Exhaled nitric oxide following repeated 6-hour immersed exercise dives at 1.35 atm

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Background

- Exhaled nitric oxide (NO_{exp}) produced by NOS (iNOS, eNOS, nNOS) in a wide variety of cells in the lungs and airways.

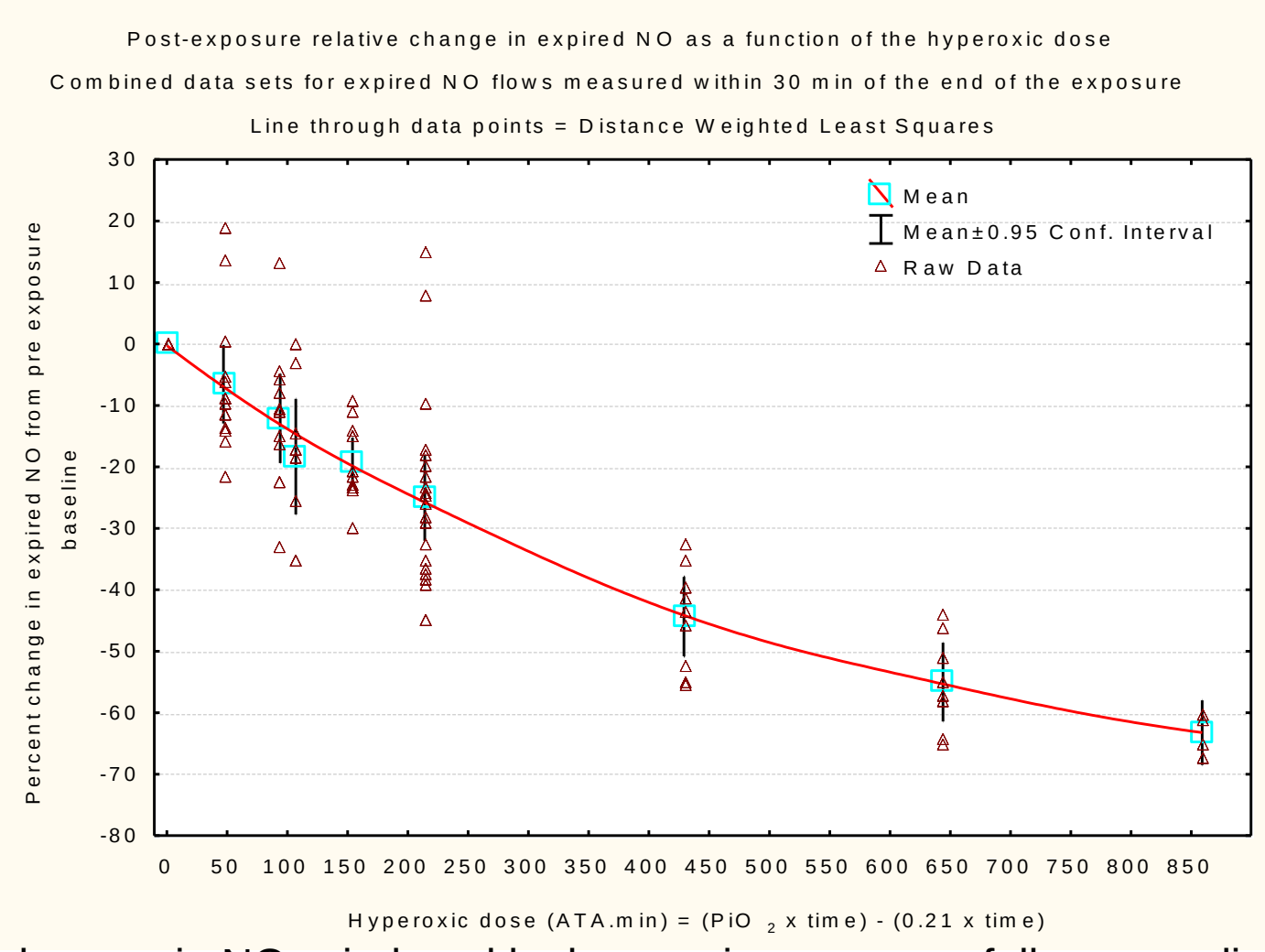
- Endogenous levels of NO in the lung may serve to protect the lung from oxidative injury (Gutierrez et al., *Free Rad. Biol. & Med.* 1996; Fothergill & Gertner *EUBS Proceedings* 2009).

