NAVSEA – Hypercapnia: Cognitive Effects and Monitoring

Year 2: Sensitivity, Reliability and Context Sensitive PO_2 Findings

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Study's Critical Questions

- Can we quantify N_2 narcosis (equivalent narcotic depth)?
  - –What is a significant level of narcosis?
  - –What mission critical skills are impaired?
- Do CO_2 and O_2 affect N_2 narcosis?
  - –Are the narcotic properties of the gases different?
  - –Are CO_2 and O_2 independently narcotic?
  - –Are the effects additive or is there a synergistic "interaction" (multiplicative)?
  - –What is the duration of their narcotic effects (adaptation)?
- Is $ETCO_2$ an adequate surrogate for $PaCO_2$?
  - –What is the relationship of $ETCO_2$ to $PaCO_2$ at depth during exercise?
  - –How can we measure and eventually predict physiologically relevant values of CO_2?

Study Design

Figure 4, Protocol summary

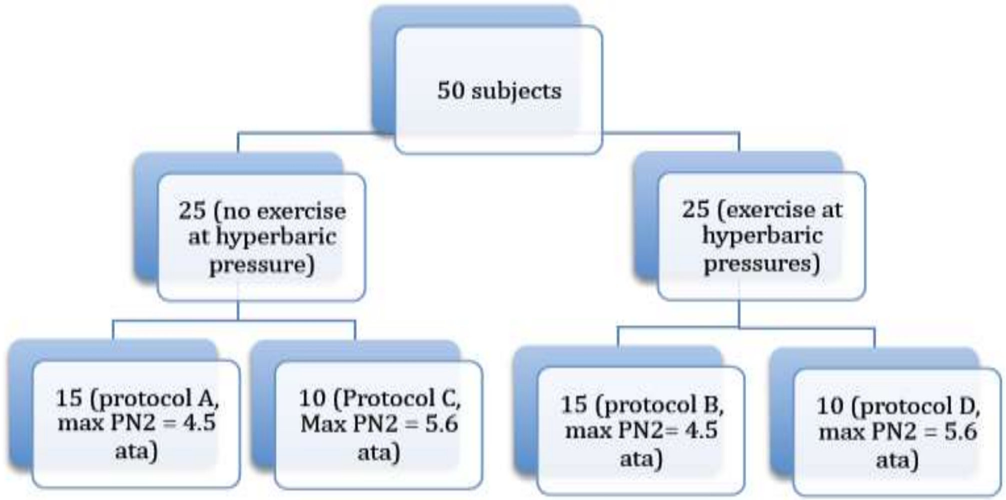


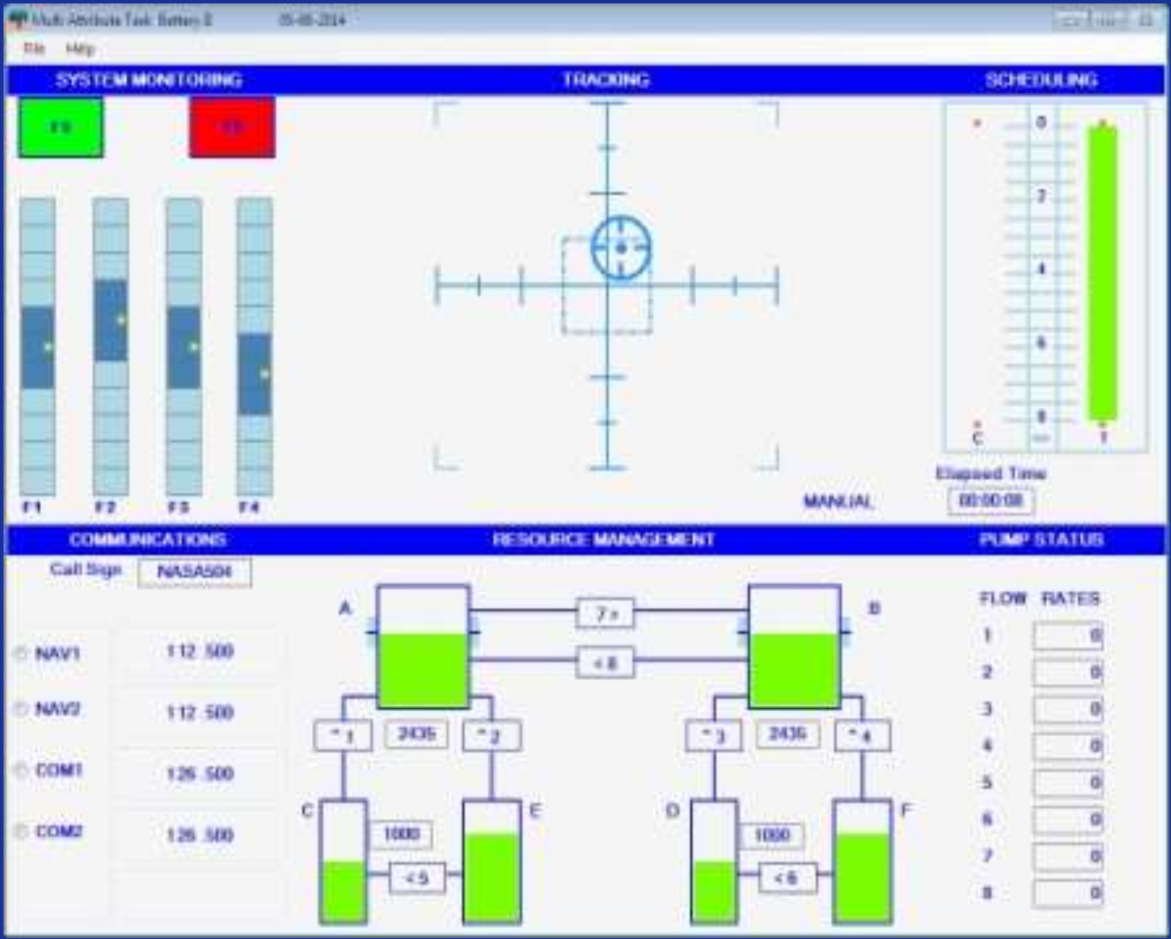
Table 2, Conditions of hyperbaric phase of Protocols A-D

Protocol name	Number of subjects	Exercise + / -	Pressures (fsw)	Added CO_2	PO_2 (ata)	PN_2 (ata)	EAD (fsw)
A	15	-	122.1 158.4	+ and -	0.2, 1.3	4.5	152
B	15	+	122.1 158.4	+ and -	0.2, 1.3	4.5	152
C	10	-	158.4	+ and -	0.2	5.6	197.5
D	10	+	158.4	+ and -	0.2	5.6	197.5

MATB Tasks

Cognitive Impairment Measurements Methods

- TRACKING (each 1/second, last 3 minutes of stage)
  - RMS pixel distance from origin
  - visual / motor
- SYSMON
  - correct response (lights and scales)
  - reaction time
  - inappropriate keystrokes
  - attention / reaction time
- COMM (5/stage)
  - correct radio
  - correct frequency
  - reaction time
  - inappropriate keystrokes
  - attention / memory / reaction time
- RESMAN (each 15 seconds)
  - tank levels
  - attention / planning / strategy



Methods:

