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Effect of cannabinoids on the feeding behaviour on the free-living ciliate *Tetrahymena pyriformis*

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Introduction: The cannabinoid system regulates feeding behaviour in mammals by inducing hyperphagia through the cannabinoid receptor, CB1 (1). Comparable data on its effect on feeding in unicellular eukaryotes, from which mammalian cells have evolved, is lacking. These cells do possess endocannabinoid compounds and endocannabinoid-metabolizing and -synthesizing enzymes but do not possess a known cannabinoid receptor (2). Even so, when presented with exogenous cannabinoids, they exhibit depressed cell growth and macromolecule synthesis, changes in cell shape and reduced/irregular motility (3,4). This study assessed whether exogenously applied cannabinoids affected their feeding behaviour.

Method: The ciliate *Tetrahymena pyriformis* was fed with an indigestible fluorescent prey (*Synechococcus* sp.) at $1.2x10^8$ cells/mL in triplicate in the presence and absence of the cannabinoids Anandamide (AEA) and Cannabidiol (CBD) at the IC_{50} concentration (4µM). The number of prey/cell, digestive vacuoles/cell and prey/digestive vacuole were determined, with fluorescence microscopy, on fixed samples throughout a 2.5h feeding period at 23^oC.

Results: Both CBD and AEA altered ciliate feeding behaviour compared to untreated cells. They acted biphasically, with a 30 minute delay in feeding and subsequent hyperphagia. CBD induced a higher ingestion rate (1.65 ±.0.6 prey/cell/min) than AEA (1.1 ± 0.06), as determined by Student's t Test based on the SEM of regression models, $p < 0.05$, $n = 3$. AEA maintained the number of prey/vacuole (16.4 ± 0.4) to that of control and CBD increased the number of prey/vacuole (25.1 ± 0.4), as determined by Independent Samples t Test, $p < 0.05$, $n = 3$. Thus, AEA produced more vacuoles, whereas CBD filled the vacuoles with more prey, making them larger.

Conclusion: This study provides novel evidence to suggest a role for cannabinoids in unicellular eukaryotic feeding behaviour. The cannabinoid compounds may act at different cellular targets or through different signalling mechanisms but further research is required to uncover those targets. Such experiments, with a model organism, could provide novel therapeutic targets for cannabinoids in humans and be pivotal in understanding the evolutionary history of the mammalian endocannabinoid system.

References:

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