Review of: "Oxytocin neurons enable social transmission of maternal behaviour"

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The presented manuscript is highly interesting because contains a new methodological paradigm and new insights into the understanding of developing parental behavior. First methodologically manuscript in line with a new direction of research of mouse behavior – a synchronized combination of behavioral task/home cage observation and one of the methods to study neuronal populations in vivo (calcium imaging, photometry, electrophysiology) in specific regions and cells of interest. Specifically in the case of this research - the behavior of cohoused dam and verging mice and neuronal recordings in PVN oxytocin neurons. Secondly, the authors demonstrated dam-virgin female interaction resulting in the social transmission of parental behavior and specific behavior of dam (Shepherding). The authors identified the role of visual cues from the dam and USV cues from pups and the role of the oxytocinergic system in those processes.

These interesting findings provide new information. From my side, I have several points to suggest.

1) Authors well discussed and showed the role of visual and auditory cues. But what about olfactory cues? It will be good to discuss the role of this cue in the introduction and discussion. For example in another context of transmission of parental information (from mother to father) – olfactory cue is one of the crucial. If a mother in transparent box visual cue is presented while the olfactory cue is disrupted, and father cannot retrieve pups)

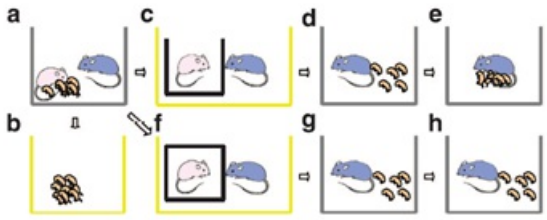
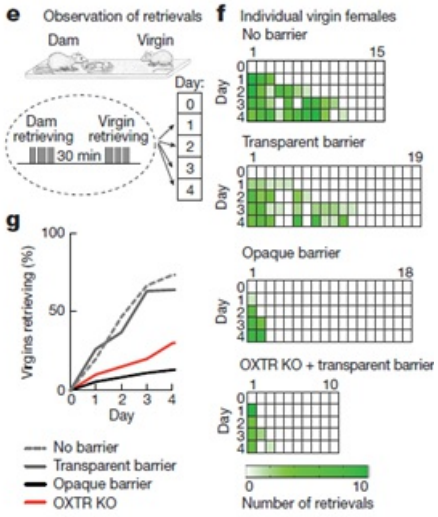


Figure 4a-h, Liu et al. Nat. Commun. 2013

However, I guess there is a big difference in the transmission of information from the dam to a virgin. Because authors performed an experiment with opaque barrier where visually cue disturbed but olfactory

cue remain and in that situation retrieving from virgin female dramatically decreased. Hence the possible role of the olfactory cue is minimal.



(Figure 3e-g; Carcea et al. Nature, 2021)

2) Authors described a link between USV emitted by pups and the oxytocinergic system by recordings from left PVN with photometry from the left auditory cortex, together with audio recordings of pup vocalizations during dam pup retrieval. The interesting point is the ability to use the setup established by authors for the investigation of other USV cues. Where the frequency of distress calls of pups goes in an interval of 40-90kHz, there is a unique distress call of dam emitted with frequency 38kHz (Liu et al. Nat. Commun. 2013). Again, this call can induce paternal behavior in the father but what about virgin females? It will be curious to see the response of PVN and the auditory cortex of virgin on this stimulus (for example in a situation where dam separated from pups and from virgin by opaque/transparent barrier, in this context dam emitted 38kHz sound)

3) Regarding the social transmission of parenting skills, what about the breeding conditions of the dam itself? The authors indicated Bl6j mice were isolated until experiments. It means, by themselves, they did not get social facilitation from other dams. And what about breeding to produce pups from the dams. They were paired one by one with male, or it was several dams with one sire? Especially interesting, level of shepherding in the dam to virgin depended on previous experience or not? Can own experience of a dam affect its activity to a virgin?

4) Regarding the long-term effect of social facilitation of alloparenting it is interesting to compare the level of infanticide in primiparous dams without prior social transmission of parenting or with it.

5) Data of DREADD inhibition of OT neurons in PVN and experiments with OXTRKO mice highlighted the

role of Oxytocin in maternal behavior itself and transmission of parenting skills. Previously known that blocked release of oxytocin in PVN (CD38KO model, Jin et al., Nature 2007) or knockout of OXTR (Takayanagi et al. PNAS, 2005) leads to moderate to a severe deficit in maternal behavior but not abolished it completely. While transmission of parental behavior can be blocked this way. For example, CD38KO fathers completely lose the ability to get cues from dams and demonstrate the total absence of paternal behavior (Akhter et al. Molecular Brain 2013). Authors enhanced that knowledge, demonstrating loss of ability to learn in virgin in OXTRKO mice and by modulation of OXT neurons in PVN by inhibitory DREADD (however did not disturb retrieval behavior itself if virgin already acquired parenting behavior). Altogether, current data suggest oxytocin is important but not critical neuropeptide for maternal behavior itself but crucial for social transmission of parenting behavior to different animals (virgin females or sires) via different sensory cues.

In conclusion, the manuscript is well-written. Authors employing a broad spectrum of models and techniques to research new aspects of parental behavior and its transmission and finally text give some ideas for future research in this direction.