Nanoparticles damage brain cells.

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Wang J, Y Liu, F Jiao, F Lao, W Li, Y Gu, Y Li, C Ge, G Zhou, B Li , Y Zhao, Z Chai and C Chen. 2008. **Time-dependent translocation and potential impairment of central nervous system by intranasally instilled TiO2 nanoparticles**.
Synopsis by Abby D. Benninghoff, Ph.D. and Wendy Hessler

Scientists have shown for the first time that very small particles of titanium dioxide (TiO2) can travel from the nose to the brain and cause damage to brain cells in laboratory mice. TiO2 is a white pigment widely used in paints, coatings, plastics, cosmetics, sunscreens and other personal care products. These results suggest that short-term exposure to nano-sized TiO2 via breathing could lead to brain injuries.

Context

Nanomaterials are very small particles that are about 1 to 100 nanometers in size. For perspective, a human hair is about 80 micrometers in width. Nano-sized particles are about 1,000 times smaller, or about 1 to 100 nanometers. At this small size, these materials can interact with atomic or molecular structures. Naturally-occurring nanomaterials include sea salt, soil dust and volcanic dust. Others are synthetic, produced as an industrial byproduct (soot from burning fossil fuels and industrial dusts) or engineered with specific, desired properties useful in manufacturing and other applications (carbon black, metal oxides, quantum dots). Very small nano-sized particles may have different physical and chemical properties than in their larger bulk forms. These differences are being exploited by chemical and physical engineers. Nanomaterials are anticipated to yield numerous advances in many fields, espcecially medicine and health care through targeted drug delivery, new cancer therapies and early disease detection. However, their special properties may also have undesirable effects.

Metal oxide nanomaterials are widely used in industry for their valuable mangnetic, electric and optical properties. TiO2 is a highly used white pigment added to paints, coatings, plastics, inks, foods, medicines, toothpaste, cosmetics, sunscreens and other personal care products. Workers may be exposed to nano-sized TiO2 particles (termed “ultrafine” by industry) during processing or applying TiO2 to manufactured goods. Consumers are exposed when using the products. The International Agency for Research on Cancer has classified TiO2 as a possible human carcinogen based upon evidence from laboratory studies in animals (IARC 2006). Breathing the nano-sized TiO2 particles significantly increased risk of lung cancer. There is also evidence from laboratory animal studies that inhaled TiO2 can deposit on lungs and cause inflammation (Oberdörster 2000; Orsier and Oberdörster 1997).

Because of their small size and chemical properties, nanoparticles can traverse the protective membrane barrier surrounding cells. It is important to note that some cells, especially nerve cells, extend long distances in the body. For example, the olfactory nerve extends from the nose into an area of the brain that deciphers smell, called the olfactory bulb. Particles inside cells, then, could reach other parts of the body and the brain, such as the hippocampus and cortex.

What did they do?

Laboratory mice breathed in nano-sized TiO2 particles to determine if the material could reach the brain, how long the journey would take and if it would damage brain tissue. The mice inhaled a preparation of 500 micrograms of TiO2 particles suspended in water every other day for 30 days. This dosing method is analogous to taking a nasal spray medicine. The researchers at the nanomaterials laboratory in Beijing, China, tested two different sizes of TiO2: nano-sized (80 nanometers) and slightly larger particles (155 nanometers).

Mice brains were examined on days 2, 10, 20 and 30 to determine how quickly the particles might travel to the brain. The content of TiO2 in specific regions of the brain was determined using mass spectrometry, an instrument that used molecular weight to measure amounts. Also, the scientists looked at the brains cells in the exposed animals using transmission electron microscopy. Finally, to determine if TiO2 exposure caused chemical changes in the brain, the authors measured levels of certain molecules called cytokines that indicate increased inflammation and cell stress.

What did they find?

After two days and only one inhalation exposure, significant amounts of both sizes of TiO2 were found in the brain, especially in the olfactory bulb. The amount of TiO2 in brain tissues increased with continued exposure, and the maximum levels were observed after 30 days (15 individual inhalations).

After 10 days of exposure, TiO2 was also detected in other areas of the brain, including the cerebral cortex, cerebellum and hippocampus. The greatest accumulation of nano-sized TiO2 occurred in the hippocampus at 30 days where the concentration reached about 280 nanograms of TiO2 per gram of brain tissue. Researchers observed significant changes in the cells of the olfactory bulb and hipoccampus regions of the brain in the TiO2-exposed mice (but not the cerebral cortex or cerebellum). In the olfactory bulb, there were more neuron cells than normal, while cells in the hippocampus appeared to be damaged and degenerating. Finally, levels of certain biomarker molecules indicative of inflammation and cell stress were higher in the brains of TiO2-exposed mice.

What does it mean?

The findings of this study are significant for three key reasons. First, it showed conclusively that inhaled TiO2 can travel from the nose to the brain. Normally, the brain is protected from toxins by the blood-brain barrier. But in the case of breathing exposures, the nanoparticles may evade this protection by traveling along the olfactory nerve from the nose to the brain. This “backdoor” pathway circumvents the brain’s natural shield that blocks unwanted chemicals from reaching sensitive brain cells. Second, this study provides evidence that inhaling TiO2 particles can damage brain cells. According to the authors, “these results imply that the function of neurons in the hippocampus would be greatly injured” from the TiO2 exposure. The hippocampus is the critical center of the brain responsible for short-term memory and spatial navigation. However, further studies are necessary to test whether breathing the nano-sized TiO2 particles impacts brain function.

Third, TiO2's effects were observed at a relatively low exposure dose and within a short period of time. The nano-sized TiO2 particles showed up in the brain within two days following one dose of 500 micrograms, which is about the size of a grain of salt. The quick transfer into the brain raises serious safety concerns for workers who may be exposed to ultrafine TiO2 during its manufacture or application to numerous industrial and commercial products.

TiO2 nanomaterials are in some cosmetics and personal care products, although it is not known what human inhalation exposure may result from the application and use of these items (such as facial powders that may be dusty).

Comments from Alan Muller, NAB Environmental Consultant August 4, 2009

TiO2 is found in incinerator ash and coal ash. Historically it's been considered harmless enough to be used in food. In 2006 it was classified by the International Agency for Research on Cancer (IARC) as an IARC Group 2B carcinogen " possibly carcinogenic to humans".

In my opinion, though, the key point here is that if TiO2 can go directly from the nose to the brain via the nervous system, presumably very small particles of other air pollutants can also do this. For example, it has been shown that Uranium travels nerves from nose to brain. So do manganese, nickel, and thallium.

These particles fall into the category of "nanoparticles" or ultrafine particles" that are not measured or regulated effectively and not well controlled by air pollution control equipment. We should therefore, require that this nose-to-brain transport of airborne pollutants be fully considered in any "environmental assessment" of incinerators or other air polluters.