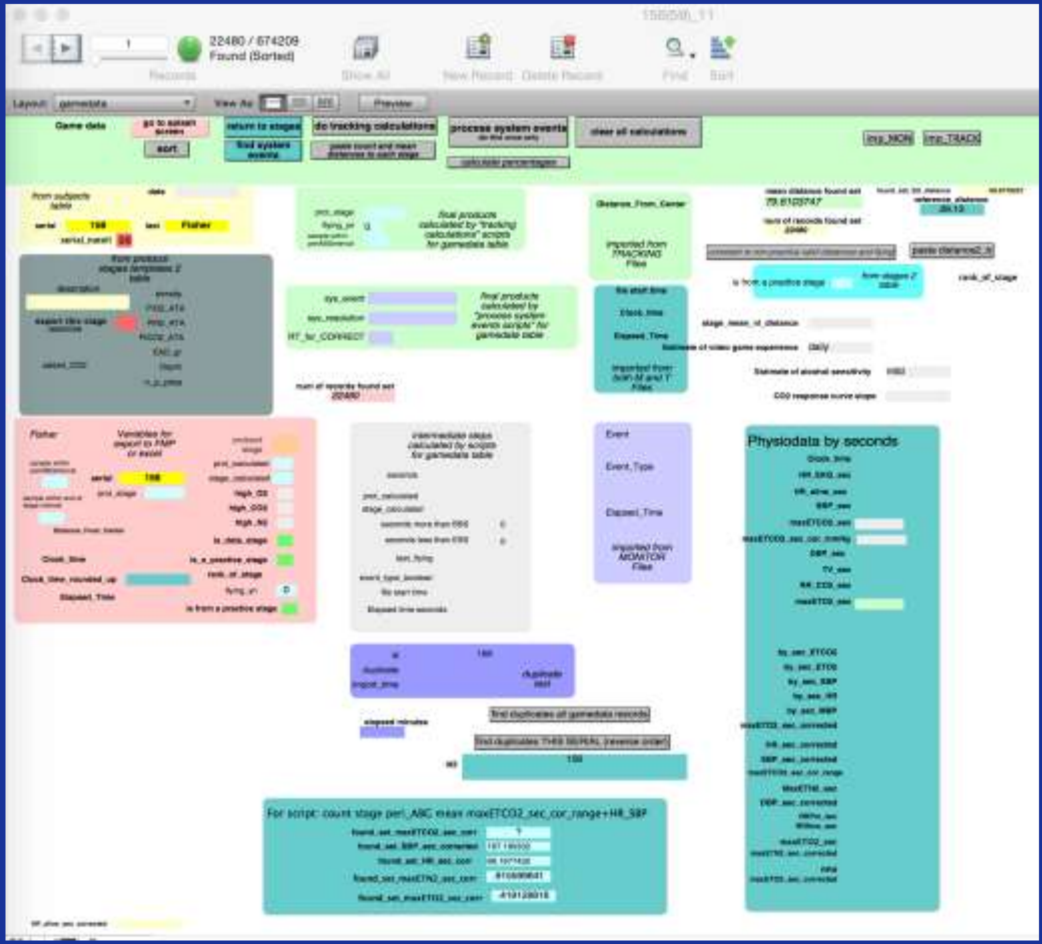
- 33 subjects
- Practice to plateau level
- Trials:
  - –PiCO2=0 and 0.075 ATA (7.5 kPa)
  - –PiO2=0.21 ATA (21.3 kPa), 1.0 ATA (101.3 kPa) and 1.22 ATA (123 kPa)
  - –PiN2=0 and 0.79 ATA (80.0 kpa), 4.6 ATA (465 kPa) and 5.6 ATA (567.3 kPa)
- Preliminary Analysis
  - –pre-to-post test correlations, means, 95% CI, repeated measures ANOVA, linear regression.
  - –controlled for recent video game experience, exercise and pre-test hypercapnic ventilatory response (HCVR)

