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European Journal of Paediatric Neurology 36 (2022) 151–158

Contents lists available at ScienceDirect

European Journal of Paediatric Neurology

The myth of vaccination and autism spectrum

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ARTICLE INFO

Article history:
Received 14 April 2021
Received in revised form
12 December 2021
Accepted 14 December 2021

Keywords:
Autism
Immunizations
Vaccinations
Children
Myth

ABSTRACT

Background: Among all of the studied potential causes of autism, vaccines have received some of the most scrutiny and have been the topic of many evidence-based studies. These efforts have led the great majority of scientists, physicians, and public health researchers to refute causation between vaccines and autism.

Rationale: This presumed association and concern has been a major contributor to parents' refusal to immunize their children and has become a major threat to public health in secluded populations over the last two decades, even prior to the COVID-19 pandemic. With the emergence of COVID-19 immunizations, sentiments towards this topic were addressed as a public health concern that may influence the ability to overcome the Corona virus worldwide.

Scientific review of data: Despite the overwhelming data demonstrating that there is no link between vaccines and autism, many parents are hesitant to immunize their children because of the alleged association.

Other contributing factors to the myths and conspiracy theories surrounding the association between vaccines and autism include the fact that the diagnosis of autism is typically made after the age of receiving the main childhood immunizations, as well as the occasional occurrence of regression after the age of first year vaccinations. In spite of vast evidence that the main contribution to the increase in incidence is from improvement of the diagnostic process, this rapid and publicized rise in autism diagnoses feeds parental concerns regarding any medical intervention that may be associated with the health of their children.

Recommendations: It is plausible that with more evidence-based studies linking autism to specific etiologies the myth will diminish and disappear eventually. In an era where conspiracy theories are prevalent on social media, it is critical that evidence-based studies relating autism to specific etiologies be made public, and that information concerning autism diagnosis and causes be made more readily available through social media and parental organizations.

1. Introduction

The topic of vaccinations and autism spectrum has been studied and reviewed extensively over the last few decades and is still a heavily debated topic — especially now in the context of the COVID-19 pandemic. When crossing the terms "vaccination" and "autism" on Google Scholar, there are 38,200 results with the leading topic being MMR (measles, mumps, & rubella) and the repeated evidence in many thousands of articles against its association with autism.

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https://doi.org/10.1016/j.ejpn.2021.12.011
1090-3798/

In spite of the strong evidence from multiple studies over the last three decades, the public sentiment of hesitancy poses a significant health risk and may influence the COVID-19 immunization plan. Global medical officials used social media to try to overcome this fear as a major measure to combat the Coronavirus pandemic by enhancing vaccination acceptance [1–3].

Before the COVID-19 pandemic, the influence of the sentiment against immunizations caused suboptimal vaccination coverage in specific populations and resulted in outbreaks of diseases easily preventable by vaccines, such as measles, resulting in significant morbidity and mortality in vulnerable individuals [4].

The largely publicized concern around the rapidly rising incidence of autism [5] continues to feed this sentiment. Other contributing factors to the myths and conspiracy theories surrounding the association between vaccines and autism include the fact that the diagnosis of autism is typically made after the age of receiving the main childhood immunizations, as well as the occasional occurrence of regression after the age of first year vaccinations. Additionally, the medical community's inability to provide conclusive answers in regard to the causes and treatment of autism further contributes to the growing concern.

In order to address this topic, we reviewed the current knowledge and the multiple publications studying the link between vaccinations and autism, as well as the public state of mind nourished by social media and non-scientific influences. Despite the numerous evidence-based studies showing no relationship between immunizations and autism spectrum, the cultural belief of this association is still reinforcing the widespread concern about vaccines, with the COVID-19 pandemic reviving this topic.

2. History of immunizations and of pandemics and epidemics that could have been prevented by immunizations

Vaccines are the most effective way to prevent infectious diseases. The history of childhood immunization has had many breakthroughs throughout the years, including Edward Janner's first smallpox vaccination on the 8-year-old James Phipps in 1796, and Louis Pasteur's first rabies vaccination on the 9-year-old Joseph Meister in 1885. Many of the efforts towards vaccine development in the 20th century targeted childhood infectious diseases, including polio, measles and diphtheria.

