



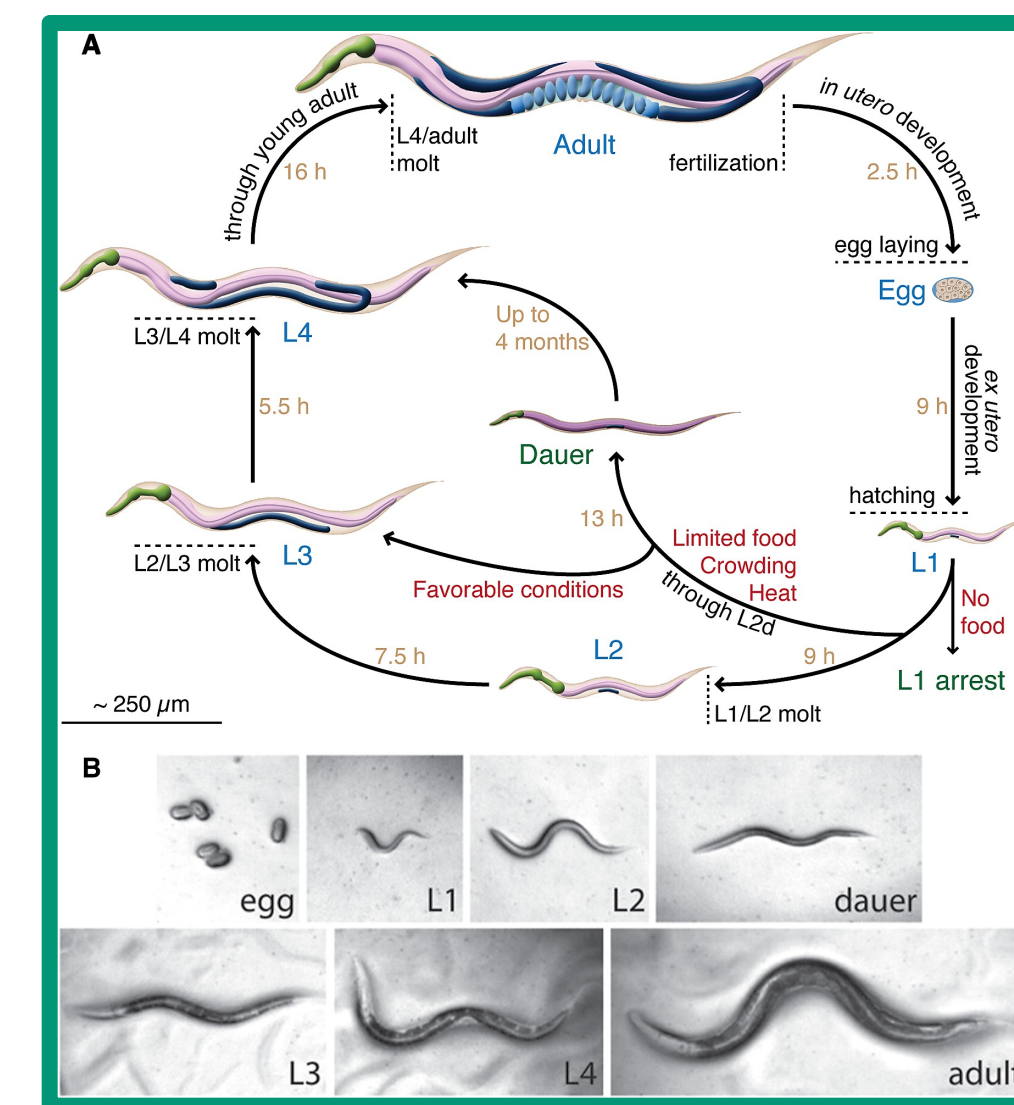
The Effect of Antihistamines on Behaviorally Trained *C. elegans*



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C. elegans: A Truly Amazing Organism

Caenorhabditis elegans, or *C. elegans*, are transparent, microscopic soil nematodes. They are ideal organisms to use in several types of experiments because of their rapid life cycle, invariant number of somatic cells, and sequenced genome. Hermaphrodites and males are the two possible genders of a *C. elegans*. Hermaphrodites contain both the male and what we consider the female reproductive systems of *C. elegans*. The instance of finding a male *C. elegans* in the wild is extremely low since males are typically only produced in times of stress. All *C. elegans* undergo four larval stages before reaching adulthood; this process is altered slightly if a *C. elegans* in the first larval stage is faced with undesirable conditions such as limited food, overcrowding, and heat, causing the worm to enter a dauer stage where it uses minimal energy and can survive for up to four months without the outside conditions improving.



