

AperTO - Archivio Istituzionale Open Access dell'Università di Torino

Metabolic and behavioral sex-related differences induced by conditional inactivation of Npy1r gene in mice

This is the author's manuscript

Original Citation:

Availability:

This version is available <http://hdl.handle.net/2318/1885174> since 2023-01-10T14:19:24Z

Terms of use:

Open Access

Anyone can freely access the full text of works made available as "Open Access". Works made available under a Creative Commons license can be used according to the terms and conditions of said license. Use of all other works requires consent of the right holder (author or publisher) if not exempted from copyright protection by the applicable law.

(Article begins on next page)

Metabolic and behavioral sex-related differences induced by conditional inactivation of *Npy1r* gene in mice

Alessandra Oberto^{abc*}, Ilaria Bertocchi^{abc*}, Angela Longo^a, Paola Palanza^d and Carola Eva^{abc}

^a Neuroscience Institute of the Cavalieri-Ottolenghi Foundation, 10043 Orbassano (Turin), Italy; ^b Department of Neuroscience, University of Turin, 10126 Turin, Italy; ^c Neuroscience Institute of Turin; ^d Department of Medicine and Surgery, University of Parma, 43100, Parma, Italy

Sex differences affect brain, behavior and metabolic functions, and contribute to vulnerability to disease; the mechanisms underlying the sex specificity of brain activity is, however, poorly known. Sex-biased effects of selective gene deletion have been reported in mice models relevant for emotional and stress-related behaviors and metabolic functions. Despite this evidence, the vast majority of rodent researchers continue to use exclusively males in their studies, and information on sex differences in these regards is sparse.

NPY is one of the most abundant neuropeptide within the CNS. In the hypothalamus, NPY is synthesized by ARC neurons, projecting to other nuclei of the circuit controlling food intake, including the PVN, VMH, and DMH nuclei. NPY is identified to date as the most potent orexigenic peptide and its chronic central administration produces hyperphagia, robust obesity and decreased thermogenesis. In addition, NPY plays a key role in the regulation of balance between reproductive functions and energy homeostasis via the activation of Y1Rs. Thus, in the hypothalamus NPY acts as integrator among feeding circuit, stress signals and neuroendocrine system.

The NPY-Y1R system is sexually dimorphic and sensitive to gonadal steroids.

We have previously generated a conditional knockout mouse model (*Npy1r^{rfb}* mice), in which the *Npy1r* gene was specifically inactivated in forebrain principal neurons starting from juvenile age. Here we demonstrated that *Npy1r^{rfb}* mice show a sex dimorphic phenotype, revealing the existence of NPY-Y1R neuronal subpopulations involved in sex-related differences of metabolic and behavioral functions.

