

Le proprietà prebiotiche delle radici di cicoria come antidoto agli effetti avversi del confinamento e dell'isolamento nelle missioni spaziali.



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Sessione “Effetti psicofisici e comportamentali causati da confinamento e isolamento. Individuazione, sviluppo ed applicazione di contromisure”.







Caputo et al. *Translational Psychiatry* (2020)10:185
<https://doi.org/10.1038/s41398-020-00869-4>

Translational Psychiatry

ARTICLE

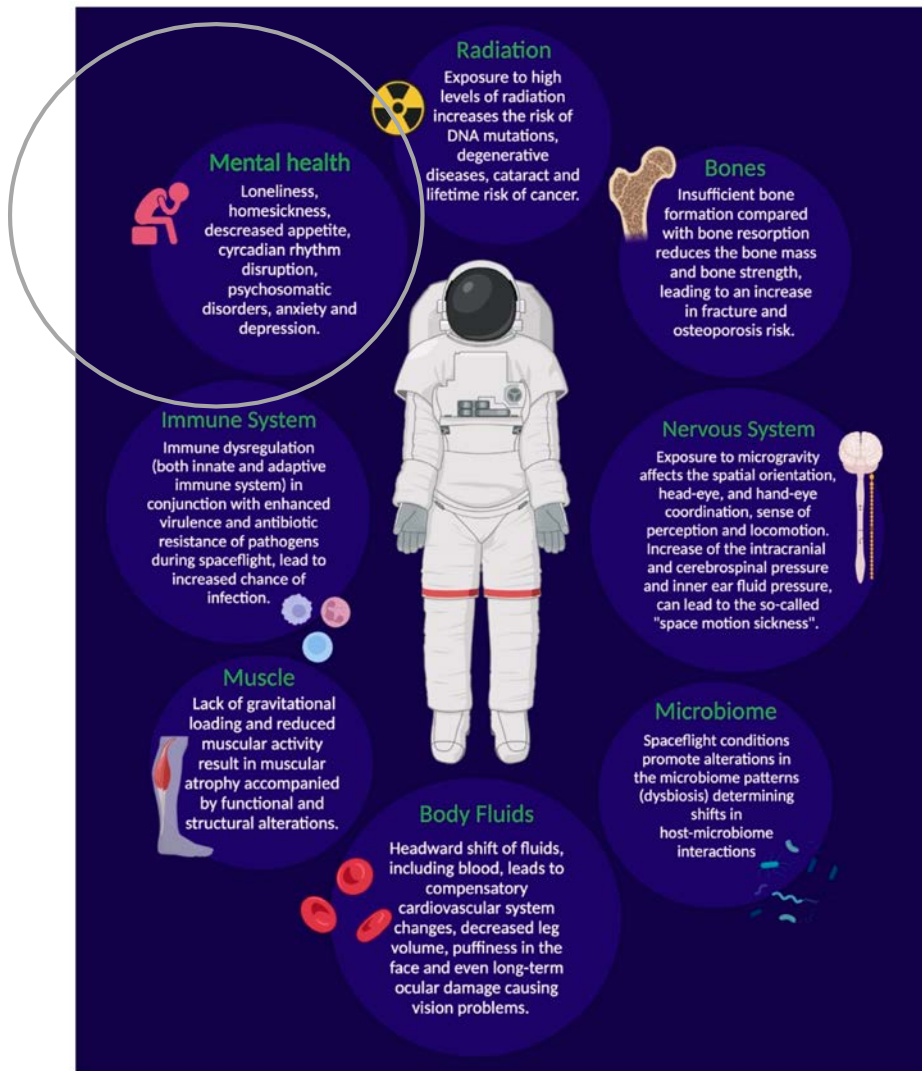
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Genomic and physiological resilience in extreme environments are associated with a secure attachment style

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Enrico Alleva⁹ and Simone Macrì ⁹



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Exposure to space-related stressors causes alterations in various systems, including behavioural and microbiome changes

→ To favour the success of these missions, it is critical to minimise the potential consequences on the well-being of crewmembers

→ **the use of prebiotics may be a promising approach**

Aim



→ Verify whether the consumption of prebiotic-rich vegetables, cultivable within the **bioregenerative life support systems**, is able to **counteract the psychophysiological alterations induced by chronic stress**



First step Selection of a species that:

- Fast growing
- Known to be edible (the full plant!)
- Contains a lot of prebiotics
- Safe
- Can grow nicely in fully controlled environment
- Respond to modulation of growth conditions



Cichorium intybus L.



	Glucose	Fructose	Sucrose	Fructans
	%SS	%SS	%SS	%SS
Average	0,51	1,17	2,61	46,12
s.e.	0,06	0,07	0,28	0,63

Almost 8 g of fibre in 100 g of fresh produce

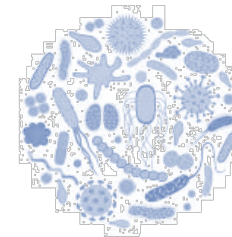
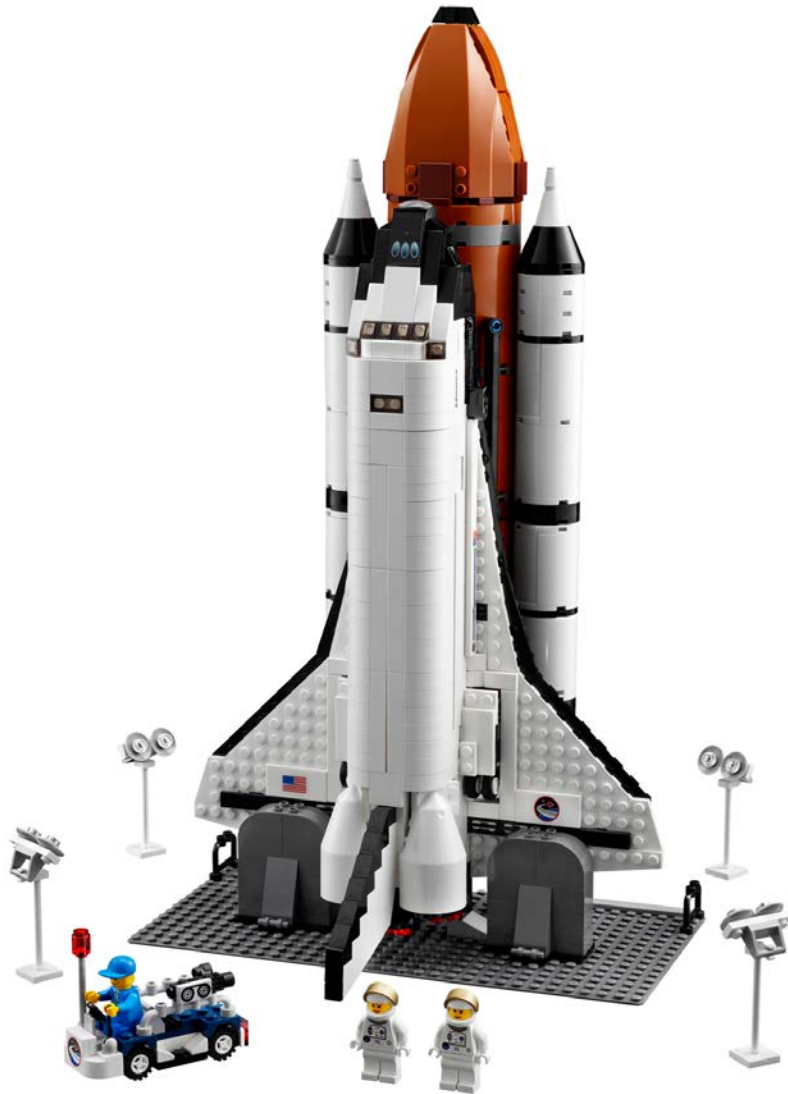
EFSA: High in fibre:at least 6 g of fibre per 100 g or at least 3 g of fibre per 100 kcal'

Paglalunga, G., Proietti, S., Cardarelli, M., Moscatello, S., Colla, G. and Battistelli, A., 2022. Chicory Taproot Production: Effects of Biostimulants under Partial or Full Controlled Environmental Conditions. *Agronomy*, 12(11), p.2816.



