Exploring the epigenome to identify biological links between the urban environment and neurodegenerative disease: an evidence review

Sophie Glover[1] (sglover08@qub.ac.uk), Dr Claire Hill[1], Prof Bernadette McGuinness[1], Prof Amy Jayne McKnight[1], Prof Ruth Hunter[1]
[1] Queen's University Belfast, School of Medicine, Dentistry and Biomedical Science, Centre for Public

Background and Aims

Over half of the global population currently reside in **urban areas** (1).

In tandem, our global population is **ageing**, with the number of people with **dementia** (a result of neurodegeneration) is expected to more than double to **139 million persons by 2050** (2).

Physical pollutants of the urban environment (e.g., **air pollution**) are identified **risk factors** of neurodegenerative disease (3) while other **urban environmental characteristics** (e.g., **urban green and blue space**) have been associated with a **reduced risk** of cognitive impairment and dementia from exposure (4).

The **biological pathways** by which the urban environment contributes to neurodegenerative disease risk and pathology are **not fully understood**.

Epigenetics (dynamic modifications to the genome) has been associated with exposure to urban environmental characteristics (5) and neurodegenerative disease (6) respectively (**Figure 1**).

This **underlying biology** may help us better understand how the **urban environment** is **linked** to **neurodegenerative disease**.

Aims:

- **Summarise** the evidence on the influence of key urban environment factors which are known to affect human cognitive function

- **Highlight** the benefits of epigenetic exploration to assess the link between the urban environment and neurodegenerative disease

- **Identify** the current understanding of biological pathways from the literature between the urban environment and neurodegenerative disease through epigenetics
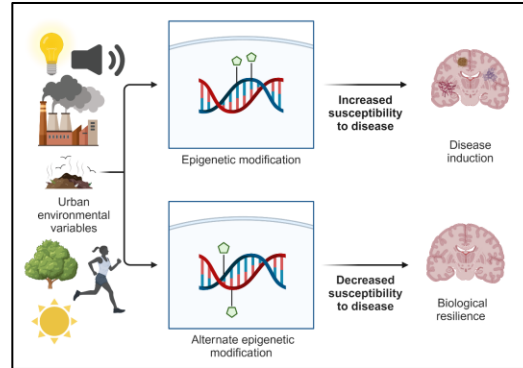

Fig 1. Exposure to urban environmental characteristics resulting in differential cognitive outcomes due to resilience.

The urban environment and cognitive function

Noise pollution — **Increased risk** of cognitive impairment from chronic exposure

Light pollution — **Sleep deprivation, oxidative stress and circadian disruption**

Air pollution — **Increased risk** of Alzheimer's disease and Parkinson's disease

Soil pollution — **Oxidative stress, blood brain barrier penetration and gene alteration**

Green and blue space — **Decreased risk** of cognitive impairment and dementia

Physical and social activity, reduced temperature, reduced stress, Attention Restoration Theory, improved mental health

Epigenetics and Analytical Techniques

Epigenetic modifications occur throughout the life course from **environmental exposure**.

Epigenetic modifications influence how **genes** are **expressed**; they can increase or decrease expression which can have **harmful consequence on health** or result in **resilience** (7).

DNA methylation is one of the most common epigenetic modifications (**Figure 2**).

Analytical techniques have been developed which allow us to visualise epigenetic modifications:
- **Epigenetic Clocks**
- **Epigenome-Wide Association studies**
- **Mendelian Randomisation**

These techniques can aid in **detecting a biological link** between environmental exposures and neurodegenerative disease.
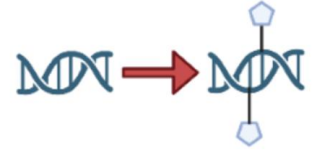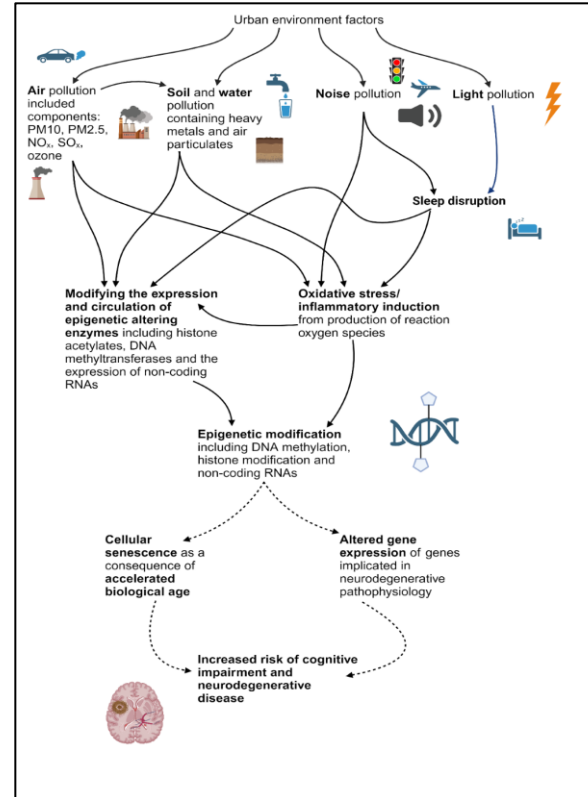

Fig 2. DNA methylation from the addition of methyl groups to a DNA molecule.

Biological Pathways

Current research allows us to **elucidate** biological pathways but not fully understand the process from environmental exposure to the disease state (**Figure 3**).

Fig 3. The biological pathways involving epigenetic mechanisms which link urban environment pollutants and neurodegenerative disease.

Conclusion

Future research will require us to:
- Perform **analysis** to assess **causal relationships**
- **Disentangle complex interactions** through taking a **systems approach**
- Use **multi-omic data**, incorporating multiple types of environmental data to understand interactions and subsequent molecular consequences

Through this research, we will **improve our understanding** of the complex relationship between the urban environment and neurodegenerative disease.

This will enable us to recommend **public and urban policy recommendations** in the hopes of **reducing the burden** of **neurodegenerative disease** on our ageing population.

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