



# Smell of autism: synthetic fragrances and cause for allergies, asthma, cancer and autism

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## Abstract

### Introduction

The widely believed notion that autism is genetically conveyed to the next generation has been seriously disputed. The recent sequencing of the exomes of autistic children and each of their biological parents, as part of recent trio investigations, cast serious doubt on this paradigm. Rather, environmental causation seems to have greater explanatory power. The link between autism spectrum disorder and exposure to toxic ingredients in perfumes, even at minute (femtomolar) levels, has been suggested by recent scholarship. Scents are known to have the capacity to reach the brain, including the brain of a foetus whose mother uses perfume that derives from synthetic scents made from mutagenic chemicals. The aim of this review was to discuss synthetic fragrances and cause for allergies, asthma, cancer and autism.

### Conclusion

The potential role of fragrances and particularly perfumes, which are mainly synthetic chemicals from petrochemicals and contain benzene ring compounds, needs investigations. These chemicals are highly mutagenic and cause foetal brain cell death at extremely low concentrations.

### Introduction

For hundreds of thousands of years humankind has adored fragrances

from flowers, fruits and living organisms. This co-evolution of civilization and fragrances has created a balance between humans and their environment, which means natural chemicals do not harm humans. This adoration of pleasant scents developed into an art form as humans devised methods to capture perfumes and store them in bottles so that they could smell their captured odours year around. The world's age-old fascination with fragrance has resulted in capacity to capture and preserve scents that promote pleasant, beautiful and positive sensory perceptions. At least that is what the term *fragrance* has come to connote. In the mid-1900s, several counter-evolutionary events emerged. Chemists began to synthesize perfumes and fragrances by utilizing benzene-ring-based petrochemicals. Tragically, benzene is a known mutagen and carcinogen, or cancer-causing agent<sup>1-2</sup>. Initially, perfumes were combinations of natural oils and synthetic compounds created in a laboratory. Gradually, most natural fragrances were replaced by their synthetic imitations; thus, perfume production has become most dependent on the scientific laboratory, where outcomes are certain, than on the natural world, where outcomes are not certain. These fragrances have now become part of our lives so much that they are now an essential part of our everyday lives, forming a part of household items where they are not needed, including soaps, detergents, car and house fresheners, hair products, candles, cosmetics, food flavours and so on. Since synthetic perfumes are unnatural and do not have the beneficial effects of natural

fragrances at the molecular level, their use has a deleterious effect on human immune systems causing many allergic reactions, such as sneezing and watery eyes, which constrict both bronchial tubes and pocketbooks. Profits reaped by corporates that manufacture synthetic perfumes come with a heavy price, higher prevalence of asthma and respiratory illnesses. Ironically, talented marketing professionals have led modern consumers by the nose to such an extent that fragrances have become an environmental hazard to a large segment of the population and have become a menace to children in particular.

This review summarizes some of the subjective concerns and attempts to date that have brought greater objective scrutiny to the debate over the safety of components used in the imprecise objects called fragrances<sup>2</sup>. A major challenge surrounding the use of such terms as *fragrance* or *perfume* is the elusive imprecision that cloaks them in what can be dangerous evasions of transparent labelling. It may make good marketing sense, and of course dollars, to describe how chemicals will impart a tropical rain forest smell to a teen's hair or a fresh smell to a baby skin, but there must be understandable substance to product descriptions in addition to clever phrases. A product that invokes the imagery of tropical rain forests should contribute positively to human lungs, eyes and skin rather than unleashing products that cause asthma, allergies, eczema or cause autism in the unborn foetus when an expecting mother is inhaling some of the most toxic chemicals found in fragrances<sup>1-2</sup>. Surely the term *fresh* should not mask carcinogens and

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foetal-brain-altering chemicals that threaten unborn, infants or humans of any age.

### Discussion

The authors have referenced some of their own studies in this review. The protocols of these studies have been approved by the relevant ethics committees related to the institutions in which they were performed.

The widely believed notion that autism is genetically conveyed to the next generation has been seriously disputed<sup>3-7</sup>. And the recent sequencing of exomes of autistic children and their biological parents, as part of recent trio investigations, cast serious doubt on this paradigm<sup>8</sup>. Rather, environmental causation seems to have greater explanatory power<sup>9-11</sup>. The link between autism spectrum disorder (ASD) and exposure to toxic ingredients in perfumes, even at minute (femtomolar) levels, has been suggested by recent scholarship<sup>1,2,4,11</sup>. Scents are known to have the capacity to reach the brain, including the brain of a foetus whose mother uses perfume that derives from synthetic scents made from mutagenic chemicals<sup>4,9,11</sup>.

