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Brain MRI Findings of Altitude Chamber Personnel: An Investigational Update

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Disclaimer and Disclosures



- ✧ ***The opinions expressed during this presentation are solely those of the authors and do not represent an endorsement by or the views of the United States Air Force, the Department of Defense, or the United States Government.***
- ✧ ***The authors have no financial disclosures.***
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Background



- ✦ From 1994-2010, there were 73 documented DCS cases in U-2 pilots. Between 1994 and 2005, the number of annual cases ranged from 0-5; between 2006 and 2010, the number of annual cases increased to 6-10.***
- ✦ Additionally, there was a trend toward more severe (neurologic and pulmonary) cases between 2006 and 2010, with 22 cases compared to 10 cases the preceding 12 yr.***
- ✦ From 2006-2010, there was an increase in the average annual flight hours per pilot to meet wartime operational needs that correlated temporally with the increase in number and severity of DCS cases.***



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Background



- ✧ ***Recent (since 2010) brain MRI studies found white matter hyperintensities (WMH) not associated with observable neurological impact/deficit***
- ✧ ***AFMSA/SG9 study grants I-11-10 and I-11-44 authorized to evaluate WMH and their impact***
- ✧ ***Study compares analysis of U-2 pilots and hypobaric physiology personnel to flight surgeon & doctorate personnel controls***



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Hypothesis



If pilots exposed to high altitudes demonstrate changes on MRI...

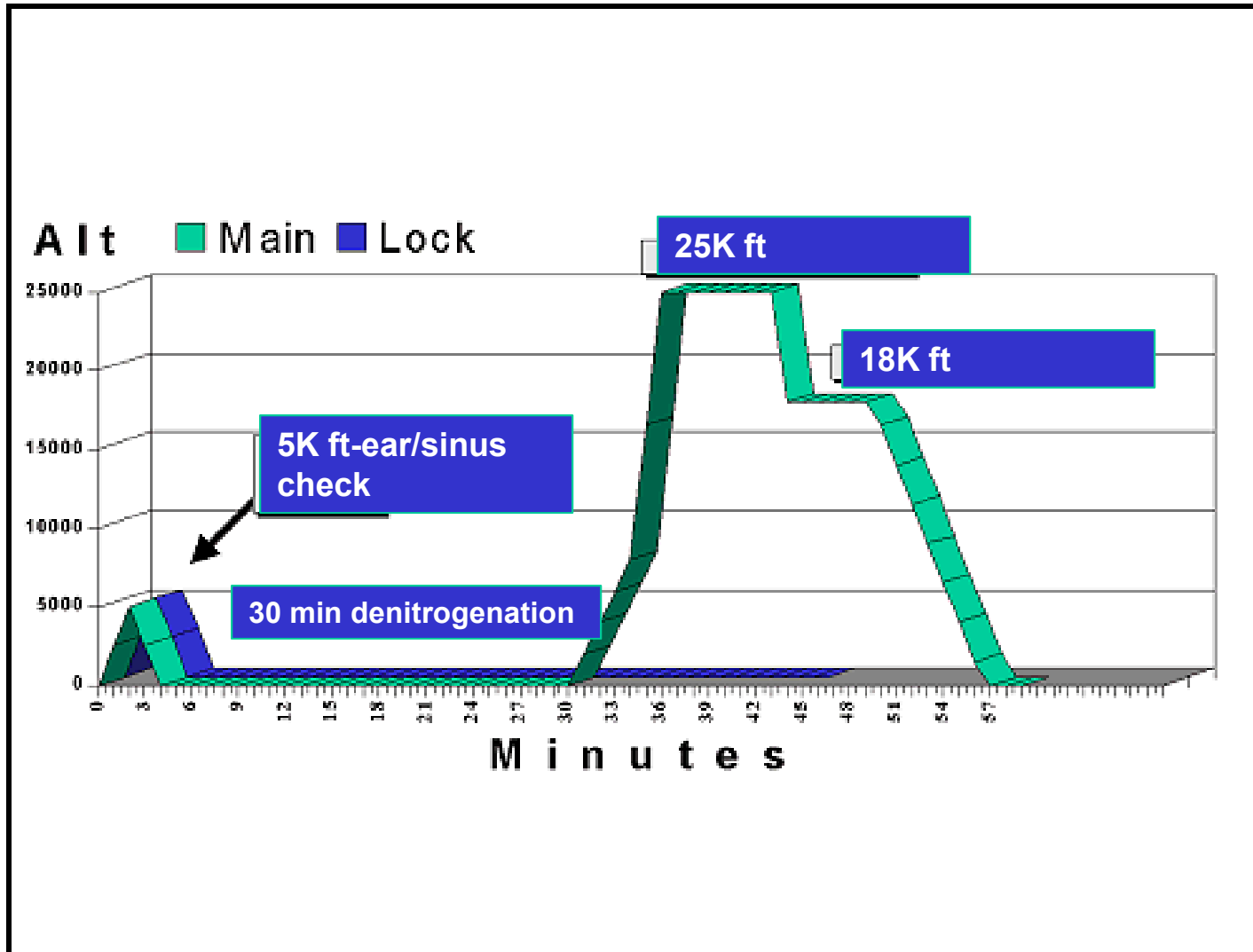
what about these folks?





