



An Investigation of Oxytocinergic Modulation of Striatal Dopamine Neurochemistry and Behavior in the Male Prairie Vole



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Prairie Voles



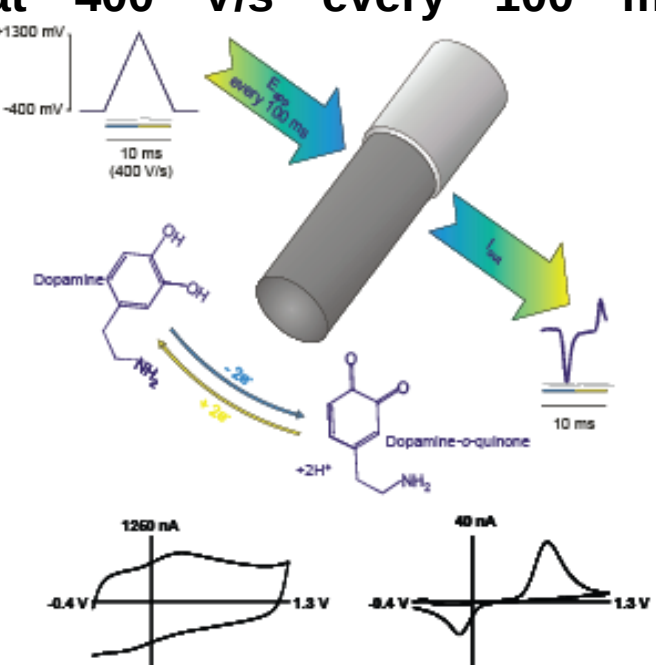
The socially monogamous prairie vole (*Microtus ochrogaster*) serves as an ethologically sound model to study social attachments as it utilizes selective social bonds in its life history strategy (Carter et al., 1995; Getz et al., 1993; Kleiman, 1977). Prairie voles form life long pair bonds that are characterized by the biparental care of offspring, mate guarding, and shared home territories (Carter et al., 1995; Getz et al., 1993).

Summary

The neuropeptide oxytocin (OXT) is notable for its diverse range of physiological and behavioral effects across mammalian taxa. Beyond OXT's well-documented role in modulating basic reproductive processes during parturition and lactation, OXT is also involved in the modulation of complex social behaviors such as pair bonding, mother-infant bonding, sexual behavior, and selective affiliation with conspecifics. Converging evidence from human and rodent studies indicate that OXT modulates a number of these behaviors via interactions with mesolimbic dopamine (DA) circuitry. Mesolimbic DA systems are strongly implicated in the attribution of salience and motivation towards cues for natural rewards and drugs of abuse (Robinson & Berridge 1997), suggesting that centrally released OXT may serve to modulate the attribution of incentive salience towards social cues. Here, we used male prairie voles (*Microtus ochrogaster*) to investigate the reinforcing effects of central administration of OXT via the conditioned place preference paradigm (CPP) and DA neurotransmission in the striatum using in vitro fast scan cyclic voltammetry (FSCV). The CPP paradigm has been extensively used to study the motivational or reinforcing properties of various pharmacological agents (Bardo & Bevins 1999). FSCV allows for the assessment of sub-second changes in DA concentration following stimulation of DA terminals in slice preparations. Such rapid measures allow DA release to be distinguished from DA uptake, and thus these measures are referred to as 'real-time' measures of DA concentration. Previous behavioral pharmacological studies have shown that access to both OXT receptors and DA D2 in the prairie vole striatum is necessary for the formation of a partner preference (Liu & Wang 2003). Furthermore, Aragona et al. (2006) showed that activation of D2-like receptors within the NAcc shell region, but not the NAcc core region, induced partner preferences in the absence of mating. Our work demonstrates that an intracerebroventricular (I.C.V.) infusion of a 100ng dose of OXT is ineffective for inducing a CPP. Additionally, we found no significant differences in DA release dynamics in the nucleus accumbens (NAcc) shell, NAcc core, and dorsal striatum following OXT experience in the CPP training paradigm. Together, these experiments demonstrate a need for further research on OXT's dose dependent effects on the mesolimbic DA system. Given OXT's promise as a potential therapy for drug addiction, autism, and schizophrenia, future research will result in novel insights regarding how OXT might be used in a clinically relevant context.