Second step

- test whether, in a **mouse model of chronic stress**, the daily consumption of **chicory roots** prompts the recovery of stress-related behavioural and physiological alterations
 - Behavioural tests
 - Analyses of physiological parameters (e.g. stress hormones, caecal microbiota composition)





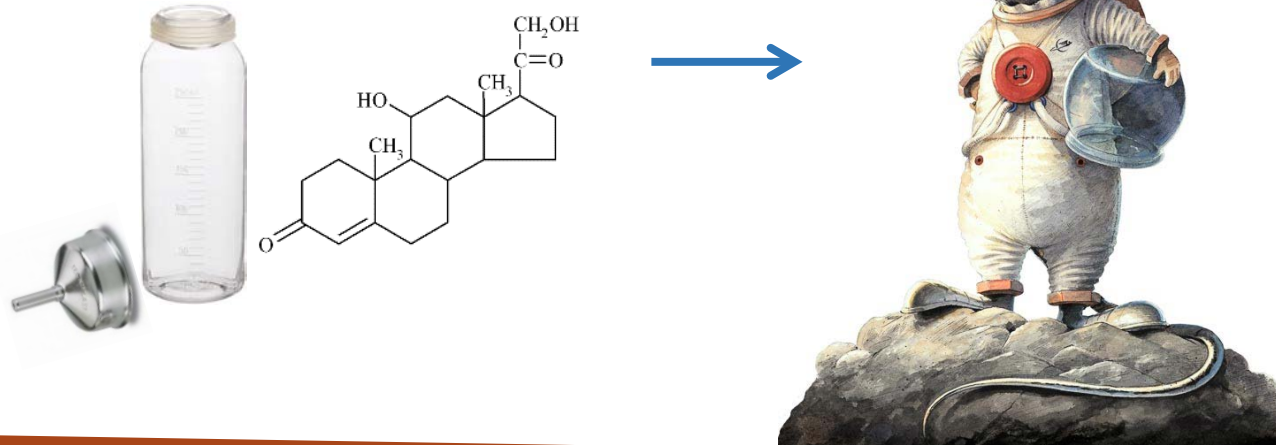
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Mouse model of chronic stress

- Chronic treatment (8-11 weeks) with a **low dose of the stress hormone corticosterone** (35 $\mu\text{g}/\text{ml}$) through drinking water to induce a moderate and persistent elevation of glucocorticoid levels
 - **mimics the effects of chronic stress** to which astronauts will be subjected during **long-duration space missions**
 - dosage: 8.60 mg/kg/die



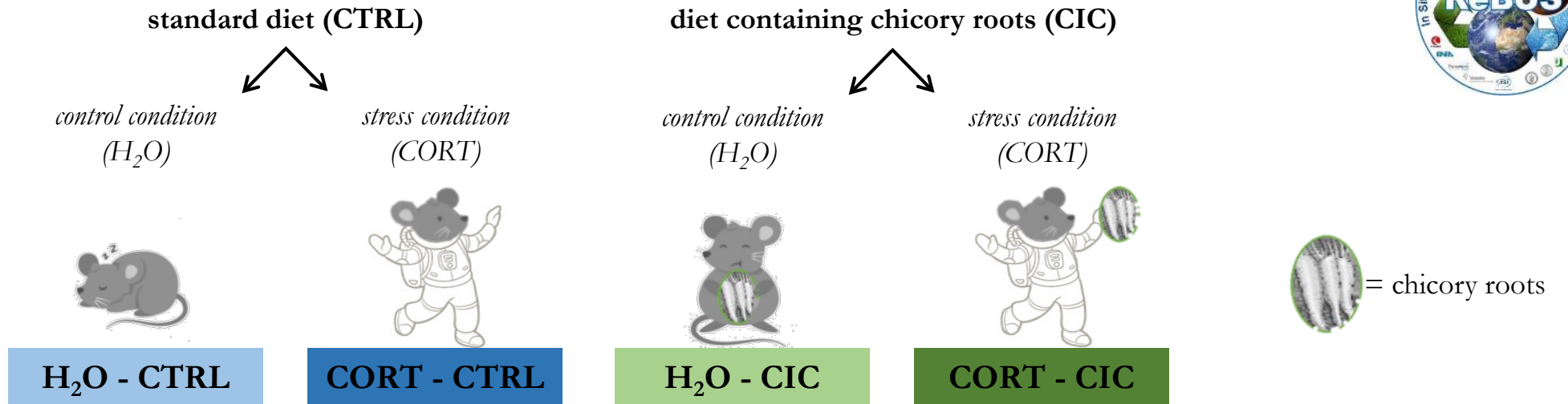
Prebiotic diet

Chicory roots (*Cichorium intybus* cv Chiavari)

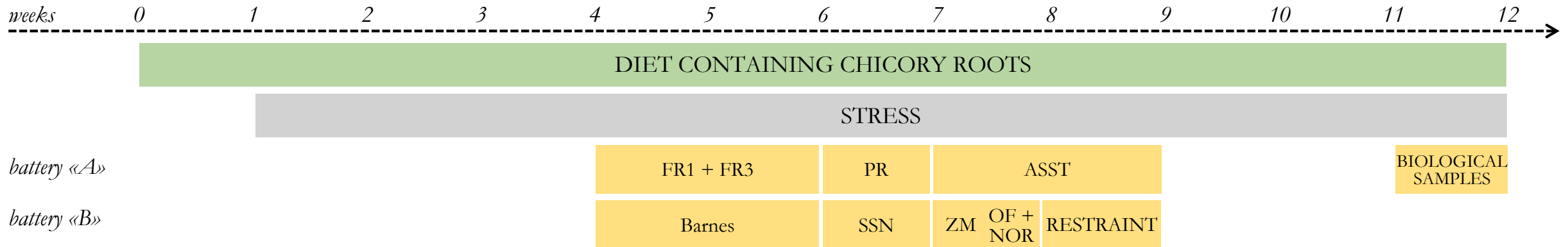
- Chronic administration (9-12 weeks) of prebiotics (fructans) through a **diet containing 25% of chicory roots**
→ **dosage**: on average 0.42 g/die of fructans (range 13.5-16.0 g/kg/day)