Cognitive Data

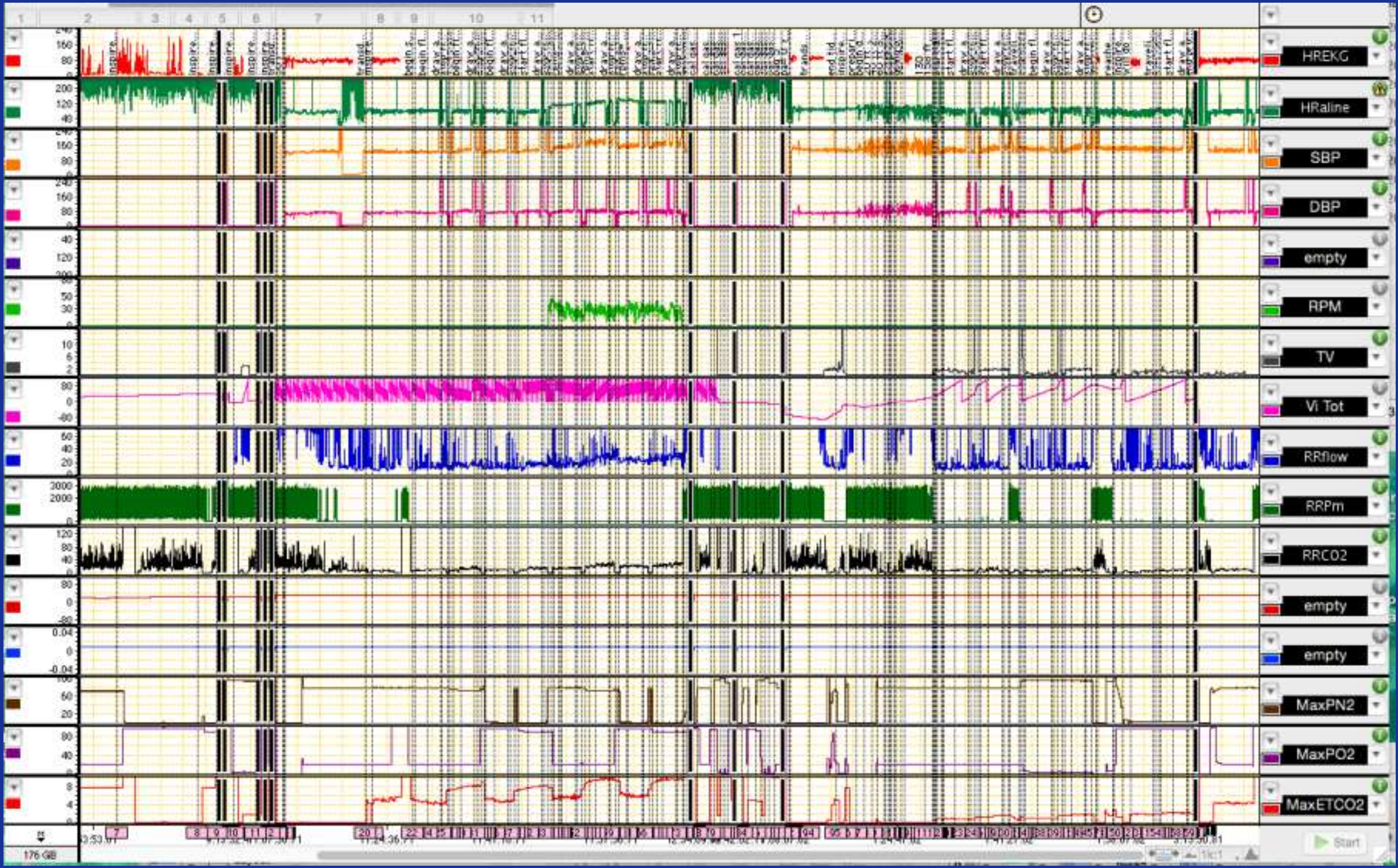
MATB-II output

Timer for gas stage

by second datapoint



Physiology Data:
Lab Chart output



Combined Data:

FMP output:

32 subjects selected

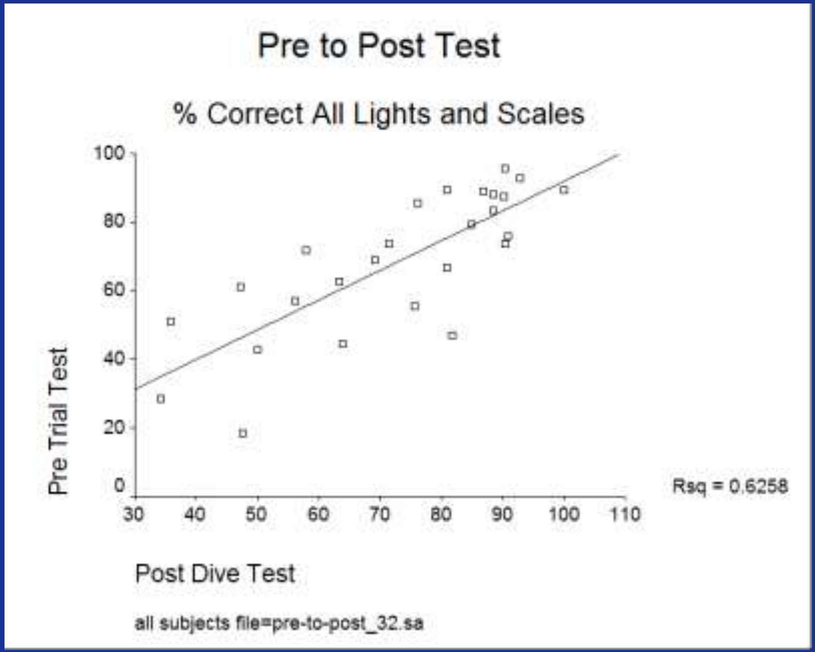
80	D	Zyla
83	C	Snyder
85	B	Spencer
86	A	Bray
89	B	Bennett
91	F	Baldwin
94	Fb	Parker
110	B	Simken