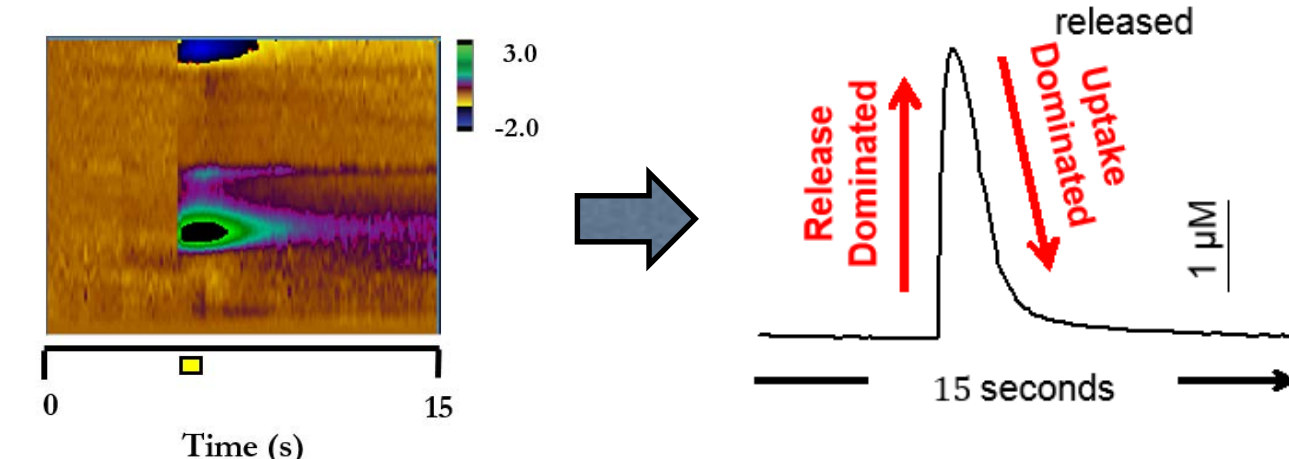
Methods

The carbon-fiber microelectrode is held at -0.4V against the reference electrode between scans and then driven to 1.2V and back in a triangular waveform at 400 V/s every 100 ms (150 measures).



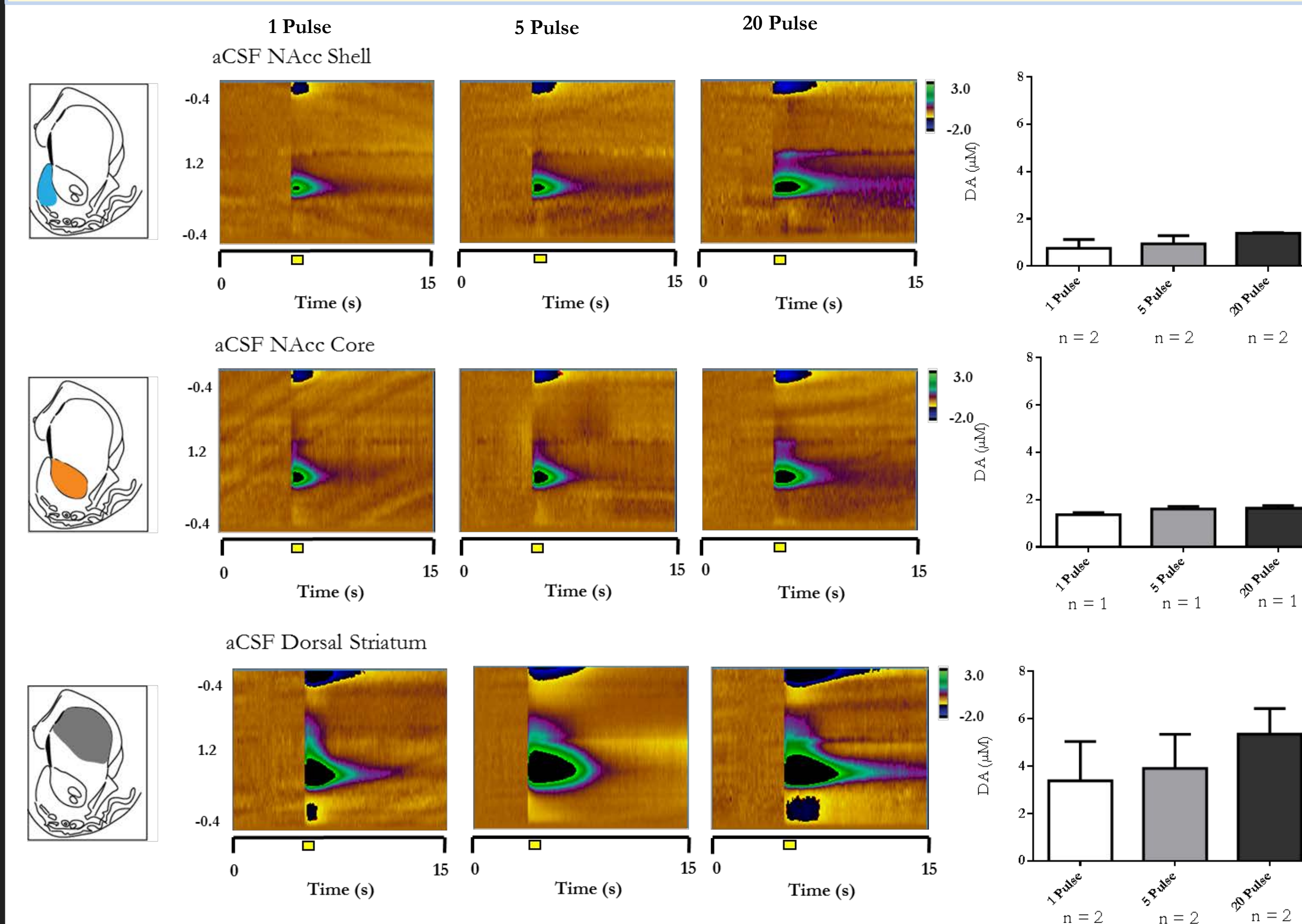
Specific chemical species are identified by the shape of their cyclic voltammograms. On the right, we show the current measured when the background is subtracted. This relatively small change in current is the result of oxidation and reduction of DA.

