Neuropeptide Y protective role on okadaic acid induced diarrhoea

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Introduction

Okadaic acid (OA) group of toxins produce Diarrheic Shellfish Poisoning after contaminated seafood ingestion leading to gastrointestinal symptoms such as diarrhoea[1,2]. These polyether compounds are synthetised by dinoflagellates of the genera *Prorocentrum* and *Dinophysis*[1,2]. Proteins Phosphatases (PPs), mainly PP1 and PP2A, are the known target of these phycotoxins[1]. However, some information arise the possibility of OA affecting other pathways that would result in diarrhoea. A wide variety of diarrheic agents have been described to alter in the Enteric Nervous System[3]. Neuropeptide Y (NPY) is a neuronal-origin peptide present in enteric and sympathetic neurons that exert an antisecretory tone[4,5]. Previous *in vitro* studies have described that OA reduces NPY expression and release[6,7]. Thus, we aimed to assess the effects of NPY on OA induced-diarrhoea.

Conclusion

NPY pre-treatment improves OA-induced damage in colon epithelial barrier at 2 h of treatment.

Methods

➢ ***In vivo assay.***

1. Mice were placed individually in metabolic caged and fasted overnight (5% glucose serum).
2. Animals were given 450 µg/kg NPY followed by 500 µg/kg OA 15 minutes afterwards.
3. Food and water were provided *ad libitum*.
4. Information regarding diarrhoea onset, changes in body weight, food and water consumption (a), along with symptoms (c) were recorded
5. During necropsy anatomopathological examination took place and samples from small and large intestines were removed and processed for Transmission Electron Microscopy (b).

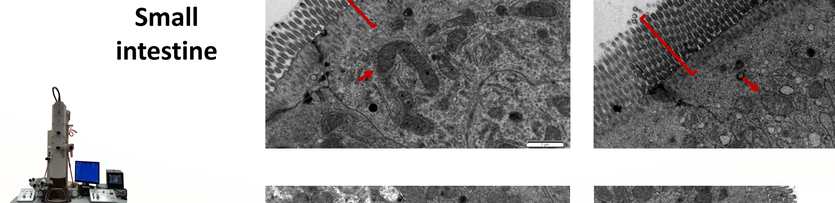
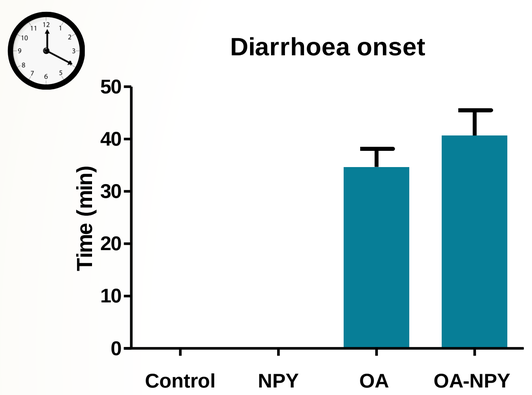
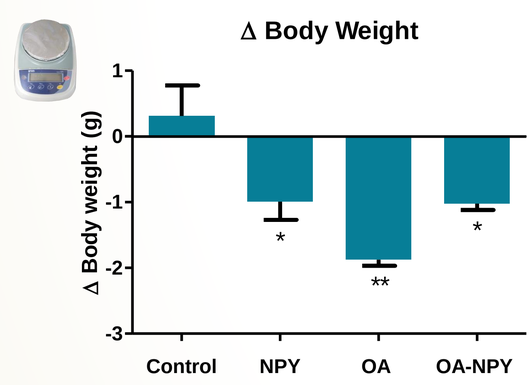
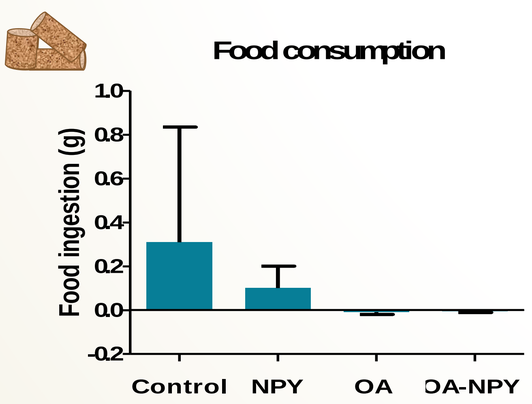


Fig. 1. Timeline scheme of the *in vivo* assessment.

a — Physiological variations







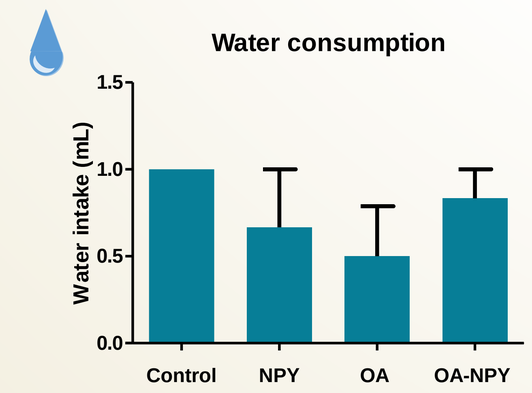


Fig. 2. Diarrhoea onset time, body weight variation, food and water intake. Asterisks indicate significant differences *versus* Control (P<0.05*, P<0.01**).

b — Symptomatology

Table 1. Symptomatology developed.

Symptoms	Control	NPY	OA	OA-NPY
Apathy	0	0	0	1
Piloerection	0	0	1	1
Cyanosis	0	0	2	1
Spasms	0	0	1	0
On-hind legs	0	0	2	2
Squint eyes	0	0	5	1
Diarrhoea	0	0	5	5
Mortality	0	0	0	0
Total mice	3	3	5	5

c — Macro- and Microscopic evaluation

Fig. 3. Anatomopathological representative images (Abdominal cavity) and Transmission Electron Microscopy of small and large intestines (scale bar 1 µm). Mitochondria (red arrows) and microvilli with the terminal web (red bracket) are indicated.

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