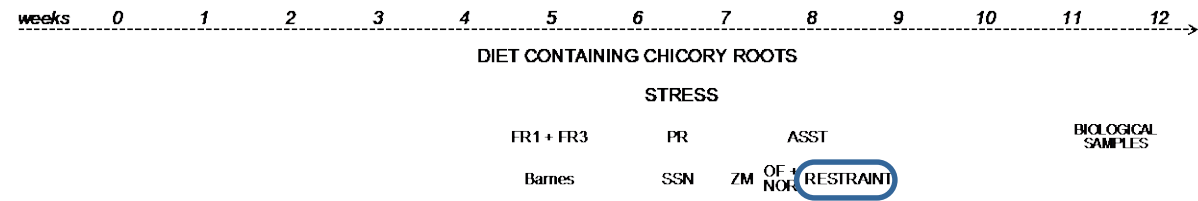
Experimental design



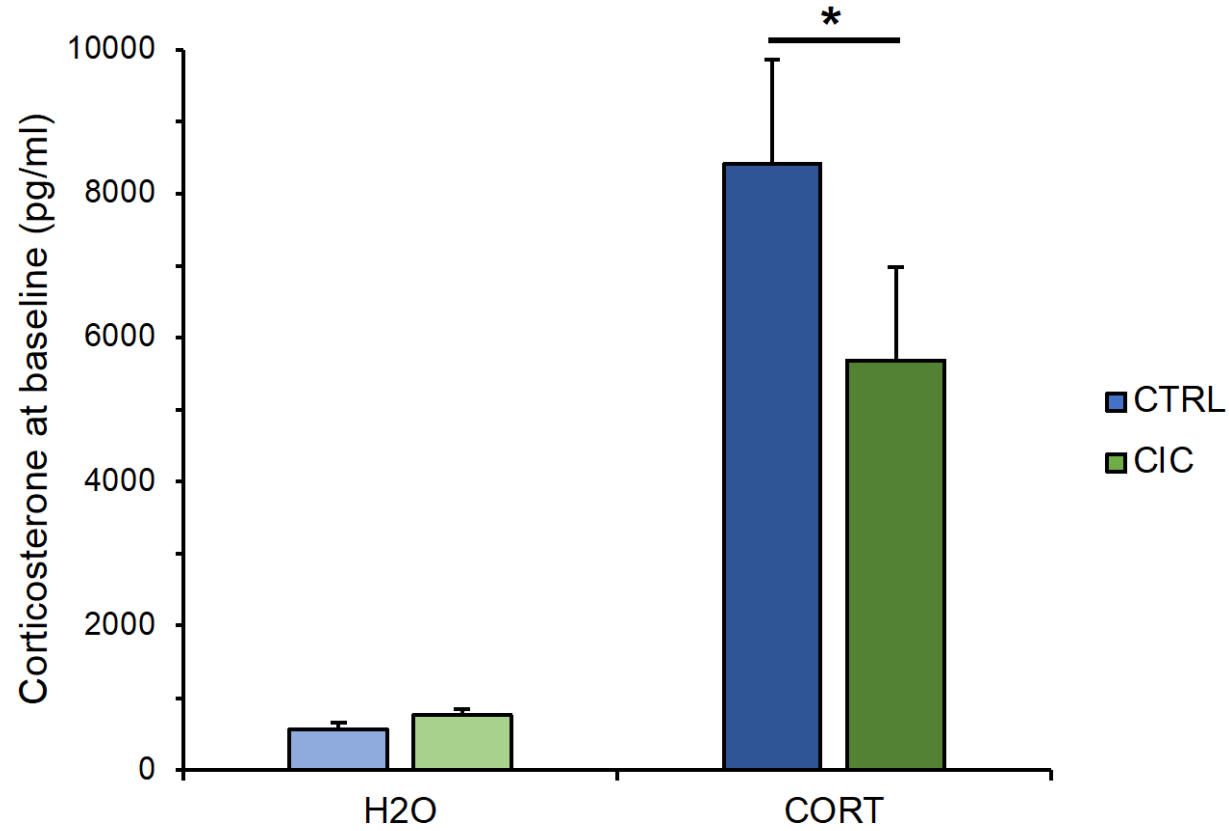
Timeline



Stress reactivity



Plasma corticosterone concentrations



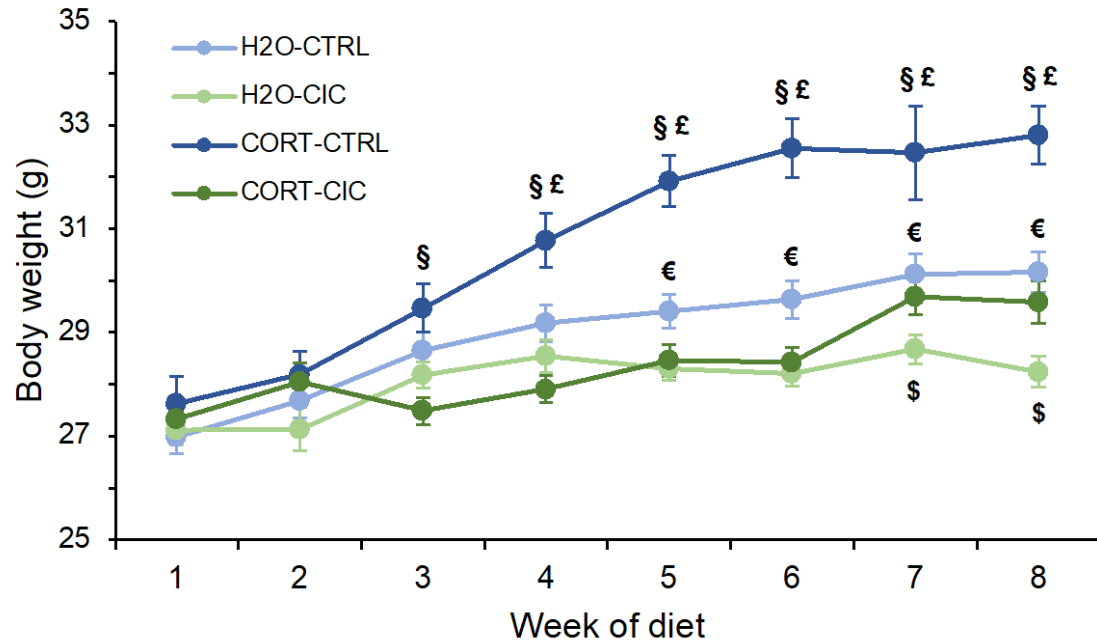
Physiological parameters



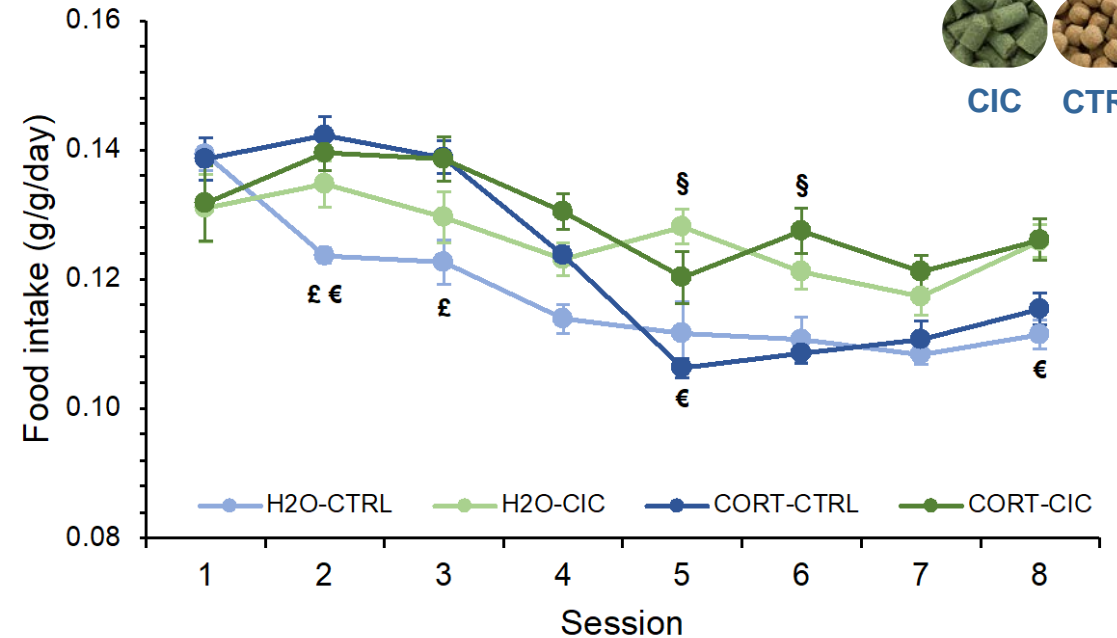
Body weight and food intake



Body weight



Food intake



£ H₂O-CTRL vs. CORT-CTRL € H₂O-CTRL vs. H₂O-CIC
 \$ H₂O-CIC vs. CORT-CIC § CORT-CTRL vs. CORT-CIC

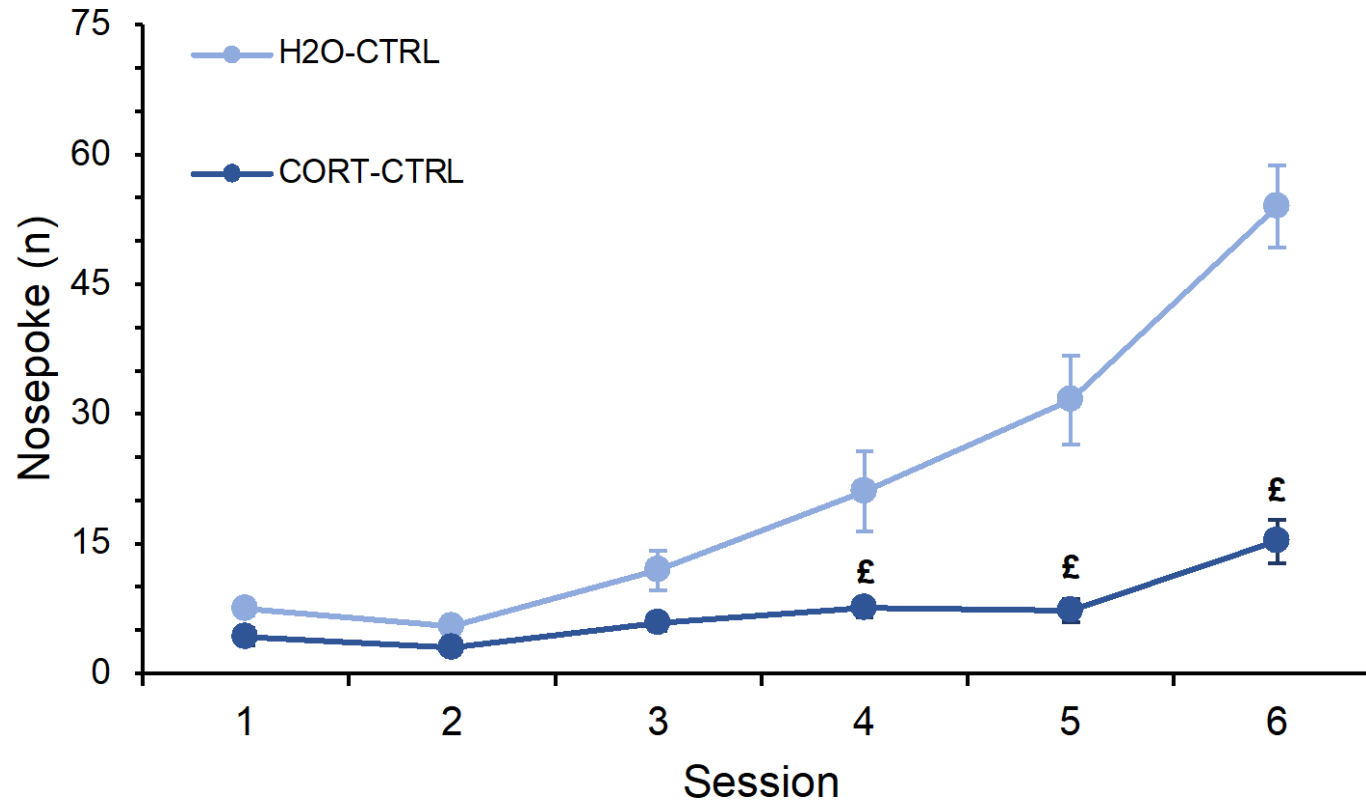


Fixed ratio test (FR)



£ H₂O-CTRL vs. CORT-CTRL

