Parental age and autism: Population data from NJ

Introduction

While the cause of autism is not known, current research suggests that a combination of genetic and environmental factors may be involved. Twin and other family studies have provided evidence of a genetic component, which recent research suggesting that autism originates prenatally. As the reported prevalence of autism has increased in recent years, so has the mean age of mothers and fathers. There have been a number of studies investigating whether certain parental and prenatal factors are correlated with autism. Advancing maternal and paternal age have been associated with a number of adverse reproductive outcomes. Paternal age, in particular, has been associated with mental illness, childhood cancers, and several other outcomes. These effects are largely associated with the increase in de novo mutations in male germ cells. The pathway through which maternal age may affect autism is not known, but advanced maternal age has been associated with adverse outcomes such as Down's Syndrome and Fragile X syndrome. One factor which complicates the potential relationship between parental age and autism is that parental age may impact ascertainment, as older parents may have greater financial resources and educational attainment, factors which are conducive to relatively early identification of developmental disabilities.

Background

A number of previous studies have found positive significant effects of parental age on autism. In a set of prospective population-based cohort studies, advanced maternal age was found to be significant and positive in a study in Denmark (Eaton et al, 2001), and in a California study by Croen et al (2002). Advanced paternal age was found to be a factor in another study in Denmark (Lauritsen et al, 2005), and in an Israeli study (Reichenberg et al, 2006). In a population-based case control study in Australia (Glasson et al, 2004), advanced maternal age was found to be significant. A study in Denmark (Larsson et al, 2005), found young maternal age and advanced paternal age to be significant.

More recently, Croen et al (2007) studied a large clinical (Kaiser Permanente-California) dataset to identify those children diagnosed with ASD. An analysis of this administrative data set found significant effects for paternal age (35-39 years and 40+ years) in adjusted models that controlled for maternal age and other demographic characteristics. When age was measured continuously, both paternal and maternal age, obtained from birth certificate data, were significantly associated with increased risk of ASD, but paternal age only was associated with autism, while maternal age only was associated with PDD-NOS and Asperger's Syndrome. While the Kaiser dataset is very large, it is not population-based, raising questions of representativeness.

Another recent study by Bhasin and Schendel (2007) analyzed cases of ASD in Metropolitan Atlanta identified through population-based ascertainment and matched with controls, examining demographic features from birth certificates, including maternal (but not paternal) age, maternal education, and median family income. Bhasin and Schendel found a significant negative effect for mothers less than twenty years, and a significant positive effect for mothers over 35 years. This effect persisted when autism cases were separated into those ASD cases with and those without mental retardation, but the adjusted odds ratio was notably higher (2.4, 1.6 – 3.6) in the case of those without MR, and barely significant (1.7, 1.0-2.8) in cases with autism and MR.

Some studies have found significant risk effects related to other parental characteristics. For example, Bhasin and Schendel, 2007, found that median family income was positively and significantly associated with autism prevalence, and this effect was greater in the case of autism cases in the absence of MR. However it is difficult to know the extent to which the observed relationship reflects a true risk factor or is an artifact of ascertainment.

A Swedish study found that mother's country of birth was significant (Hultman, et al, 2002). Lauritsen et al (2005) also found mother's country of birth to be significant, and also found an effect when parents were born in different countries, particularly if the mother was born outside of Europe or North America. The reason for this is not clear, but one theory advanced by the authors was that this may be a marker for paternal traits, as socially awkward males may be disproportionately likely to marry women from other countries.

Overall, most prior studies have been conducted in fairly homogenous populations. The two studies by Croen et al (2002 and 2007) and the Atlanta study (Bhasin and Schendel, 2007) involved diverse populations, but while these studies controlled for race and ethnicity in their adjusted models, the differential effect of parental age on autism by race and ethnicity has not been considered explicitly.

