



NemaMetrix

THE ENDOGENOUS CANNABINOID ANANDAMIDE CAUSES HYPERPHAGIA IN *C. elegans*

DO NEMATODE WORMS GET THE MUNCHIES?

PURPOSE

The NemaMetrix ScreenChip System is a microfluidic platform for recording electropharyngeograms (EPGs) from the nematode worm *Caenorhabditis elegans* and other nematode species. A key feature of the system is semi-automated loading from a reservoir of hundreds of nematodes, which increases throughput by 10 to 100 fold over previous methods for counting pharyngeal pumps. This technical note demonstrates the utility of the ScreenChip system in pharmacology, taking as an example compounds chemically related to Δ^9 -tetrahydrocannabinol (THC), the primary psychoactive compound in marijuana (*Cannabis sativa*).

Cannabinoid drugs mimic endocannabinoids, endogenous signaling molecules used by the brain to regulate synaptic transmission, learning and memory, and other fundamental processes. One of the legendary effects of cannabinoid drugs is increased motivation to eat, or hyperphagia. The two main human endocannabinoids are anandamide and 2-AG, both of which are present in *C. elegans*¹. Here the ScreenChip is used to test the hypothesis that anandamide produces hyperphagia in *C. elegans*, a potential correlate of marijuana munchies.

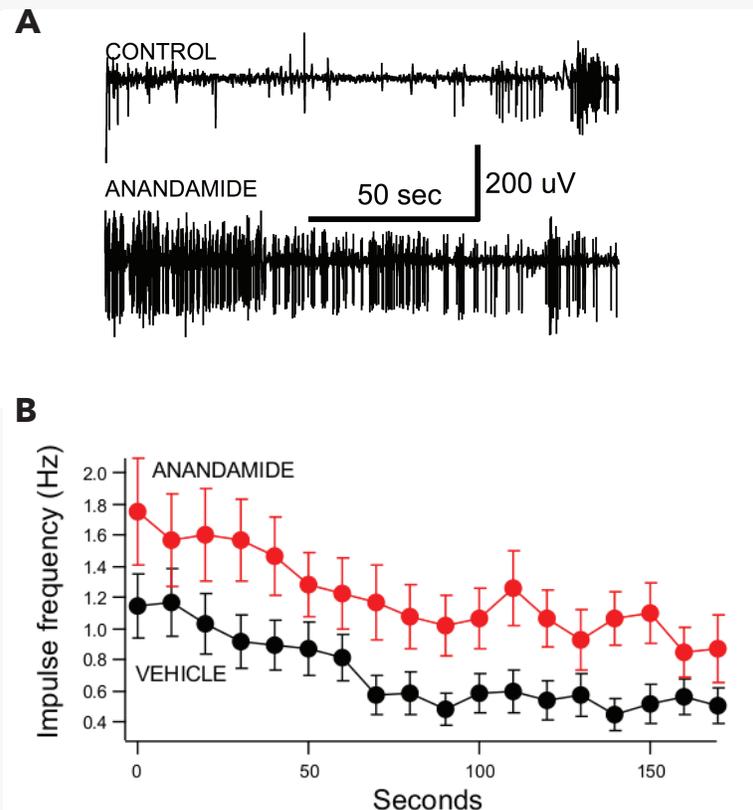


Fig. 1. Effect of anandamide on feeding rate in *C. elegans*.

A. Representative electropharyngeograms (EPGs) from control and anandamide-exposed worms. **B.** Mean pump frequency versus time in 10 sec. bins (Anandamide, $N = 27$; Control, $N = 41$). STATISTICS in B: Data are shown as mean \pm SEM. ANOVA, Treatment, $F(1,66) = 7.26$, $p = 0.009$.



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RESULTS

Well-fed adult worms were pre-exposed to the drug by soaking them for 20 min. in a tube of fluid containing 100 μ M anandamide. Control worms received the same treatment but without the drug. Immediately before recording, a suspension of edible bacteria solution was added to the tube. Worms were drawn from this tube into the chip and recorded individually for 3 min. Pumping was activated in both groups of worms but anandamide approximately doubled the pumping frequency (Fig. 1). The overall decline in pumping frequency with time possibly resulted from depletion of food in the vicinity of the worm's mouth during the recording (Fig. 1B).

CONCLUSION

We conclude that anandamide causes hyperphagia in *C. elegans*. This finding provides the basis for genetic screens to identify cannabinoid signaling pathways.

METHODS

Strains, cultivation, and food. Synchronized worms (N2) were cultivated at 20°C to the first day of adulthood on plates containing nematode growth medium (NGM) seeded with *E. coli* OP50^{2,3}. During EPG recordings, worms were fed *Comamonas sp.* at an initial concentration of 0.8 optical density units, suspended in M9 buffer³.

Electropharyngeograms. Pharyngeal pumping frequency was measured using methods described in the ScreenChip User Guide (www.nemamatrix.com). In the experimental group, the food suspension contained 100 μ M anandamide.

REFERENCES

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2. Stiernagle, T. Maintenance of *C. elegans*. (2006).
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