During in vitro slice experiments, a bipolar stimulating electrode is placed in the Nacc shell, Nacc core, or dorsal striatum. DA release is evoked by electrical stimulations (1, 5, and 20 pulse) and release and uptake are assessed with the carbon-fiber electrode.

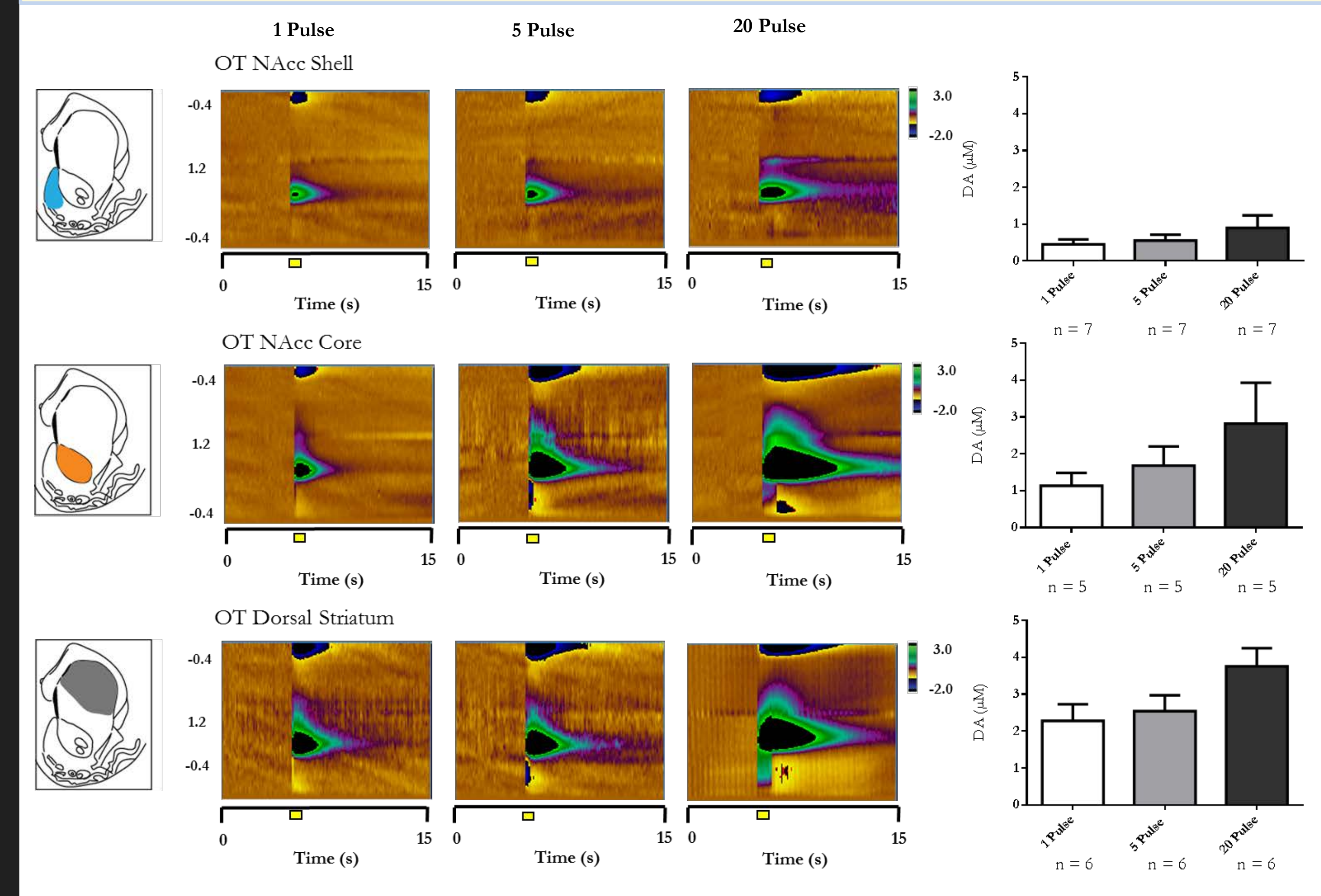


This 'color plot' shows changes in current at all points along the 150 measure scan. Electrode calibrations are performed in order to convert current to DA concentration.

