Decoding sleeping sickness signals could aid quest for treatments

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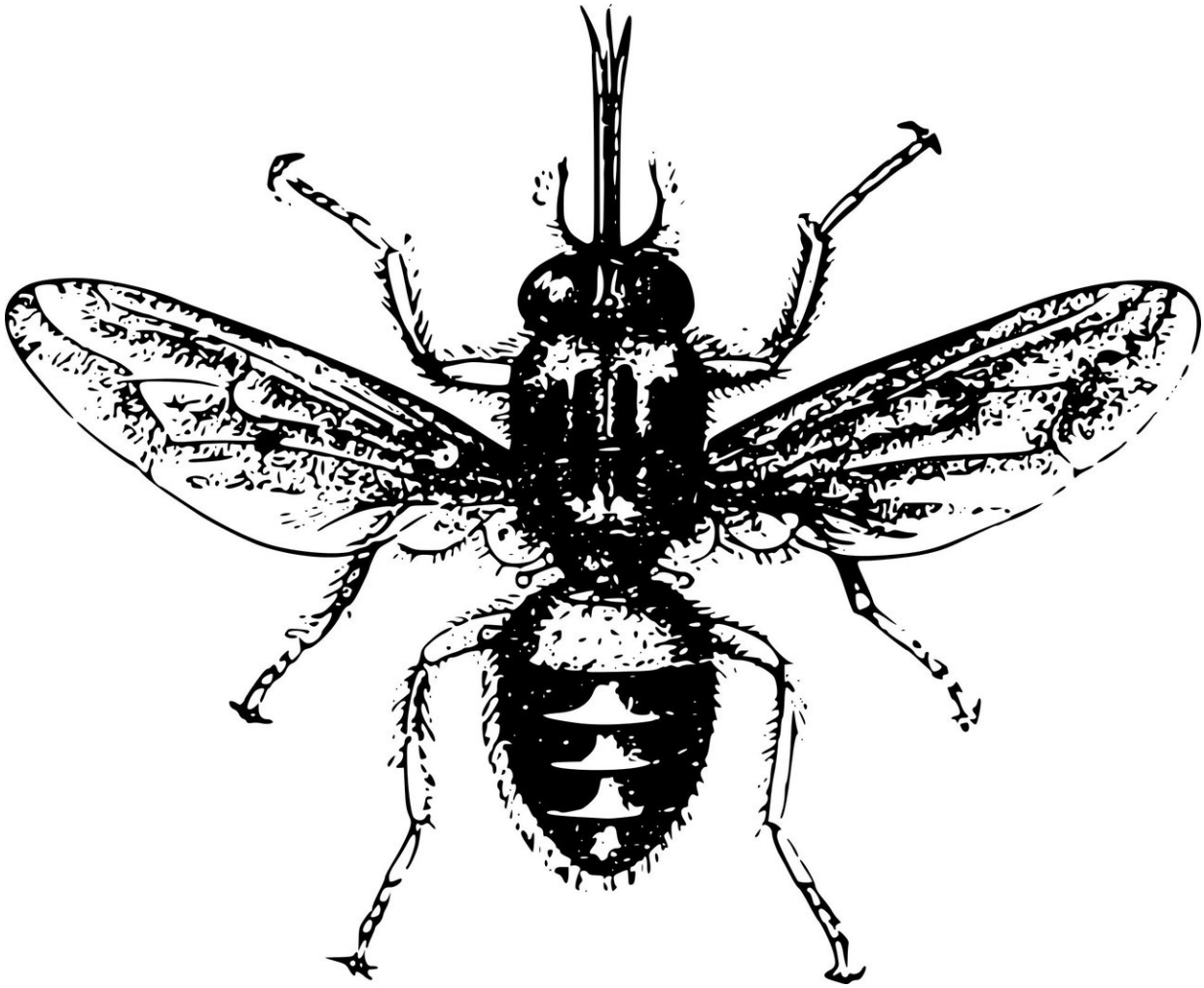

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Key insights into how the parasites behind sleeping sickness boost their ability to spread could aid efforts to beat the disease.

The finding resolves a decades-long puzzle about the behaviour of the parasites, which are spread by the bite of the tsetse fly, and cause disease in people and animals.

Researchers studied how parasites in the bloodstream send chemical signals to one another to undergo a physical change that is needed for them to spread disease.

Scientists have pinpointed details of the signal that enables parasites to change from a form in which they can quickly boost their numbers, to one that is more suited to aiding their transmission and survival in flies.

Scientists led by the University of Edinburgh found that the parasites release enzymes, called peptidases, which break down proteins in the blood into smaller molecules.

These small molecules, known as oligopeptides, are sensed by a protein—GPR89—which is found on the surface of the parasite. This triggers the parasites' transition into a state in which they can be taken up and transmitted by flies.

Oligopeptides also act as nutrients for the parasites and are taken up by the same surface protein.

Disrupting this process by designing drugs that interfere with the GPR89 protein could offer a new way of tackling the disease, the team suggests.

The approach could limit drug resistance in two ways—by restricting the supply of nutrients and stopping transition to the state required for disease to spread, researchers say.

Researchers also suggest that the parasites could be disarmed by an artificial form of the signalling molecule. This would trick the parasites into prematurely arresting their growth.

The study, published in *Cell*, was carried out in collaboration with the University of St Andrews and was funded by Wellcome.

Professor Keith Matthews, of the School of Biological Sciences, who led the study, said: "Understanding how these parasites communicate with each other has been a mystery for decades. The mechanism we have discovered provides new opportunities to develop much-needed drugs for this devastating disease."

Mike Turner, Head of Infection and Immunobiology at Wellcome, said: "This study solves one of the most fundamental questions about the sleeping sickness parasite and will help researchers around the world look for new ways to limit the severity of the disease.

"This ability of the sleeping sickness parasite to regulate how they switch between states so that they can be transmitted by tsetse flies was first described in 1972 and since then many groups have failed to solve it until this beautiful study by Professor Matthews' group."

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