The Age Estimation Science Advisory Committee

AESAC

Interim report on the scientific feasibility of using DNA methylation to assist in assessing the age of unaccompanied asylum-seeking children - Research Template

Topic background & key issues

The Home Office Chief Scientific Adviser (HO CSA) has commissioned the Age Estimation Science Advisory Committee (AESAC) to undertake a review of DNA methylation in relation to its potential use for assessing the age of unaccompanied asylum-seeking children (UASC) whose ages are questioned. The interim report concluded that further research work would need to be/should be undertaken before DNA methylation could offer any substantive evidence for application in Scientific Age Assessment (SAA).

The Panel have collated this guidance to enhance the recommendations of the interim report, by indicating the issues that would need to be taken into consideration if further research work on DNA methylation for age assessment of UASCs is commissioned. It builds on the knowledge and expertise that AESAC has acquired in the formulation of the interim report.

Overview of the strength of available evidence in the area.

DNA methylation is an epigenetic process whereby molecules known as methyl groups, separate from those that dictate the genetic sequence, can become attached to an individual's DNA. This methylation occurs at certain locations in the genome. These areas are known as known as CpG sites (cytosine followed by guanine, separated by one phosphate group). The proportion of CpG methylation that occurs at specific sites in the DNA sequence can be used to provide an estimate of an individual's age that is strongly correlated with their chronological age. Other life-associated processes can also influence methylation status and when age is assessed without regard to these, the measure is referred to as 'biological age.'

If the right combination of methylation sites is incorporated into an appropriate model, it may be possible to estimate the individual's age to within an agreed level of accuracy.

This process is not straightforward. Factors such as the sample tissue type, the demographics of the population being considered, and the environmental conditions they have been exposed to may lead to significant variation in the levels of DNA methylation in a given sample. DNA methylation sites should therefore be selected to minimise bias and uncertainty caused by variation in the fitted model.

To date, most research on using DNA methylation to estimate chronological age has been conducted on primarily white populations in Western Europe and North America. This is not representative of the asylum-seeking population, in which variation in both genetic characteristics and exposure to environmental factors such as acute stress may lead to variation in DNA methylation patterns.

As a result, AESAC presently recommend against the use of DNA methylation as an age assessment tool. This is because there is not enough current, applicable scientific data to be able to develop a representative model and determine its efficacy. Nevertheless, AESAC acknowledge the potential advantage of this approach in comparison with current methods of age assessment, subject to further research and review.

There is ongoing interest in producing an age assessment model that would limit the impact of certain epigenetic factors, such as disease and account for environmental genetic factors such as geographic origin and population stress. Mitigating the impact of these factors through research, would make assessment of chronological age more accurate.

The Panel outline the questions that must be considered if undertaking such a study, below.

The efficacy of age assessment tools must be determined both independently and in conjunction with other SAA methods, to ascertain if an accurate combination approach can be applied to SAA.

Considerations and Requirements for this research

The factors that must be considered to enable DNA methylation to be assessed as an appropriate method to determine chronological age are:

<u>Ethical underpinning of the research</u>

It must be ensured the research process is ethically sound and appropriate from beginning to end. The target population is particularly vulnerable, so this must be assured at all research stages. Ideally, independent ethical approval should be sought prior to undertaking this research.

Factors such as:

- how to store participant-identifiable data in a secure way and comply with General Data Protection Regulations
- how often the study should be independently reviewed
- how participants can decline DNA methylation analysis without negative inference.

Population study – Establishing a reference group of DNA methylation samples

Conduct of this research would require a large cross-sectional dataset of tissue samples from suitable individuals of confirmed age, to act as a reference group. The tissue samples would be from individuals of similar characteristics to UASCs, including, but are not limited to: age range, geographic origin, life experience, protected characteristics and socioeconomic status. The individuals would have their tissue samples processed and scientifically age assessed through DNA methylation.

Second phase of the study

The age of individuals of unconfirmed age can be assessed in different ways including Merton-compliant age assessment and biological assessment of the hand/wrist or third molar. The likelihood of the age assessed by biological methods and/or Merton assessment can be combined using the likelihood ratio. The resulting age can then be compared to the age proposed by DNA methylation.

This stage of the research should be coupled with a questionnaire to capture detail on the level of stress the UASC has experienced. As talking about their trauma may trigger repressed emotions, interpreters and psychological support should be provided to the study participants to ensure that they are supported appropriately.

Appropriate sample collection methods

The degree of DNA methylation can be estimated using blood samples. However, this would be inappropriate for UASCs, where use of invasive methods should be minimised in a vulnerable population to reduce potential of further harm and trauma. Therefore, a non-invasive sample collection method such as a buccal swab would be preferable.

DNA methylation site selection

DNA methylation sites should be selected that are strongly associated with chronological age and agnostic of the subject UASC’s genetic and environmental background.

Impact of Stress/Trauma

Where possible, the tissue samples should be derived from individuals who have experienced similar stresses to UASCs. As such, a comprehensive understanding of factors that might impact on the stress of UASCs and others is required.

It should be noted that the experience of stress and trauma, and its effects on the body, will be unique to each individual. The challenge in quantifying this must be acknowledged as a limitation to the DNA methylation age assessment model.
Proposed timescale and funding for completion The research process should be timely to reflect current understanding and methodology and be flexible to advances in epigenetic understanding and research over time. Alternatively, if DNA methylation age assessment is shown not be sufficiently accurate, the study should be halted until epigenetics is better understood and developments in this field of study have progressed.

Glossary

Biological age: The biological age of an individual is a measure of how their body has changed over time taking into account environmental and genetic factors, it is a relative measure of chronological age which reflects the fact that the body physiologically changes over time.

Chronological age: Chronological age is defined as the time elapsed since birth.

Epigenetics: The study of heritable traits, or stable changes of cell function, which occur without changes to the DNA sequence.