

Breakthrough in treatment of sleeping sickness

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(PhysOrg.com) -- Scientists at the University of Glasgow have made a significant breakthrough in the treatment of Sleeping Sickness, otherwise known as Human African Trypanosomiasis.

The experts, from the university's medical, veterinary and life sciences faculties, believe the discovery, published this week in 'Brain', a leading neurological science journal, could potentially lead to the development of safer drugs for sleeping sickness in the future.

Sleeping Sickness is widely recognised as one of Africa's neglected diseases killing up to 50,000 people every year. It causes an infection of the [brain](#) that is always fatal if untreated. But current treatments are far from safe or effective.

Melarsoprol, an arsenic based drug, is the most common treatment given for sleeping sickness. However, it is so toxic that it kills one in 20 patients who are given it. With most fatalities, patients die from a very severe [brain inflammation](#) triggered by Melarsoprol.

University of Glasgow researchers have now identified that by inhibiting a particular metabolic pathway in the brain, known as the kynurenine pathway, they can significantly reduce the inflammation found in the brains of animals infected with the [parasites](#) or trypanosomes which cause sleeping sickness. It is inflammation in the brain which kills patients, rather than the parasite itself.

The study published in Brain was led by Peter Kennedy, Burton Professor of Neurology at the University of Glasgow, and builds on previous research carried out by study co-authors Professor Trevor Stone, Professor Mike Barrett and Dr Jean Rodgers.

Professor Kennedy explains: "The kynurenine pathway is a major metabolic pathway in humans active in many tissues including the brain. It can

induce inflammation when stimulated.

Pharmacologists have found that specific drugs aimed at the pathway can be useful in dampening down inflammation. Professor Stone and his research group showed a similar involvement of the kynurenine pathway in the fatal brain inflammation that occurs in cerebral malaria.

"It has been known for sometime that Melarsoprol is capable of killing patients by profoundly damaging their brains. Exactly how this happens remains unclear, but it seems likely that the drug kills the parasites very rapidly and profound inflammatory responses to those dying parasites cause damage to the brain cells in their vicinity. This can lead to death of the patients."

Scientists now hope the new finding could mean drugs intended to dampen down inflammatory reactions within the brain could be given to patients to reduce the risk of the drug induced toxicity when treating sleeping sickness.

Professor Kennedy continues: "We are unquestionably one step closer to developing safer combination drugs for the treatment of sleeping sickness. Our study with mice showed that if you inhibit the kynurenine pathway with an anti-inflammatory drug or agent you minimise damage to the brain. This lessens the risk of death. Therefore, we believe that when treating patients with Melarsoprol it would be possible to minimise brain damage if a specific anti-inflammatory drug was administered before the patient received melarsoprol. We will of course need to test this theory, but this finding is extremely promising."

Sleeping Sickness occurs in 36 countries in sub-Saharan Africa and is a major health problem in Angola, the Democratic Republic of Congo, Uganda and Sudan. The trypanosome parasite is transmitted by the tsetse fly. If untreated, the trypanosome crosses the blood-brain barrier to invade the nervous system inducing confusion,

paralysis, coma and a reversal of the normal the sleep cycle - where the disease gets its name.

Professor Kennedy is the author of 'The Fatal Sleep' published in 2007 by Luath Press.

More information: A copy of the paper is available at: brain.oxfordjournals.org/cgi/content/full/awp074
Kynurenine pathway inhibition reduces central nervous system inflammation in a model of human African trypanosomiasis, Brain, Advance Access published on March 31, 2009
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