From: Chen & Karimella, Toxmas (2015). The *C. elegans* dauer larva as a paradigm to study metabolic, depressive and dissociative responses. *PLoS* 12(2): e0172304. doi:10.1371/journal.pone.0172304

Materials and Methods

Four experiments were performed. The first three consisted of first synchronizing *C. elegans* to ensure they were of the same age at the time of the training, later training them to stop responding to a series of vibrating taps applied with a Philips Sonicare HealthyWhite HX6711/02 Toothbrush on the first vibration setting to the side of the agar-filled petri dishes the nematodes were on, and finally exposing the *C. elegans* to two commonly available and used antihistamines, diphenhydramine (Benadryl) and cetirizine (Zyrtec). Doses of 1.3 mg/ml of sterile water for Benadryl and 0.4 mg/ml of sterile water for Zyrtec were used. These amounts were based on the recommended doses for adult patients taking both medicines. Each medication was crushed using a mortar and pestle and added to 10 mLs of sterile autoclaved water. 10 mLs of sterile water was used as a control. The fourth experiment was performed the same way except for the omission of the training of the the *C. elegans* prior to their exposure to the antihistamine and control solutions. This aimed to ensure that the antihistamines were not affecting the *C. elegans* in any other way which could jeopardize the validity of the results.



Antihistamines: A Menace to the Mind?

Antihistamines are a commonly used class of drugs that prevent histamine from binding to cell receptors and triggering histamine release and symptoms of allergic reactions (1, 2). Recent studies have correlated the use of antihistamines with an increased risk of dementia (4-6), which is alarming since the US population has an increasing incidence and prevalence of diagnosed food or seasonal allergies (3), and antihistamines are often a first-line medication recommended for initial treatment of these allergies.



Abstract

The goal of this investigation was to explore the association between antihistamines and dementia. To study this, antihistamine use and resulting behavior change or memory dysfunction was researched in the nematode *C. elegans*. It was hypothesized that behaviorally trained *C. elegans* that had ceased reacting to vibrations would recommence reacting to vibrations after exposure to antihistamines. To avoid the possibility of differential responses based on larval stage, *C. elegans* were synchronized to the L3 larval stage using a bleaching technique. Groups of ten synchronized *C. elegans* per culture dish were conditioned to stop reacting to exposure of vibrations applied with a standard electric toothbrush to the side of the dish. The toothbrush was touched to the dish 20 times over a span of ten seconds. After the ten second exposure, the *C. elegans* were allowed to rest for one minute and exposed to vibrations again. This process was repeated for a total of 102 minutes over two days, resulting in the *C. elegans* showing signs of becoming accustomed to the vibrating “taps”, as indicated by the decline of the percentage of *C. elegans* responding to the vibrations. After conditioning, diphenhydramine (Benadryl), cetirizine (Zyrtec), or sterile water solutions were added to the top of the semisolid medium of the petri dishes at a concentration of 1.3 mg/ml for diphenhydramine or 0.4 mg/ml for cetirizine, to ensure direct exposure of the *C. elegans*. Groups exposed to diphenhydramine and cetirizine exhibited loss of conditioned response of the behavioral training, while the control group retained the conditioned response to the vibration stimulus. The results suggest a possible link between antihistamines and behavior change or memory dysfunction in the nematode *C. elegans*. Further studies are needed to confirm and elucidate the mechanism of this response.

My Hypothesis

It was hypothesized that behaviorally trained *C. elegans* that had ceased reacting to vibrations would recommence reacting to vibrations during exposure to antihistamines.

