Editorial

Integrative Pediatrics and Child Care Autism and its Obstetrical Causes

BM Petrikovsky*

Professor of Obstetrics and Gynecology, New York Institute of Technology, USA

***Correspondence:** Boris M Petrikovsky, Professor of Obstetrics and Gynecology at New York Institute of Technology, USA, E-mail: bpetriko@gmail.com

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Autism spectrum disorder (ASD) is a developmental disorder characterized by abnormal social interaction and communication and manifested by repetitive behavior. Parents notice signs of autism in the first two or three years of their child's life.

There are numerous speculations about the cause of ASD. Some theories include vaccinations, toxic nutrients, maternal obesity, prenatal fever, use of oxytocin, among others [1]. The report from the Department of Developmental Services from California has been widely quoted as evidence for the epidemic of autism [2]. This increase may reflect the adoption of a broader concept of autism, changes in diagnostic criteria, and improved identification of patients with autism attributable to better medical services [3][4].

Studies of twins suggest that heritability is 0.7 for autism and as high as 0.9 for ASD, and sibling of those with autism are about 25 times more likely to be autistic than the general population. Typically, autism cannot be traced to a Mendelian mutation or a chromosome abnormality. Numerous candidate genes have been located, with only small effects attributable to any particular gene. The large number of autistic individuals with unaffected family members may result from structural variation (deletion, duplications or inversions).

Recently, Rosman et al. [5] studied whether there is a relationship between the frequency, timing, and duration of prenatal ultrasonography and autism. The data collected included gestational age and time of exposure, frame rate, soft tissue thermal index, Doppler use, and the length of time of using 3-dimensional (3-D) imaging. The authors evaluated ultrasound exposure by trimester. They concluded that the ASD group had a greater mean depth of ultrasonographic penetration than the control group in the first trimester.

Autism's symptoms result from maturation-related changes in the brain. Its mechanism can be divided into two areas: the pathophysiology of brain structures and the neuropsychological linkages between brain structures and behaviors. The immune system is thought to play a role in autism. Children with autism have been found to have inflammation of the peripheral and central immune systems as indicated by increased levels of pro-inflammatory cytokines and significant activation of microglia. Biomarkers of abnormal immune function have also been associated with impairments in behaviors that are characteristic of the core features of autism. Transient changes to the brain's electrical activity were detected in response to stimuli, in autistic individuals.

Ultrasound has been considered safe during pregnancy. A large cohort study of infants found that those exposed to ultrasound have increased odds of being left-handed, a finding that was confirmed in subsequent meta-analyses [6][7][8]. These studies suggest that ultrasound exposure can influence cerebral hemispheric specialization. Animals

studies have shown that ultrasonography may have an adverse effect on the developing brain [9][10]. In mice, exposure to the ultrasound in utero caused a failure in the neurons to acquire their normal cortical position. ACOG recently declared: "ultrasound energy delivered to the fetus cannot be assumed to be completely innocuous, and the possibility exists that such biological effects may be identified in the future." In another recent statement, ACOG has endorsed the "prudent use" of ultrasound in obstetrics, discouraging its use for nonmedical purposes, e.g., solely to create keepsake photographs or videos [11]. The AIUM also advocates the responsible use of ultrasound during pregnancy. Although there are currently no confirmed detrimental biological effects from an ultrasound during pregnancy, the possibility exists that such biological effects may be eventually identified. Doppler studies pose the high risk of thermal effects on the fetus and may cause a substantial temperature increase in the fetal brain [12]. ACOG claims that there are no clear clinical benefits of 3-or 4-D imaging and suggests that conventional 2-D ultrasonography be the recommended standard of care [13]. Most of the ACOG guidelines follow the ALARA (as low as reasonably achievable) principle during pregnancy, but even the ALARA principle does not provide any specific, evidence-based limit for safe use.

A World Health Organization (WHO) study, on the other hand, reviewed 6,717 citations obtained from a systematic search of MEDLINE and the Cochrane Central Register of controlled trials electronic databases between 1950 and 2007. The final analysis included 61 publications on short and long-term effects of in utero exposure to ultrasound from 41 different studies: 16 controlled trials, 13 cohort studies, and 12 case-control studies. The outcome includes analysis of low birth weight, preterm birth, low Apgar scores, need for neonatal resuscitation, presence of seizures, admission to a neonatal intensive care unit, perinatal mortality, childhood growth, neurologic development, behavioral scores, hearing and visual impairment, cognitive function, attention deficits, and motor skills, among others. The only finding was the previously reported weak correlation between ultrasound exposure and left-handedness in males [8]. If we assume the assertion of an increased recent prevalence of autism to be adjusted for the purposes of the study, then it is fair to state that the increased prevalence of ASD parallels the increased use of ultrasound during pregnancy. At the same time, there has been an increased use of cell phones and personal computers over the same time period [14]. It is unclear if this rise in autism is due to an increase in diagnoses or an increase in its prevalence. Some researchers argue that physicians are doing a better job at diagnosing autism, particularly in minority populations.

Therefore, if an association between prenatal ultrasonography and autism exists, it doesn't necessarily imply causation. The question remains, however, what is the current status of the problem and what further steps are warranted? The continued lack of scientific data may result in conspiracy theories and the risk of creating unjustified public fear [14]. On the basis of the current information, we conclude that currently, there is no credible evidence that a cause-effect relationship exists between in utero exposure to ultrasound and development of ASD.

While infection with rubella during pregnancy causes less than 1% of cases of autism, vaccination against rubella can prevent many of those cases.

Current Recommendations

Ultrasound use should be restricted to medical indications and performed by trained professionals [14]. In the meantime, certain measures, in light of ACOG and AIUM recommendations can be considered, e.g., establishing time limits for performing 1st, 2nd, and 3rd-trimester ultrasound examinations. In our experience, computer-assisted detection of fetal abnormalities shortens the timing of fetal ultrasound exposure without compromising its diagnostic accuracy [15]. This software works by overlapping various sonographic features of fetuses we are studying over analogous features from the database containing various genetic abnormalities and other fetal syndromes. We recently published a study on the duration of ultrasound examinations performed by radiologists as compared to maternal-fetal medicine (MFM) specialists (a total of 10,000 scans). A wide variety in the duration of sonographic examinations had been observed. It appears that MFM specialists take more time performing sonographic examinations than radiologists. The reported data can be utilized in developing timing guidelines for obstetrical sonography [16][17].

In conclusion, until further research eliminates any association between obstetrical ultrasound and autism, caution should be exercised to avoid extended exposure to ultrasound [18].

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