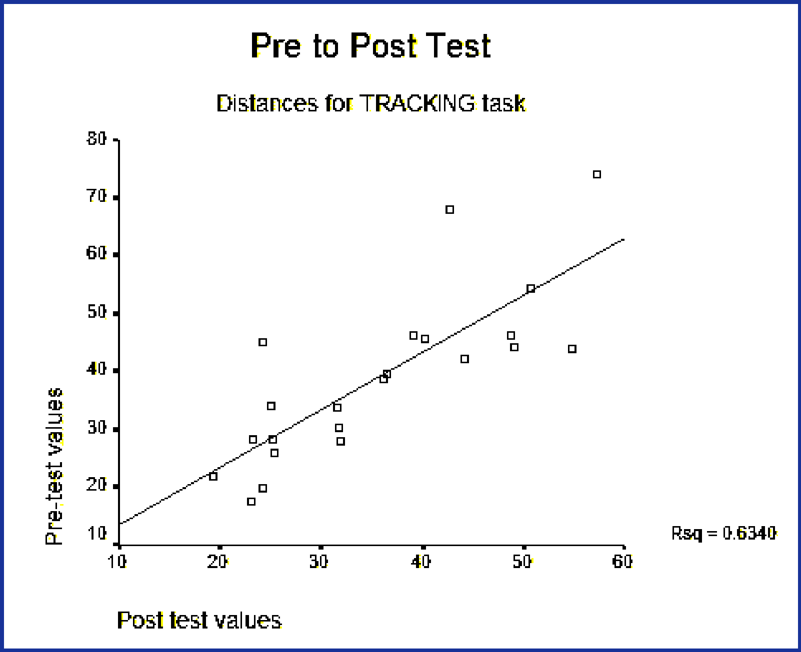
gas num	narcosis group	description	mean distance	normal dist	N subjects	N distances	CV	mean_SD distance	%RED	RT RED	% GREEN	RT GREEN	% SCALES	RT SCALES	N	HR	SBP	DBP	MBP	n
1	air	01_rest_surface_air	43	100	32	5540	0.60	29	69	1.25	72.2	2.00	64	2.82	30	69.	154	97	107	29
2	CO2	02_rest_surface_CO2	48	115	32	5696	0.65	32	68	1.62	67.3	1.89	58	2.92	30	77.	167	106	117	29
3	O2	03_rest_O2_1ATA	41	100	32	5646	0.60	29	65	1.56	74.6	1.62	60	2.74	30	69.	157	98	109	30
4	O2CO2	04_rest_O2_1ATA_C	43	106	32	5948	0.58	26	73	1.49	74.0	1.84	67	2.93	30	75.	163	100	112	30
1	air	05_ex_surface_air	43	104	32	5860	0.62	30	71	1.35	65.0	1.84	61	3.39	30	98.	181	103	118	30
2	CO2	06_ex_surface_CO2	62	140	32	5941	0.85	41	65	2.44	61.2	2.83	51	2.88	29	111	197	110	128	28
3	O2	07_ex_O2_1ATA	43	105	32	5855	0.61	30	76	1.39	65.1	1.74	61	3.16	31	106	177	100	114	29
4	O2CO2	08_ex_O2_1ATA_CO	46	112	31	5538	0.69	33	69	1.10	67.2	1.70	57	2.70	31	113	193	108	124	29
1	O2N2	11A_rest_1.2_4.5	48	110	6	1111	0.76	37	68	1.95	50.6	2.33	41	3.15	6	74.	152	105	121	5
1	O2N2	11B_ex_1.2_4.5	47	119	10	1754	0.74	36	74	4.04	63.7	2.26	55	2.94	10	102	174	89	110	8
6	N2	11C_rest_.21_5.6	39	95	2	305	0.77	37	70	0.89	65.0	1.10	59	2.12	2	82.	171	116	134	2
6	N2	11D_ex_.21_5.6	96	179	10	1826	1.61	78	73	1.82	61.9	3.42	43	3.68	9	104	192	100	117	10
5	O2N2CO2	12A_rest_1.2_4.5_CO	45	105	6	1042	0.62	30	77	1.60	56.5	2.33	43	2.79	6	86.	185	124	145	5
5	O2N2CO2	12B_ex_1.2_4.5_CO2	98	236	10	1598	1.15	56	45	1.91	40.8	2.77	24	2.96	10	109	196	111	130	8
9	N2CO2	12C_rest_.21_5.6_C	36	93	2	368	0.59	28	69	0.99	72.2	1.16	56	1.89	2	82.	186	115	139	2
9	N2CO2	12D_ex_.21_5.6_CO2	77	183	8	1644	0.94	46	56	1.84	48.2	2.79	30	3.40	8	115	192	119	128	10
6	N2	14A_rest_.21_4.5	40	93	7	1230	0.50	24	60	1.17	80.6	1.86	66	2.63	6	77.	172	120	137	6
6	N2	14B_ex_.21_4.5	37	100	8	1424	0.50	24	69	1.23	69.0	1.89	54	3.10	8	120	178	82	106	7
7	N2CO2	15A_rest_.21_4.5_CO	50	113	7	1220	0.69	33	67	1.56	74.1	2.05	62	3.37	6	88.	187	119	141	6
7	N2CO2	15B_ex_.21_4.5_CO2	51	132	8	1396	0.62	30	66	1.35	72.8	2.07	48	2.88	8	124	195	106	126	7
3	O2	19_USN_deco_40_fs	43	88	13	2251	0.52	25	62	1.33	58.9	1.64	54	2.60	17	77.	149	94	107	11
	air	20_post_dive_test	37	94	28	5211	0.51	25	82	1.28	73.3	1.88	72	2.73	27	73.	164	104	121	21
				total N	380	68404								total N	366					