Most children worldwide receive immunizations against childhood diseases, with an estimated 2–3 million deaths prevented every year [6]. Nowadays, the CDC-recommended childhood vaccinations include: Hepatitis B, Tetanus, Diphtheria, Pertussis, Polio, Haemophilus influenzae B, Pneumococcus, Rota-virus, Measles, Mumps, Rubella, varicella, Hepatitis A, Papilloma-virus and Influenza [7]. The global vaccination coverage (i.e., proportion of children that receive recommended vaccines worldwide) remains unchanged in recent years. Both the lack of access to vaccines and the lack of confidence in vaccines are the two main causes for low rates of children immunization in specific communities [8,9]. These communities are mostly comprised of developing countries, however developed countries such as the US and England have also reported decreasing rates of childhood vaccination in the past few years [10].

Vaccination during the early phases of life (i.e., infants and children) is crucial due to the immaturity of the immune system, leaving individuals susceptible to vaccine-preventable diseases and even life-threatening conditions. Moreover, lower immunization rates among children may cause vaccine-preventable disease outbreaks in the general population and endanger elderly or immunosuppressed individuals. Immunizations as early as the neonatal phase is hypothesized to have beneficial health effects such as fewer required vaccination for immunogenicity or immunomodulatory boosting effect [11].

Ironically, the success of vaccinations in eliminating vaccine-preventable diseases caused many individuals to become more concerned about the adverse effects of vaccinations than the actual disease, resulting in lower vaccine acceptance rates and greater risks of vaccine-preventable diseases to the general population and especially children, as per parental choice. Accordingly, along with the rational of vaccinating children during the vulnerable first years, there is a key challenge to be addressed-the hesitancy of caregivers to vaccinate their children due to fear of adverse effects that vaccinations may cause [12]. In fact, vaccine literacy and misconceptions regarding the safety of childhood vaccination and their involvement in long-term adverse effects is the major cause for vaccination refusal [8].

The main misinformation surrounding vaccine safety involves the belief that vaccine formulations contain harmful substances. (e.g., adjuvants, preservatives etc.). Another misconception is that there is an excessive number of vaccinations. Others are concerned about the negative effect on the immune system of children, as well as the proposed correlation to conditions such as autism, diabetes etc. [13–15].

2.1. Vaccine safety

The safety of childhood vaccination has extensively and repeatedly been evaluated over the years [14,16,17]. The meta-analysis of Taylor et al. proved evidence for non-correlation of vaccination and autism for a compelling number of more than 1,256,407 children [18]. Nevertheless, all vaccination can potentially cause mild and short-lasting side effects. Vaccines adverse events (AE) in children that should be noted include local events such as pain and swelling in the injection site, as well as systemic events such as fever, irritability, drowsiness, and rash [7]. Serious adverse events (SAE) may include severe rash, severe infections, encephalitis or even death, however such SAE are rare.

Some children with neurological disorders, either progressive and neurodegenerative such as mitochondrial (Leigh Syndrome), or neurodevelopmental genetic disorders, such as Dravet Syndrome (due to SCN1A mutation), may be susceptible to fever with seizures and regression occurring after a febrile episode. Fever after vaccinations may be perceived by the parents as the cause of those syndromes.

Multiple meta-analyses have been performed to assess AE following each childhood vaccination. The results included local and systemic AE, as well as SAE in very low frequencies. According to a study that assessed 61 meta-analyses that evaluated vaccine safety, specific safety outcomes such as maternal events (e.g., stillbirth or spontaneous abortion) or cardiovascular events were found to be unaffected or even less likely following vaccination [19]. These results, taken in consideration with the rigorous safety tests that vaccines undergo before being clinically approved, as well as the continuous monitoring for AE by health organizations like the CDC and the WHO, provide reassuring evidence in terms of safety profile of the recommended childhood vaccinations.

3. Autism diagnosis and epidemiology

The American Academy of Pediatrics recommends screening all children for ASD at 18 and 24 months followed by a comprehensive evaluation for children with developmental concerns [20]. However, in recent years it has been recommended that they be evaluated at a younger age and that the diagnosis be made during the second year of life [21–23]. When it comes to age of diagnosis, there is still a large gap between “state-of-the-art” research on autism and mainstream practice. This gap varies in its magnitude between countries, among communities, and in relation to

socioeconomic status. In addition, there may be a delay of a few years between detection of early signs and final diagnosis [24]. Nevertheless, parental concerns and initiation of a diagnosis process commence mostly during the second year of life and this is the period when most childhood immunizations are provided [25,26].