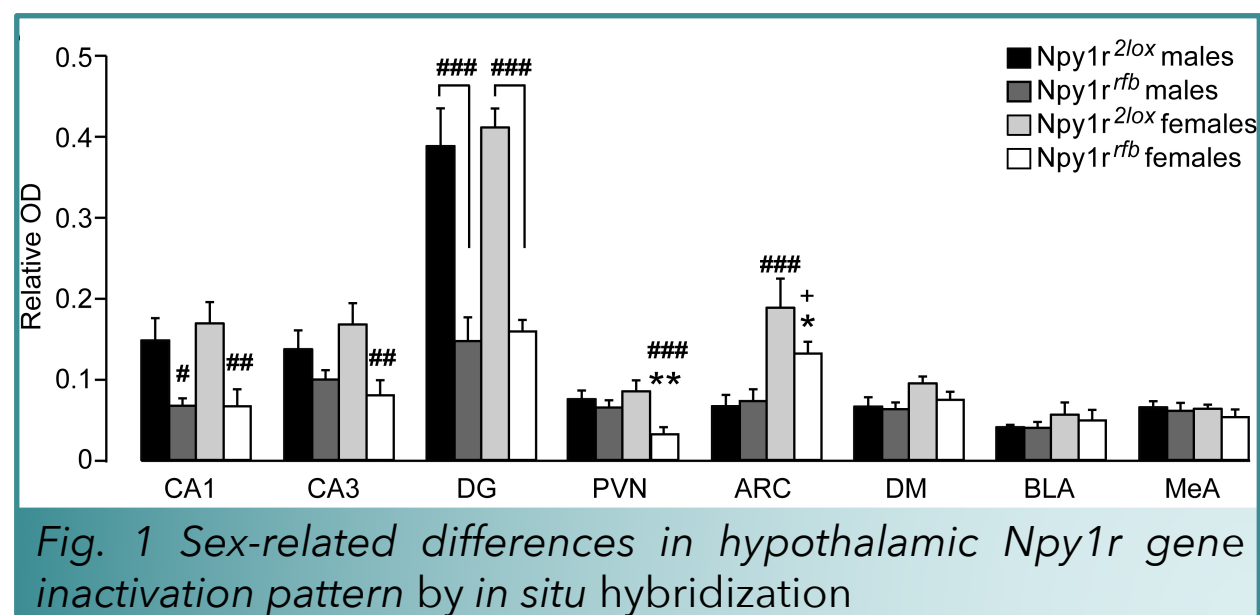


Fig. 1 Sex-related differences in hypothalamic *Npy1r* gene inactivation pattern by *in situ* hybridization