- Studies conducted at the NSMRL have shown that NO_{exp} temporarily decreases following dry resting hyperbaric oxygen exposures in a dose dependent manner.

- The strong relationship between the post-dive relative change in NO_{exp} and the hyperoxic dose of the preceding dive suggests that NO_{exp} may provide a useful noninvasive measure of lung oxidative stress following prolonged hyperoxic exposures.

NO_{exp} following dry hyperoxic exposures

Summary of results collected at NSMRL (2007-2012)



The changes in NO_{exp} induced by hyperoxic exposures follow a predictable dose response relationship with the level of oxidative stress [hyperoxic dose] ($r = -0.857$; $p<0.00001$)

Project Goal

- To determine if consecutive multi-day dives, immersion, and exercise significantly affect the post-dive hyperoxic mediated decrease in $NO_{exp.}$

Vs

Methods

IRB Protocols

- NSMRL.2010.0002: Exhaled nitric oxide (NO) and carbon monoxide (CO) as noninvasive markers of hyperbaric oxidative stress in humans
- NEDU.2008.0006: Mechanisms of fatigue and exercise intolerance following multiple 6-hour dives at 1.35 atm PO_2: Phase 1 – multiple 6-hour resting and exercise dives
- NEDU 2013.0004. Air dive comparison: Human performance and pulmonary O_2 toxicity guidance for repeated 6-hr exercise dives at 1.35 atm.

Dive Exposures

O_2 Dives (n=12): Five six-hour dives on sequential days (with 18 hr surface intervals) breathing 100% oxygen at 1.35 atm in NEDUs heated test pool:
(water temp 87 ± 3 ° F (31 ± 2 ° C).

Air Dives (n=14): Same as O_2 dives except that divers breathed air at 1.35 atm

Exercise protocol

Repeated cycles of 30 min mild cycle ergometer exercise (target heart rate of 95 ± 5 beats per) followed by 30 min rest for 6 hr

