Adrenergic regulation of immunosenescence and cognitive function across the life course: preliminary data

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Introduction

- The **sympathetic nervous system** (SNS) is involved in brain-immune communication[1].
- Ageing is associated with changes in the immune system, which can result in age-related morbidities[2].
- Increased adrenaline and noradrenaline (A/NA) levels and immune ageing have separately been linked to **cognitive decline**[3] (Fig. 1).

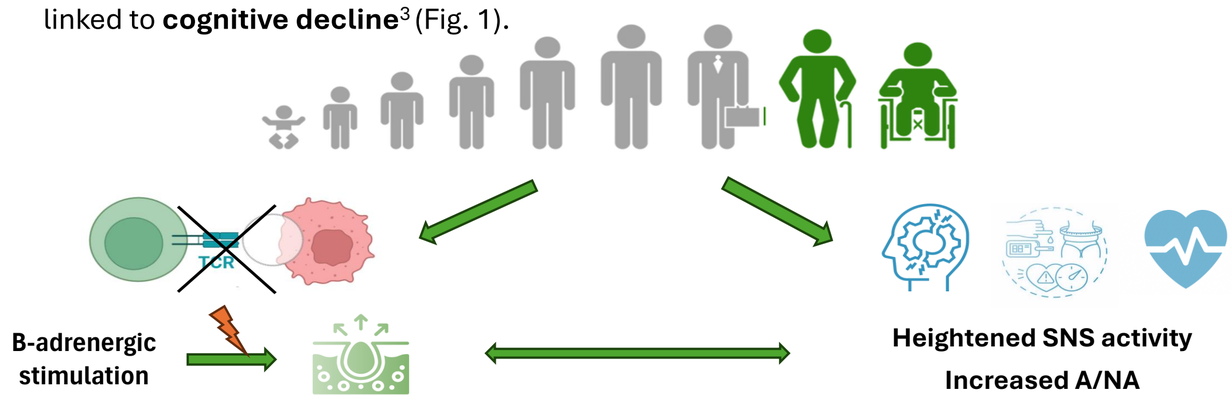
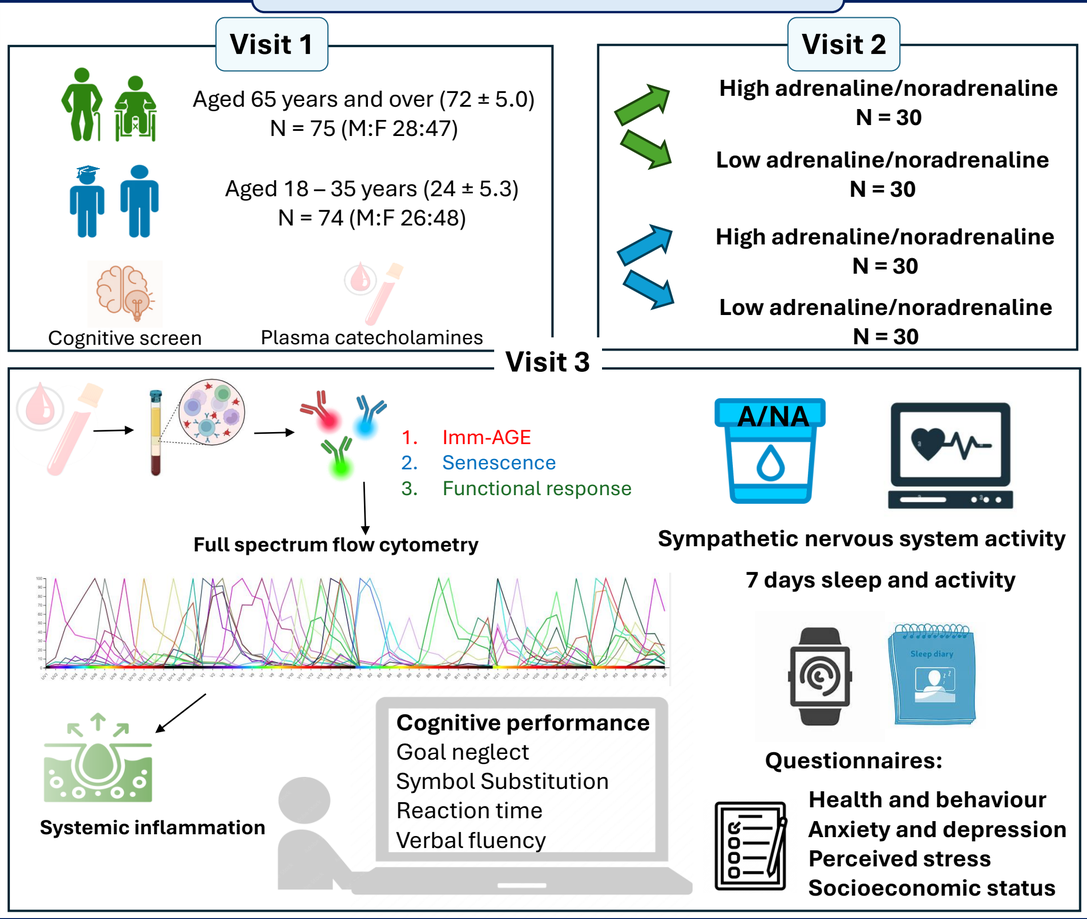