PeriABG max cor ETCO2	mean PaCO2	mean PaO2	mean pH	n ABGs	% Freq	% Radio	% inapp	RT COMM	% pump A	% pump B
35.12	33.00	107	7.49	28	95	98	7	1.64	91	88
57.79	49.32	142	7.35	28	89	92	7	1.04	87	85
32.10	30.85	543	7.49	28	92	96	8	1.31	91	89
55.38	48.23	506	7.35	27	93	97	8	1.09	91	91
36.64	35.29	103	7.44	27	93	96	7	2.27	89	90
65.24	54.86	145	7.30	27	93	97	7	2.43	89	89
36.94	36.41	545	7.42	27	91	94	6	1.97	88	89
64.87	53.65	492	7.31	27	93	97	5	0.98	88	90
34.90	35.64	379	7.47	[illegible]	81	100	9	3.99	91	84
39.19	37.92	342	7.43	[illegible]	75	90	5	3.70	84	85
36.71	34.85	127	7.47	[illegible]	80	100	3	1.92	100	100
40.53	40.59	112	7.41	[illegible]	90	100	8	0.93	84	85
63.89	55.34	341	7.33	[illegible]	89	93	5	2.80	89	89
69.19	56.31	370	7.31	[illegible]	58	62	8	2.13	85	85
59.76	52.25	149	7.34	[illegible]	86	86	0	2.37		
66.58	62.19	163	7.26	[illegible]	71	80	13	1.73	86	87
36.10	34.23	140	7.45	[illegible]	92	100	10	2.16	89	91
39.68	42.14	133	7.41	7	88	89	5	1.76	88	89
64.79	53.32	160	7.33	[illegible]	94	93	5	1.08	92	80
71.08	58.56	143	7.30	7	73	78	4	6.10	86	88
30.45	34.15	990	7.48	11	98	96	2		92	94
36.14	33.32	101	7.49	[illegible]	95	98	6		89	89
445			total N	[illegible]						