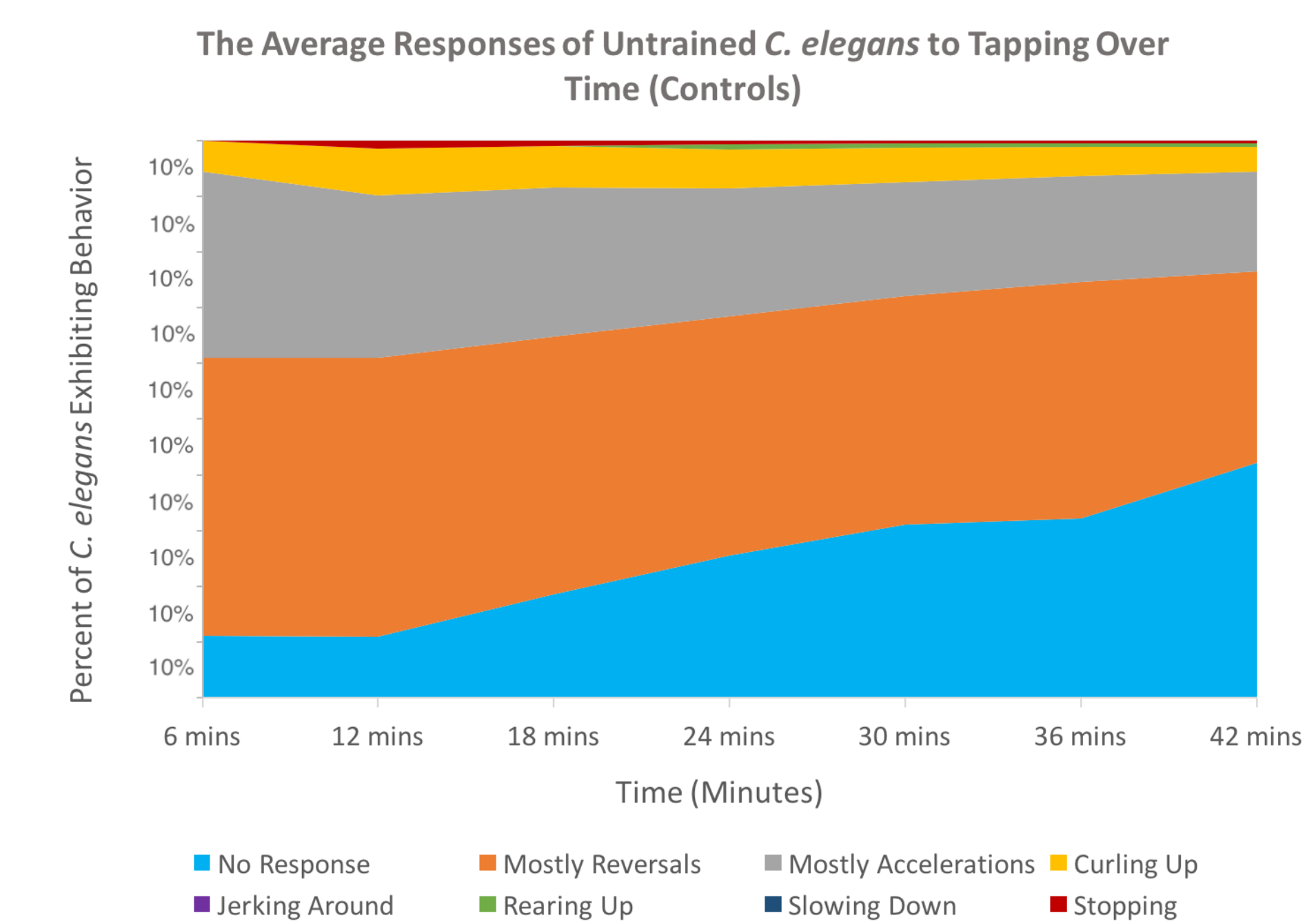
Results

The results for the three identical experiments are shown combined in the six graphs on the right. All were similar in their findings. The protocol utilized caused the *C. elegans* to become used to the taps and behaviorally trained to not react in a conditioned response. When exposed to the antihistamines, the *C. elegans* seemed to forget their training, as they recommenced responding to the tap stimuli. Interestingly, these new responses varied from the responses observed before the exposure to the antihistamines. This is particularly fascinating because dementia has caused people to behave erratically, sometimes irrationally. The fourth experiment *C. elegans* were not killed by the antihistamines when exposed; they were still thriving a week after the experiment was performed. These results suggest a possible link between antihistamines and behavior change or memory dysfunction in the nematode *C. elegans*. Further studies are needed to confirm and elucidate the mechanism of this response; this project is continuing and different routes of experimentation considered, including studying antihistamines and memory in a mutated strain of *C. elegans*.

