NASA 14 Day Undersea Missions:
A Short-Duration Spaceflight Analog for Immune System Dysregulation?

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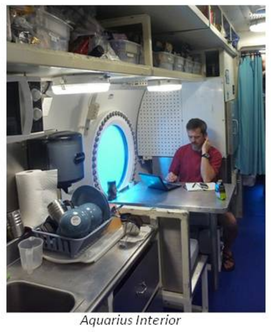
BACKGROUND

Spaceflight-associated immune dysregulation occurs during spaceflight and may represent specific clinical risks for exploration-class missions. An appropriate ground analog for spaceflight-associated immune dysregulation would offer a platform for ground evaluation of various potential countermeasures. This study evaluated the NASA Extreme Environment Mission Operations (NEEMO), consisting of 14 day undersea deployment at the *Aquarius* station, as an analog for this phenomenon. Given the comparatively short duration, NEEMO is viewed as a Space Shuttle analog. For this study, assays included measures of adaptive immunity, viral reactivation and stress factors. Sixteen Aquanauts from missions NEEMO-12, 13 and 14 participated in the study.



Aquarius Interior

AQUARIUS

-Seafloor depth: 62 feet
-Operating depth (on stilts): 47 feet
-Interior pressure: ~2.5 Atos; ambient pressure hab
-Main living space: cylinder 43 ft. x 9 ft.
-Mission durations: up to 2 weeks
-Saturation diving conditions:17 hour decompression required for surface return
-Aquanauts: up to 6-9 hours diving per day

METHODS

•A total of 16 subjects participated in this study, representing the NEEMO 12, 13 and 14 missions. Informed consent was obtained from all subjects, and relevant institutional CPHS/IRB approvals were obtained.

•All NASA general immune and viral assessment methods used for this study were performed as previously described: *Aviation and Space Environmental Medicine, 2009 May, 80(5 Suppl): A37-44.*

ASSAYS

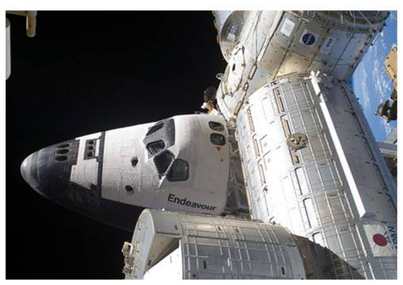
(ESA)
PMN number, function, bactericidal
In-vitro DTH
Apoptosis/necrosis
Cellular mRNA expression
Plasma purine markers of inflammation/hypoxia
Erythropoietin activity
Stress test
Stress hormones
Components of exhaled air

(NASA)
VirLeukocyte subsets*
T cell function*
Intracellular/secreted cytokine profiles*
us specific T cell number/function
Latent herpesvirus reactivation
Circadian rhythm analysis

**data included in this presentation*

SAMPLING SCHEDULE

	PRE MISSION						UNDERSEA													POST MISSION							
BLOOD (20.5 ml)	X											X							X	X							X
LIQ. SALIVA (1-2 ml)	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
DRY SALIVA (<1.0 ml)	X											X							X								X
URINE (45 ml)	X																										X
EXHALED AIR	X		X			X		X				X				X			X	X		X					X
JSC HEALTH SURVEY	X																			X							
ESA STRESS SURVEY	X		X			X		X				X				X			X	X		X					X
ESA SPIELBERGER SURV.	X																			X							
	6	5	4	3	2	1	1	2	3	4	5	6	7	8	9	10	11	12	13	14/ 0	1	2	3	4	5	6	7	8
	L-						Mission Day-													MD14/R+0 Surfacing Day (Samples after surfacing)	R+							



Analogous?

Figure 1: Location of Aquarius Station, exterior photograph

Figure 2: Mean Peripheral Leukocyte Subsets (n=16)

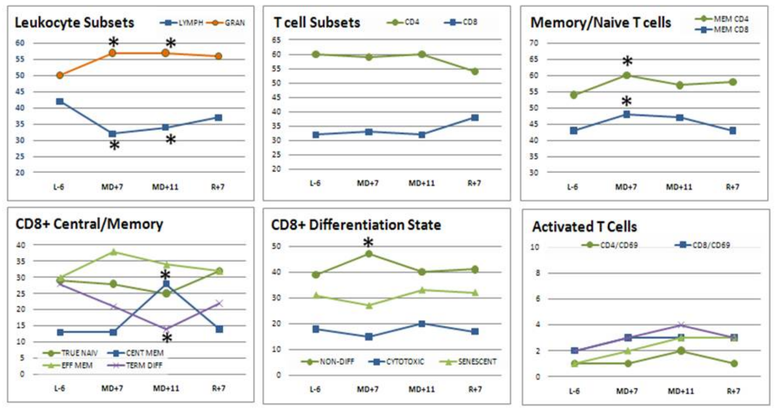


Figure 3: Individual Crew Data, Selected Functional Parameters (n=16)

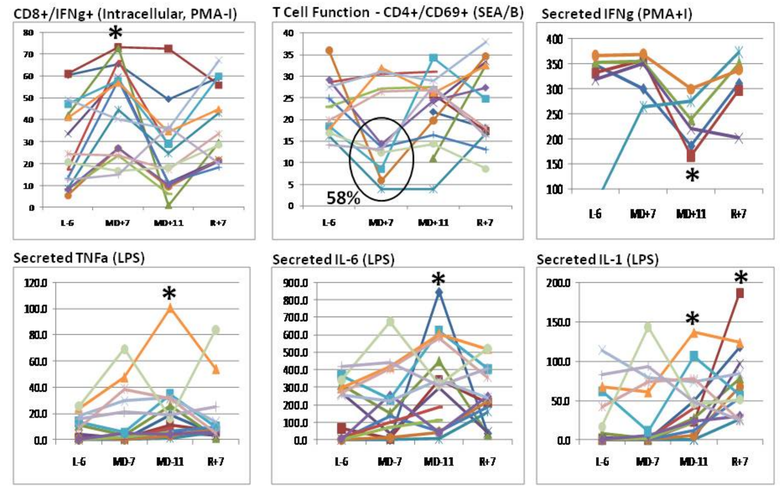


Figure 4: Virus-Specific Immunity, Cortisol, NfKB (n=16)