*Fragrance* is a seemingly innocuous term added to health and beauty products. Ultimately, this mysterious term may actually undermine both health and beauty. Fragrance is a common euphemism for an undisclosed blend of chemical ingredients drawn from an arsenal comprised of about 3,100 total ingredients. 'Musky' may increase sales, 'exotic' may attract customers and 'floral' may sound beautifully natural, but these terms may also conceal the existence of petrochemicals and other synthetic chemicals that, when blended with natural ingredients, can form dangerous cocktails of fragrance<sup>1,2,11</sup>. In a careful recent study of 17 name-brand products, 38 different chemicals were unidentified. Dolce and Gabbana Light Blue hid the fewest number of fragrance ingredients from the public ( $n = 7$ ), whereas American Eagle Seventy

Seven concealed over three times that amount<sup>12</sup> and outdid all 16 other name-brand products. Chanel Coco came in second with 18 hidden ingredients. Among the other culpable popular fragrances were Britney Spears Curious<sup>13</sup>, Quicksilver<sup>14</sup> and Abercrombie & Fitch Fierce<sup>11</sup>. One might wish for fewer, if any, secrets in the 13 hidden fragrance chemicals in Victoria's Secret Dream Angels Wish. Calvin Klein's Eternity for Men<sup>15-16</sup> has one more covert chemical than its for-women brand, Calvin Klein Eternity, which veils 14 chemicals to produce its enticing fragrance<sup>16</sup>. So what are some of these chemicals that are found in the majority of these fragrances? These include limonene, alpha-pinene, diethyl phthalate, butylated hydroxytoluene, musk ketone, benzyl benzoate, benzophenone, octinoxate and so on. Many are known mutagens, carcinogens and may cause alterations in human foetal brain development<sup>1,2,4</sup> (also unpublished data from Bagasra lab). One of the saddest situations is that after the publication of Silent Spring in 1962 and establishment of EPA and hundreds of environmentalist activist groups against DDT and many other insecticides and chemicals, the fragrance industry realized that they need to find a way to limit any lawsuits resulting from adverse effects of fragrances. Therefore, in 1973 the US lawmakers passed The Federal Fair Packaging and Labelling Act<sup>14</sup>, exempting fragrance makers from declaring the list of ingredients that form part of fragrances created. Therefore, fragrance concealment is not illegal and is often used by the industry to hide from the public the full list of ingredients, including substances that can cause grave health problems, including breast cancer and autism<sup>2,17-20</sup>. We have recently provided evidence, obtained from Ames test analysis of foetal brain cell lines, that exposure to femtomolar concentrations of various perfumes leads to mutagenesis and neuromodulations in human foetal brain cells<sup>21</sup>.

The NPD Group reported that annual global perfume industry sales revenue has reached US\$27.5 billion in 2011, and it is most likely an underestimation.

In response to public concern over the impact of chemicals on cancer levels, the President's Cancer Panel issued in 2010 a report on the risks of cancer from chemicals. Their main conclusion was troubling: there is a positive correlation between environmental chemicals and cancer rates. Given that many chemicals are known or suspected carcinogens, it should come as little surprise that such is the case. Of particular note in the 2010 publication was the assertion that the number of cancer cases that were environmentally prompted had been vastly underestimated. Benzene, commonly an ingredient in synthetic fragrance products, was of particular concern.

In spite of concerns over the safety of fragrances for humans, their use is on the rise, not declining. We hypothesize that one of the major reasons for the alarming rise in autism and autism spectrum disorder is the rise in use of fragrances<sup>2</sup>. It should be noted that autism used to be a relatively rare diseases at the turn of the 20th century<sup>2-6,22-24</sup>, but it has now been found that 1 out of 88 children is suffering from ASD; again, this may be an underestimate. Since a neonate's brain is still developing after birth, we should expect a rise in other neurological but related conditions (e.g. attention deficit hyperactive disorder [ADHD], regressive autism; for example, a child is born normal but begins to show signs of autism after 18 months or later)<sup>21-24</sup>. ASD is a developmental condition characterized by deficits in social interaction, verbal and nonverbal communication and obsessive/stereotyped patterns of behaviour. In addition, there is evidence of impoverished language and empathy and a profound inability to adopt another's viewpoint—a failure to construct a 'theory of mind' for interpreting another person's