The prevalence of autism has rapidly been rising over the last two decades. From the last CDC report in 2020, about 1 in 54 children has been identified with autism spectrum disorder (ASD) according to estimates from CDC's Autism and Developmental Disabilities Monitoring (ADDM) Network. In earlier years, autism was associated primarily with severely affected individuals and the rate of autism was estimated to be only about 1 in 10,000 people. The rapid increase from 1 in 150 children in 2007 to the current 1 in 54 is causing significant concern among many expecting parents [27,28]. The best evidence that the rise in prevalence is mainly due to changes in diagnostic measures is found in studies performed in adult populations that used the new tools and diagnostic criteria to show approximately the same prevalence as in children, of about 2% [29].

Despite the vast evidence that the main contribution to the increase in incidence is from improvement of the diagnostic process, this rapid and publicized rise in autism diagnoses feeds the parental concerns regarding any intervention that may be associated with the health of their children.

The additional myth feeding those theories is that there is no known cause for autism – however, in reality, there are many known etiologies. There is not a single cause, but a realm of causes: genetics (more than 100 gene mutations have been associated with autism), advanced paternal age, prenatal and perinatal brain insult and prematurity are among those known causes [30–32].

4. Immune system in autism

In recent years, there has been extensive research conducted to better understand the relationship between the immune system and autism. Decades of research has revealed the vast and intricate connection between the immune system, the nervous system, and behavior [33]. There is abundant evidence suggesting the presence of a pathophysiological relationship between the immune system and autism [33]. Variation in levels of several cytokines, including Transforming Growth Factor Beta (TGF-β), Macrophage Inhibitory factor (MIF), Leptin, Interferon- γ, and many different Interleukins have been observed in individuals with autism compared to individuals without autism [33–35]. Many studies have also described various autoimmune phenomena among individuals with autism and among family members of individuals with autism [35,36]. Epigenetic regulation of the immune system has also been studied in the context of autism. These studies have provided evidence that certain genes involved in immunity are expressed at higher rates in autistic individuals, further demonstrating the connection between the immune system and ASD [37].

Maternal immune activation during pregnancy has also been comprehensively researched in order to better understand potential etiologies of autism. Infectious outbreaks, particularly the Rubella outbreak of the 1960s, provided substantial evidence that supported maternal immune activation as a risk factor for autism, proving that the disease caused but Rubella virus (and not the vaccine) is directly causing significant brain damage resulting in intellectual disability, autism and blindness [37,38]. Rubella infection is a hallmark of viral infection causing brain damage in the fetus and subsequent neurodevelopmental impairments including intellectual disability and autism. Other TORCH viruses can damage the fetal brain and cause severe neurodevelopmental impairments including autism [39]. Herpes viruses have to potential of causing severe damage and impaired outcome when causing infection even postnatally-such as Herpes virus 1,2 [40]. Direct brain damage is also caused by Zika viral infection [41].

Other viruses are known to cause post-infectious brain damage resulting in declining neurological function years after the infection. Subacute Sclerosing Panencephalitis (SSPE) is a neurodegenerative disorder in late childhood that may develop 2–10 years after the original viral attack, due to reactivation of the measles virus or an inappropriate late immune response. Successful measles vaccination programs directly and indirectly protected the population against SSPE and have the potential to eliminate SSPE through the elimination of measles [42].

The Maternal Immune Activation (MIA) model served as an experimental model to study the link between maternal exposure and atypical behavior in offspring [34,38]. This model involves introducing a pathogen to pregnant rodents and observing behavioral abnormalities within the offspring [34]. Data from both human and animal studies indicate that the timing of immunogen exposure during pregnancy affects the phenotypic variations in behavior seen in offspring [37]. Studying the relationship between the immune system and autism is useful in for the search of potential biological markers for the identification and treatment of ASD (see below the link between fever and behavior in children with autism).

When developing an understanding of the risk factors for autism, the importance of the immune system and its association with the nervous system cannot be ignored. However, this association should be studied and reported with caution, since it not only may be misunderstood by the public and perceived as causation, but also because this is a large generalization of the concept of individual differences in autism.

