## **Title:** Comparison of structural brain abnormalities and cognitive function in COPD patients after hospitalisation, stable COPD patients and healthy age-matched controls

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## **Introduction and Objectives:**

## Cognitive impairment is a common co-morbidity in chronic obstructive pulmonary disease (COPD) and is associated with poor disease management, greater disability and mortality [Chang et al J Am Geriatr Soc, 2012;60:1839-46]. We have previously shown that cognitive impairment is worse in COPD patients during and after hospitalisation for exacerbations, than in those with stable disease [Dodd et al Chest, 2013;144:119-27]. Our aim was to use multimodal brain magnetic resonance imaging (MRI) to compare structural brain abnormalities between hospitalised and stable COPD patients and healthy controls.

## **Methods:**

23 COPD patients hospitalised for exacerbations within the last year (hospitalised), 17 COPD patients not hospitalised within the last year (stable) and 23 healthy age-matched controls, were recruited. Exclusion criteria included neurological or psychiatric disorders, cerebrovascular disease or hypertension. Cognition was measured using the Montreal Cognitive Assessment. T1-weighted (T1W), diffusion tensor (DTI) and Fluid Attenuated Inversion Recovery (FLAIR) were acquired using a Philips 3T scanner. The following brain indicators were calculated: normalised whole brain and ventricular volumes (scan: T1W, software: SIENAX), white matter microstructural fractional anisotropy and mean diffusivity – compared voxelwise using tract–based spatial statistics (DTI, FSL), and white matter lesion volume (FLAIR, *dispunc*). Ethical approval was obtained (15/LO/0425).

## **Results:**

Cognition was clinically impaired in hospitalised COPD (median (IQR); 23.0(5)) but not in stable patients (27.0(2)) or controls (28.5(3)), with a significant difference only between hospitalised patients and controls (*p*<0.0001). No significant differences were found in normalised whole brain volume, however, normalised brain ventricular volume was significantly greater in hospitalised COPD, compared to stable COPD (*p*=0.046) and controls (*p*=0.028). Hospitalised and stable COPD patients had widespread significant reductions in fractional anisotropy and increased mean diffusivity throughout the white matter skeleton, compared to controls (*p*<0.001). Hospitalised patients had the highest white matter lesion volume, however this was not significantly different between groups.

## **Conclusions:**

Hospitalised COPD patients have greater cognitive impairment compared to stable COPD and controls with evidence of greater ventricular and white matter lesion volumes and damaged white matter microstructure. Mechanisms behind these neuropathological processes and possible links to observed cognitive dysfunction remain unclear, but may involve ischaemic small-vessel disease.

Table 1: Clinical, demographic and MRI indicators in hospitalised and stable COPD patients and controls

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | Hospitalised COPD | Stable COPD | Controls | *P* value | Post hoc tests |
| Number (n) | 23 | 17 | 23 | - | - |
| Age (years)1 | 69±11 | 67±7 | 66±7 | 0.477 | - |
| Gender (% male)2 | 61% | 60% | 46% | 0.540 | - |
| FEV1 (% predicted)3 | 51±18 | 54±24 | - | 0.604 | - |
| Smoking (pack years)4 | 43 (35) | 60 (25) | 0 (3) | <0.0001 | H>C\*\*S>C\*\* |
| Cognitive function (/30)4 | 23.0 (5) | 27.0 (2) | 28.5 (3) | <0.0001 | H>C\*\* |
| White matter lesion volume (ml)5 | 8.9 (17.0) | 7.4 (16.5) | 3.0 (7.2) | 0.026 | - |
| Normalised whole brain volume (ml)5 | 1399 (113) | 1424 (121) | 1381 (111) | 0.736 | - |
| Normalised brain ventricular volume (ml)6 | 71.1±27.6 | 52.8±22.8 | 53.1±19.1 | 0.016 | H>S\*H>C\* |

Values are given as mean±standard deviation or median (interquartile range). Statistical tests: 1. One-way analysis of variance; 2. Pearson Chi-square test; 3. Independent t test; 4. Kruskal-Wallis test with post hoc Dunn-Bonferroni; 5. Kruskal-Wallis test; 6. One-way analysis of variance with post hoc Bonferroni; \**p*<0.05; \*\**p*<0.0001.