Associative learning learning to perform 1 nosepoke to obtain 1 food reward



Days to criterion:
 H₂O-CTRL: 4.43 ± 0.29
 £ CORT-CTRL: 6.82 ± 0.23

weeks 0 1 2 3 4 5 6 7 8 9 10 11 12

DIET CONTAINING CHICORY ROOTS

FR1 + FR3
Barnes

STRESS

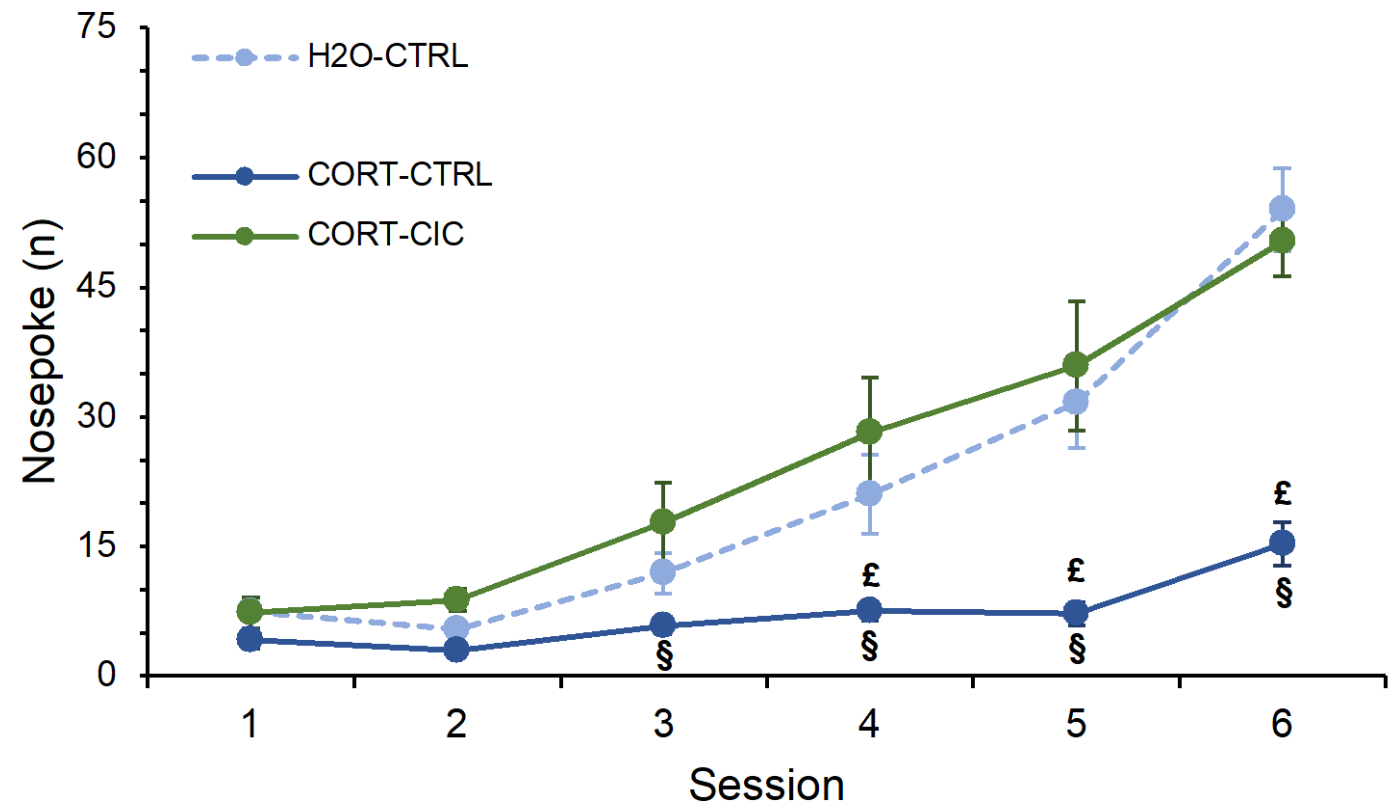
PR SSN ASST ZM OF + RESTRAINT NOR

BIOLOGICAL SAMPLES

Fixed ratio test (FR)



Associative learning learning to perform 1 nosepoke to obtain 1 food reward



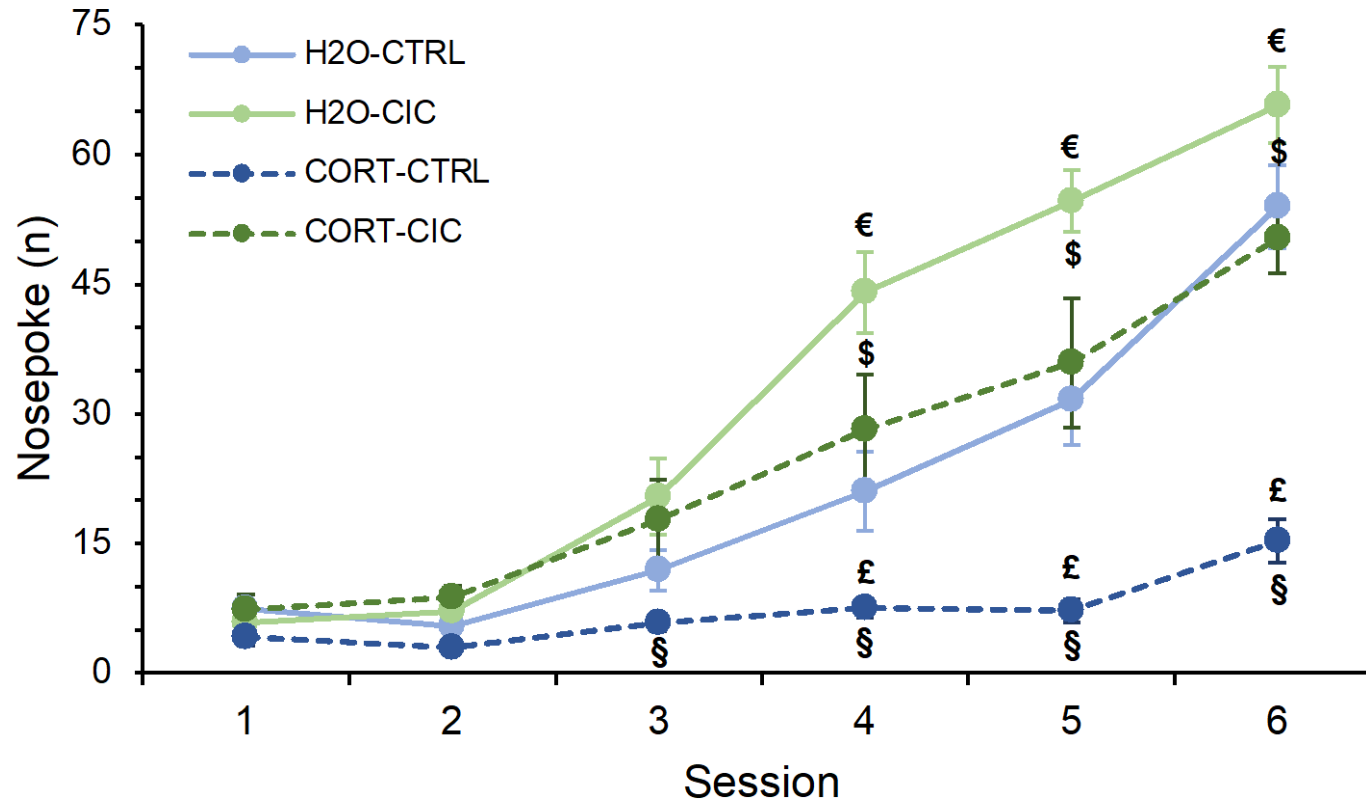
£ H₂O-CTRL vs. CORT-CTRL
 § CORT-CTRL vs. CORT-CIC