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A Typical Altitude Chamber Exposure





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Investigative Study



- ✧ ***Age 26-50 active duty***
- ✧ ***FC-II neurological standards***
 - ✧ ***Exclusionary criteria:***
 - ✧ ***Significant head trauma/surgery***
 - ✧ ***Significant headache/migraine history***
 - ✧ ***Significant psychiatric history***
 - ✧ ***Family history of degenerative neurological disease***
 - ✧ ***History of seizure after age 6***
 - ✧ ***History of DCS***
- ✧ ***Doctorate limb (n=212)***
- ✧ ***Flight surgeon limb (n=82) – ≥ 1 operational tour***
- ✧ ***Altitude exposure limb (n=82) – > 50 exposures $> 20,000$ ft***
- ✧ ***Calibration limb (n=20)***
- ✧ ***Imaged at WHASC***



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Imaging



- ✧ ***Magnetom Verio 3T - Siemens Healthcare***
- ✧ ***3D Flair MRI high resolution (isotropic 800 μm)***
- ✧ ***WMH were identified and characterized by our neuroscientist team using post-processing software***
- ✧ ***Also collected were DTI, MRS, and ASL data not included in this report***



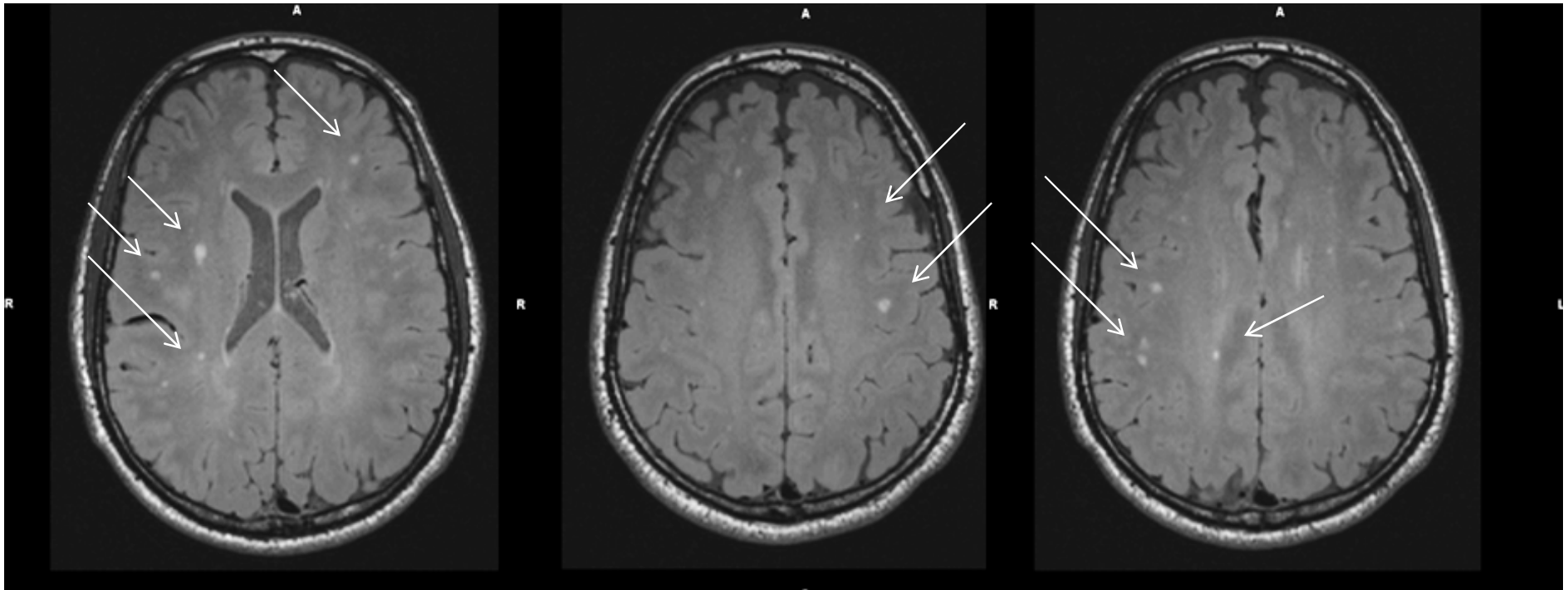
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Methodology