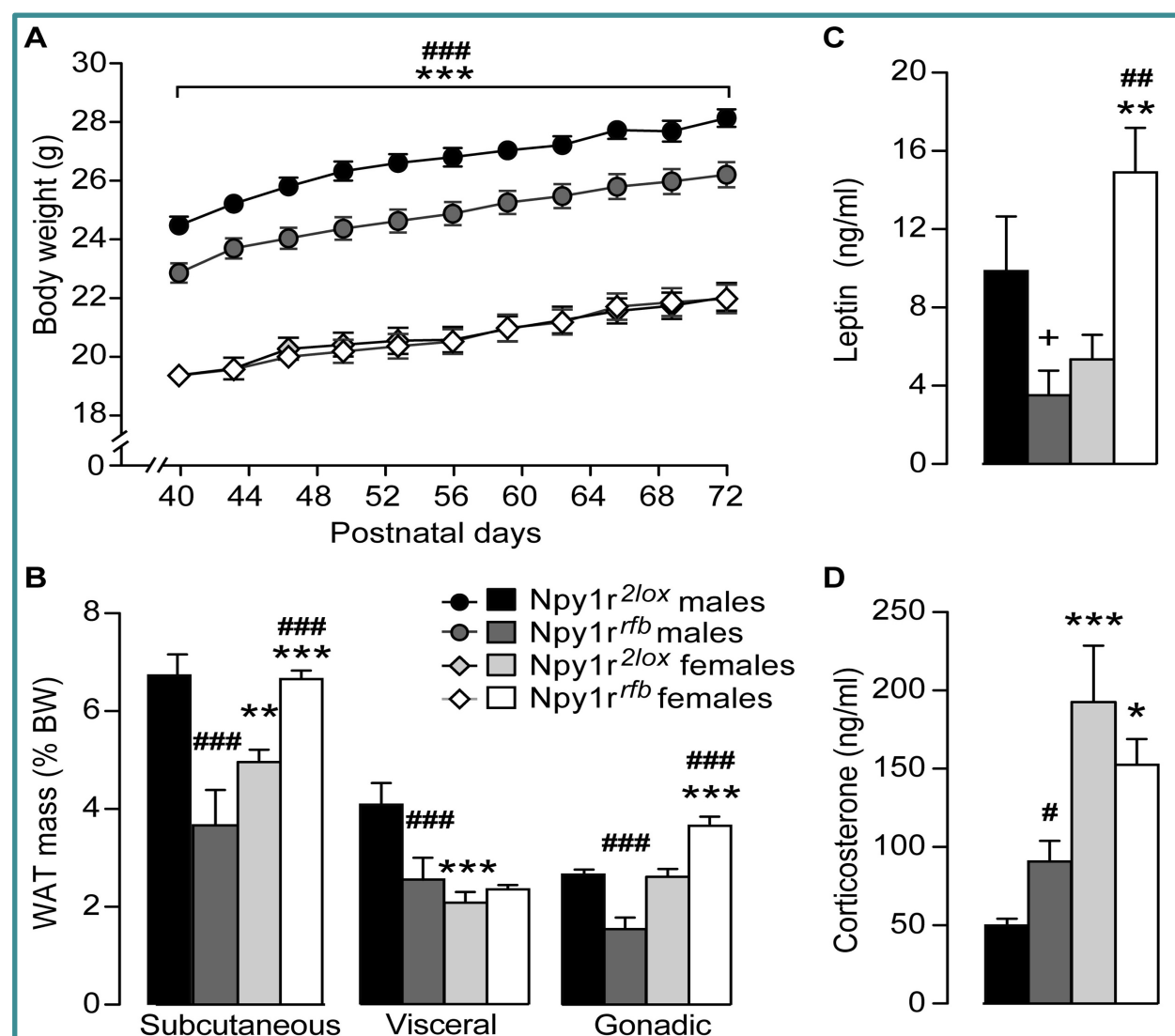


Fig. 2 Conditional *Npy1r* gene inactivation diversely affected body weight growth, WAT weight and hormone serum levels in male and female mice