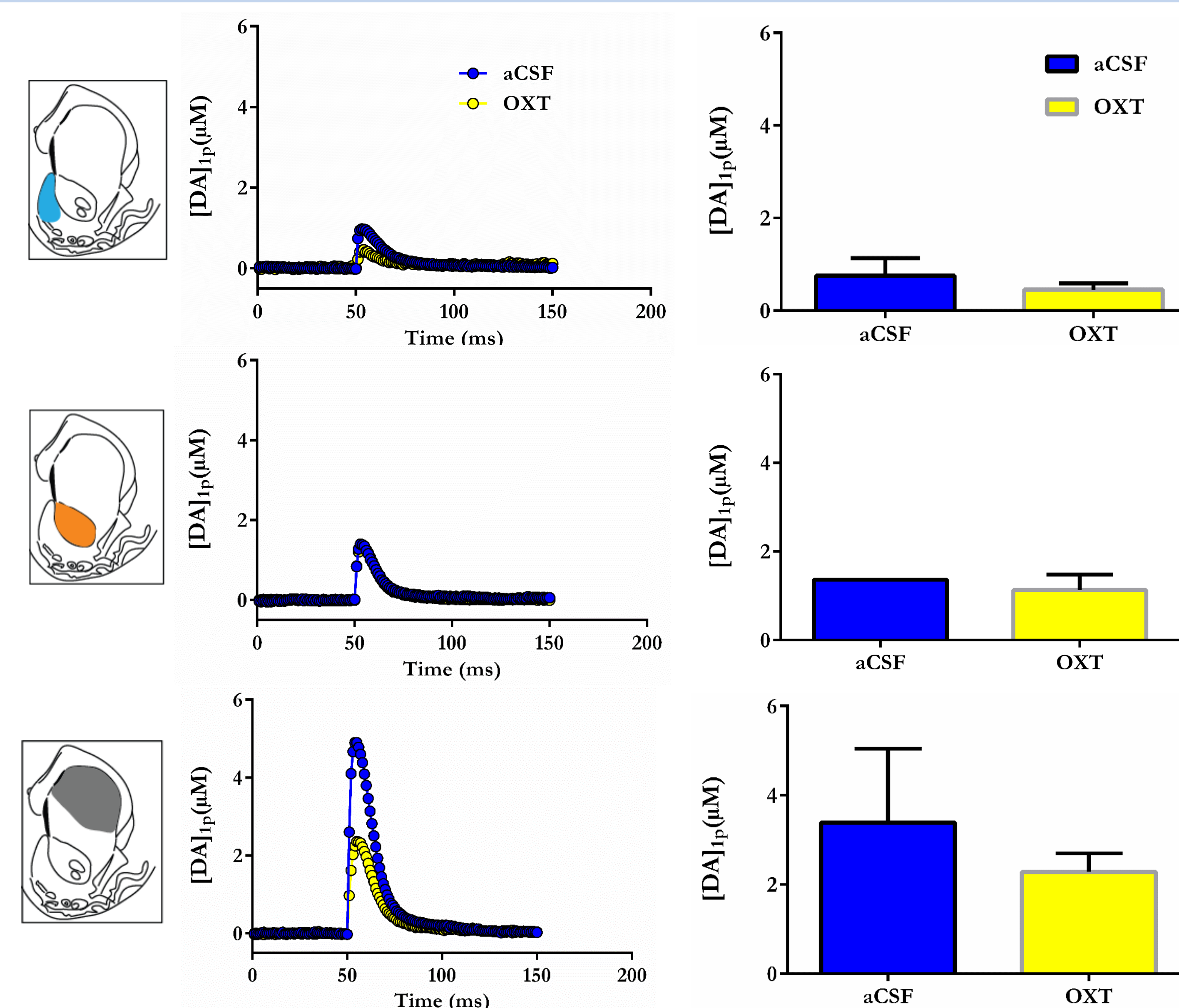
aCSF Dose



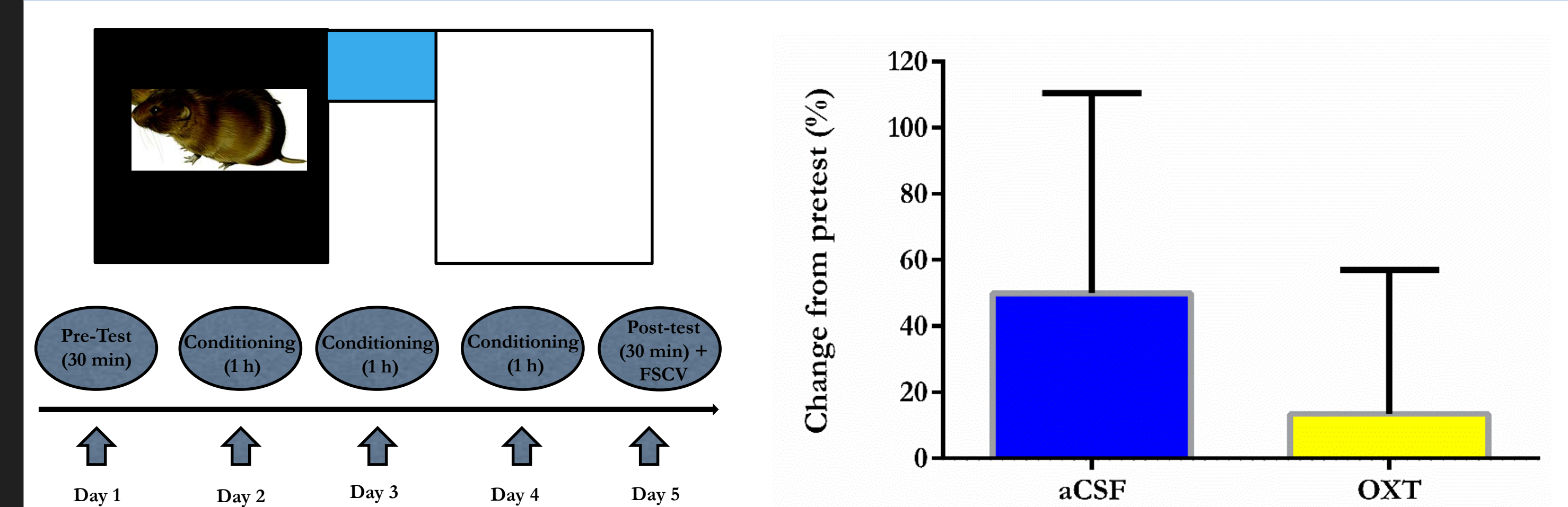
100ng I.C.V OXT Dose



No Effect of 100ng OXT on Dopamine Transmission



No Reinforcing Effects of 100ng OXT



Acknowledgements

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