Fig 1. Heightened SNS activity and adrenergic signalling are found in many age-related morbidities including cognitive decline and are also known to induce features of the immune system associated with ageing.

Aim: to determine whether heightened SNS activity is associated with increased immune ageing and if this is linked to cognitive function.

Methods



Results

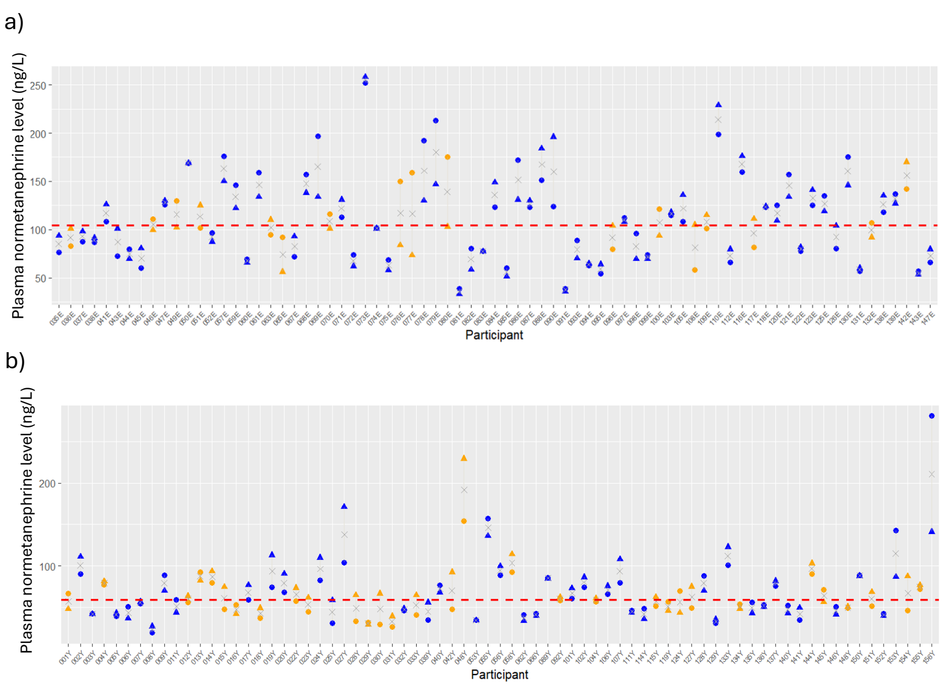


Fig 2. Normetanephrine levels at visit 1, visit 2 and mean of visits (y axis) per a) older and b) younger participant (x axis). The dashed red line shows the age group specific median value across both time points. Those in orange are excluded based on inconsistency of values across visits and those in blue are included based on having the highest or lowest values and consistency across time-points.