With the increasing understanding of many genetic etiologies causing autism, more syndromes are being revealed as involving the immune system and the brain. One example is Velo-cardio-facial syndrome in which the deletion of 22q11.2 including PRODH and COMT genotypes express a phenotype including immune deficiencies, autism and neuropsychiatric disorders such as schizophrenia [43]. Other genetic syndromes linking immune disorders and autism are Phelan-Mc Dermid syndrome (SHANK3 gene), Down Syndrome, CHARGE Syndrome and channelopathies [44–46].

In addition, prematurity becomes a major etiology causing autism, as well as immune vulnerability [30].

5. Fever, immune system and autism

Another notable association between autism and immunity is the suggested improvement in behavior in children with ASD during fever [47]. There have been many anecdotal reports that the disturbed behaviors in autism, especially stereotypic behavior and inappropriate speech, are noticeably decreased during febrile episodes, with the degree of improvement being unrelated to the severity of fever or ASD [47]. The up-regulation of heat-shock proteins and other mechanisms involved in cellular processes during fever may explain the improvement in cerebral-cortical connectivity that is diminished in ASD [48]. Singh et al. conducted a study that assessed the behavioral outcomes in patients with ASD who received sulforaphane, a substance that also up-regulates the heat shock response including protection from oxidative stress, inflammation, DNA damage, and radiation [48]. Their study indicated that there were statistically significant improvements in behavior during treatment with sulforaphane, further suggesting that the up-regulation of cellular defense mechanisms can ameliorate behavioral issues.

Studying the relationship between the immune system and autism by large double-blinded randomized controlled trials and

taking into account the anecdotal reports of improvement in communication during fever, may provide additional insight into potential biological markers for the identification and treatment of ASD, unrelated to the cause of the fever.

6. Mercury poisoning and its link to developmental disabilities and autism

One of the main misconceptions encouraging the myth of vaccinations and autism is the use of mercury-based adjuvants in some of the vaccinations. There is a robust body of evidence stating that significant amounts of neurotoxic substance uptake in the early stages of life can cause severe developmental disorders, including ASD.

Mercury has been well established as a neurotoxic factor, including its involvement in several malignancies as a result of organic mercury exposure (mostly methylmercury, MeHg) via dietary consumption (e.g., contaminated seafood, grains etc.), medical treatment (e.g., syphilis treatment or teething powder), occupational settings (e.g., chronic exposure to mercury vapors) or any other form of exposure to mercury pollution in the environment [49,50].

The toxic effects of mercury have been demonstrated many times throughout history. One of the most famous cases is the Minamata Disaster in Japan, where industrial mercury pollution was discarded in the Minamata bay thus creating a biomagnification of mercury in the consumed seafood in the bay, causing severe mercury poisoning to the area's population [51]. The toxic effects of mercury poisoning include numerous neurological alterations, such as ataxia, dysarthria, disequilibrium etc., and even mental disorders. The toxic effects of mercury are not limited to the nervous system and include other organs, such as the pancreas and kidneys, and can even result in mortality. Mercury was also identified as fetotoxic, causing disruption to the cerebral architecture in fetal brain development, leading to various neurological disorders in newborns exposed to mercury during pregnancy [52]. Fetuses are at higher risk of mercury toxicity due to the fact that organic mercury passes through and accumulates in the placenta [53].

Metal poisoning in very large doses, including mercury, can cause ASD as well as other severe neurodevelopmental disorders [54]. This link is hypothesized to be driven by metal-induced oxidative stress in the nervous system. In addition to the possible effects of mercury to cause ASD, several studies found enhanced mercury levels in ASD patients or their mothers [55], as high levels of mercury in subjects' blood, hair, teeth, and urine were positively associated with ASD [56]. There is a similarity between biological abnormalities in ASD patients and pathologies caused by mercury poisoning, as well as other neurodevelopmental disorders [49]. However, the main emphasis is on poisoning and not on negligible levels. Any substance influencing brain function may, when in excess, cause brain damage, such as lipid soluble vitamins (A, D, K, E) as well as vitamin B12 and folate [57].

6.1. The use of thimerosal in vaccines

Thimerosal is an organic mercury-containing (ethylmercury, EtHg), FDA-approved preservative used in vaccines to prevent bacterial and fungal contaminations. EtHg is involved in many similar toxic mechanisms as MeHg [58], however, it is broken down and eliminated from the body faster, thus presenting a more favorable safety profile in general and is specifically less neurotoxic than MeHg [59].