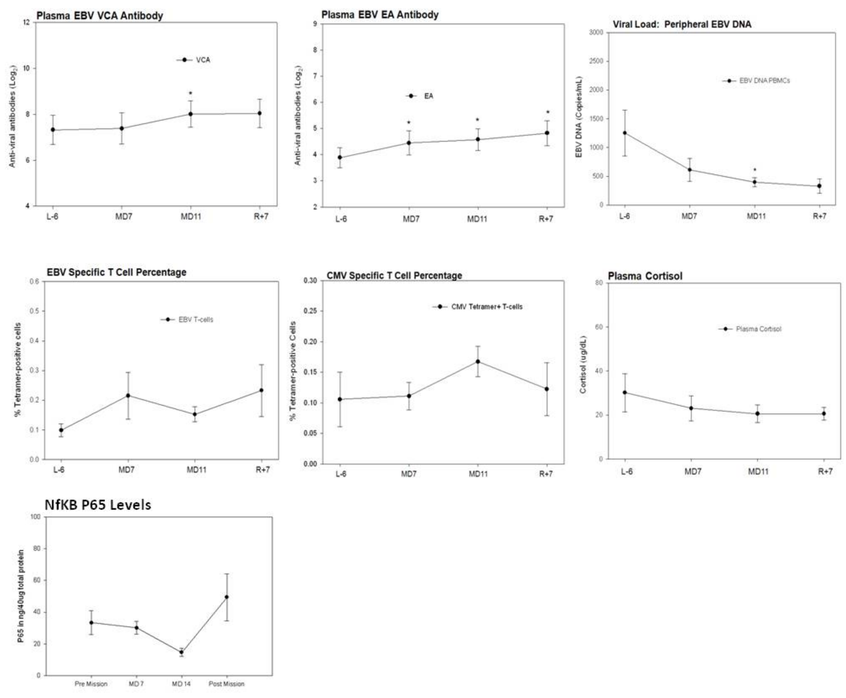
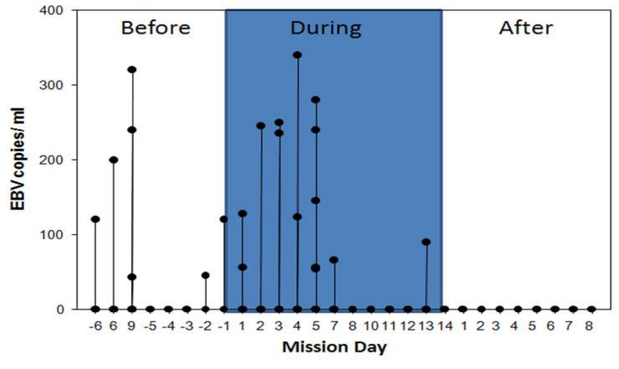


Table 1: Crewmembers with Reactivation of Latent Herpesvirus during NEEMO Missions (n=16)

	L-6	During	R+8
EBV	3	8	0
VZV	0	2	0
CMV	0	0	0

Figure 5: Shedding of EBV in Saliva during NEEMO Missions (n=16)



RESULTS

Mid-mission alterations leukocyte distribution occurred, including granulocytosis, elevated memory T cells, CD8+ T-cells subsets, constitutively activated T cells (Figure 1).

General T cell function was reduced during NEEMO missions in roughly 50% of subjects. Although the percentage of T cells secreting IFNg rose, the bulk production declined by MD11. Production of several inflammatory cytokines rose during NEEMO missions. (Figure 2).

Assuming R+7 to be the appropriate baseline: T cell production of IFNg, IL-5, IL-10, IL-2, TNFa and IL-6 were all reduced before and during the mission. Conversely, monocyte production of TNFa, IL-10, IL-6, IL-1b and IL-8 were elevated during mission, more so at the MD-14 time point (data not shown).

Granulocyte adhesion molecule expression (e.g. CD11b, CD62L) as assessed in NEEMO-14 indicated high activation during mission (data not shown).

Antibodies to Epstein-Barr virus (EBV) viral capsid antigen and early antigen were increased in approximately 40% of the subjects (Figure 4).

Changes in EBV tetramer-positive CD8+ T-cells exhibited a variable pattern. Antibodies against Cytomegalovirus (CMV) were marginally increased during the mission (Figure 4).

Herpesvirus reactivation was determined by PCR. EBV viral load was generally elevated at L-6 (Figure 4). Higher levels of EBV reactivation were found before and during the NEEMO missions (Figure 5), VZV reactivation occurred in 2 NEEMO crewmembers, no CMV reactivation was observed in any of the NEEMO mission or control samples (Table 1). Plasma cortisol was elevated at L-6.

CONCLUSION

Some changes in leukocyte distribution, T cell function, cytokine production, virus specific immunity and viral reactivation that occur during NEEMO missions are similar to those observed during or immediately following spaceflight.

Unfortunately, 6 days prior may be too near to mission start to serve as an appropriate baseline measurement.

The NEEMO platform may have utility for short-duration, ground-based spaceflight-immune research, such as investigations of mechanism or countermeasures validation.