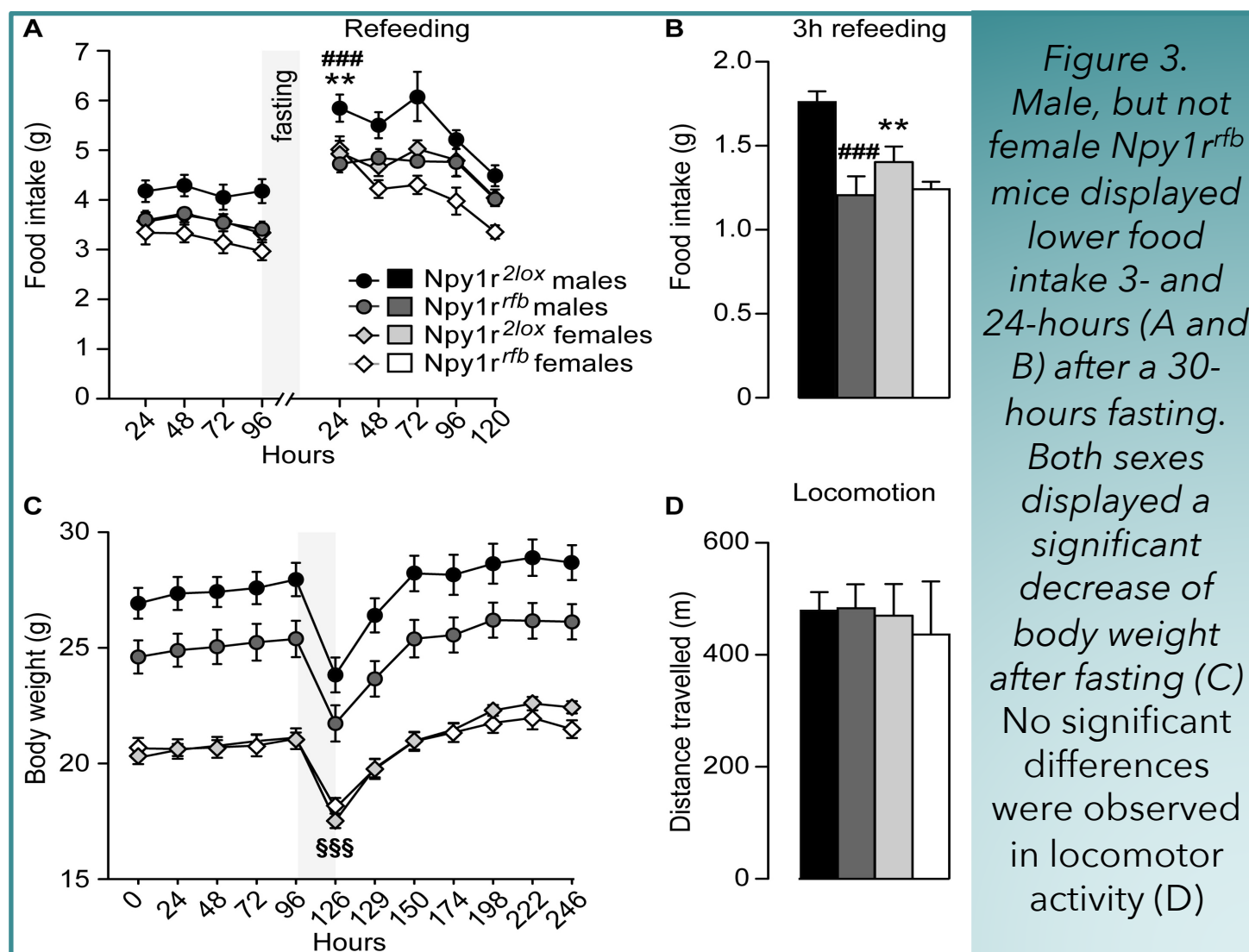


Figure 3. Male, but not female *Npy1r^{rfb}* mice displayed lower food intake 3- and 24-hours (A and B) after a 30-hours fasting. Both sexes displayed a significant decrease of body weight after fasting (C) No significant differences were observed in locomotor activity (D)