Due to public safety concerns led by anti-vaccination groups, and the concern of cumulative mercury exposure during the first 6 months of life, the use of thimerosal has been excluded from childhood vaccines in the US since 2001, as well as in the European Union and a few other countries [60,61]. According to the CDC, current thimerosal-containing vaccines include four quadrivalent influenza vaccines (Afluria, Flucelvax, Flulaval and Fluzone) and one tetanus and diphtheria vaccine (TDVAX) [62]. The minimum age of use for these approved thimerosal-containing vaccines is 7 years. Moreover, all of these vaccines have a non-thimerosal containing alternative [62]. The World Health Organization supports the continued use of thimerosal-containing vaccines in developing countries given that they are less expensive, are widely available, and are logistically suitable for these regions, while also being safe and effective [61].

As the link between ASD and organic mercury is-well established, concerns have arisen regarding the use of thimerosal-containing childhood vaccines and the cumulative EtHg exposure as a result. Numerous peer-reviewed studies and meta-analyses investigated the risk for ASD due to thimerosal exposure and found no increased risk of ASD associated with thimerosal-containing vaccines [13,62]. The link between thimerosal and other developmental disabilities (e.g., speech problems or learning difficulties) has also been evaluated and found to demonstrate no association between exposure to thimerosal in vaccines and these disabilities [13]. In contrast, longitudinal studies have found a correlation between higher thimerosal exposure from vaccines and ASD diagnosis [63,64].

Despite research that found no risk for ASD from thimerosal, the exposure to thimerosal in childhood vaccines has been limited worldwide due to the concerns of these effects. Nevertheless, this concern continues to feed the myth, and common words used in anti-vaccine campaigns still include mercury/thimerosal and ASD [65,66], including the current COVID-19 vaccine which does not contain thimerosal.

7. Measles, mumps, and rubella vaccination and autism

The concerns surrounding the MMR vaccine and its posited link to autism have stemmed from a now-disproven publication that falsely claimed there to be a connection between autism and the MMR vaccine [37]. This study's profound impact on subsequent vaccine hesitancy has warranted widespread research into the matter in order to address the concerns regarding its safety. Over the past few decades, many studies have repeatedly disproven the claims associating MMR vaccination with increased incidence of autism. Nevertheless, this ominous and subsequently rejected publication from 1999 in Lancet journal, continues to weaken the acceptance of all accumulating medical evidence for the last 22 years. For this reason, we would like to refrain from mentioning the author, but a note-worthy fact is that this publication still appears as the first mention among 38,200 publications on Google Scholar when searching for the combination “vaccination and autism”.

The evidence against this link was examined thoroughly in many studies. The following is a short list of some of the many reputable studies that have declined any risk of MMR vaccination causing autism:

- **Measles, Mumps, Rubella Vaccination and Autism: A Nationwide Cohort Study**: A nationwide cohort study in Denmark that analyzed population registries in order to link information on MMR vaccinations, other childhood vaccinations, autism risk factors, and autism diagnoses. Their study, which included 5,025,754 person-years of follow-up, supported that MMR vaccination does not increase the risk for autism, nor does it provoke autism in susceptible individuals. It also found that there is no associated clustering of ASD cases after MMR vaccination [67].

- **A population-based study of measles, mumps, and rubella vaccination and autism**: A retrospective cohort study that assessed MMR vaccination status and psychiatric diagnoses among 537,303 children born in Denmark between 1991 and 1998. The study provides evidence against a causal relation between MMR vaccination and autism. Their data demonstrated a similar risk of autism in vaccinated versus unvaccinated children, a lack of temporal clustering of autism cases after immunization, and that neither autistic disorder nor ASD were linked to MMR vaccination [68].
- **The combined measles, mumps, and rubella vaccines and the total number of vaccines are not associated with development of autism spectrum disorder: the first case-control study in Asia**: a case-control study that looked at MMR vaccination history, including number of vaccine injections, and compared data between patients with and without ASD in a genetically homogenous population. The data showed that neither MMR vaccination nor increasing number of vaccine injections is associated with an increased risk of ASD [69].
- **Autism and measles, mumps, and rubella vaccine: no epidemiological evidence for a causal association**: a population-based study in the UK that looked at the incidence of autism before and after the introduction of MMR vaccination. Their analyses showed no causal association between MMR vaccination and autism and no indication of temporal clustering between MMR vaccination and autism diagnoses (B [70].
- **Lack of association between measles virus vaccine and autism with enteropathy: a case-control study**: a case-control study that assessed whether children with GI disturbances and autism were more likely than children with GI disturbances alone to have measles virus RNA and/or bowel inflammation, and if the onset of autism and/or GI episode related temporally to receipt of MMR vaccination. The data provided evidence against an association between autism and persistent measles virus RNA in the GI tract or history of MMR vaccination [71].
- **Early exposure to the combined measles-mumps-rubella vaccine and thimerosal-containing vaccines and risk of autism spectrum disorder**: a case-control study that examined 413 vaccination histories of patients with and without ASD to determine whether MMR vaccination and thimerosal dosage are related to ASD. The study found no significant differences in MMR vaccination and thimerosal dosage between cases and controls [72].

