Sleeping sickness finding could lead to earlier diagnosis

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Sleeping sickness creates a metabolic 'fingerprint' in the blood and urine, which could enable a new test to be developed to diagnose the disease, according to new research published today in the journal *Proceedings of the National Academy of Sciences*.

Sleeping sickness, or human African trypanosomiasis, is usually fatal if it is not diagnosed and treated in time. The disease is newly detected in around 30,000 people in sub-Saharan Africa every year. Researchers estimate that the real number of cases is likely to be around ten times this number, as so few patients are accurately diagnosed.

Sleeping sickness is typically passed on through a bite from an infected tsetse fly, which transmits a subspecies of a parasite known as Trypanosoma brucei into the bloodstream.

The new study shows that, in a mouse model, infection with the parasite creates distinct metabolic 'fingerprints' in the blood and urine and that these fingerprints are different at different stages of the disease. This fingerprint was visible in the blood as early as one day after infection.

The researchers, from Imperial College London and institutions in Switzerland and the USA, hope that their findings could ultimately enable a fast and accurate test to be developed so that people can be tested and treated more quickly, improving their chances of survival.

Sleeping sickness is currently difficult to diagnose because its symptoms,

which in its first stage include headache, weakness, and joint pain, are shared by many other conditions. The disease is found in over 20 countries in sub-Saharan Africa and doctors there rarely have the resources to carry out the necessary diagnostic tests or to treat infected cases.

Doctors have to use both a blood test and a lymphatic fluid test, using a needle inserted into the lymph node, in order to confirm a positive diagnosis. They then use a painful and invasive lumbar puncture to work out which stage the disease has reached, in order to select the best drug for treatment.

It is important to catch the disease as early as possible in order to give the patient a chance of recovering. In the second stage of the disease, when the parasite progresses into the patient's brain, doctors have to use a different, less effective set of drugs. One of these drugs, melarsoprol, can cause devastating side-effects, such as a brain disease, or encephalopathy, which causes fatality in 50 percent of cases.

Professor Elaine Holmes, corresponding author of the research from the Department of Biomolecular Medicine at Imperial College, said: "Sleeping sickness is a shattering disease and it is often not spotted until it is too late. Its initial symptoms can be quite mild and non-specific and doctors in sub-Saharan Africa don't usually have the time or money to carry out the tests to check if someone has it. This means a lot of people are dying and if there was a simpler way of testing people, doctors might be able to save many of them.

"Our research is at a very early stage, but our results suggest that scientists could in the future create a better way to test for sleeping sickness. So far we have only looked at a mouse model, and we have not yet investigated what happens when there are multiple parasites in the body, but these are promising findings," she added.

For the new study, the researchers used NMR spectroscopy to analyse the metabolic profiles of twelve mice infected with the parasite Trypanosoma brucei brucei, using blood and urine samples. They carried out their analyses two days before infection and at a series of points over a 33-day period after infection. Twelve uninfected mice acted as controls.

Trypanosoma brucei brucei cannot infect humans with sleeping sickness but it is very closely related to the parasites Trypanosoma brucei gambiense and Trypanosoma brucei rhodesiense, which do.

The next step for this research is to determine whether the findings in mouse models can be replicated in humans. The researchers also want to explore whether other parasitic infections create their own metabolic fingerprints, and how such fingerprints can be distinguished from one another where a person has multiple parasitic infections.

The researchers are also keen to investigate whether the parasite that causes sleeping sickness has become more virulent. In the current study, a separate group of mouse models was used to ascertain how quickly the disease progressed. This revealed that the parasite crossed into the brain much sooner than had been shown previously. Earlier studies had shown that the parasite was established in the brains of mouse and rat models 21 and 13 days after infection, respectively. The new study showed that the parasite crossed into the brain within seven days of infection.

Source: Imperial College London