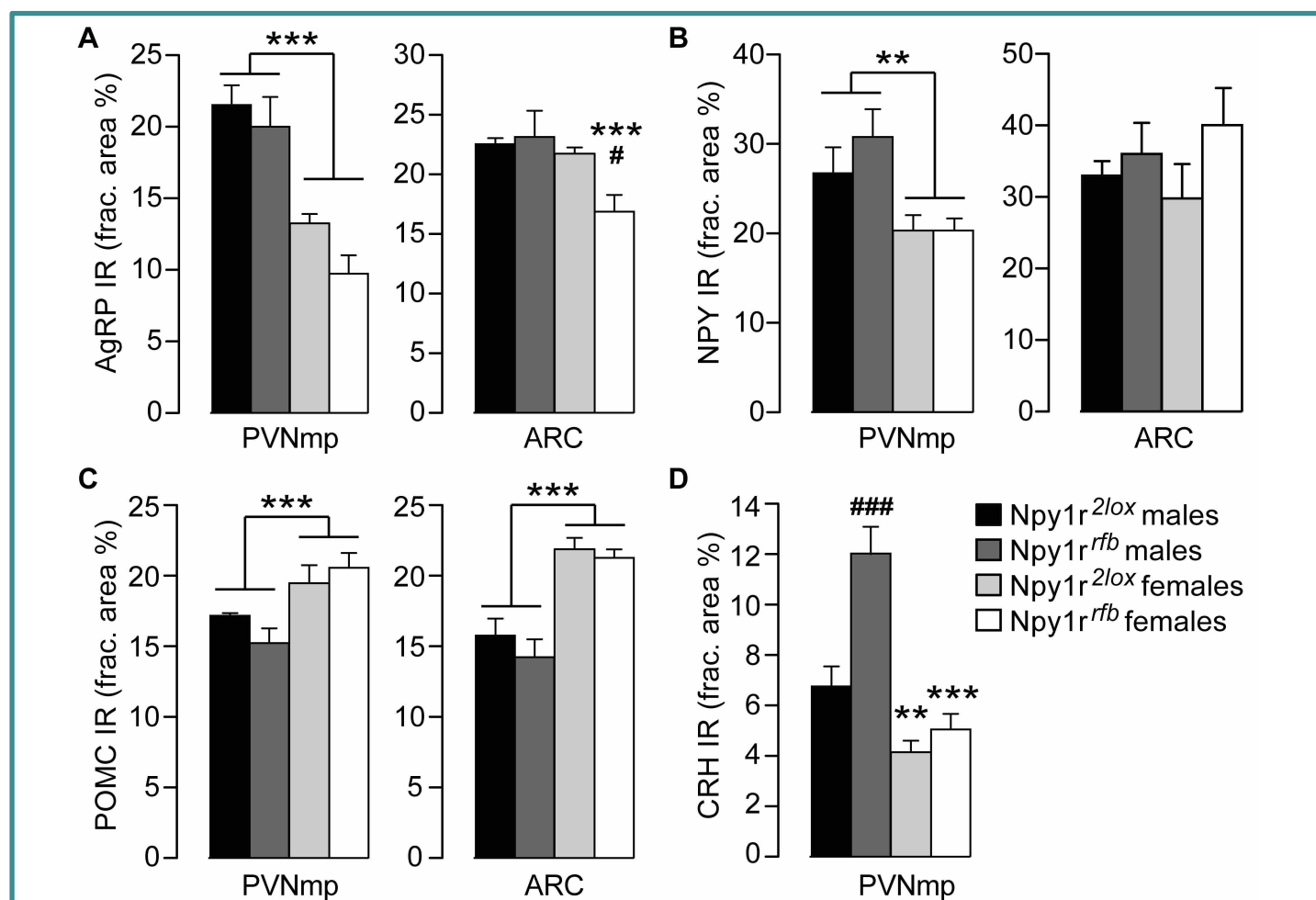


Fig. 4 Female mice showed lower AgRP, NPY and CRH-IR signal in the PVNmp and higher POMC IR in PVNmp and ARC compared to males. Female, but not male, *Npy1r^{rfb}* mice showed a significant decrease of AgRP-IR in the ARC. Male, but not female, *Npy1r^{rfb}* mice displayed an increase in CRH-IR in the PVNmp compared with male *Npy1r^{2lox}*

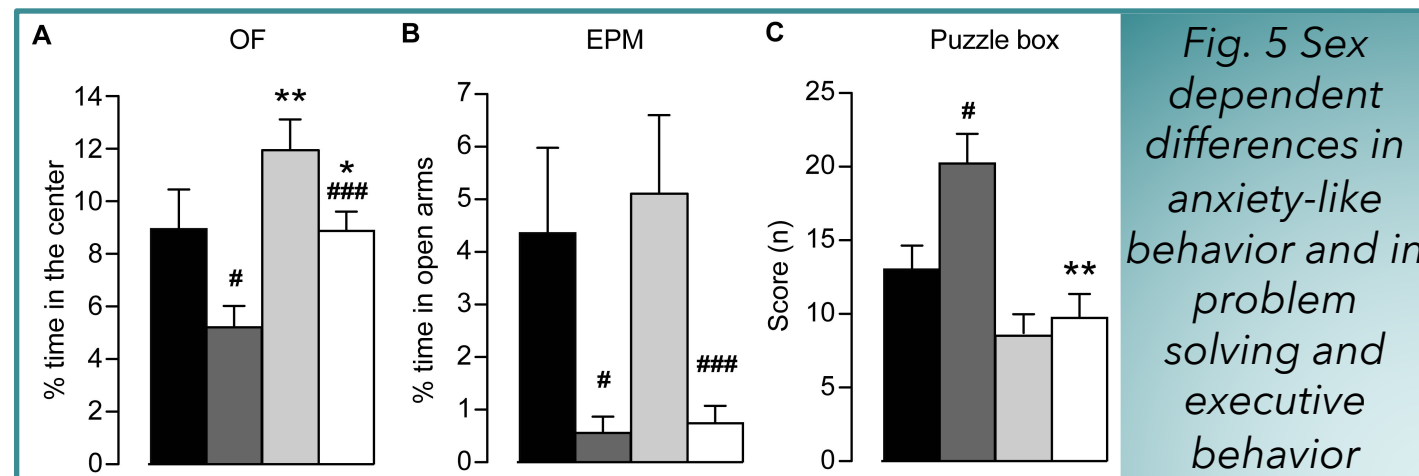


Fig. 5 Sex dependent differences in anxiety-like behavior and in problem solving and executive behavior