Days to criterion:
 H₂O-CTRL: 4.43 ± 0.29
 £ CORT-CTRL: 6.82 ± 0.23
 § CORT-CIC: 4.42 ± 0.50

Fixed ratio test (FR)

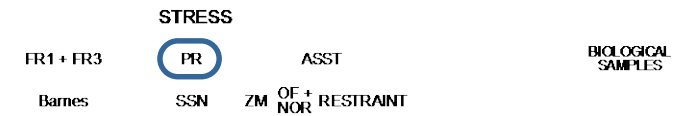


Associative learning learning to perform 1 nosepoke to obtain 1 food reward



£ H₂O-CTRL vs. CORT-CTRL
 \$ H₂O-CIC vs. CORT-CIC
 € H₂O-CTRL vs. H₂O-CIC
 § CORT-CTRL vs. CORT-CIC

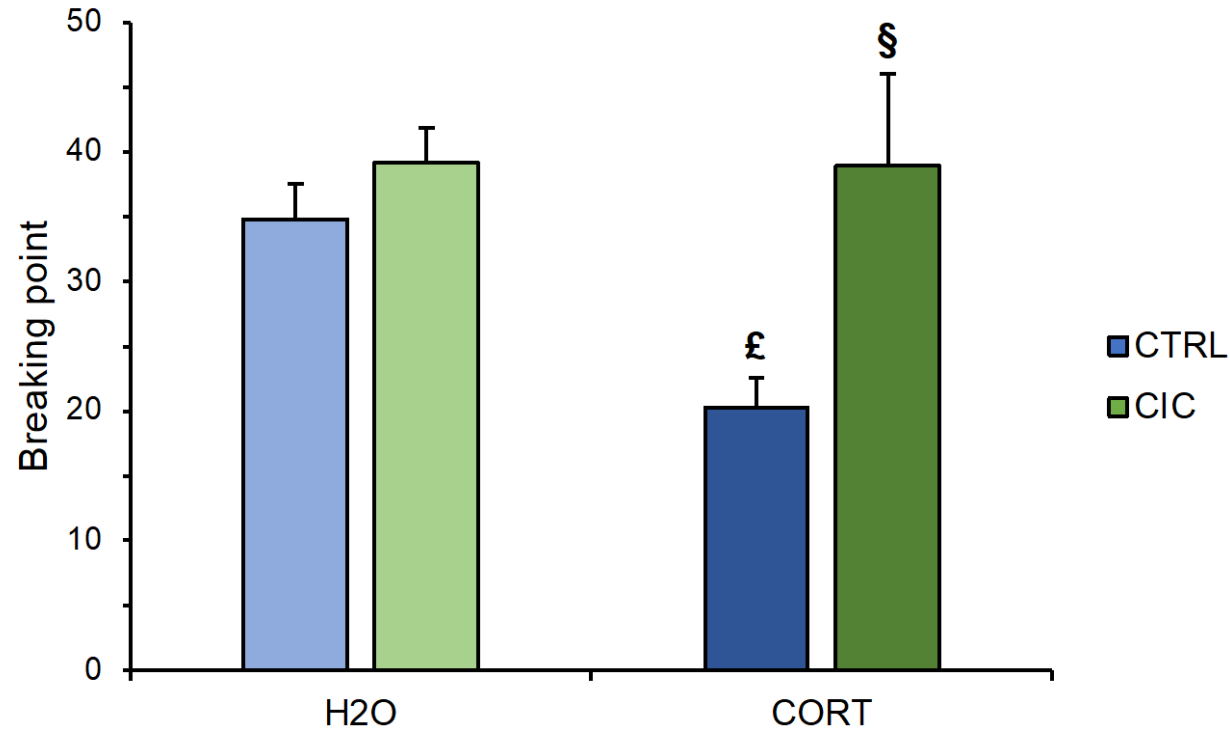
Days to criterion:
 H₂O-CTRL: 4.43 ± 0.29
 CORT-CTRL: 6.82 ± 0.23
 CORT-CIC: 4.42 ± 0.50
 H₂O-CIC: 3.73 ± 0.21



Progressive ratio test (PR)



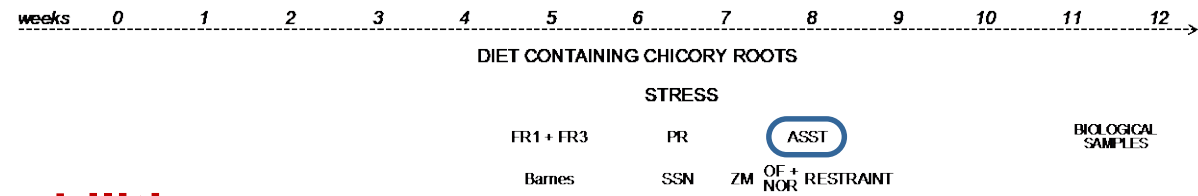
Motivation effort the subject is willing to make to obtain a reward



£ H₂O-CTRL vs. CORT-CTRL
 § CORT-CTRL vs. CORT-CIC

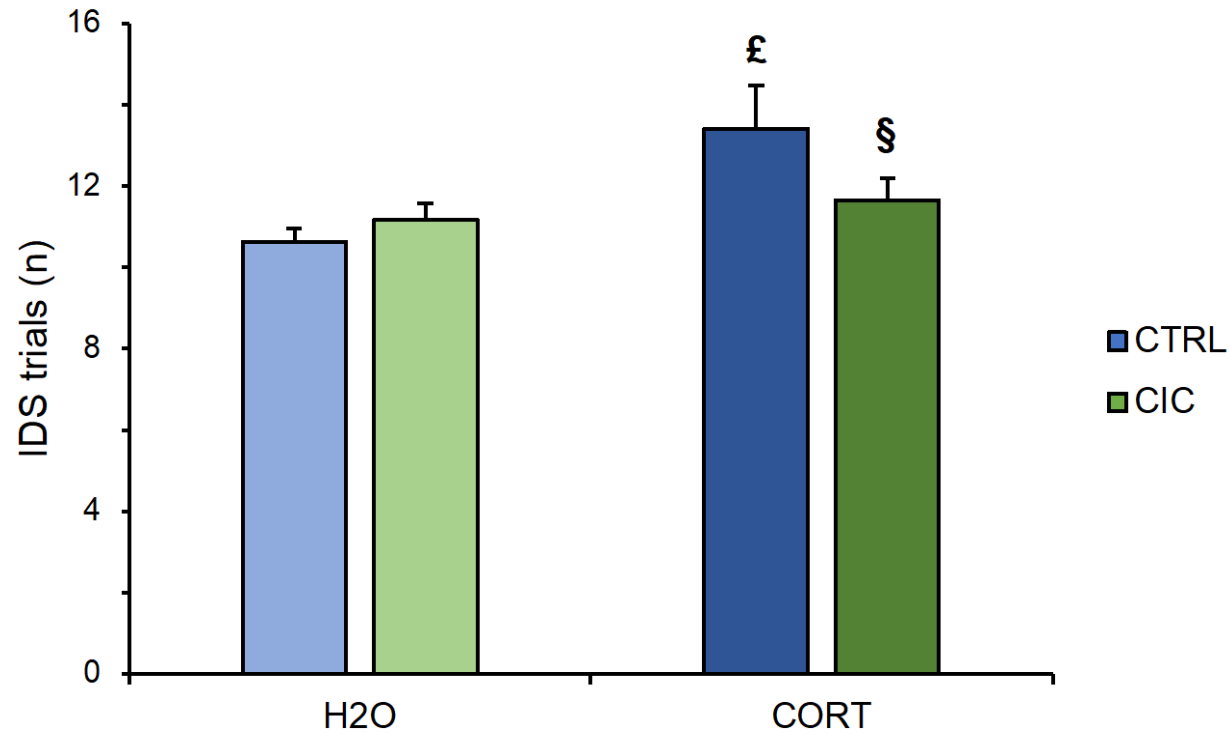
pellets	nosepokes per pellet (breaking point)	total nosepokes
1 st	3	3
2 nd	3	6
3 rd	6	12
4 th	6	18
5 th	10	28
6 th	15	43
7 th	21	64
8 th	28	92
9 th	36	128
10 th	45	173