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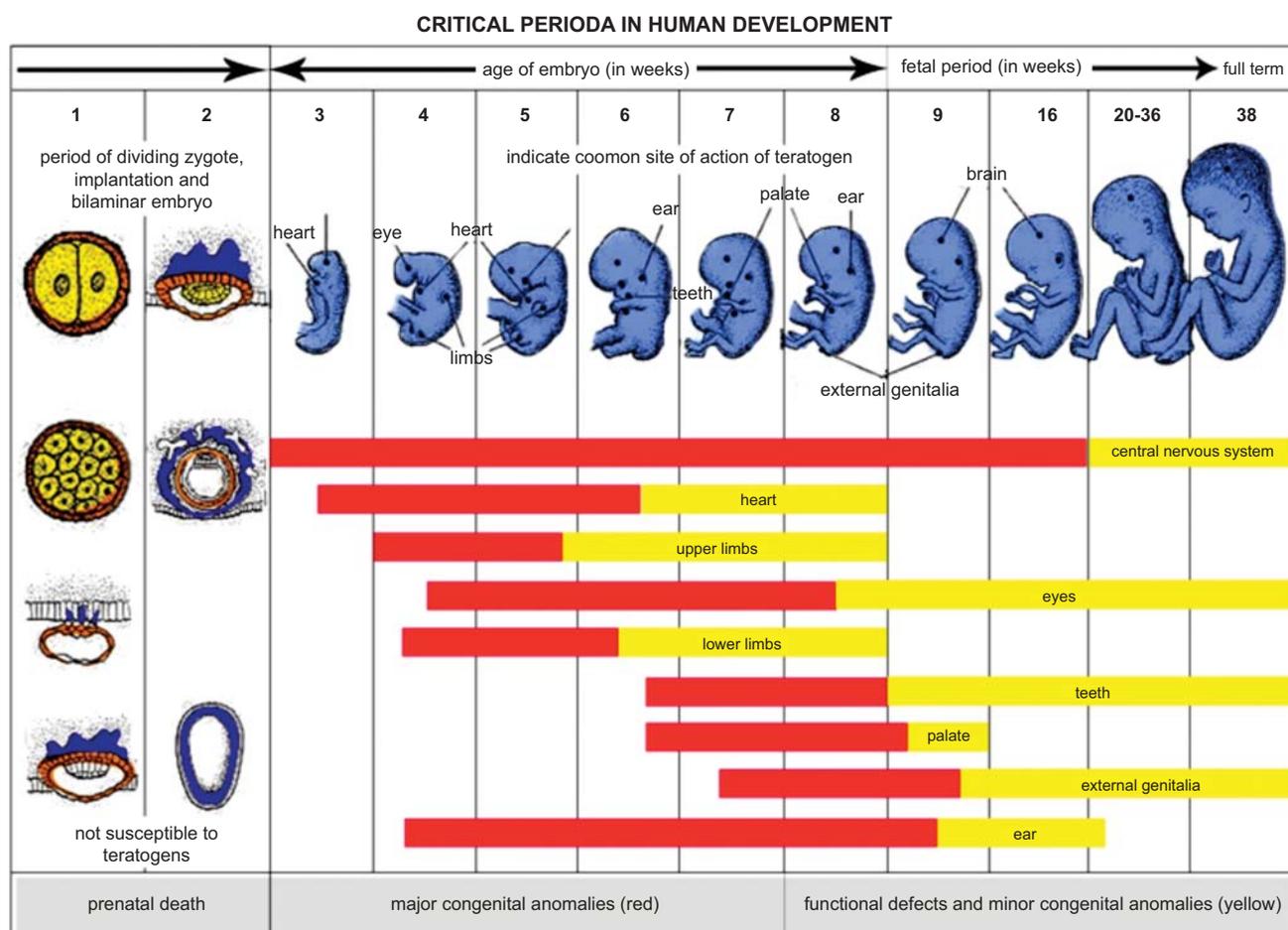
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thoughts and intentions<sup>3-4</sup>. Although there is no reliable neurophysiological marker associated with ASDs, dysfunction of olfactory bulb (OB) and mirror neuron system (MNS) has been documented<sup>3-4,24</sup>. The bars shown in Figure 1 indicate periods when organs are most sensitive to damage from teratogenic agents. It is noteworthy that most of the research literature does not mention development of olfactory system. The brain starts developing 18 days after fertilization, and many times mothers who become pregnant do not know they are pregnant until after a few weeks have passed. Therefore, mothers who

are exposed to certain synthetic fragrances, either through inhalation and epidermal exposure, and food-flavour chemicals, through ingestion (e.g. teas, chewing gum and other food flavours), may put their embryo at risk without even knowing it (Figure 1).

It may seem counterintuitive, but humans do not always make rational choices. Even though they are almost always well-informed to make logical decisions, they do not always do so. Fragrances are significant in producing not only perfumes but also detergents, foods, drugs, hygienic items, household products, solvents and industrial greases.

