Region-specific effects of IGF-1 and oxytocin in MeCP2 KO mice

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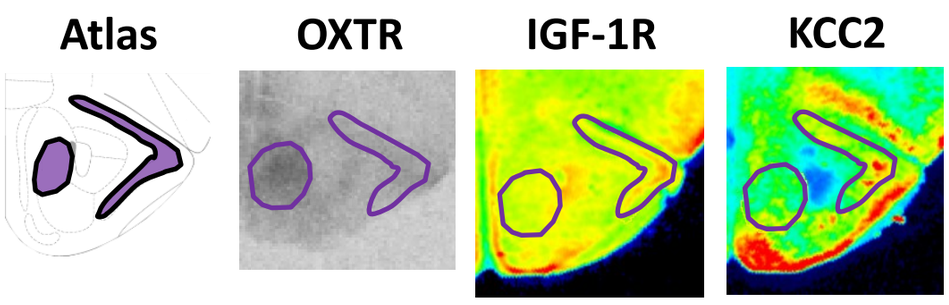
INTRODUCTION

- The K^+/Cl^- cotransporter 2 (KCC2) is one of the main regulators of the excitation:inhibition (E/I) balance in neurons (*Chamma et al., Front. Cell. Neurosci., 2012*).
- The neuropeptide Oxytocin (OXT), via its oxytocin receptor (OXTR), modulates KCC2 perinatally to establish an appropriate E/I balance (*Leonzino et al., Cell Rep., 2016; Tyzio et al., Science, 2014*).
- Methyl-CpG binding protein 2 (MeCP2) hemizygous knock-out male mice (MeCP2 KO) show deficits in KCC2, and treatment with rhIGF-1 rescues the phenotype of these mice by normalising KCC2 levels (*Banerjee et al., PNAS, 2016*).

IS KCC2 A COMMON TARGET OF IGF-1 AND OXT IN MeCP2 KO MICE?

METHODS

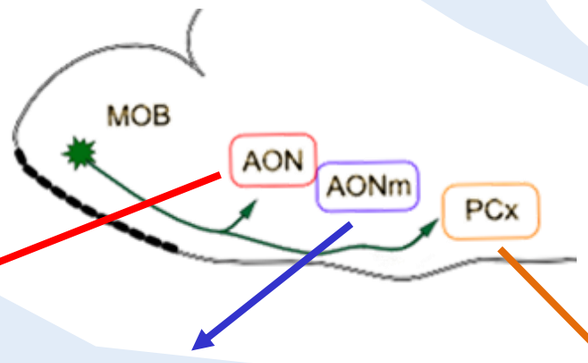
- We studied the olfactory system and the hippocampus CA2/3, because they are very plastic, and express high levels of OXTR and IGF-1 receptor (IGF-1R).
- We treated mice with vehicle, rhIGF-1 (0.25 mg/kg, i.p., for 10 days) or OXT (≈20 µg/kg, i.n., twice/day for 10 days).
- Autoradiography with selective iodinated radioligand for OXTR mapping and quantification.
- Infra-Red immunostaining for IGF-1R and KCC2 mapping and quantification.