Attentional set-shifting task



Attentional capabilities

number of trials performed to reach the criterion in the intra-dimensional shift (IDS)



£ H₂O-CTRL vs. CORT-CTRL

§ CORT-CTRL vs. CORT-CIC

Microbial distribution

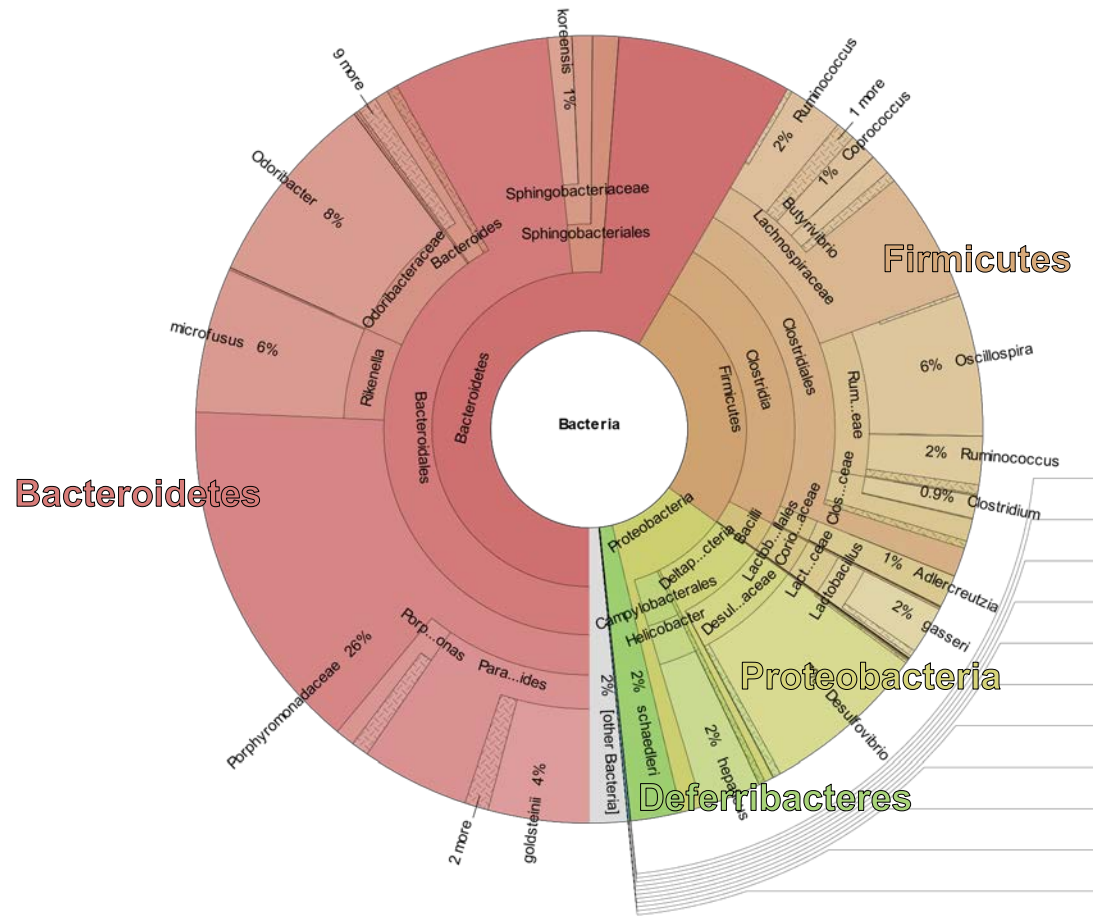
DIET CONTAINING CHICORY ROOTS

STRESS

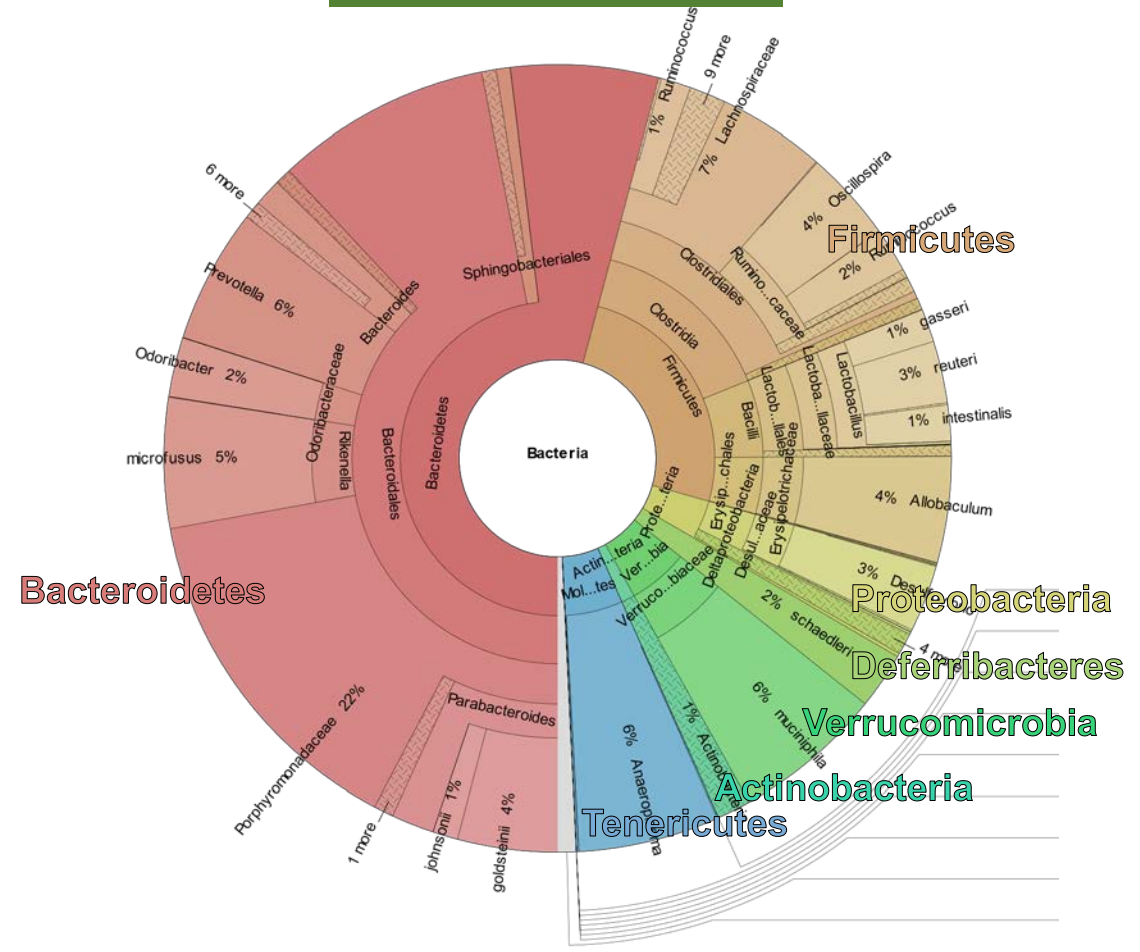
FR1 + FR3 PR ASST
Barnes SSN ZM OF + RERAINT
NOR

BIOLOGICAL SAMPLES

CORT - CTRL



CORT - CIC





	CORTICOSTERONE Detrimental effects (H ₂ O-CTRL vs. CORT-CTRL)	PREBIOTIC DIET Beneficial effects (CORT-CTRL vs. CORT-CIC)
→ Associative learning (FR)	✓	✓
→ Motivation (PR)	✓	✓
→ Attentional capabilities (ASST)	✓	✓
→ Cognitive flexibility (ASST)	✗	n/a
Spatial memory (BARNES)	✓	(✓)
Anxiety (ZM and OF)	✓	✗
Recognition memory (NOR)	(✓)	✗
Sociability (SSN)	✗	n/a
Social memory (SSN)	✗	n/a
Body weight	✓	✓
→ Basal corticosterone	✓	✓



Can we translate this study to the ISS?