Public policy responses show sufficient sensitivity towards problems posed by fragrances, but only in limited instances. Some hospitals and government offices have limited the use of scents in their premises. Those wearing fragrances are not allowed to enter into the Tuttle, Oklahoma City hall. Portland city, Oregon, has requested that custodians utilize cleaning products that are unscented and prohibits city employees from wearing fragrances<sup>21</sup>. Consistent with its policy for other employees, resident physicians in South Carolina's Palmetto Health System have been instructed that fragrances, including



**Figure 1:** The bars indicate periods when organs are most susceptible to damage from teratogenic agent. It is noteworthy that research literature does not mention much about the development of olfactory system. The brain starts developing 18 days after fertilization and many times mothers who become pregnant do not know they are pregnant until after a few weeks have passed. Therefore, mothers who are exposed to certain synthetic fragrances, either through inhalation and epidermal exposure, and food-flavour chemicals, through ingestion (e.g. teas, chewing gum and other food flavours) may put their embryo at risk without even knowing it.

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but not limited to colognes, after shaves and perfumes, are not to be worn during work time. The policy has a well-founded rationale: fragrances are a potential cause of allergic reactions in coworkers and patients<sup>25</sup>. Such a trend in public policy is understandable, especially since it has been found that a number of ingredients in fragrances have either been inadequately analysed or regulated.

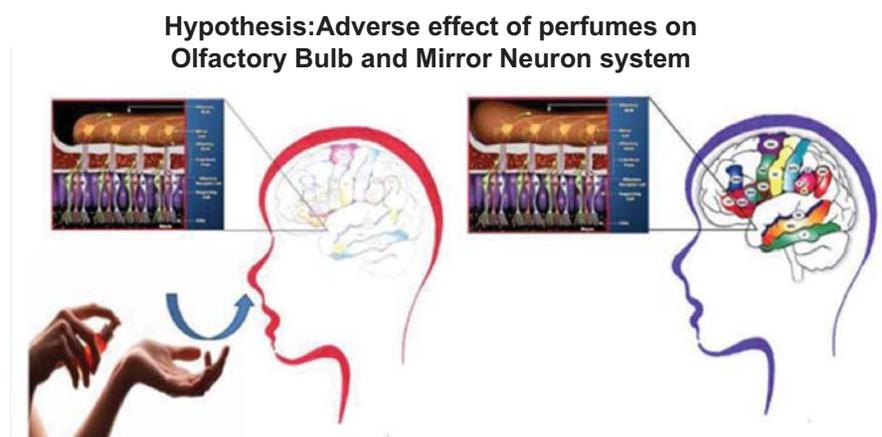
These are not new concerns, but analysis and regulation seem to have not kept pace with aggressive marketing and sales pitches carried out to promote synthetic scents in the marketplace. In 1986 the National Academy of Sciences had identified the category 'fragrances' as one of the six areas that should receive high priority in the field of neurotoxicity testing. The remaining categories were solvents, selected air pollutants, heavy metals, insecticides, food additives and solvents. It is definitely a matter of concern that synthetic petroleum-based compounds accounted for as much as 95% of the chemicals from which fragrances derive their desirable scents. If a product is advertised directly and openly, revealing the potential harms associated with a perfumed product, sales would likely plummet, particularly if it were reported to consist of carcinogens known to cause birth defects and autism, trigger allergic responses, and harm the central nervous system. What would happen to sales if labels were to openly mention the presence of carcinogenic ingredients such as aldehydes, dioxine, chloromethane, butanone, pinene, limonene, linalool, benzene derivatives and other toxins, alerting the public about the dangers these fragrance ingredients can cause?

Concerns about neurotoxicity have been raised over the inclusion of ingredients such as zinc pyridinethione, isobutanol, 1-butanol, 2-butanol, tert-butanol, acetyl-ethyl-tetramethyl-tetralin, t-butyl toluene, hexachlorophene and 2,4-dinitro-3-

methyl-6-tert-butylanisole. Testicular atrophy has been observed in lab tests with animals, as has been neurotoxicity (myelin disease). Nerve damage is an obvious threat when the myelin sheath, which shields nerves from damage, is damaged (Figure 2). Time does not bring the regeneration one might hope for because the myelin sheath is not capable of regeneration. The logic behind US Environmental Protection Agency (EPA) codes is to protect the population from hazardous practices and substances, including ethanol, methyl isobutyl ketone, methyl ethyl ketone, benzal benzoate, butylated hydroxytoluene and methylene chloride<sup>26</sup>. Each of these hazardous substances, according to code, is to be disposed of according to prescribed hazardous waste disposal guidelines. EPA code regulations are put in place primarily to protect people. Ironically, each of these toxic substances has been found in fragrances<sup>26</sup>. Throughout US history, time and time again governments have stepped into regulate industry practices in public interest. Self-regulation by businesses themselves has made its contributions, but the potential for self-interested self-regulation and for unethical collusion are very real in a capitalistic society. Yet greater federal regulation