NO_{exp} measurements

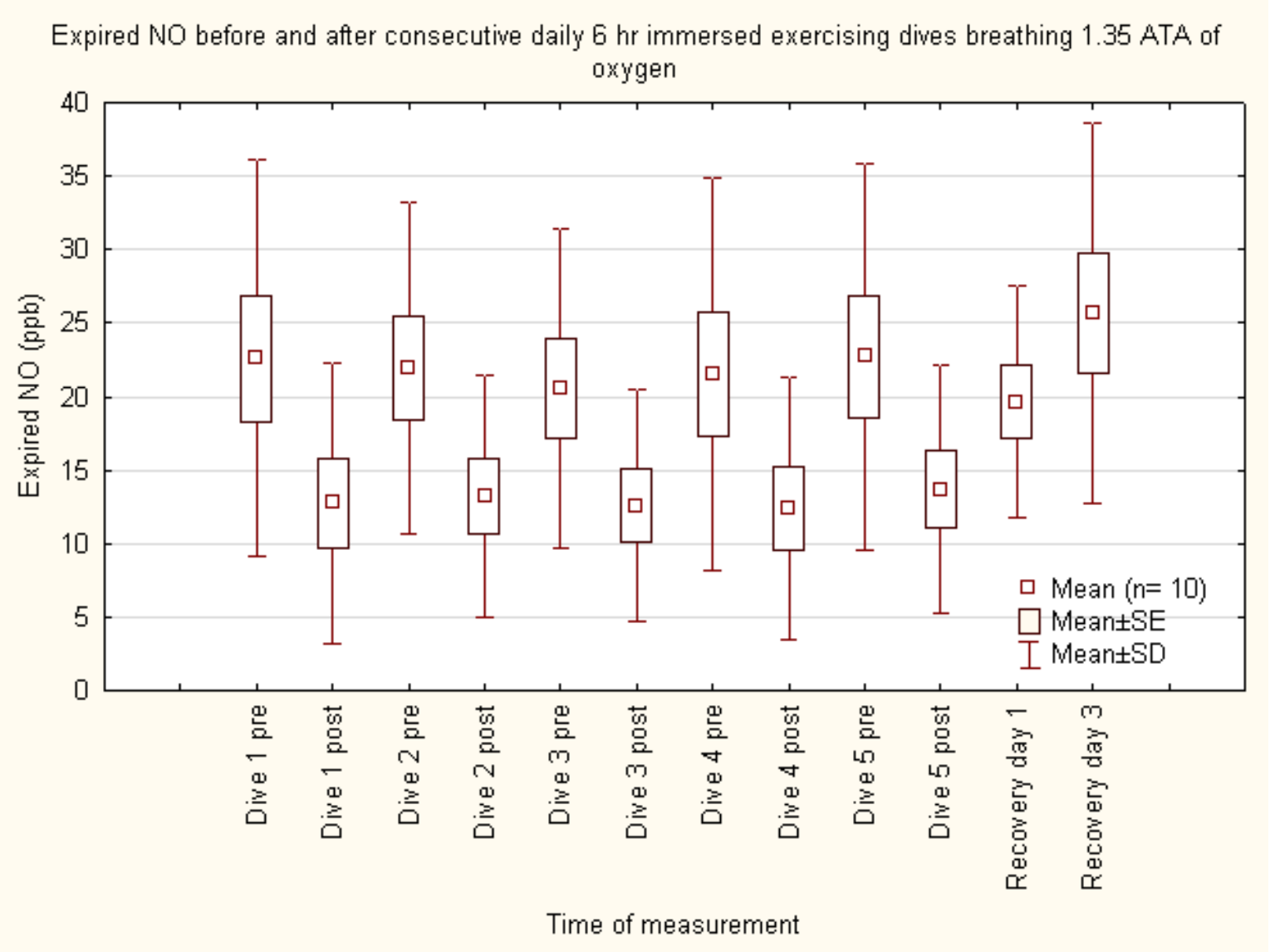
Niox Mino, Aerocrine Inc, Sweden
(electrochemical sensor technology)

- Measurement range: 5 – 300 ppb
- Lowest Detection Limit: 5 ppb
- Analytical Accuracy: ± 5 ppb or max 15%
- Exhalation time: 10 s at an exhalation pressure of 10 – 20 cm H2O, to maintain a fixed flow rate of 50 ± 5 mL/s.
- NO_{exp} value = mean of 2 measurements that are within 4 ppb , if not within 4 ppb take median of 3 measurements
- No calibration gas needed

NO_{exp} measured:

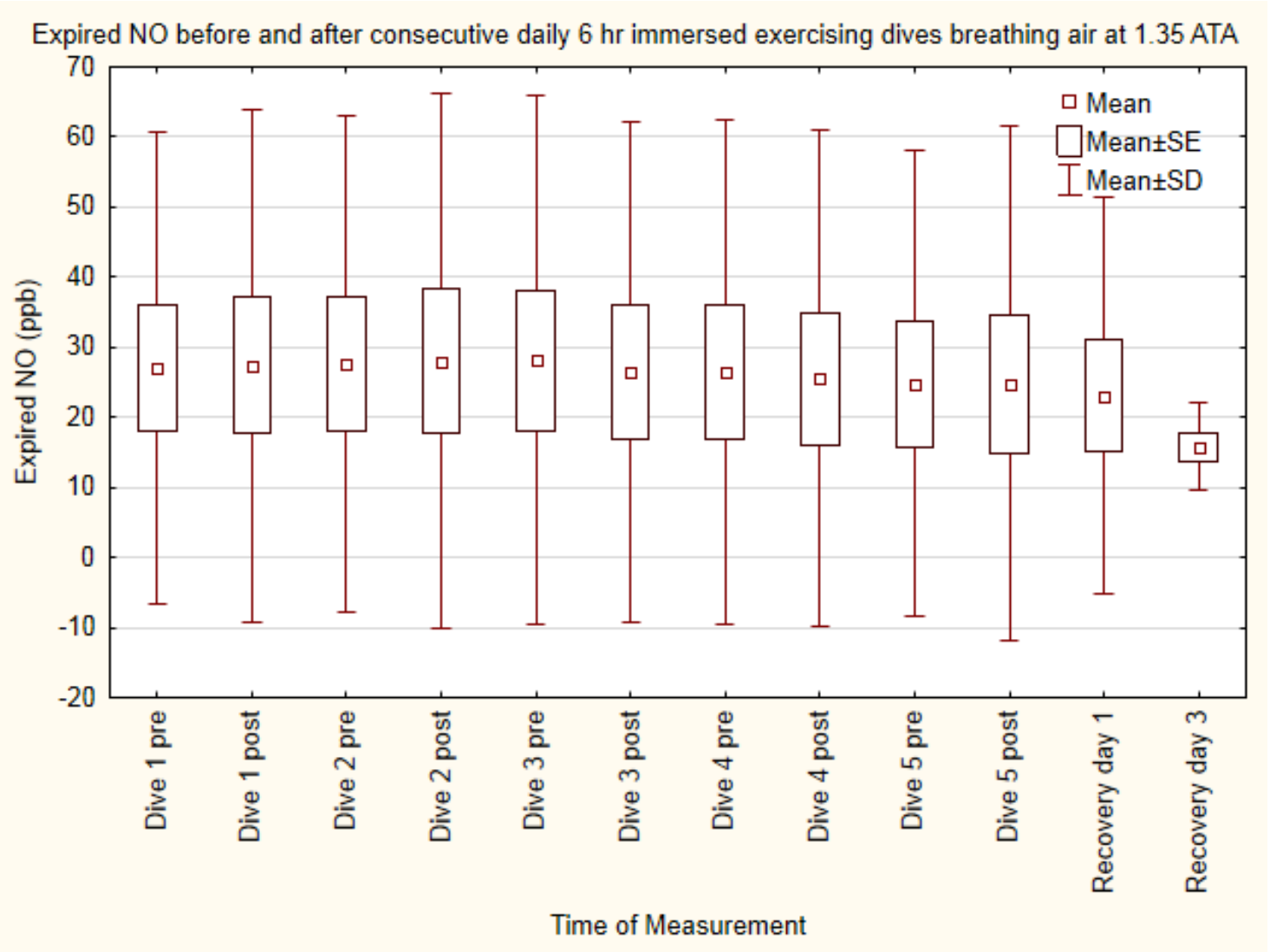
1. immediately before each dive
2. after each dive within 30 min of exiting the water
3. on recovery day 1 (approx. 18 hr. surface interval)
4. on recovery day 3