- ✧ ***All participants underwent MRI***
- ✧ ***Data analyzed using nonparametric Mann-Whitney test***
- ✧ ***We considered a $p\text{-value} \leq 0.05$ statistically significant***
- ✧ ***Data compared between hypobaric physiology personnel and Air Force officer controls (doctorate degree group), respectively***

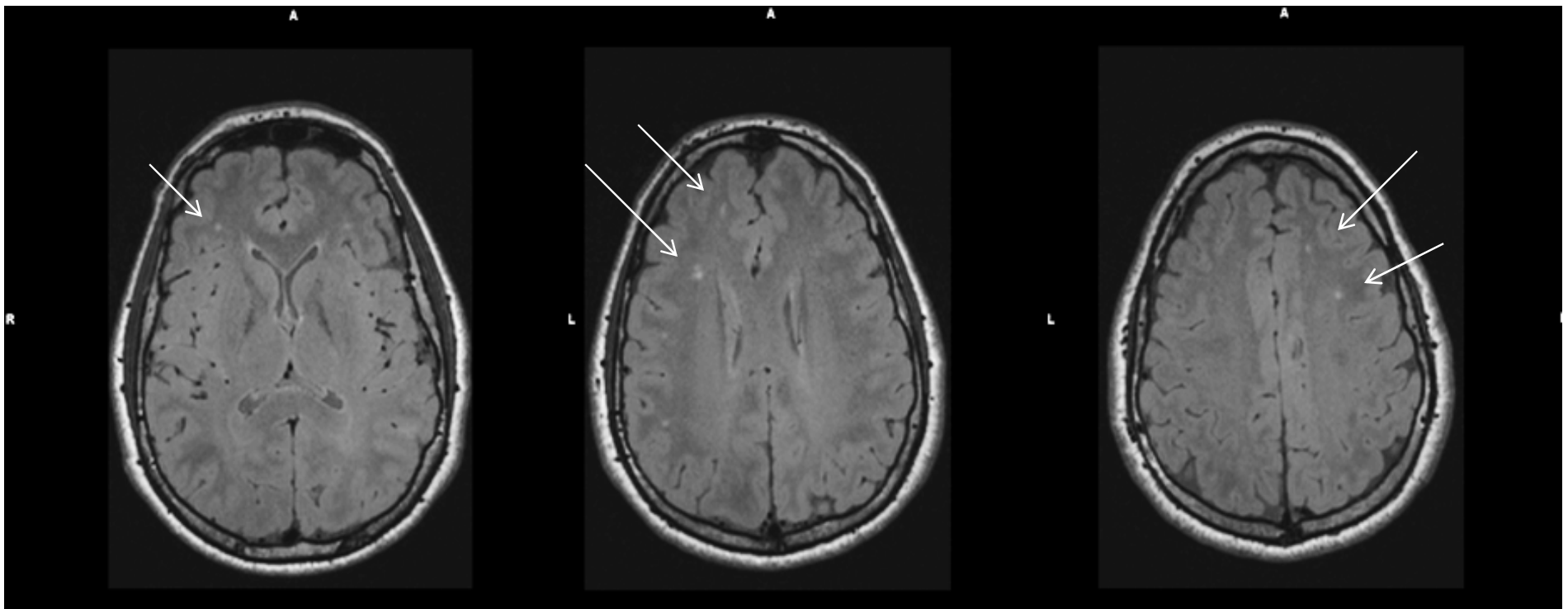
MRI Abnormalities in 2 Altitude Chamber Technicians





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MRI Abnormalities in 2 Altitude Chamber Technicians





WMH Comparison – Chamber

12/31/2012



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	<i>PHY (n=57)</i>	<i>DOC+FSG (n=102)</i>	<i>p-value (2-tailed Mann-Whitney)</i>
<i>Subcortical WMH vol</i>	<i>0.157±0.481 cm³</i>	<i>0.042±0.076 cm³</i>	<i>p=0.029</i>
<i>Subcortical WMH count</i>	<i>7.4±12.8</i>	<i>3.3±5.6</i>	<i>p=0.022</i>

✧ ***Significant difference between control (DOC+FSG) and PHY (hypobaric physiology personnel)***

