Brain mapping of selective acetylcholine receptor activation with pharmacological MRI

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The central cholinergic system and muscarinic cholinergic receptor activation have long been associated with cognitive function.
Furthermore, acetylcholine and muscarinic receptors regulate growth, differentiation, and plasticity in the cortex of the developing central nervous system. The aim of the current study was to assess the feasibility of pharmacological MRI (phMRI) to detect cholinergic neuronal activity in rat brain. Adult male Lewis rats were anesthetized with isoflurane and endotracheally intubated. A lateral tail vein was cannulated. Then, the animals were placed in a stereotaxic head frame and mechanically ventilated with 3% isoflurane in O_2/N_2O (1/2). Vital functions were monitored by pulse oximetry and capnography. Peripheral muscarinic effects were blocked by injection of methyl-scopolamine (0.2 mg/kg, i.v.). BOLD MRI was performed at 4.7 T (SISCO/Varian systems) using a gradient echo multi-slice sequence: TR= 300 ms; TE =17.5 ms; pulse angle = 41°; data matrix = 64 x 64; field-of-view = 35 x 35 $mm^{2;}$ 16 1.2-mm slices. After 10 minutes of baseline measurements, pilocarpine was administered (2.5 mg/kg i.v.). MRI was continued up to 50 minutes following injection. Arterial blood pressure response to pilocarpine was recorded off-line (n=5). Brain activation maps were generated using a Student's t-test that compared baseline measurements to the first 10 minutes after injection. After intravenous injection of pilocarpine, a non-selective muscarinic receptor agonist, phMRI demonstrated regional activation in basal forebrain, cortex, hippocampus and thalamus. This brain activation pattern corresponds to the cholinergic muscarinic receptor distribution in rat brain (Fig. 2). Despite a pilocarpine-induced rise in blood pressure, the spatial and temporal pattern of the BOLD signal increases suggests a selective neuronal activation pattern. In conclusion, this study demonstrates the feasibility of phMRI to assess cholinergic neuronal activation *in vivo*, which provides a basis for future studies on plasticity of cholinergic networks in relation to brain injury.

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Poster Session of Choice: Neuroscience 2 on Thursday, June 3rd (bij voorkeur naast of in de buurt van poster Jet van der Zijden, Utrecht, getiteld "Mapping cortical projections in rat brain after stroke...")