Results from the O_2 Dives



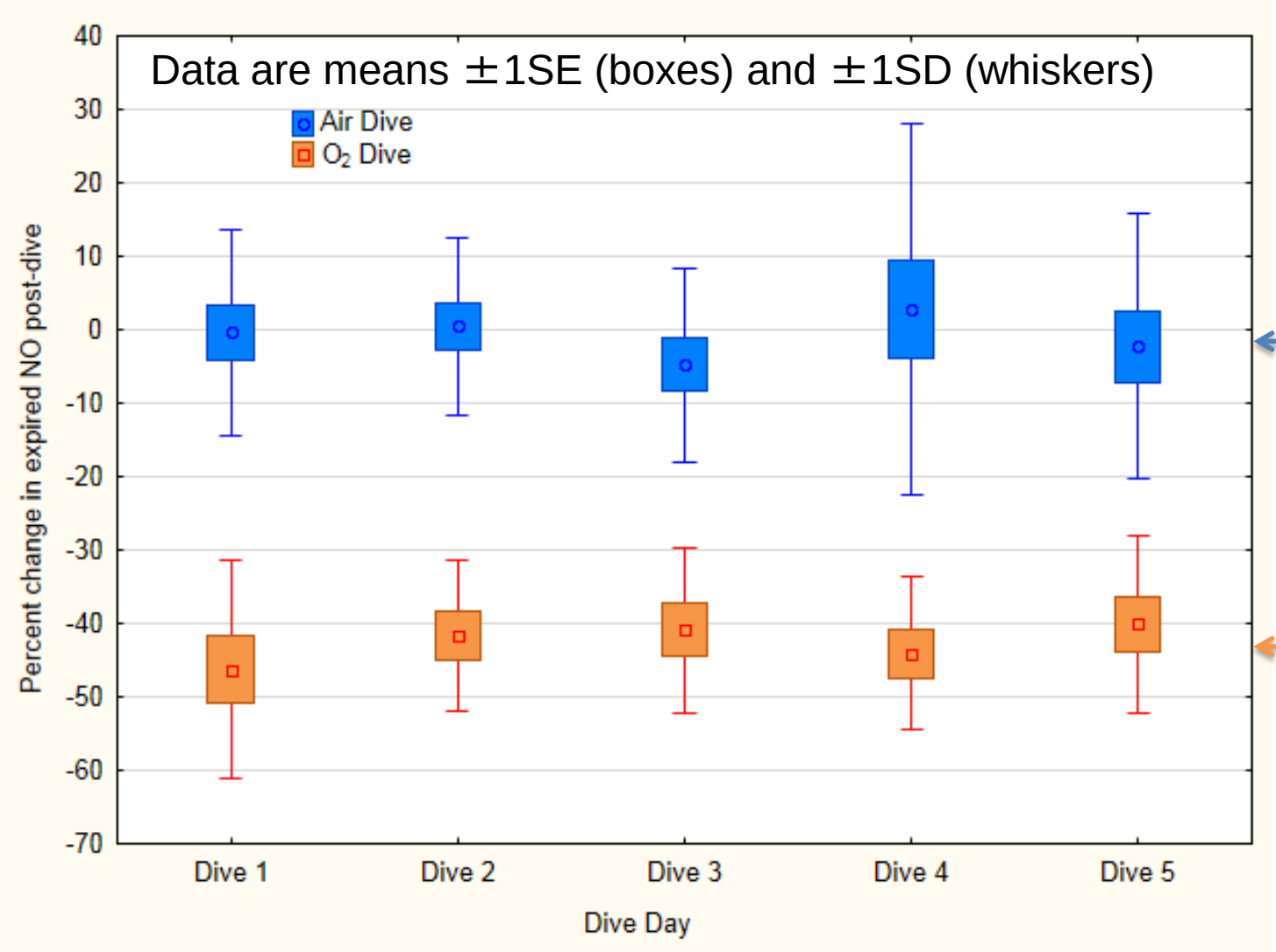
NO_{exp} significantly decreased following the dives (Main effect Pre vs Post; $p<0.0001$)
Day x Pre-post interaction NS ($p=0.686$)

Results from the Air Dives



The post-air dive NO_{exp} did not differ significantly from the pre air dive values at any point during the dive week ($p=0.643$; $n=14$).