In addition to the many individual studies showing no correlation between MMR vaccination and ASD, a 2014 meta-analysis further reinforced the lack of connection between the two (L. E [18]. The CDC provides online resources explaining the recommendation for the MMR vaccine. In the article titled "Understanding MMR Vaccine Safety", the CDC provides answers to several questions regarding the safety and necessity of the MMR vaccine. While there is abundant proof that there is no relationship between the MMR vaccine and autism, vaccine hesitancy among parents is still prevalent and poses a serious public health risk.

8. Vaccine safety

The hesitancy surrounding vaccine safety has highlighted the need for reliable information to be made available to the public. The CDC has made extensive efforts to provide reputable resources that reassure the public about the safety and efficacy of vaccinations. On their website, they encourage people to participate in reporting any possible adverse events associated with receiving vaccinations. The reporting systems they have in place include the Vaccine Adverse Event Reporting System (VAERS) and the Vaccine Safety Datalink (VSD). Additionally, the CDC established the Clinical Immunization Safety Assessment (CISA) Project that connects healthcare providers with vaccine safety experts regarding issues pertaining to individual patients or issues that are not already addressed by the CDC.

9. Conspiracy theories and solutions

"Conspiracy theories" are attempts to explain the ultimate causes of significant social and political events and circumstances with claims of secret plots by two or more powerful actors [73–75]. While often thought of as addressing governments, conspiracy theories could accuse any group perceived as powerful and malevolent. Conspiracy theories appear to provide broad, internally consistent explanations that allow people to preserve beliefs in the face of uncertainty and contradiction. Consistent with this analysis, research suggests that belief in conspiracy theories is stronger under conditions of uncertainty [76]. Franks and Colleagues [77] note that conspiracy theories have been communicated as devices to cope with collective trauma. Consistent with this reasoning, studies have demonstrated that conspiracy beliefs are associated with feelings of powerlessness [78–80]. Autism is a disorder perceived as mysterious and unpreventable, parents are feeling powerless and doubt the ability of medical professionals to provide help and healing.

The origin of the conspiracy beliefs about vaccines and autism stems from the 1998 Lancet paper previously mentioned [81]. One of the leaders in disproving the vaccine/autism link states that the main conspiracy theory fueling vaccine hesitancy centers around scientific data being faked and harmful side-effects of vaccines being hidden from the public to ensure that pharmaceutical companies and governments are able to profit [82,83]. The conspiracy theory concerning the government hiding information may play the biggest role in antivaccine sentiment. Blaming large pharmaceutical companies as the culprit is also an easy target since they are often imagined as withholding a cure by individuals who are left feeling powerless when they are diagnosed with serious illnesses [84].

Belief in conspiracy theories has been fueling vaccine hesitancy. Even though there has been no published studies that significantly illustrate a relation between vaccines and autism, vaccine hesitancy continues as the conspiracy is rooted in individuals not trusting the scientific information that is being released. By fueling conspiracy theories, the feeling of fear increases, leading to ultimately detrimental effects on public health. Vulnerable populations with less resources are at risk to contagious diseases as well as those with weakened immune systems [85]. Investing energy in trying to decrease antivaccine sentiment should parallel uncovering the actual etiologies of autism.