✧ ***WMH distribution similar in pattern to DCS (U-2 pilots)***

✧ ***Unrelated to clinical episodes of NDCS***

✧ ***Correlation with exposure hours not yet performed***

✧ ***Difference noted for cortical thickness as well***



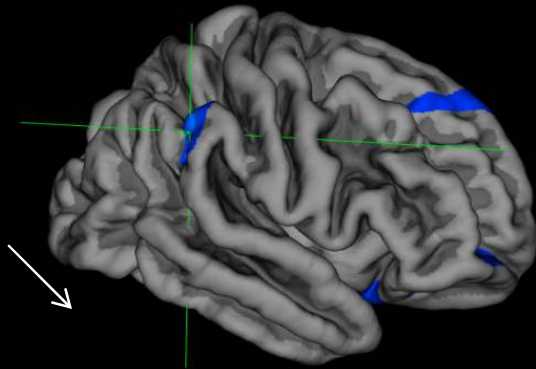
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Cortical Thickness

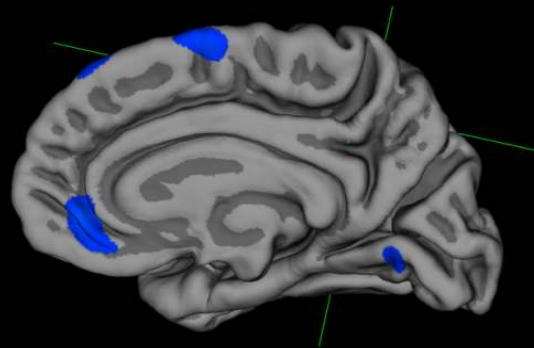
(*n*= 52 PHY; 75 DOC+FSG)



Does the average thickness differ between PHY and NRM?
Nuisance factors: Age
Contrast: rh-Diff-PHY-NRM-Intercept-thickness
n=127, DOF=123

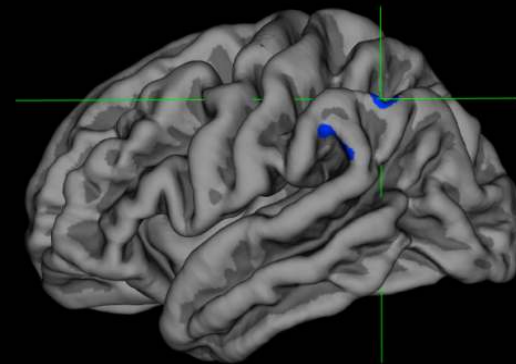


Does the average thickness differ between PHY and NRM?
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n=127, DOF=123



Blue-shaded regions represent areas of relative thinning of cortex compared to normative controls

Does the average thickness differ between PHY and NRM?
Nuisance factors: Age
Contrast: lh-Diff-PHY-NRM-Intercept-thickness
n=127, DOF=123





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WMH in Other Populations

- ✧ WMH nonspecific – seen in a variety of neurological conditions as well as a consequence of aging***
- ✧ WMH reported in high-altitude mountain climbers, even in the absence of clinical symptoms of mountain sickness – attributed to a combination of hypoxia and hypobaria***
- ✧ WMH change present in 23% (26/113) of Turkish military divers with no history of DCS compared with 11% (7/65) of controls***
- ✧ WMH change was found in 43.7% of French military divers with no history of DCS compared with 21.8% of controls***

Fayed et al. Am J Med 2006; 119(2):168.e1-6

Erdeml et al. Aviat Space Environ Med 2009;80:2-4

Gempp et al. Aviat Space Environ Med 2010; 81:1008-12



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Thus far...



- ✧ ***The data collected thus far in this investigation utilizing state-of-the-art, high-resolution MRI technology indicate increased volume and number of subcortical WMH in physiology personnel occupationally exposed to high altitudes vs. our control cohort.***



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- ✧ *The etiology of these microemboli remains elusive, with gas microemboli, platelet-thrombin aggregates, and inflammation all possibilities.*



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- ✧ ***The data collected thus far in this investigation utilizing state-of-the-art, high-resolution MRI technology indicate increased volume and number of subcortical WMH in physiology personnel occupationally exposed to high altitudes vs. our control cohort.***
- ✧ ***Based on a uniform WMH distribution, we postulate an underlying microembolic (<30- μ m) phenomenon as a cause for these WMH.***
- ✧ ***The etiology of these microemboli remains elusive, with gas microemboli, platelet-thrombin aggregates, and inflammation all possibilities.***
- ✧ ***Further investigation into the pathophysiology of WMH is warranted.***



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Implications?



- ✧ ***WMH associated with impairment of executive processing in other neurological diseases***
 - ✧ ***Statistical but not clinical deficits noted in U-2 pilots***
 - ✧ ***Is there a threshold effect?***
- ✧ ***Presumably a “static” process***
- ✧ ***Standard treatment for NDCS is hyperbaria***
 - ✧ ***Should this be augmented by anti-thrombotic or anti-inflammatory treatment?***
- ✧ ***Is there a dose:effect relationship to exposure?***



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Questions?





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Questions?



✧ Answers?



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Questions?



✧ *Answers?*

✧ *Thank you*