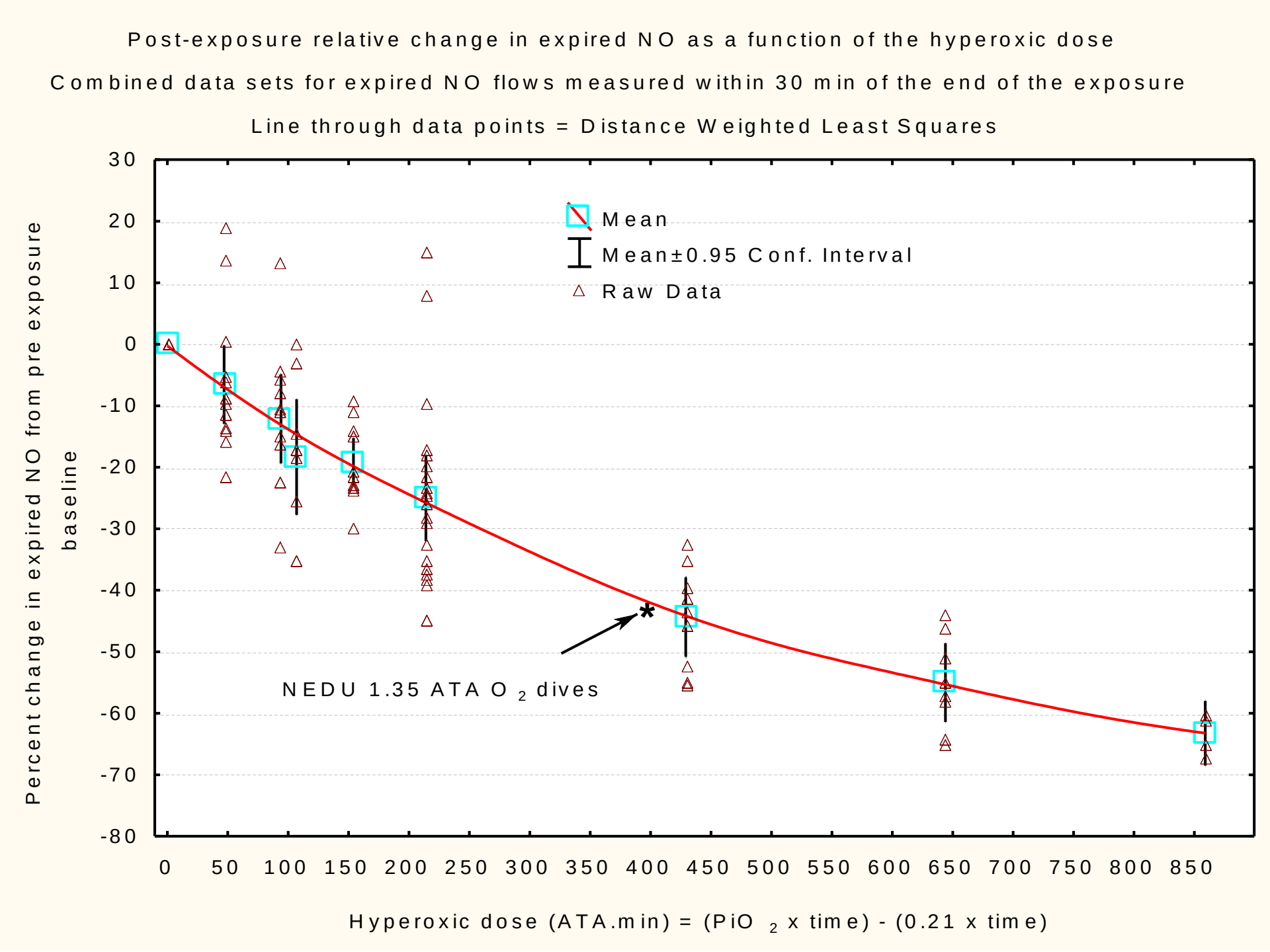
Relative change in NO_{exp} following the air and O_2 dives



Mean % change in the post-dive NO_{exp} across the 5 days:

Air dives
-0.8%

O_2 Dives
-42.4%


Post-exposure relative change in expired NO as a function of the hyperoxic dose
Combined data sets for expired NO flows measured within 30 min of the end of the exposure
Line through data points = Distance Weighted Least Squares
Mean
Mean±0.95 Conf. Interval
Raw Data
NEDU 1.35 ATA O 2 dives
Percent change in expired NO from pre exposure baseline
Hyperoxic dose (ATA.min) = (PiO 2 x time) - (0.21 x time)
30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850

Conclusions

- Immersion and mild exercise do not significantly affect the hyperoxic mediated post-dive decrease in NO_{exp}.

- Consecutive multi-day dives also do not appear to modulate the magnitude of the hyperoxic mediated post-dive decrease in NO_{exp}.

Acknowledgements and Disclaimer

- *This work was supported by the Office of Naval Research (ILIR grant N0001410WX30014) to DF and a NAVSEA 00C grant (N0002411WX02303) to JPF.*

- *The views expressed in this article are those of the author and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, nor the U.S. Government.*

- *The study protocol was approved by the NSMRL and NEDU Institutional Review Boards in compliance with all applicable Federal regulations governing the protection of human subjects.*

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