Conspiracy theories are reinforced by the very basis of Internet search engines. There are "discussion groups" on any topic and user communities. Searching for information will inevitably lead to any source of information, regardless of its validity. Opponents of vaccines build sites, discussion groups, etc., so that a "reasonable person" who writes the phrase "vaccines, autism, against" this will inevitably reach sites that deal extensively with the subject, and that may seem scientific and authoritative the general public and may create a false representation of the topic. Communication styles within the media [86–88] revealed that vaccination and antivaccination comments use different kinds of language in their communication of information [89]. In addition, the vaccine-skeptical sites were highly interactive, with spaces for community discussion, and oriented towards the creation of people that believe to be affected by vaccination. In contrast authoritative pro-vaccination sites offer limited interactivity and focus on evidence-

based knowledge and perceived as aloof and dictatorial [82,90,91].

Political views [92] or words from celebrities sent on social media can then lead to the spread of misinformation and propagation of beliefs about vaccines causing autism [93].

The perceived unexplained rise in autism incidence and the mystery surrounding the causes of autism continues to feed the myth linking autism to immunizations schedule. A study in Italy that investigated vaccine beliefs in Italian mothers concluded that "When trying to make sense of the unpredictable nature of ASD, parents blamed vaccines and their toxic components to try and rationalize the mysterious cause of autism in their child" [94]. This study shows that belief in the theory that vaccines cause autism can be a way for concerned, confused parents to bring more clarity into their situation, reducing their overall anxiety with the disease.

Rachel Casiday, a medical anthropologist who studied British parents' attitudes toward MMR says that scientists should work on making dry scientific facts more compelling and centered around a story [85] and that vaccine information should also be presented in an emotional context. For example, compelling stories that we are aware of as clinicians, but have not been researched systematically, involve the personal stories of families who refrained to immunize their following children after their first child was diagnosed with ASD. Later on the additional siblings of those families who were not vaccinated were still diagnosed with ASD, thus refuting the family's belief in vaccinations as a cause for autism and supporting a more genetic etiology. Most families refrain from expressing their change in opinion and decline participating in research.

9.1. Solutions to conspiracy theory misinformation

- Presenting anti-conspiracy arguments before the conspiracy theory-presenting anti vaccine arguments rooted in facts can help those who do not want to vaccinate shift their beliefs, but in order to shift population behavior the scientific arguments should be presented *before* the individuals have been exposed to the conspiracy theory [95]. In regard to those who have been already exposed to conspiracy theories, stronger measures can be taken such as excluding non-vaccinated children from the educational system. Another option which has recently passed in the U.S. state of Oregon requires parents or guardians to watch an education video before they are allowed a vaccination exemption [95].
- In the realm of mass information we are in today, it is crucial that information hygiene is embraced as a society, where individuals deem all information as pathogenic before they accept or propagate it [96]. Social media has shown a clear impact on the public's understanding of science and medicine, as well as the spread of conspiracy theories so it is important to address the misinformation that is surfacing. In order to best appeal to the inflexible minds of victims to conspiracy theorists, communicating messages in an emotional context that is both warm and inclusive of all opinions may serve as the best option for instilling true change in their misguided beliefs. Social media's role in the propagation of misinformation has been significant, so it is important to find ways to influence the media to portray a more accurate picture about the nature of vaccines.

10. Summary

In spite of vast evidence of vaccine safety and its lack of connection to autism, this myth is still influencing parents to children with autism and general public and increases vaccination refusal rates. A lot of the distrust in vaccinations is rooted in the forceful nature it is put on individuals, without an explanation that is fully understandable to the general public in regards to the reasons of autism. With more evidence of genetic and epigenetic etiologies along with earlier diagnosis of autism the mystery surrounding autism symptomatology should be unveiled.

Medical information about vaccine safety should be provided in an effective manner, with special attention paid not only to the content of the information but also to how it is presented, with a focus on providing a welcoming environment for open discussion about the benefits and risks.

This psychological response to diagnosis should guide us into a cautious and empathetic approach when explaining the genetics of autism. This explanation may pose additional burden on the parents, although most mutations related to ASD are de-novo and not inherited [31]. It may be easier for the parents to blame an environmental external factor such as vaccinations, thus this sentiment poses significant health concerns to vulnerable populations. The COVID-19 pandemic, however, clearly exemplified that the diseases that immunizations prevent are far more severe than the vaccinations themselves. It is plausible that with more evidence-based studies linking autism to specific etiologies the myth will diminish and disappear eventually.

Declaration of competing interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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