

## SCA 20

**LONGITUDINAL ASSESSMENT OF NEUROCOGNITIVE DYSFUNCTION IN RATS FOLLOWING CARDIO-PULMONARY BYPASS: EVIDENCE FOR PERSISTENT DEFICITS**

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**Introduction:** Neurologic and neurocognitive dysfunction following cardiopulmonary bypass (CPB) have been demonstrated in clinical (1) and experimental settings (2). However, the incidence of cerebral injury in the literature is variable and strongly related with both the methodology and timing of the brain impairment assessment. Although short-term outcome has been repeatedly demonstrated in rats, longitudinal assessment of neurocognitive dysfunction following CPB has not been reported. The objective of this study was to evaluate long-term neurocognitive dysfunction utilizing a CPB model in rats.

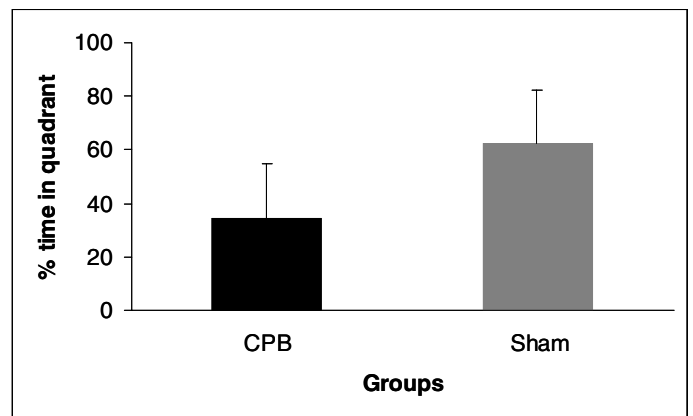
**Methods:** Male Sprague-Dawley rats (330-360g; n=36) were prepared for CPB (2,3) and randomized into two groups: I. CPB group (n=19) in which normothermic CPB was carried out for 75 min; II. Sham group (n=17) where the rats were cannulated but did not undergo CPB. On days 3, 7, 14 and at 6 weeks after surgery, the rats were submitted to a standardized neurological test (neuroscore 0-9; 9=normal behavior). In addition, the animals underwent both short and long-term cognitive testing in the Morris water maze, including basic (memory acquisition), probe (spatial memory testing), and reversal trial (working memory testing) protocols during the first 17 post-operative days (short-term cognitive outcome) and then repeated 6 weeks after surgery (long-term cognitive outcome). Statistical analysis of the neuroscore (median [IQR]) was compared using the Mann-Whitney U test. The water maze data was compared using repeated measures ANOVA, followed by the Student t test. P value < 0.05 was considered significant.

**Results:** The CPB group had worse neuroscores (day 3, 5[2]; day 7, 7[2]; day 14, 5[1]; 6 weeks, 5[1]) compared to the Sham group (day 3, 7[2]; day 7, 7[1]; day 14, 7[1]; 6 weeks, 7[1]) at all the time points tested (P<0.05). In the Morris water maze, the CPB group demonstrated short-and long-term neurocognitive dysfunction displaying persistent impairment in both spatial and working memory (Figures 1 and 2).

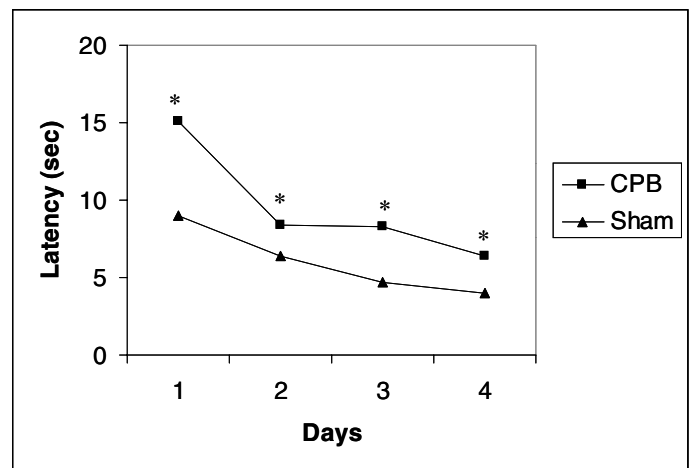
**Conclusions:** Compared to sham-operated controls, rats undergoing CPB demonstrated worse neurologic and neurocognitive outcome. Importantly, these deficits were seen early after surgery and appeared to persist long-term. These findings serve to reinforce the relevance of rat models of CPB to test both mechanisms of injury and assess neuroprotective strategies in the setting of CPB (3).

**References:**

1. N Engl J Med 2001; 344: 395-402
2. Anesthesiology 2001; 95: 1485-91
3. Anesthesiology 2003; 98: 690-8

**Short-term cognitive outcome (Probe trial)**

**Figure 1.** Deficit in spatial memory in the CPB group is shown by reduced time spent in a quadrant where the platform was placed compared to the Sham group (P< 0.05).

**Long-term cognitive outcome**

**Figure 2.** The animals in the CPB group took longer time to find a hidden platform compared to the Sham group, thus demonstrating a persistent working memory deficit (\*P<0.05).