Software for psychometric testing



<https://spinoff.nasa.gov/fine-motor-skills-app>.

CREDIT: NASA/ P. Whitson

Packing and delivery of chicory roots



https://en.wikipedia.org/wiki/Space_food#/media/File:ISSSpaceFoodsAssortment.jpg.

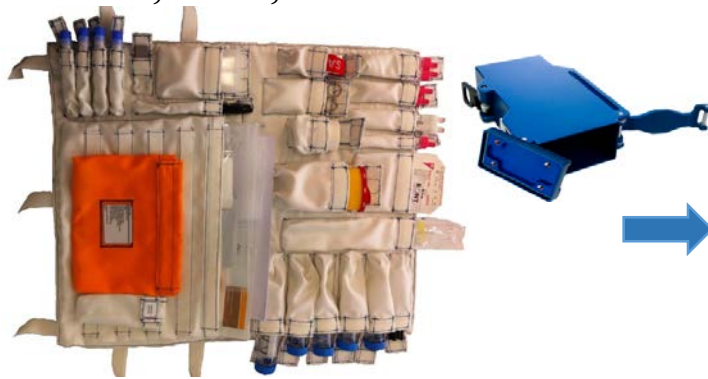
CREDIT: WIKIPEDIA



Design and development of sampling kits to collect blood, faeces, urine, and hair

On board facilities to collect, process, and keep biological samples

ISS



CREDIT: Kayser Italia



CREDIT: NASA



CREDIT: ESA



CREDIT: ESA/NASA/ T. Pesquet

Upload of sampling kits



Analysis of samples



Download of samples





Grazie dell'attenzione

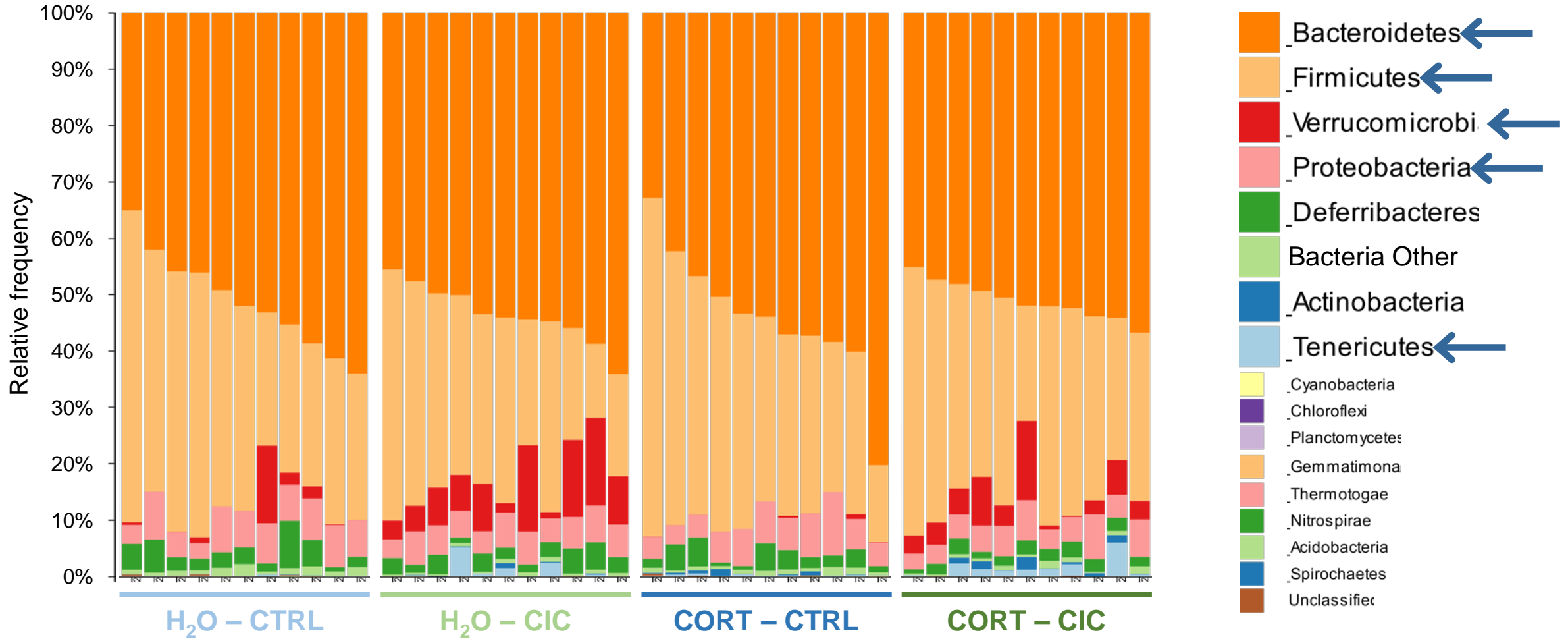


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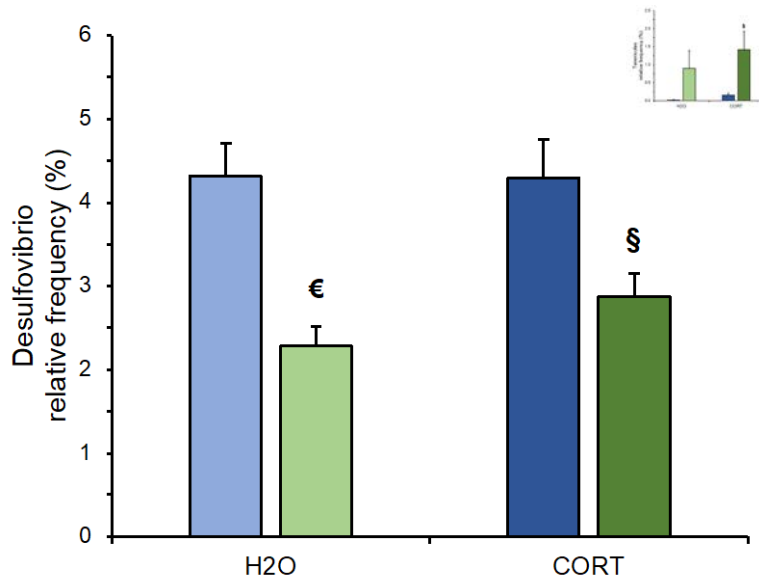
Microbial distribution at phylum level



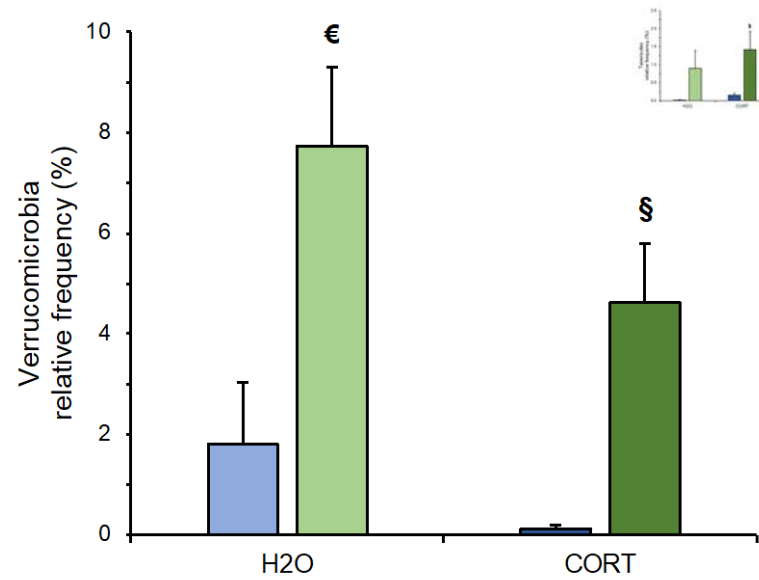
- Prebiotic supplementation effectively shifted microbiota composition in both non-stressed and stressed animals