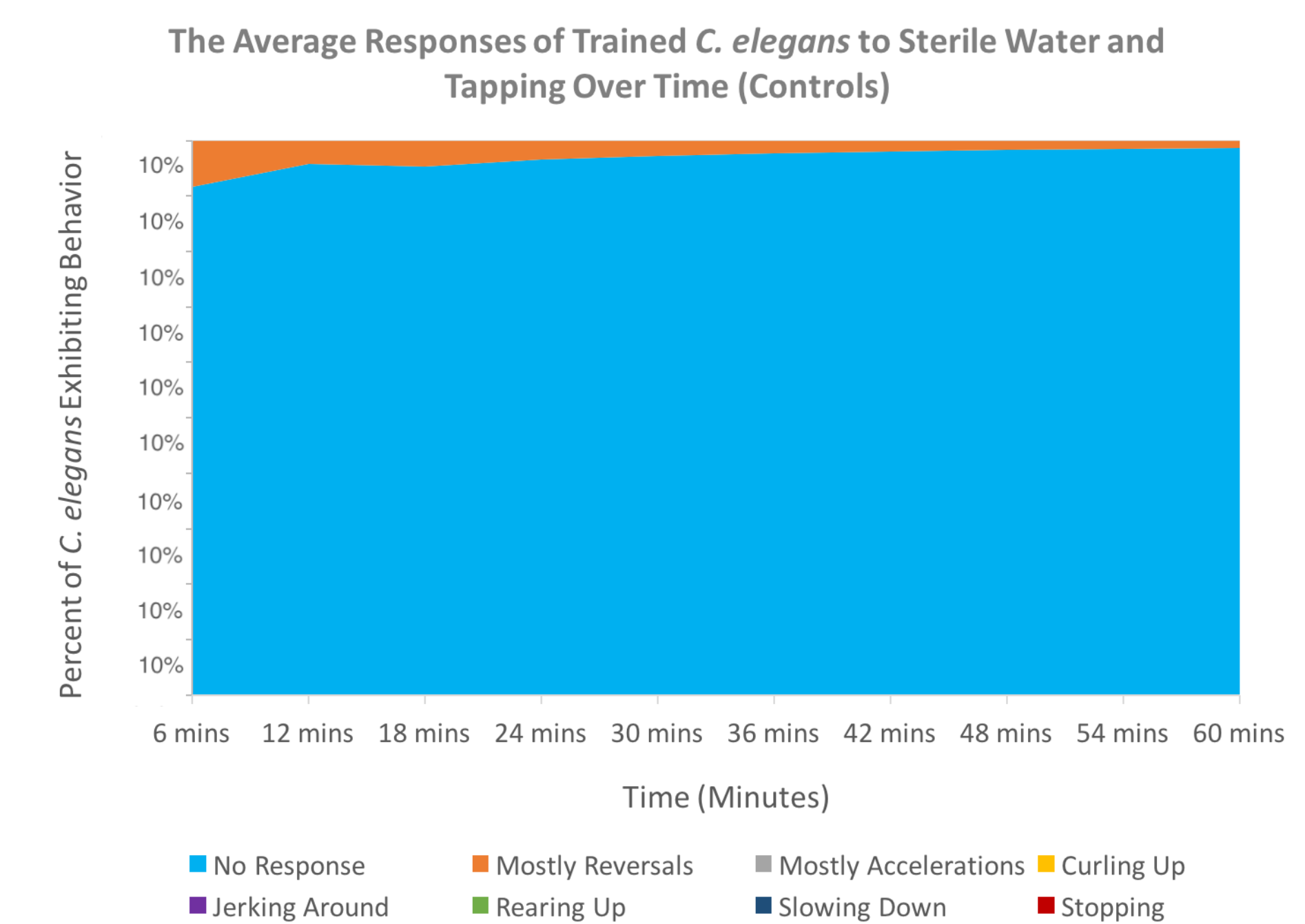
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