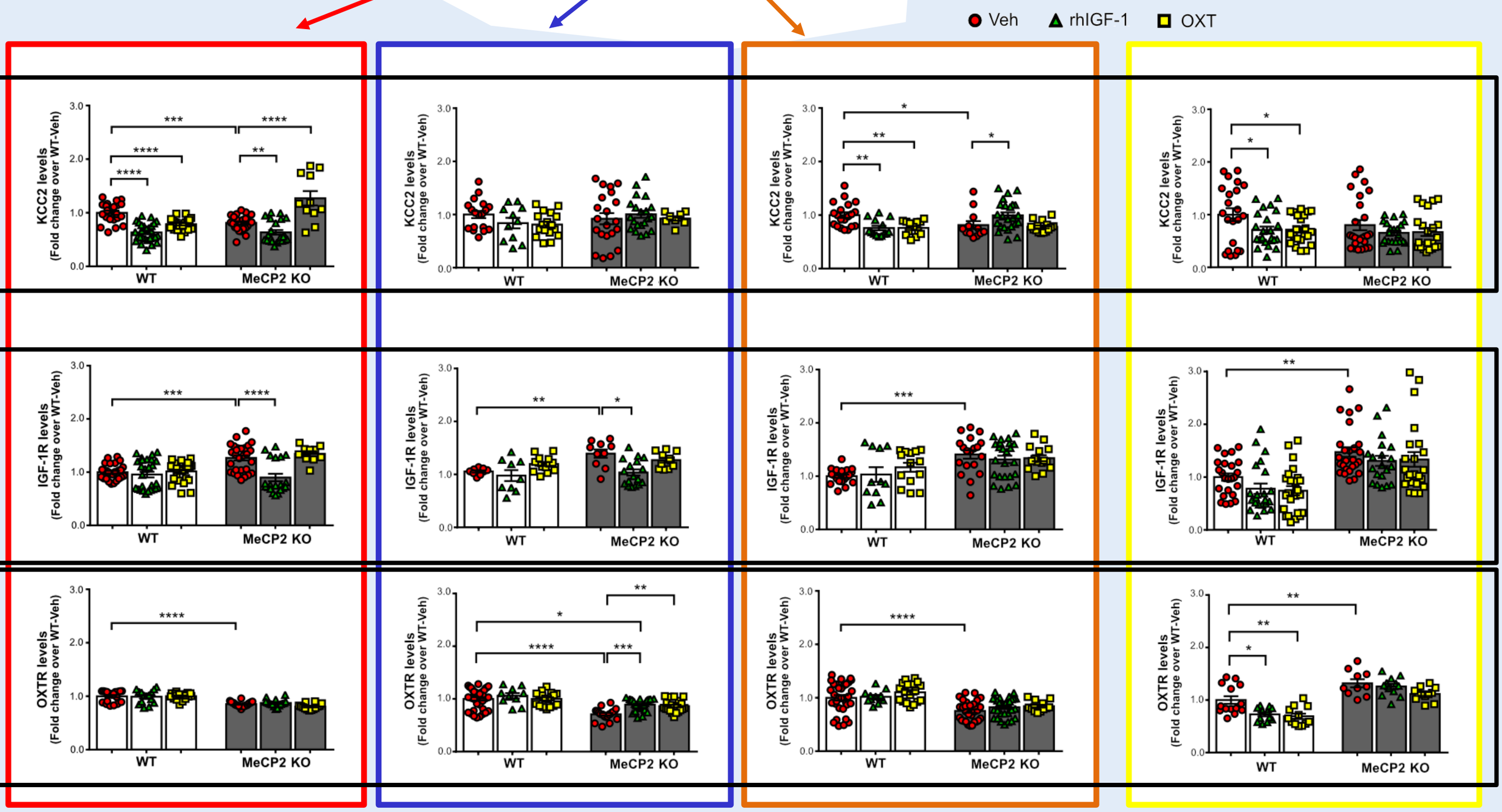
RESULTS

OLFACTORY SYSTEM:

Anterior Olfactory Nucleus (AON)
Anterior Olfactory Nucleus, medial part (AONm)
Piriform Cortex (PCx)



HIPPOCAMPUS CA2/3



Single observations (left and right hemisphere) are displayed; N = 2-3 mice/group, 4-8 observations per mouse. *p<0.05, **p<0.01, ***p<0.001, *p<0.0001, Two-way ANOVA and Bonferroni *post hoc* test.

CONCLUSIONS

1) The alterations of the OXTergic and IGF-1R system in olfactory areas suggest that combinations of OXT and IGF-1 may have combinatorial therapeutic effects in Rett syndrome patients.
2) The region specific variations in OXTR and IGF-1R levels in different brain regions before and after treatment suggest the need to evaluate region-specific therapeutical treatments.
3) The alterations of the OXTergic system in olfactory areas need further investigation to understand whether they may subtend social behavioural alterations in MeCP2 KO mice.