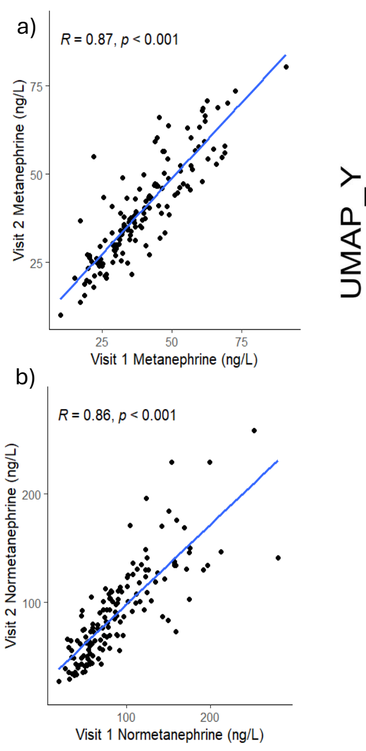


Fig 3. Correlation between levels of a) metanephrine and b) normetanephrine at visit 1 and 2.

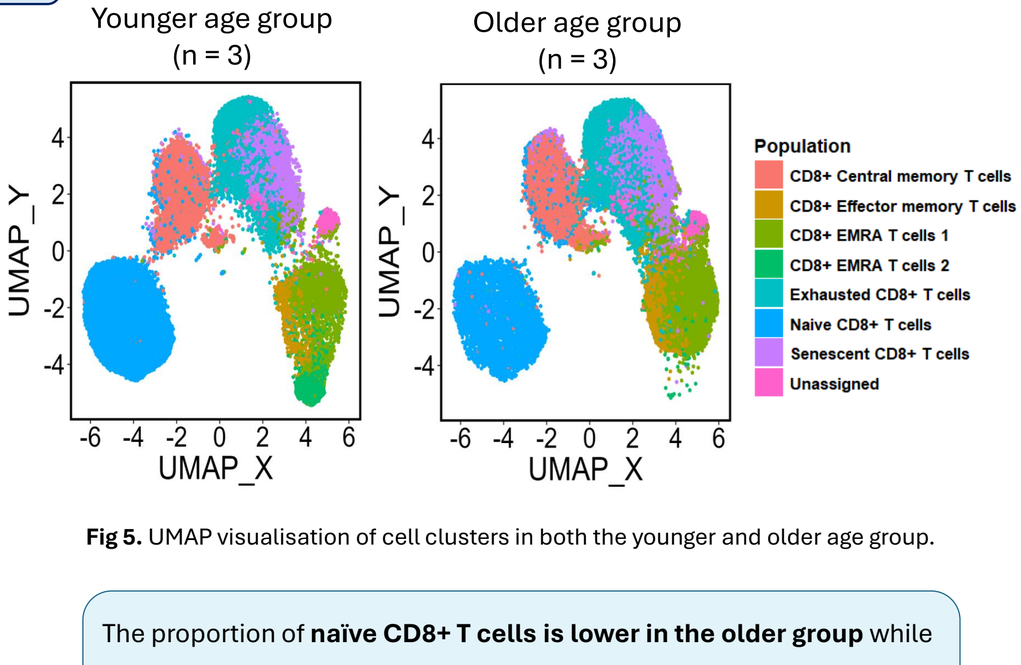


Fig 5. UMAP visualisation of cell clusters in both the younger and older age group.

The proportion of **naïve CD8+ T cells is lower in the older group** while proportions of terminally differentiated and **senescent CD8+ T cells are higher** in the older group.

Participants were stratified based on plasma levels of catecholamines at visit 1 and visit 2. Only those **with consistently high or consistently low values**, compared to the age-group median, were invited back for visit 3.

There was a strong, significant correlation between visit 1 and visit 2 levels of both metanephrine (r = 0.87, p <0.001) and normetanephrine (r = 0.86, p < 0.001).