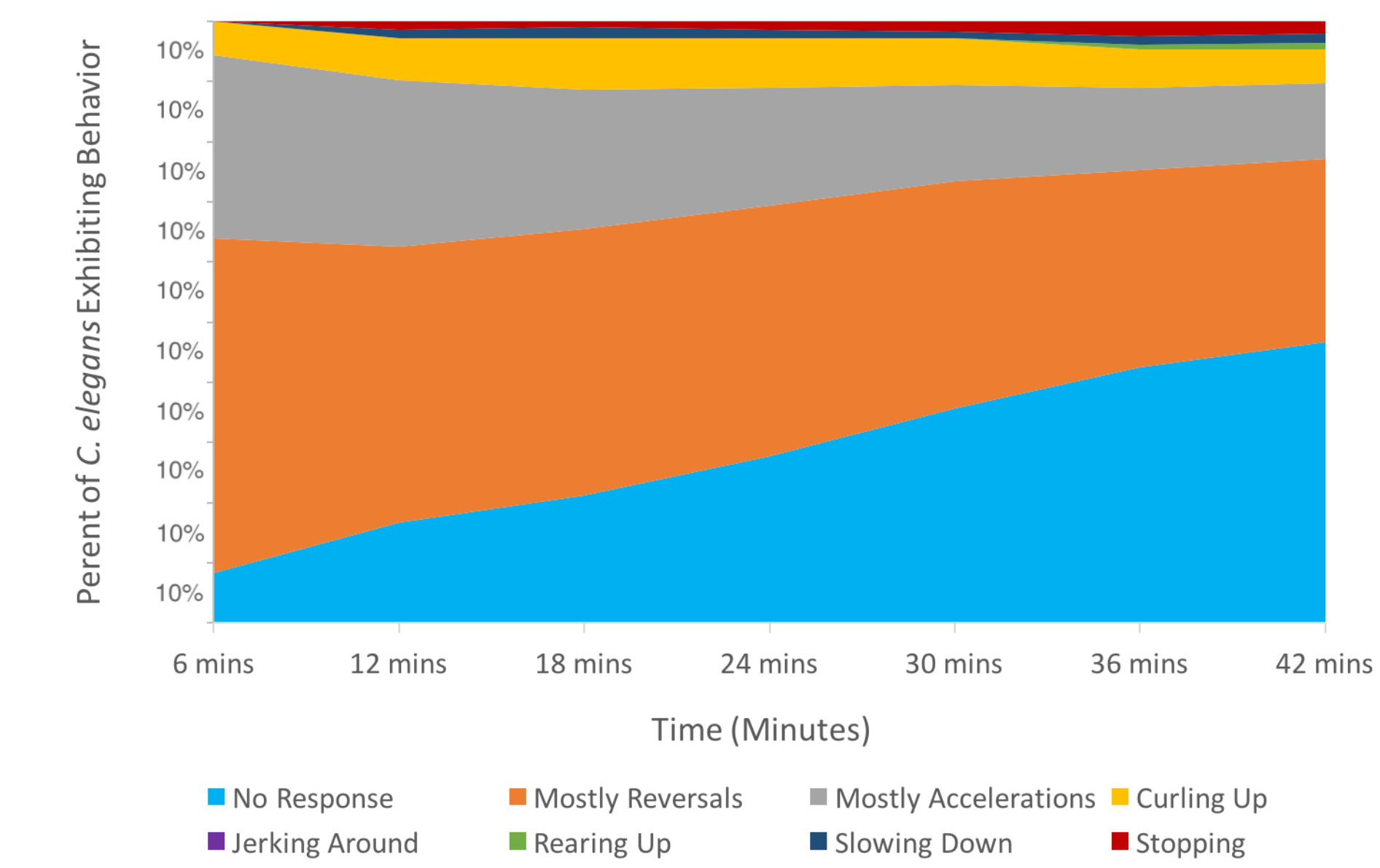
Results: The First Training Day



