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Parental report of vaccine receipt in children with autism spectrum disorder: Do rates differ by pattern of ASD onset?

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ABSTRACT

A contentious theory espoused by some parents is that regressive-onset of autism spectrum disorder (ASD) is triggered by vaccines. If this were true, then vaccine receipt should be higher in children with regressive-onset ASD compared with other patterns of onset. Parental report of rate of receipt for six vaccines (DPT/DTaP, HepB, Hib, polio, MMR, varicella) was examined in children with ASD ($N = 2755$) who were categorized by pattern of ASD onset (early onset, plateau, delay-plus-regression, regression). All pairwise comparisons were significantly equivalent within a 10% margin for all vaccines except varicella, for which the delay-plus-regression group had lower rates of receipt (81%) than the early-onset (87%) and regression (87%) groups. Findings do not support a connection between regressive-onset ASD and vaccines in this cohort.

Most scientists agree that the majority of autism spectrum disorder (ASD) cases are likely caused by some combination of genetic and environmental factors [1,2]. Although twin and sibling studies demonstrate high heritability for ASD [3–7], genetic causes can be identified in only 15–20% of cases [8,9]. Lacking a clear etiological mechanism, parents often devise their own explanations for their child's ASD, yet little is known about parents' beliefs about causes of ASD. A limited number of studies found that most parents believe in a combination of internal (i.e., innate to the child; genetics, brain structure) *and* external causative factors (i.e., extrinsic to the child; diet, pollution, vaccines) [10,11]. However, less is known about *how* and *when* parents' beliefs are formulated and why some parents endorse some causes over others.

A highly contentious belief held by some parents and perpetuated by the popular media is that ASD, especially regressive-onset ASD, is triggered by vaccinations [12,13]. This notion was initially put forth by Andrew Wakefield in a paper published in 1998 that has since been retracted. Wakefield proposed that the measles, mumps, and rubella (MMR) vaccine caused intestinal inflammation, thereby allowing chemicals in the vaccine to enter the bloodstream, travel to the brain, and cause regressive-onset autism. Though the study was fraudulent, fears about an autism-vaccine connection have persisted and expanded to include other concerns about vaccine safety, the recommended immunization schedule, and vaccine ingredients [14–16]. Numerous epidemiological studies have been conducted worldwide, with results failing to support a link between vaccines and ASD (e.g., [17–21]). Unfortunately, fears regarding an association between autism and vaccines persist.

This belief that vaccines play a causal role in autism may be perpetuated, in part, by parents of children with ASD who exhibit

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developmental regression. Initially, the emergence of ASD was characterized as either *early onset*, for which symptoms appeared within the first year, or as *regressive onset*, where seemingly typical development was marked by a loss of previously acquired skills, usually in language and/or social skills [12]. Because regression is reported at an average age of 21.4 months [22] and the majority of childhood vaccines are given before 2 years of age, parents may mistakenly attribute their child's regression to the vaccines they received before the observed loss of skills, even when developmental delays are already present. In a qualitative study of 128 parents of children with ASD, 71% of parents of children with regressive onset specified external factors as the cause of their child's ASD, compared with 7% of parents of children with early-onset ASD; conversely, 93% of parents of children with early-onset ASD specified genetic factors as the cause of their child's ASD, compared with 29% of parents of children with regressive onset [12]. More recently, Goin-Kochel, Mire, and Dempsey [13] found that parents of children with a history of regression were more likely to blame "toxins in vaccines" as the cause of their children's ASD than were parents of children with ASD without regression.

Despite the overwhelming scientific evidence demonstrating that there is no association between vaccines and ASD, the beliefs that parents hold about such a link may influence actual vaccination behaviors. Fears about an autism-vaccine connection have prompted some parents of children with ASD to either delay or refuse vaccinations for their *subsequent* children. For example, Bazzano and colleagues [23] found that half of parents of children with ASD discontinued or changed vaccination practices for subsequent children because of their beliefs that vaccines contributed to ASD. Likewise, Kuwaik and colleagues [24] found that MMR-vaccine receipt was significantly higher for older siblings diagnosed with ASD compared to their younger counterparts (90% vs. 43%, respectively). Moreover, the odds of delaying or omitting a vaccine in a series – compared to receiving the entire series – are much higher among families endorsing vaccines as the cause for their older children's ASD [25].