Plasma normetanephrine is correlated with measures of depression, perceived stress, attention and executive function.

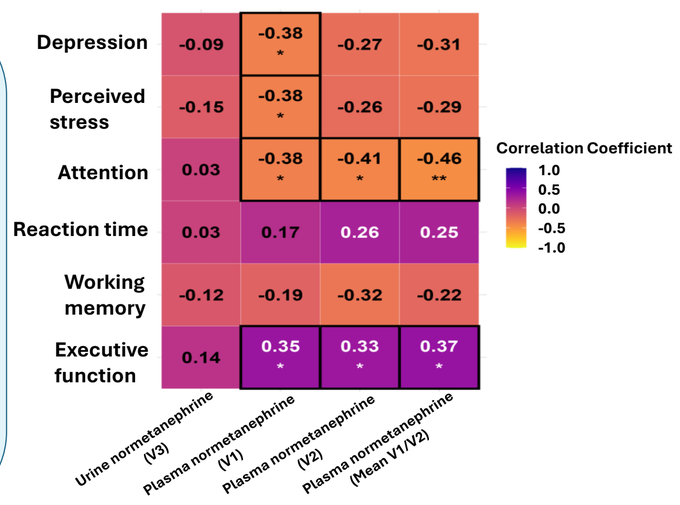


Fig 4. Correlation between catecholamines, stress and cognition.

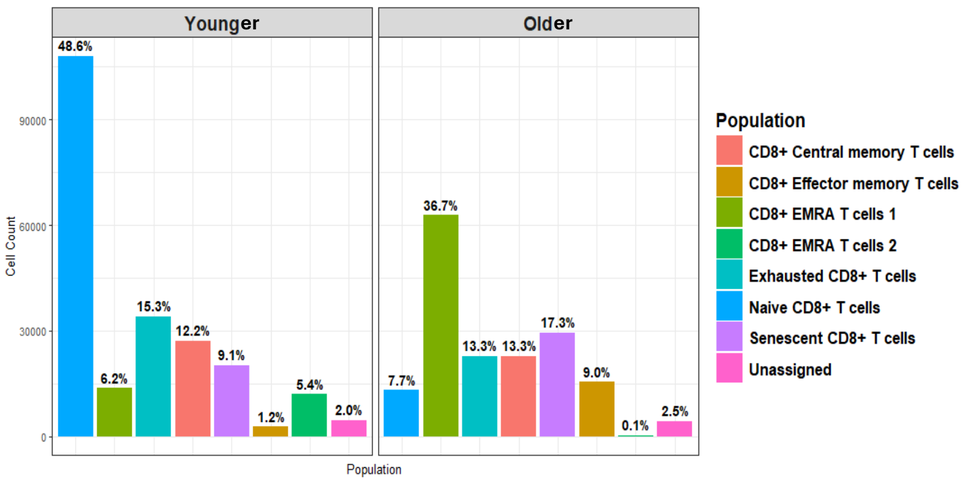


Fig 6. Percentage of each cell population shown in the UMAP for both the younger and older age group.

Conclusions

Visit 1 and 2 plasma catecholamine levels showed strong agreement between visits conducted 4 – 8 weeks apart.

Participants have been stratified and invited back for visit 3 in four groups: **younger, lower SNS activity and higher SNS activity; older, lower SNS activity and higher SNS activity** (n = 30 in each group)

Preliminary analysis of a 27 – marker flow cytometry panel for senescence shows a **reduced proportion of naïve cells and increased proportion of some terminally differentiated cells** in the older age group compared to the younger age group, as expected. Ongoing analysis is examining how SNS activity impacts these changes in immunity.

Next Steps

Complete study visit 3 for all 120 participants

Begin analysis with participants stratified by sympathetic nervous system activity

Calculate Imm-AGE score and investigate relationship with cognition and sympathetic nervous system activity

Assess ex vivo functional responses to stimulation

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