

## Fluid delivery system for gustatory tasks in fMRI

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**Introduction:** A common requirement in gustatory reward expectation and anticipation tasks is the ability to deliver small amounts of liquid to the subject's mouth in a precise and repeatable manner. Previous studies [1,3,5,6] with such requirements have used programmable syringe pumps with long tubing (typically over six meters) running from the apparatus in the scanner control room into the bore in the magnet room. In our experience, the use of such long tubing adds considerable error to the delivered amount, increases off-cue taste delivery via dripping, precludes the use of fluids above or below room temperature, and requires difficult and messy setup to prime the tubes with fluid. Our study improves the existing design by implementing a hydraulic relay system to allow the fluid delivery component to be as close to the magnet as necessary, which eliminates the previously mentioned design flaws. The system was designed to examine BOLD activation in mesocorticolimbic brain regions rich in  $\mu$ -opioid receptors. Activation in these regions is elicited upon the expectation and receipt of palatable liquid food stimuli, and we hypothesised that opioid antagonists would produce measurable effects on fMRI markers of food reward processing.

**Materials and Methods:** Three Harvard Apparatus Model 22 programmable syringe pumps were used. Each pump drives one 50mL syringe, which transfers degassed, deionised water through inelastic pneumatic tubing to another 50mL syringe in the scanner room. This syringe is connected 'plunger to plunger' with a third syringe, containing the reward fluid, and comprises the pressure transfer array [Fig 1]. The final syringe is connected via a short tube to the gustatory manifold in the subject's mouth, and all components in the final stage are disposable, for hygiene reasons. All tube connections were 'luer locked' to prevent leakage under pressure and air traps were created on the pump end using three-way stopcocks. Pump control software was written in Borland Delphi 5.0, and a stimulus-response PC was synchronised to the scanner TR interval using a fibre-optic / TTL converter. Two fMRI sessions were performed on each of 14 subjects with a clinical Siemens 3T Tim Trio (Siemens Healthcare, Erlangen, Germany) using TR=2200ms, TE=31ms, PI=2, BW= 2298Hz/pix, matrix=64<sup>2</sup>, FA=70°. To test the effects of opioid antagonists on fMRI response to gustatory reward expectation, a Food Reward Expectation and Delivery task [4] was run; this contained photographs of high-calorie/appetising and low-calorie/non-appetising foods predictive of liquid stimuli with equivalent appetitive appeal. The liquid stimulus was delivered to the subject's mouth shortly after the image presentation via the afore-mentioned apparatus, in order to assess receipt-related brain activity.

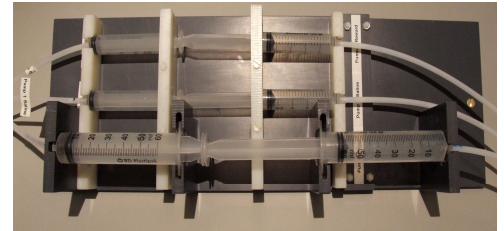


Fig 1. The pressure transfer array which transfers the programmable syringe pump motion into fluid delivery. It is located near the subject in the scanner bore to keep delivery tubes as short as possible.

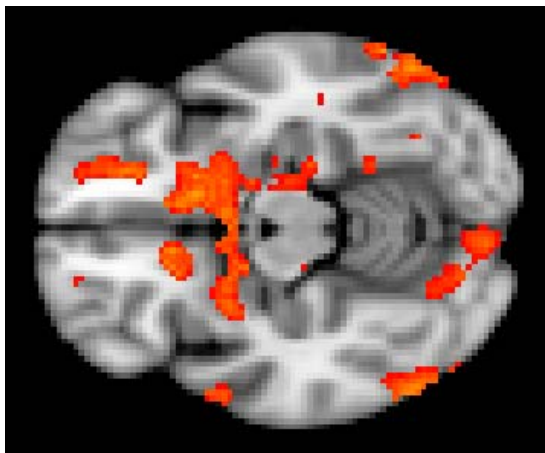


Fig 2. fMRI gustatory reward activation across N=14 baseline visits. Strong activation is seen in the ventral striatum and OFC.

**Results:** The hydraulic-relay taste delivery apparatus was successfully used in all subjects, totalling 28 scans. Following a preprocessing stage that included motion correction, spatial filtering at 6mm FWHM, temporal detrending and fieldmap-based EPI unwarping, the data were fit to a preconvolved stimulus paradigm to give parameter and noise variance estimates for each subject. Group statistics [Fig 2] were computed across the N=14 baseline visits using a full mixed-effects analysis and inference performed with a corrected clusterwise significance threshold of  $p=0.05$ . Excellent activation is noted in the ventral striatum and orbitofrontal cortex (OFC), as would be expected in a reward paradigm [1-4]. Motion parameters [Fig 3] indicate an absence of large head movements due to swallowing or changes in mouth position. Our findings show that high affinity opioid antagonists produce effects on fMRI markers of food reward processing and that these effects are related to variability in  $\mu$ -receptor occupancy associated with different doses of the drug. This corroborates previous research in healthy adults [7] and alcoholics [8] which demonstrated that BOLD response to reward receipt and anticipation is modulated by treatment with opioid antagonists with a high affinity for the  $\mu$ -opioid receptor.

**Discussion:** Gustatory reward expectation and anticipation tasks are technically difficult and require an accurate fluid delivery system. In the system described above, significant attention was given to reducing fluid elasticity at all points.

This resulted in a cleaner, smaller, easier setup and a quick interchange of a fresh refill syringe set. The mechanism facilitates minimal amounts of taste to be given without the immediate need to swallow, obviating throat muscle activation and movement artefacts, and enables accurate delivery of small quantities of liquid in precise time frames.

**References:** 1. O'Doherty, *Neuron* 2002;5:815-826. 2. Filbey *Neuropsychopharmacology* 2008;33:1391-1401. 3. Frank, *J Neuroscience Methods* 2003;131(1-2):99-105. 4. Stice, *Science* 2008;322:449-452. 5. Kami, *J Neuroscience Methods* 2008;172(1):48-53. 6. Marciari, *J Neuroscience Methods* 2006;158(2):186-194. 7. Petrovic, *J Neurosci.* 2008;28:10509-10516. 8. Myrick, *Arch of Gen Psych.* 2008;65:466-475.

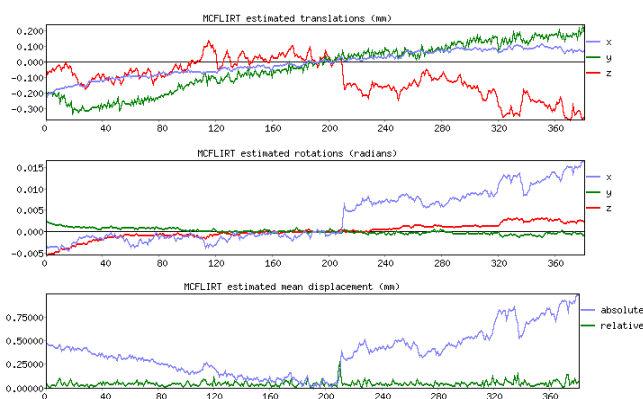


Fig 3. An illustration of the estimated motion curves for a six parameter rigid body motion correction algorithm. We observe that net overall motion is well within acceptable limits (< 1mm) and that there is no evidence of motion due to swallowing.