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## **WHITE MATTER HYPERINTENSITIES AND IMPLICATIONS FOR FUTURE ALTITUDE CHAMBER RESEARCH**

*HYPERINTENSES DE LA SUBSTANCE BLANCHE ET IMPLICATIONS POUR LA RECHERCHE FUTURE SUR LA CHAMBRE D'ALTITUDE*

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**Introduction:** Repeat exposure to non-hypoxic decompression stress is associated with increased white matter hyperintensities (WMH) on brain magnetic resonance imaging (MRI) of U-2 pilots, altitude chamber workers and divers. However, retrospective survey of altitude chamber participants in low intensity decompression stress associates excess WMH in a minority with past mild traumatic brain injury (MTBI). Further data are available following prospective study of brain MRI before and after altitude chamber studies in 2017.

**Methods:** Volunteers for hypobaric oxygen system assessments underwent entry (screening) and exit MRI (high resolution volumetric FLAIR) at the University of Nottingham, UK. For test-retest validity and to avoid bias, MRI data were analysed independently for total subcortical WMH number and volume at the University of Maryland, USA. Entry criteria were <6 WMH up to 0.08 mL total volume. The survey findings were updated and outcomes reviewed to consider implications for future altitude chamber research.

**Results:** Eleven research participants in 160 hypobaric exposures up to equivalent altitudes between 18,000 ft and 40,000 ft pressure altitude had eight WMH (total volume 0.166 mL) on study entry and five (0.184 mL) on exit. To date, 28 participants in 1577 hypobaric exposures over 15,000 ft do not manifest altitude-associated WMH. Excess WMH in four UK participants screened to date (12%, N=33) remain attributable to past MTBI, Fisher Exact Test statistic 0.0031 ( $P < 0.05$ ).

**Conclusions:** Low intensity (brief, infrequent) hypobaric exposure, including occasional hypoxia familiarisation, has not promoted WMH in healthy UK volunteers. The chosen altitude study entry criteria appear pragmatic, with just one screening failure (63 WMH occupying 2.38 mL); it may remain prudent to exclude volunteers with excess WMH from altitude research. A negative history of MTBI has 100% sensitivity and 100% negative predictive value for excess WMH (zero false negatives) in UK volunteers scanned to date (N=33).