Preliminary Results Summary

- Pre-to-post test scores were well correlated
- Arterial CO_2 and O_2 and end-tidal CO_2, O_2, N_2 and their interactions are significant predictors of performance
- Strong narcosis / cognitive impairment signal for 0.075ATA CO_2.
- Low to moderate narcosis signal for 4.5 to 5.6ATA N_2
- The effect of O_2, depends on its context (interactions with other gases)



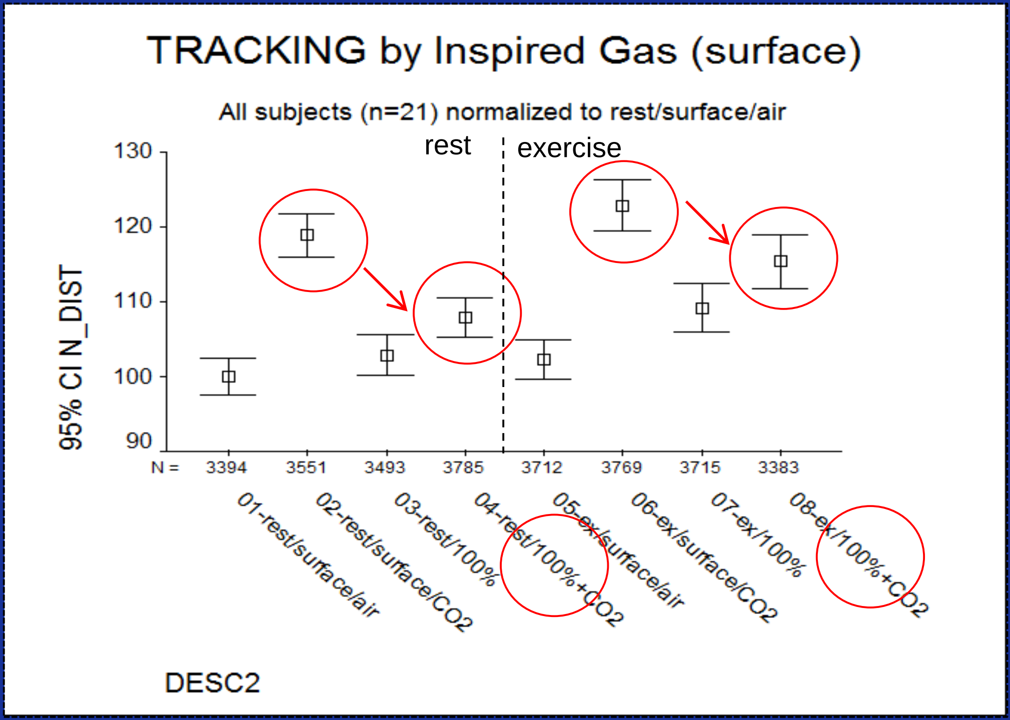


Surface Oxygen effect: performance improved (Figure 1)

On the surface O_2 appears to counteract CO_2 associated cognitive impairment. 100%

- CO_2 caused a 17 to 31% performance decrement rest and exercise respectively ($p<.001$ ANOVA with Tukey's HSD post-hoc correction)
- Stages with higher PiO_2s in that only a 7-12% decrement was observed.
- Confirms the findings of Gill and Vann