Relative abundance of phyla Proteobacteria, Verrucomicrobia and Tenericutes

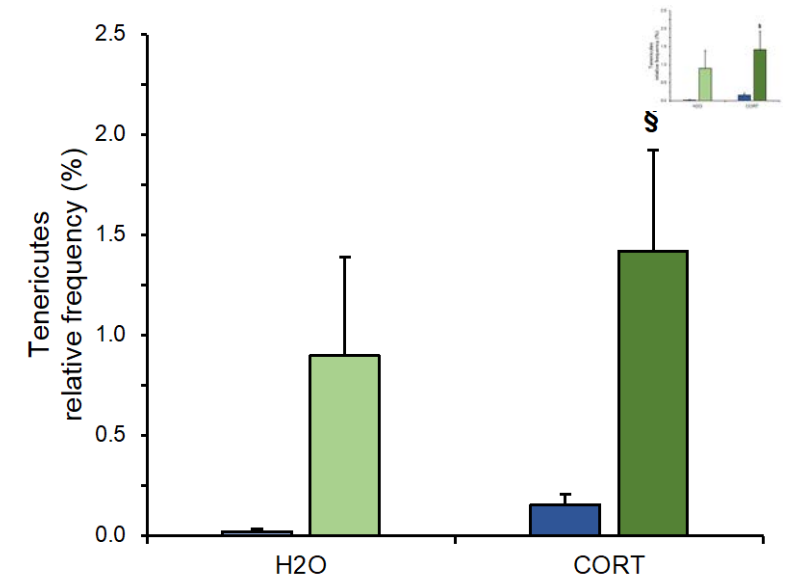
genus *Desulfovibrio*
(main representative of
phylum Proteobacteria)



phylum Verrucomicrobia
(entirely composed of
species *Akkermansia muciniphila*)

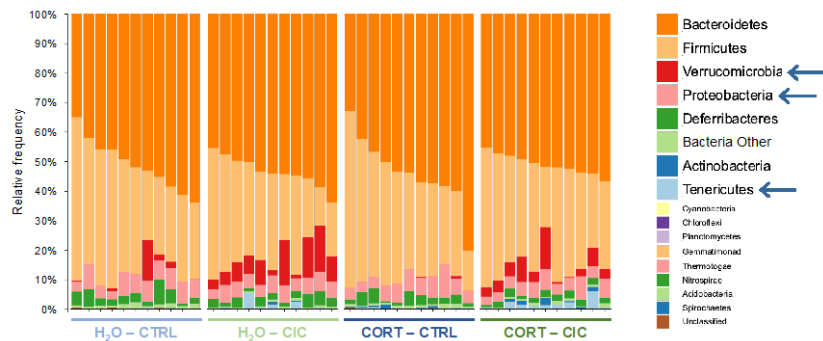


phylum Tenericutes
(entirely composed of
class Mollicutes)



€ H₂O-CTRL vs. H₂O-CIC

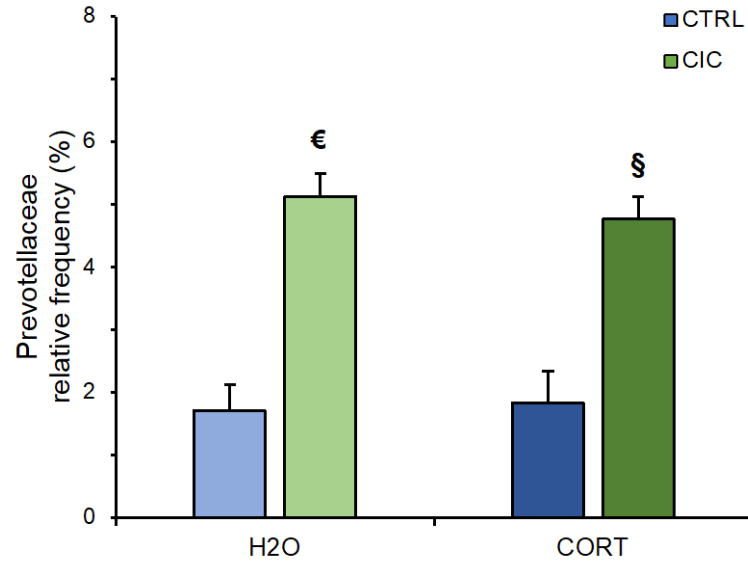
§ CORT-CTRL vs. CORT-CIC



- Significant decrease in the phylum Proteobacteria and increase in the phyla Verrucomicrobia and Tenericutes between control and prebiotic-treated mice, in both non-stressed and stressed groups

Relative abundance of selected genera of phyla Bacteroidetes and Firmicutes

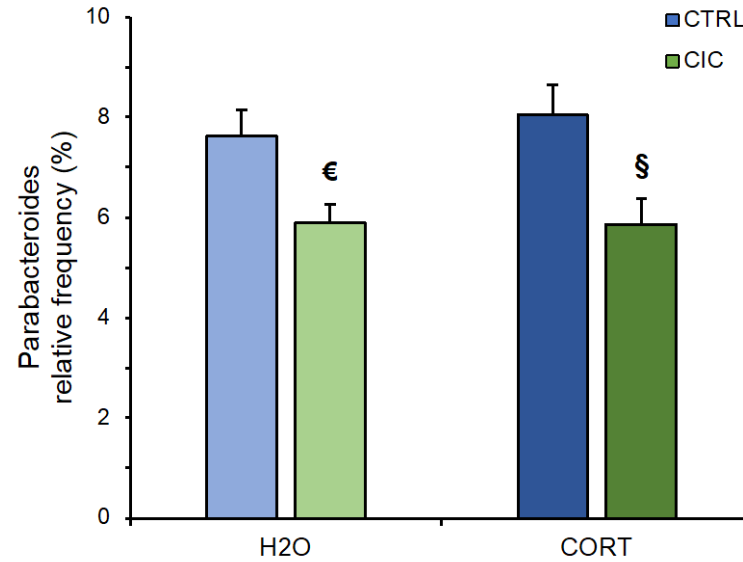
family *Prevotellaceae*
(belonging to phylum Bacteroidetes)



£ H₂O-CTRL vs. CORT-CTRL

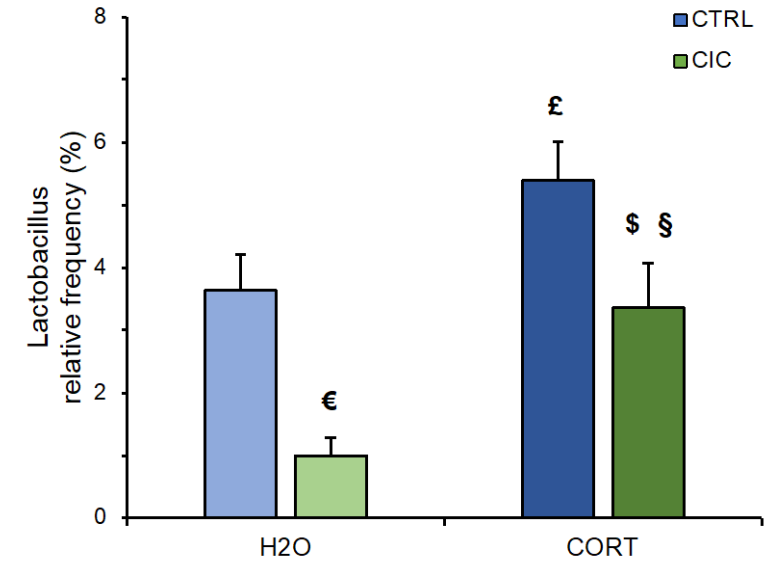
\$ H₂O-CIC vs. CORT-CIC

genus *Parabacteroides*
(belonging to phylum Bacteroidetes)

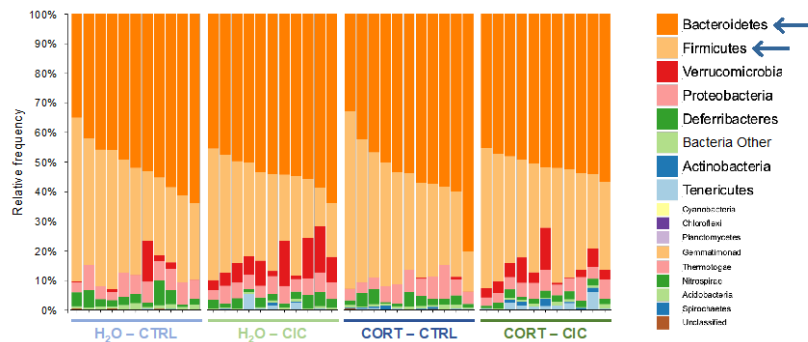


€ H₂O-CTRL vs. H₂O-CIC

genus *Lactobacillus*
(belonging to phylum Firmicutes)



\$ CORT-CTRL vs. CORT-CIC



- Prebiotic supplementation significantly increased *Prevotellaceae* and decreased *Parabacteroides*, regardless of stress exposure.
- *Lactobacillus* was significantly affected not only by the chicory diet but also by chronic stress → the stress-induced increase was fully normalized by prebiotics