Results: In 2022, there were 91 deaths for the city and county (14.8/100,000) significantly higher than (8.14/100,000) in England and Wales (X^2=16.4, p<0.00001). The city had significantly more deaths (N=67;25.0/100,000, X^2=95.6, p<0.00001) versus the county (N=18;5.2/100,000). Mean age of death 43.2±9.0 and 23% were women. Most deaths in the county occurred in urban areas. Median age of death for Males was 42.6 yrs. and Females 45.2 yrs. (SD±9.0). Most implicated drug causing death was heroin and morphine (23.1%), methadone (16.5%) like national data, whilst benzodiazepines (15.4%) were higher than national (p>0.05). Most deaths were caused by more than one implicated drug 82.4%. 64.8% of deaths occurred in a person known to be using drugs. Many deaths had methadone implicated (N=28; 30.8%) and 50 deaths had methadone at PM of which 11 were prescribed. Most deaths (N=55; 64.7%) occurred in the top decile of IMD and occurred in the top 4.4% most deprived neighbourhoods.
Conclusion: Socioeconomic deprivation was associated with higher rates of drug-related deaths; most deaths occurred in the most deprived areas. Addressing deprivation-related risks in economically challenged areas is critical to effectively tackling drug deaths and health inequalities. The cause of death was most often opioids and strategies such as take-home naloxone and optimising opioid substitution treatment will be vital to reduce deaths. We note a high proportion of deaths had methadone, which was not prescribed, present at postmortem, indicating that prescribed methadone may have been diverted. Drug services may consider strategies to increase use of supervised consumption as per guidelines to reduce diversion and associated deaths.

A Spatial Covariance ^{123}5IA-85380 SPECT Study of α4β2 Nicotinic Receptors in Dementia with Lewy Bodies

Dr Judith Harrison[1,2], Dr Sean Colloby[1], Prof John O'Brien[3] and Prof John Paul Taylor[1,4]

[1]Translational and Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Newcastle, United Kingdom; [2]Northumbria NHS Healthcare Foundation Trust, Newcastle, United Kingdom; [3]Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom and [4]Central Newcastle Tyne and Wear (CNTW) MHS Foundation Trust, Newcastle, United Kingdom

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Aims: Cholinergic dysfunction is key in dementia with Lewy bodies (DLB), and likely to influence the cognitive and psychiatric symptoms of this condition. However, patterns of spatial covariance in DLB in terms of nicotinic acetylcholine receptors (nAChRs) is unknown. In this study we used ^{123}I-5-iodo-3-[2(S)-2-azetidinylmethoxy] pyridine (^{123}5IA-85380) SPECT (α4β2 nAChR assessment) to investigate the covariance patterns in DLB and their associations with cognition.
Methods: Fifteen DLB and 16 healthy controls underwent ^{123}5IA-85380 and rCBF (^{99m}Tc-exametazime) SPECT scanning. We applied voxel principal components (PC) analysis, generating a series of PC images representing common intercorrelated voxels across subjects. Linear regression generated specific α4β2 nicotinic and rCBF covariance patterns that contrasted DLB from controls.
Results: A α4β2 pattern that distinguished patients from controls ($F_{1,29}$ = 165.1, p<0.001), showed relative decreased uptake in bilateral temporal pole, inferior frontal, amygdala, olfactory cortex, insula, anterior/mid cingulate and putamen, as well as relative preserved/increased uptake in sensorimotor, fusiform and occipital lobe, implicating regions in a nicotinic receptor expression sense, within limbic, salience, default mode, olfactory, sensorimotor and visual networks. We then successfully derived from patients, α4β2 nicotinic receptor patterns that correlated with $CAMCOG_{total}$ (r=−0.52, p=0.04), MMSE (r=−0.68, p=0.01) and $CAMCOG_{memory}$ (r=−0.70, p=0.01), demonstrating a common 'cognitive' topography of relative decreased binding in lateral/medial prefrontal, lateral temporal, inferior parietal and thalamus along with relative preserved/increased binding in cingulate, insula, occipital and medial temporal regions, structures representing a range of networks supporting executive, language, social cognition, attention and sensory functions.
Conclusion: In conclusion, disease and cognitive related patterns of cholinergic α4β2 nicotinic receptor binding were apparent in DLB and could inform future therapeutic targets of these receptors in this condition.

Clozapine and Risk of Haematological Malignancies: Insights from a Meta-Analysis

Dr Omar Kassar[1,2], Dr Osama Hassan[3,4], Dr Moaz Elsayed Abouelmagd[5], Dr Muataz Kashbour[6] and Dr Omar Shaheen[1]

[1]Faculty of Medicine, Alexandria University, Alexandria, Egypt; [2]Medical Research Group of Egypt, Negida Academy, Arlington, Massachusetts, USA; [3]Central and North West London NHS Foundation Trust, London, United Kingdom; [4]Faculty of Medicine, Zagazig University, Zagazig, Egypt; [5]Faculty of Medicine, Cairo University, Cairo, Egypt and [6]Dignostic Radiology Department, National Cancer Institute, Misrata, Libya

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Aims: Clozapine, the first and most effective atypical antipsychotic for schizophrenia, is typically reserved for treatment-resistant cases due to its serious adverse effects. Recent studies have linked clozapine to an increased risk of haematological malignancies (HM). This meta-analysis is the first to systematically investigate this association.
Methods: We performed this study in accordance with the Cochrane Handbook for Systematic Reviews and Meta-analysis of Interventions. Eligible studies included involving patients treated with clozapine, regardless of the primary psychiatric diagnosis, cohort, case-control, cross-sectional that reported the association between clozapine use and the risk of haematological malignancies.
Results: Five studies were included in our meta-analysis (three retrospective cohorts and two case-control studies) involving a total of 211,427 patients. The overall odds of developing HM were significantly higher in the clozapine group compared with the control group (OR=2.1, 95% CI, 1.39–3.18, p=0.00005, I2=83%). Sensitivity analysis was conducted, and heterogeneity was resolved by exclusion of the study by Brainerd et al. The overall effect after its exclusion suggested a significant increase in the odds of HM (OR=2.45, 95% CI, 1.75–3.43, p< 0.00001, I^2=48%). Subgroup analysis showed that the odds of developing leukaemia (OR=4.02, 95% CI, 2.22–7.27, p<0.00001), and lymphoma (OR=6.27, 95% CI, 2.83–13.9, p<0.00001) were significantly higher than the combined risk for all HM. There was no significant association between clozapine and HM with a cumulative dose of <999 defined daily