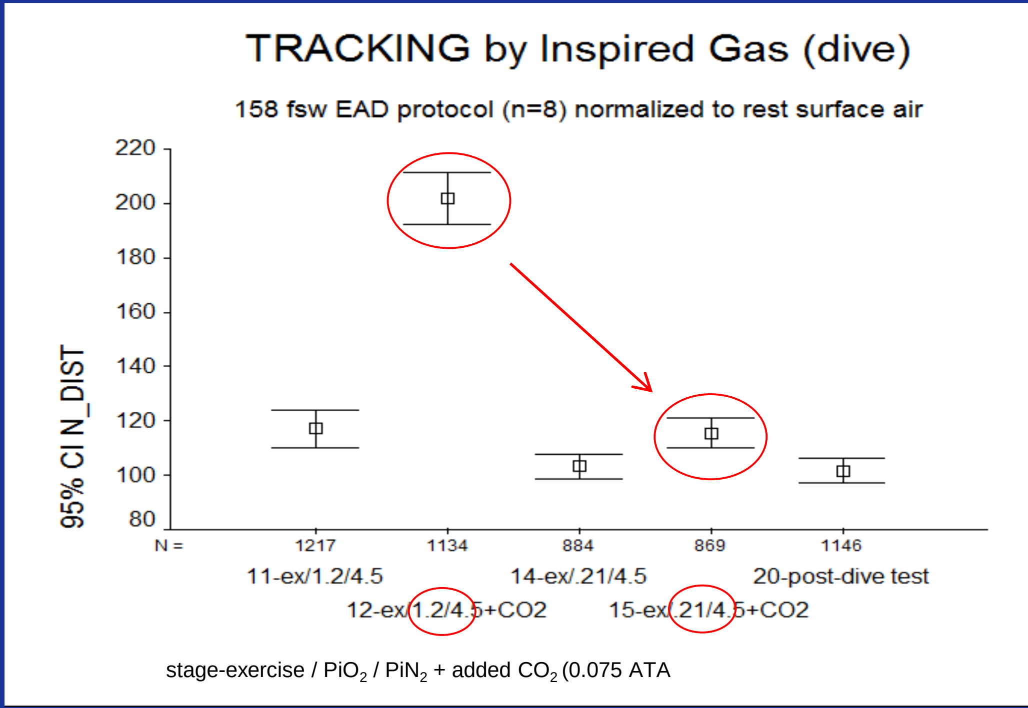
__Figure 1__ shows the mean TRACKING distances (± 95% CI) for immersed surface conditions. Performance impairment from 0.075ATA CO_2 was reversed by increased PiO_2=.925. (higher scores are worse)



Dive Oxygen effect: performance impaired (Figure 2)

- Elevated PiN_2 alone at 4.5 ATA did not significantly impair TRACKING performance (p=.366),
- **At constant 4.5ATA** an elevated PiO_2 (1.2ATA) was associated with a 15% (normocapnic) to 85% (hypercapnic) performance decrement ($p<.001$) compared to a normoxic PiO_2 (0.21ATA).
- PiO_2 = 1.2ATA was associated a 50% failure rate
- O_2 narcotic effect versus toxicity?

__Figure 2__ shows the severe impairment of TRACKING performance during 0.075ATA CO_2 challenge at 158 feet seawater while breathing a gas with a PiO_2=1.2ATA. Scores were improved by switching to a lower PiO_2=0.21ATA.



Preliminary Conclusions:

1. According to the Meyer-Overton theory of anesthetic potency, O_2 should cause cognitive impairment when breathed at hyperbaric pressures.
2. Prior investigators have noted mixed effects, however, this may be because oxygen is a substrate for cellular respiration, a potent vasoconstrictor, and it is CNS toxic at > 1.4 ATA.
3. Accordingly, a partial pressure below 1.4 ATA may be insufficient to detect a measurable narcotic effect. Additional subjects and gas partial pressures should be tested to confirm these preliminary findings.
4. Incipient CNS O_2 toxicity secondary to CO_2-mediated release of protective O_2 cerebral vasoconstriction will need to be distinguished from narcosis.

Review of Critical questions:

Do CO_2 and O_2 affect N_2 narcosis?

- Are CO_2 and O_2 independently narcotic?
  - probably
- Are the effects additive or is there a synergistic (multiplicative) interaction with N_2?
  - interaction (O_2 and CO_2), (N_2 and CO_2?)
- Are the narcotic properties of the gases different?
  - probably but pending

Upcoming Results

- Create the algorithm to compute the “equivalent narcotic depth” based on gas partial pressures
  - –Test the lower limits of gas partial pressures (40 additional subjects)
  - –inclusion of subjective findings, adaptation (divers versus non-divers)
  - –hypercapnic ventilatory response, VO2 max
- Assess the relationship between end-tidal and arterial partial pressure of CO_2 (PCO_2) to predict elevated arterial PCO_2

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