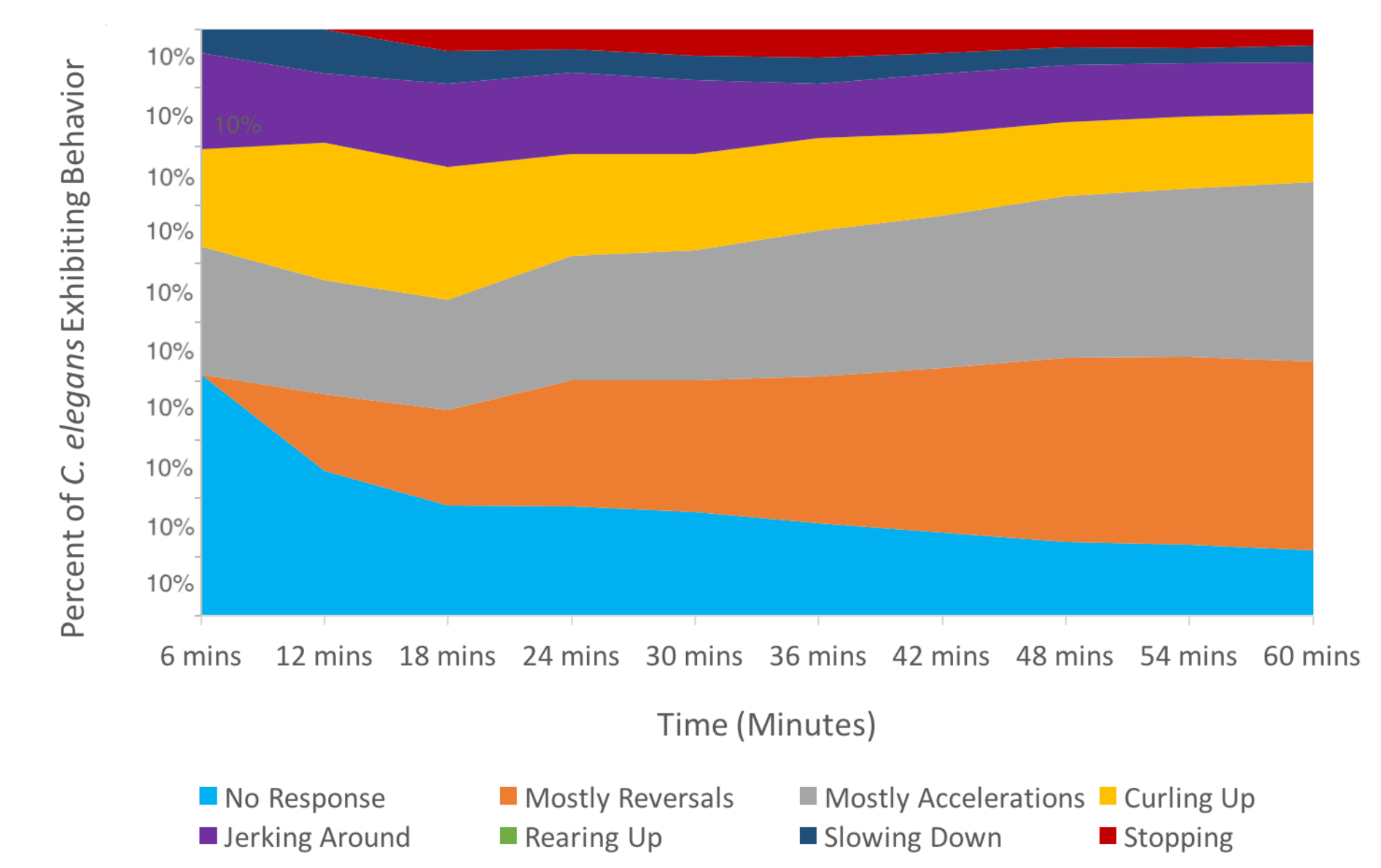
Results: Exposure Day



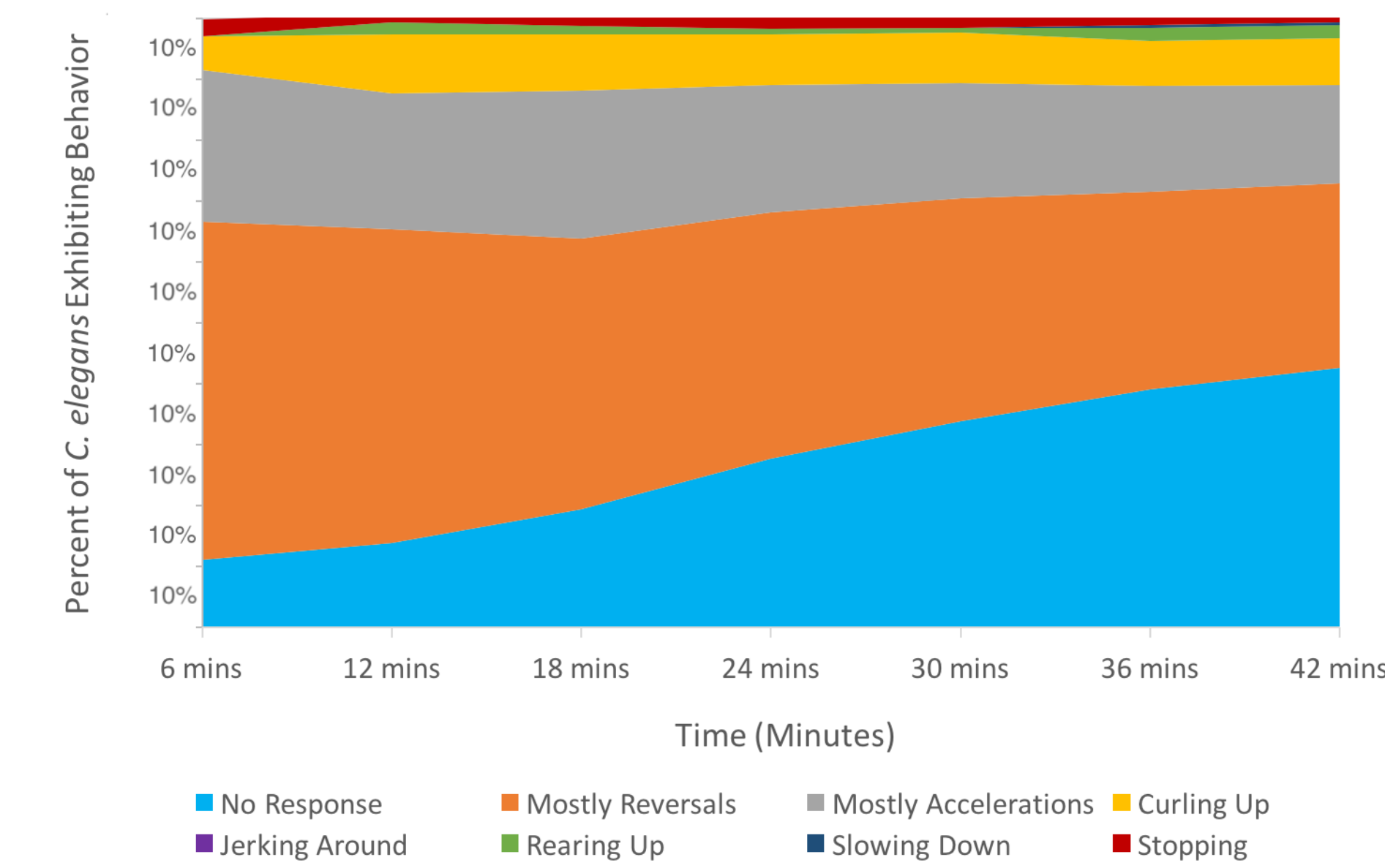