Data and Methods

This study investigated an ASD case population derived from active, population-based surveillance implemented in four New Jersey counties. This surveillance was undertaken as part of the CDC-funded autism and developmental disabilities monitoring network, or ADDM. New Jersey was one of six sites participating in 2000 and one of fourteen sites in 2002. (MMWR, 2007). The ADDM was founded in 2000 by CDC as a multiple-site, multi-source records-based surveillance system designed to identify children with ASD and other developmental disabilities. The ADDM network relies on systematic screening of developmental records rather than reliance on prior diagnoses of ASD. Since prior studies have identified age eight as the approximate peak in autism prevalence, the ADDM network uses age eight as the index year for its surveillance. Educational and health records of eight year olds in the study counties, therefore, were reviewed to identify cases. The fact that case identification is done at age eight eliminates some of the concern with ascertainment bias which may lead to more early identification of cases by parents with more resources.

New Jersey had significantly higher prevalence estimates than did the other states, a fact which may be attributable to greater numbers of educational evaluations available to reviewers. (MMWR, 2007). In New Jersey, children with ASD born in 1992 and 1994 and residing in four counties (Hudson, Union, Essex and Ocean) during the study years, 2000 and 2002, were identified through a two-phase process involving screening of data contained in special education and clinical records and independent, expert analysis and case determination using DSM-IV TR criteria. The cases were identified through an active population-based ascertainment process. In phase one, special education and clinical records of children residing in the surveillance region were reviewed/screened for autism triggers. Case information, including diagnoses, test findings, behavioral descriptions was abstracted from all records with one or more ASD trigger. A composite case file representing all information abstracted from education or health was analyzed by a panel of developmental disabilities professionals, familiar with autism, using study-specific definitions for Autistic Disorder and Autism Spectrum Disorder.

The two birth cohorts were linked to their birth certificate information. Children without ASD, that were born in 1992 and 1994 in the same census tracts as case children, served as population controls. Demographic information contained in the NJ birth certificate was analyzed to examine possible correlates of autism.

Results

Table 1 shows some descriptive results. (To be inserted.)

Table 2 shows results from a series of logistic regressions. The first columns show unadjusted results while the second one shows adjusted results. The adjusted results include controls for year and month of birth, sex, race and ethnicity of mother, age difference between mother and father, gestational age, birth weight, birth order, plurality, and presence or absence of any of the twenty two congenital anomalies recorded on the New Jersey birth certificate. The analysis is first conducted on the total population, and separately for whites and blacks.

For the unadjusted results for the total population, there is a significant effect for maternal age in the categories 30-34 years and 35-39 years. Paternal age was not significant. However, when measured continuously, both paternal and maternal age are significant, although the effect is quite small. In the adjusted models for the total population, however, none of the measures of maternal and paternal age are significant. For the model which is restricted to non-hispanic whites, neither maternal nor paternal age is significant in either the unadjusted or adjusted models, whether measured categorically or continuously. However in the model for non-Hispanic blacks, the effect of parental age is quite a bit stronger. In the unadjusted model, both paternal and maternal age are significant, both categorically and continuously. In the adjusted model for blacks, however, only maternal age (30-34 years) was significant (OR: 1.99, 1.02-3.82). A similar set of models estimated for Hispanics (not shown) had similar results to that for non-hispanic whites, in that no measure of parental age was significant in either unadjusted or adjusted models.

Table 2. Parental age and autism in New Jersey, 1992 and 1994 birth cohorts, adjusted and unadjusted odds ratios

Total

Parental Age	Unadjusted OR	95% C.I. Lower	95% C.I. Upper		Adjusted OR	95% C.I. Lower	95% C.I. Upper
Categorical							
Paternal							
<20	**0.748**	*0.392*	*1.427*		**0.745**	*0.333*	*1.665*
20-24	**0.838**	*0.595*	*1.180*		**0.814**	*0.540*	*1.227*
25-29	**Reference**				**Reference**		
30-34	**0.944**	*0.741*	*1.203*		**0.886**	*0.674*	*1.166*
35-39	**1.094**	*0.849*	*1.408*		**0.956**	*0.694*	*1.318*
>40	**1.257**	*0.954*	*1.656*		**1.101**	*0.712*	*1.702*
Maternal							
<20	**0.972**	*0.621*	*1.520*		**0.948**	*0.513*	*1.750*
20-24	**1.121**	*0.837*	*1.502*		**1.112**	*0.791*	*1.565*
25-29	**Reference**				**Reference**		
30-34	**1.279**	*1.007*	*1.625*	*	**1.291**	*0.982*	*1.698*
35-39	**1.526**	*1.149*	*2.028*	*	**1.430**	*0.976*	*2.095*
>40	**1.352**	*0.745*	*2.452*		**1.171**	*0.584*	*2.349*
Continuous							
Paternal	**1.018**	*1.004*	*1.032*	*	**1.006**	*0.962*	*1.051*
Maternal	**1.022**	*1.006*	*1.039*	*	**1.023**	*0.977*	*1.071*