If vaccines are associated with developmental regression in children with ASD, then it follows that vaccination rates should be significantly higher in children who had regressive onset. To our knowledge, only two studies have investigated whether rates of MMR-vaccine receipt are different between children with ASD with or without a history of regression. Fombonne and Chakrabarti [18] examined rates of regression per the *Autism Diagnostic Interview – Revised* (ADI-R) – a standardized, parent interview that queries early child development and past/present behaviors indicative of autism – in three U.K.-based samples of individuals with ASD, two of which had the opportunity to receive the MMR vaccine and one of which predated this vaccine; regression rates were not significantly different across samples. Similarly, Uchiyama and colleagues [26] examined rates of regression among children with ASD in Japan before, during, and after an MMR-vaccine program was initiated, with no differences observed for any time period. However, both of these studies only focused on the MMR vaccine, with the latter study further limited by selection biases (i.e., private ASD clinic) and non-standardized assessment of regression status. Additional research in this area is necessary to further examine possible associations between vaccines and specific patterns of ASD onset. Toward this end, the goals of this study were to (a) investigate rates of vaccine receipt in a large, well-characterized sample of North American children with confirmed ASD diagnoses and standardized assessment of regression status and (b) examine whether there are differences in parent-reported rates of vaccine receipt by pattern of ASD onset. We hypothesized that rates of parent-reported vaccine receipt would be equivalent across ASD-onset categories.

1. Methods

1.1. Participants

Participant data were obtained via the Simons Simplex Collection [SSC; 27], a repository of clinical and genetic data from families who have a single child diagnosed with ASD and no other first- through third-degree relatives with ASD or suspected ASD. Twelve sites across North America collected data on behalf of the SSC between 2007 and 2011 (i.e., rolling enrollment). Rigorous standards were applied to the evaluation of ASD in participating children, which included administrations of both the *Autism Diagnostic Observation Schedule* [ADOS; [28]] and the *Autism Diagnostic Interview—Revised* [ADI-R; [29]]. Details about inclusion/exclusion criteria and recruitment tactics can be found in Fischbach and Lord [27].

1.2. Measures

1.2.1. ASD-onset types

The dichotomous characterization of ASD onset was previously expanded by Shumway and colleagues [30], who identified four distinct ASD-onset patterns using various combinations of responses to select items from the ADI-R: early onset (symptoms of ASD in the first year with no skill loss), delay-plus-regression (early symptoms of ASD as well as loss of language and/or social skills), plateau (no symptoms of ASD in the first year or later loss of skills), regression (no symptoms of ASD in the first year but loss of language and/or social skills). Their same method was applied in the current work to generate distinct ASD-onset groups.

1.2.2. Vaccine receipt

Vaccination history was obtained during an extensive Medical History Interview (MHI) conducted with children's parents. Parents were specifically asked (a) whether their child had received a particular vaccine and, if so, (b) whether it was "given on schedule" or "delayed but received." Study coordinators were allowed to request vaccine records as evidence of the child's vaccination history, and some parents indicated that they were looking at their child's vaccine record when answering these items during the MHI. However, because the SSC did not track which participants had a vaccine record collected, we conservatively assumed all responses to be parental report. Based on review of files at our study site, we estimated that approximately 50% of the sample had vaccination records as the source for this information. Because (a) dates of vaccine receipt were not queried and (b) some parents may not know whether a vaccine was truly "given on schedule" or not (e.g., in cases of supply shortage, child illness, provider error), we interpreted endorsement of "given on schedule" to mean that they accepted the vaccine *at the time that it was initially offered to them*, rather than opting to decline or delay receipt of the vaccine. This afforded delineation of those who never received a specified vaccine, those who received it when it was first offered, and those who received it but were delayed.

The following is the list of all vaccines as queried on the MHI: old diphtheria, pertussis, and tetanus vaccination (DPT); new diphtheria, pertussis, and tetanus vaccination licensed in 1991 by the U.S. (DTaP)[1]; hepatitis B (HepB); Haemophilus influenzae type b vaccination (Hib); polio-oral; polio-injected; polio-unknown method of administration; mumps, measles, rubella (MMR); influenza (flu shot); tetanus booster; travel-related vaccines; chicken pox/varicella. Two option boxes also allowed inclusion

[1] DTaP was licensed for the 4th and 5th doses (given after 12 months of age) in 1991 but not licensed for the first three infant doses until 1996.

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