60	59
Vezina et al.	Observed	111	86	96	106
	Expected	95	101	107	96
Henderson et al.	Observed	42	39	27	35
	Expected	35	38	33	29
Total Observed		636	584	599	574
Total Expected		574	620	616	586

that persons born in February and April had lower values of 5-HIAA. These researchers related their findings to the previous literature that reported lower monoamine metabolites to be associated with depression, suicidal behavior, impulsivity, and excessive mortality. An excess of births in March, April, May, and June was found in persons who later developed multiple sclerosis.¹² A disproportionate number of persons with Down syndrome were born in the first four months of the year.¹³ This Down syndrome finding may be especially relevant to Alzheimer's disease because there is an excess of relatives of Alzheimer's disease patients who have Down syndrome, and because of the large percentage of persons with Down syndrome who manifest Alzheimer's-like brain changes when they are over the age of 40.^{14,15} The same sort of "harmful influences" such as inadequate nutrition, infection and various environmental factors posited for other disorders with seasonality of birth could be relevant in the etiology of Alzheimer's disease. It has been suggested by Hoffer,^{16,17} Hagberg,¹⁸ Evans,¹⁹ Weiner,²⁰ Braverman,²¹ Abalon,²² and Berry and Borkan,²³ that nutritional deficiency may play a role in the treatment of Alzheimer's disease. The present research was carried out with late-onset Alzheimer's disease patients. Our findings may or may not apply to early-onset Alzheimer's disease. Possibly relevant to this matter is that it was predicted and found that schizophrenia (paranoid) with a presumably lesser genetic distribution had greater seasonality of births than did persons with catatonic and hebephrenic schizophrenia.⁸ These authors inferred that with lesser genetic predisposition other etiological factors would have to be stronger to produce the disorder. Since early-onset Alzheimer's seems to have a greater genetic predisposition than late-onset Alzheimer's disease,⁶ it is entirely possible that the latter has lesser seasonality. Future seasonality of birth re-

search that is capable of assembling a sufficiently large number of early-onset Alzheimer's disease cases is recommended.

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