Whites

Parental Age	Unadjusted OR	95% C.I. Lower	95% C.I. Upper		Adjusted OR	95% C.I. Lower	95% C.I. Upper
Categorical							
Paternal							
<20	**1.732**	*0.695*	*4.315*		**2.150**	*0.600*	*7.709*
20-24	**0.766**	*0.430*	*1.365*		**0.907**	*0.454*	*1.811*
25-29	**Reference**				**Reference**		
30-34	**0.852**	*0.617*	*1.176*		**0.727**	*0.501*	*1.054*
35-39	**0.937**	*0.668*	*1.314*		**0.721**	*0.465*	*1.119*
>40	**1.256**	*0.872*	*1.810*		**1.016**	*0.556*	*1.857*
Maternal							
<20	**1.214**	*0.557*	*2.646*		**0.619**	*0.197*	*1.944*
20-24	**0.964**	*0.610*	*1.525*		**0.878**	*0.510*	*1.511*
25-29	**Reference**				**Reference**		
30-34	**1.155**	*0.846*	*1.575*		**1.299**	*0.902*	*1.871*
35-39	**1.409**	*0.978*	*2.030*		**1.482**	*0.887*	*2.476*
>40	**1.233**	*0.565*	*2.688*		**1.152**	*0.451*	*2.944*
Continuous							

Paternal	**1.014**	*0.993*	*1.036*		**1.003**	*0.937*	*1.073*
Maternal	**1.020**	*0.995*	*1.045*		**1.021**	*0.952*	*1.096*

Blacks

	Unadjusted				**Adjusted**			
		95% C.I.				**95% C.I.**		
Parental Age	**OR**	**Lower**	**Upper**		**OR**	**Lower**	**Upper**	
Categorical								
Paternal								
<20	-	-	-		-	-	-	
20-24	**1.057**	*0.533*	*2.096*		**1.292**	*0.595*	*2.805*	
25-29	**Reference**							
30-34	**1.466**	*0.801*	*2.681*		**1.064**	*0.546*	*2.073*	
35-39	**2.245**	*1.293*	*3.897*	*	**1.508**	*0.760*	*2.994*	
>40	**2.113**	*1.190*	*3.752*	*	**1.269**	*0.525*	*3.064*	
Maternal								
<20	**0.389**	*0.114*	*1.327*		**0.425**	*0.111*	*1.633*	
20-24	**1.497**	*0.799*	*2.807*		**1.654**	*0.816*	*3.352*	
25-29	**Reference**							
30-34	**2.277**	*1.249*	*4.152*	*	**1.991**	*1.021*	*3.882*	*
35-39	**2.162**	*1.030*	*4.539*	*	**1.768**	*0.721*	*4.335*	
>40	**1.719**	*0.395*	*7.478*		**1.468**	*0.288*	*7.489*	
Continuous								
Paternal	**2.162**	*1.030*	*4.539*	*	**1.018**	*0.940*	*1.103*	
Maternal	**1.051**	*1.016*	*1.087*	*	**1.025**	*0.939*	*1.118*	

Adjusted models include age of the other parent, maternal and paternal education,
year and month of birth, sex, mother's race, gestational age, birthweight, certain congenital anomalies.
Includes only observations for which maternal and paternal age are known.

Discussion

This study finds relatively little evidence for an effect of parental age on the probability of autism. However, there are some notable differences by race. In particular, for the population where the mother was black, the effect of maternal and paternal age on the probability of autism was greater. However, most of this effect disappeared in the adjusted models, with only the effect of maternal age 30-34 years remaining.