Results: Exposure to Benadryl



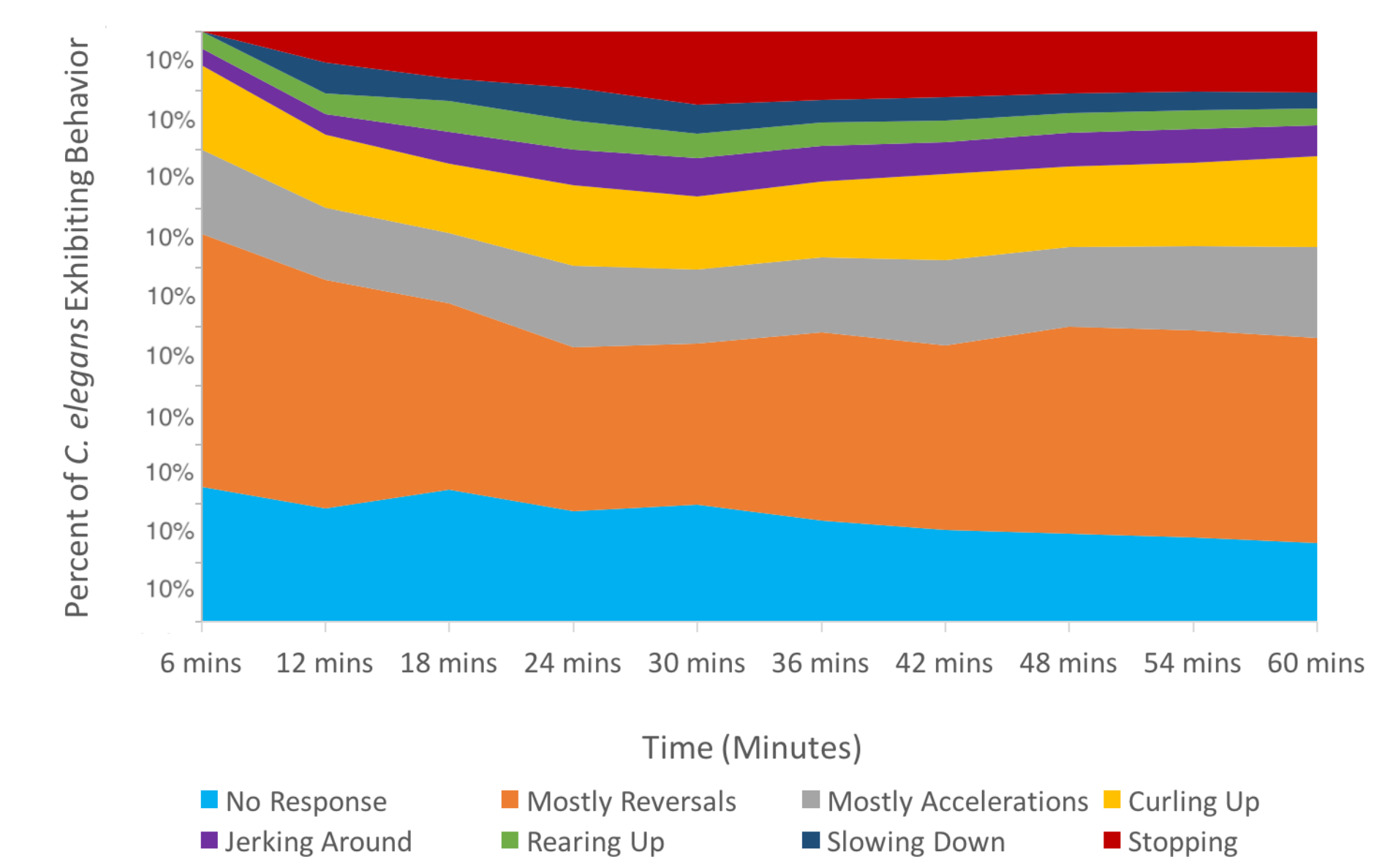
Results: Exposure to Benadryl



Results: Exposure to Zyrtec



Results: Exposure to Zyrtec



Citations

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