of fragrances seems in order. One National Institute of Occupational Safety and Health report stated that from a partial list of 2,983 fragrance chemicals, some 884 were identified as toxic. If such toxins were smeared on a person's skin involuntarily, a lawsuit may be brought; ironically, individuals seeking to wear the scents of success and popularity inadvertently may be damaging their or others' central nervous system, especially an unborn foetus who has even inhaled a single breath of air get can get affected by these toxins that will never allow him/her to be protected against 'these wonderful fragrances' that kill olfactory neurons. As a result of this exposure to hazardous fragrances, a child would never know the smell of them in his/her entire life, since the exposure had killed his/her neurons that would have developed into smell-recognizing senses<sup>3-4</sup> (Figure 2).

Awareness of the potential negative side effects of perfumes is growing. In January 2013, a team from the Department of Cardiology at Kasturba Hospital (Manipal, Karnataka, India) reported an unusual situation; a hospitalized dental patient suffered from a totally unexpected case of cardiac arrest, and succumbed on the ninth day of hospitalization due



**Figure 2:** The illustration demonstrates the hypothesis that exposure to perfumes capable of modulating olfactory bulb development could cause autism spectrum disorder (ASD), which results in damaged or underdeveloped neuronal pathways.

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to sepsis. They concluded that some poison, perhaps from a hand sanitizer, had triggered the peculiar anaphylactic reactions. Suspecting the role of potential toxins in this case, doctors found that a commonly used hand sanitizer had perfume added to Isopropyl alcohol and glycerine<sup>27</sup>. In a study of 256 Turkish university students regarding barriers to sleep, as much as 53.1% mentioned 'room scents (sweat, perfume, humidity, naphthalene, etc.)'<sup>28</sup>.

Advertisers have been creative in their use of advertisement strips scented with cologne or perfume. They have paid greater attention to profits than to the adverse effects such strips might have on persons allergic to their products, including asthma patients; for example, can the inhalation of perfume embedded in magazine scent strips exacerbate asthma? A research team headed by P. Kumar found the answer to be yes. Following perfume challenges, one in five (20.7%) of the asthmatic patients they tested experienced wheezing and tightness in the chest. Asthmatic exacerbations of some sort were experienced by 36% of patients suffering from severe asthma, with declining yet still troubling rates for those with moderate asthma (17%) and mild asthma (8%). Scented strips can obstruct airways, particularly in those who are already asthmatic. We maintain that fragrances should be studied for their potential effects on the molecular pathogenesis of ASD<sup>3-4</sup>.

### Conclusion

There are numerous hypotheses and thousands of articles published in peer-reviewed journals, defining the illnesses associated with and potential causes of ASD. However, numerous investigations into the genetic basis of ASD have only limited definitive associations. We hypothesized that a better understanding of the interplay between genes and environment should speed up the progress in the field of ASD. In particular, the

development of OB and MNS, which are generally found to be underdeveloped in the brain of autistic children, can be investigated in the context of foetal development. Of note, the whole maternal-foetal unit is a highly integrated metabolic, endocrine, neuropeptides and neurodevelopment co-system and is influenced by environmental factors. Therefore, the foetal brain development must be explored in light of brain-modulating factors to which the pregnant mothers are exposed during their pregnancies, and this may provide us clues to the aetiology of ASD. This article brings forth a new way of looking at the pathogenesis of ASD and the role of fragrances, which are found in every part of the modern society and may be an important contributing factor in ASD. These chemicals may be harmful to the developing foetal brains and to adults (e.g. it may be a risk factor for Alzheimer's and Parkinson's diseases). Most of the fragrances have a benzene ring as a base and are petrochemical in nature, which may be a cause of cancers, severe asthma, obesity and other neurological illnesses; the occurrence of these ailments can increase corresponding to an increase in the usage of synthetic fragrances. Our hypothesis combined mutagenic and neurodevelopmental aspects of perfumes, and it proposed to determine the mechanisms by which environmental factors such as perfumes and other fragrances can modulate the neurodevelopmental pathways, taking into account the role of hormones and neuropeptides that may cause male gender bias.

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