Press release

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For the first time, investigating the heart as a whole:

Artificial nanoparticles influence the heart rate

Artificial nanoparticles are becoming increasingly pervasive in modern life. However, their influence on our health and the mechanisms by which they affect the human body remain largely shrouded in mystery. Using a so-called Langendorff heart, a team of scientist from the Technische Universitaet Muenchen (TUM) and the Helmholtz Zentrum Muenchen has now for the first time shown that selected artificial nanoparticles have a direct effect on heart rate and heart rhythm. The scientists are presenting their results in the journal ACSNano.

In light of the increasing demand for artificial nanoparticles in medicine and industry, it is important for manufacturers to understand just how these particles influence bodily functions and which mechanisms are at play – questions to which there has been a dearth of knowledge. Studies on heart patients have shown for decades that particulate matter has a negative effect on the cardiovascular system. Yet, it remained unclear whether the nanoparticles do their damage directly or indirectly, for example through metabolic processes or inflammatory reactions. The reactions of the body are simply too complex.

Using a so-called Langendorff heart – an isolated rodent heart flushed with a nutrient solution in place of blood – scientists from the Helmholtz Zentrum Muenchen and the TU Muenchen were for the first time able to show that nanoparticles have a clearly measurable effect on the heart. When exposed to a series of commonly used artificial nanoparticles, the heart reacted to certain types of particles with an increased heart rate, cardiac arrhythmia and modified ECG values that are typical for heart disease. "We use the heart as a detector," explains Professor Reinhard Nießner, Director of the Institute of Hydrochemistry at the TU Muenchen. "In this way we can test whether specific nanoparticles have an effect on the heart function. Such an option did not exist hitherto."

Scientists can also use this new model heart to shed light on the mechanism by which the nanoparticles influence the heart rate. In order to do this, they enhanced Langendorff's experimental setup to allow the nutrient solution to be fed back into the loop once it has flown through the heart. This allows the scientists to enrich substances released by the heart and understand the heart's reaction to the nanoparticles.

According to Stampfl and Nießner, it is very likely that the neurotransmitter noradrenaline is responsible for the increased heart rate brought on by nanoparticles. Noradrenaline is released by nerve endings in the inner wall of the heart. It increases the heart rate and also

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plays an important role in the central nervous system – a tip-off that nanoparticles might also have a damaging effect there.

Stampfl and his team used their heart model to test carbon black and titanium dioxide nanoparticles, as well as spark-generated carbon, which serves as a model for airborne pollutants stemming from diesel combustion. In addition, silicon dioxide, different Aerosil silicas used e.g. as thickening agents in cosmetics, and polystyrene were tested. Carbon black, spark-generated carbon, titanium dioxide and silicon dioxide led to an increase in the heart rate of up to 15 percent with altered ECG values that did not normalize, even after the nanoparticle exposure was ended. The Aerosil silicas and polystyrene did not show any effect on the heart function.

This new heart model may prove to be particularly useful in medical research. Here, artificial nanoparticles are increasingly being deployed as transportation vehicles. Their intrinsically large surfaces provide ideal docking grounds for active agents. The nanoparticles then transport the active agents to their destination in the human body, e.g. a tumor. Most of the initial prototypes of such "nano containers" are carbon or silicate based. So far, the effect of these substances on the human body is largely unknown. The new heart model could thus serve as a test organ to help select those particles types that do not affect the heart in a negative way.

Artificial nanoparticles are also used in many industrial products – some of them since decades. Their small size and their large surfaces (compared to their volume) impart these particles with unique characteristics. The large surface area of titanium dioxide (TiO_2), for example, leads to a large refractive index that makes the substance appear brilliant white. It is thus often used in white coating paints or as a UV blocker in sunscreens. So-called carbon black is also a widely used nanoparticle (mainly in car tires and plastics) with over 8 million tons produced annually. The small size of these nanoparticles (they measure only 14 nanometers across) makes them well suited as dyes, e.g. in printers and copying machines.

With their enhanced Langendorff heart, the researchers have now for the first time developed a measurement setup that can be used to analyze the effects of nanoparticles on a complete, intact organ without being influenced by the reactions of other organs. The heart is a particularly good test object. "It has its own impulse generator, the sinus node, enabling it to function outside the body for several hours," Andreas Stampfl, first author of the study, explains. "Additionally, changes in the heart function can be clearly recognized using the heart rate and ECG chart."

"We now have a model for a superior organ that can be used to test the influence of artificial nanoparticles," Nießner explains further. "The next thing we want to do is to find out why some nanoparticles influence the heart function, while others do not influence the heart at all." Both manufacturing process and shape may play an important role. Hence, the scientists plan

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further studies to examine the surfaces of different types of nanoparticles and their interactions with the cells of the cardiac wall.

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