DISCUSSION

Here we demonstrated that the conditional knockout of *Npy1r* gene differentially affected male and female phenotype, with males showing metabolic, hormonal and behavioral effects and females being only marginally impacted. Our results indicate that female mice are resilient to the effects of limbic *Npy1r* gene inactivation on hormone and metabolic functions, suggesting the presence of an estrogen-dependent relay necessary to ensure the maintenance of the homeostasis also in case of Y1R malfunctioning.

Sources: This work was supported by Cariplo Foundation, Compagnia di San Paolo, Torino and Fondazione CRT, Torino



<https://forum2020.fens.org/poster-presentations/>

Per info su come fare il poster

The FENS 2020 Virtual Forum platform is designed to allow you and neuroscientists from all around the globe to easily navigate hundreds of sessions and thousands of e-posters AND find your research amongst them. You will be able to share your research and interact live with your fellow delegates during your allocated poster sessions and also have the option to make your e-Poster and audio recording after the Forum for up to 3 months.

All accepted poster presenters are invited to upload an e-poster as a 1-page file.

Please note that the upload service will be available until 2 July 2020

The link to upload your e-poster will be sent in June. You will also be informed of the scheduling of your poster sessions.

What will my e-poster look like?

Each e-poster consists of a pdf and a mp3 audio file. All poster presenters may record a 3-min MP3 file to introduce their poster and a chat window will be permanently open for every poster. The recorded introduction will be accessible from the e-poster viewing center, accompanied also by the submitted abstract.

Technical specification for e-poster preparation

In order to create your e-poster, you can [download](#) the PowerPoint template which already has the right dimensions and recommended font sizes. Please save your final e-poster as a **PPTx** before uploading.

Please submit your e-poster as a 1-page PPTx-file in portrait orientation.

Please note the following technical requirements:

File format: PPTx only

Poster size in pixel: 1080 width x 1536 height – portrait orientation

Poster size in cm: 38,1 width x 54,2 height – portrait orientation

Font size: ≥16

In case you wish to add a video to your e-poster, please keep these requirements in mind:

File format: .PPTx only

Video formats: .mp4, .mpg, .mov, .avi

Max. file size: 50 MB

Max. number: 5 videos

Sound: not supported

Recording your MP3 audio file inside your e-poster

For instructions on how to record a short audio file inside your e-poster click [here](#).

For tips on recording your e-poster audio guide, please watch the video [below](#).

How will networking be organised for my e-poster?

The FENS 2020 Virtual Forum will host seven topically oriented poster sessions where presenters of each poster will be featured at two different sessions. Authors are requested to remain in attendance during the entirety of these two sessions dedicated to their topic, and are furthermore encouraged, if at all possible, to include a URL, linking to their own personal or institutional e-meeting rooms, where they can then meet other delegates face to face during their poster presentation. Zoom and other e-meeting services offer that owners may schedule "[recurring meetings](#)" with one fixed URL.

How can I secure my e-poster and presentation when it is online?:

FENS enforces a strict non-tolerance for illegal copying of content that is presented via the virtual FENS Forum platform (see [Code of Conduct at FENS Forums](#)). Presenters are encouraged to clearly indicate in their presentations that the content presented shall not be shared or copied. Presenters are furthermore strongly advised to secure a Digital Object Identifier (DOI) for their presentation by uploading it to an open data sharing repository for posters and slides such as the [Gates Open Research platform](#) or similar.

Presenters are strongly encouraged to clearly indicate whether or not photography/recording of the poster, presentation and sharing/remixing of the material is permitted. To aid in this process, FENS will provide presenters with a digital graphic Image to incorporate into their slides/poster or to print and display. The images are available [here](#).

Tips for your e-poster audio guide