Multi-omics microsampling for the profiling of lifestyle-associated changes in health

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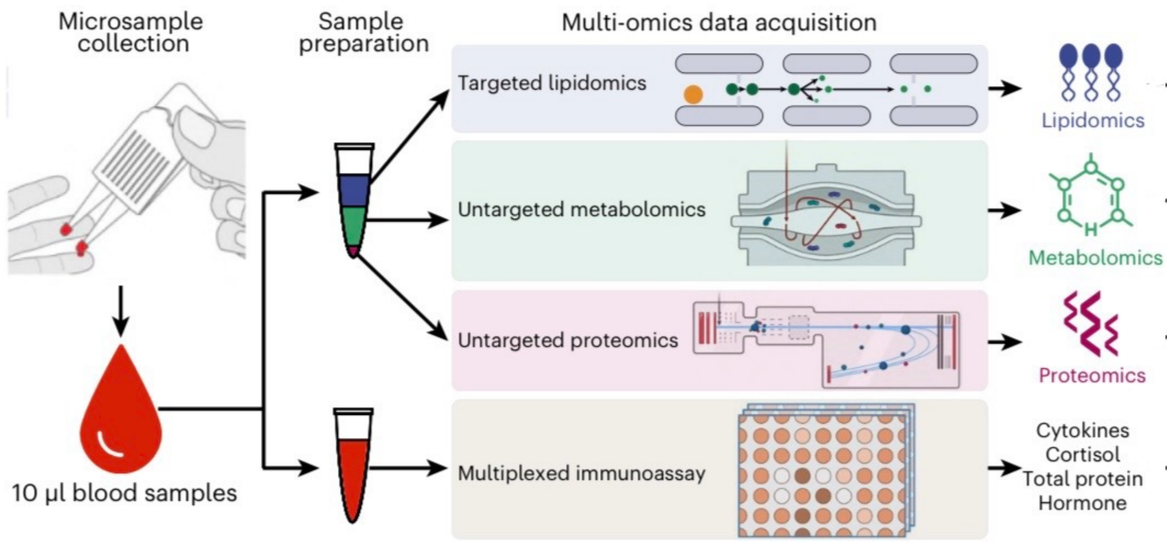
BACKGROUND

- Traditional healthcare methods used to examine blood biomarkers tend to be reactive, sparse and infrequent, limiting their efficacy in clinical practice.
- This study explores the viability of using finger prick blood drop collections of 10 µl coupled with wearable sensors to concurrently analyse biological molecules.
- It aims to discover and profile patients' responses towards various interventions, facilitating the personalisation of healthcare for the individual.

METHODS

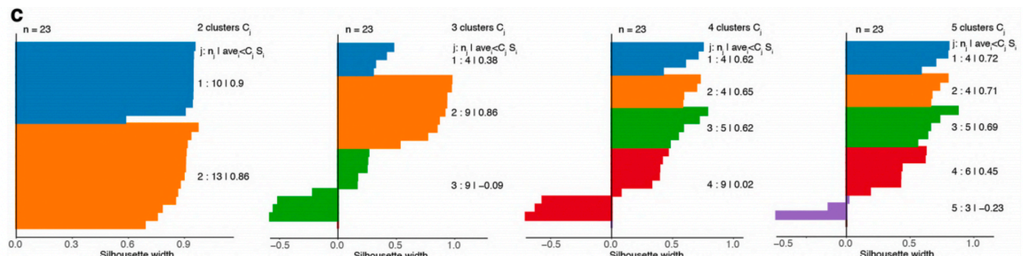
- This study comprises four sub-studies, with participants who were enrolled under an IRB-approved protocol with written consent.
- The first part involved checking the stability of microsampling by assessing the stability of proteins, metabolites, and lipids in microsamples under varying storage durations, temperatures, and their interaction.
- The second assessed the reliability and accuracy of microsampling to obtain molecular profiles, as compared to traditional venous sampling. Untargeted metabolomics and lipidomics data were generated and analysed.
- The third evaluated metabolic response (metabolomics, lipidomics and cytokines) to drinking of Ensure shake at 5 timepoints as measured by microsamples, which were used for multi-omits data acquisition. Statistical analysis continued to group it further into clusters.
- The last section was a 24/7 personalised whole physiome study using wearable and multi-omics data of a single participant, with microsamples collected every 1-2h during waking hours over 7 days. General patterns in the data were searched and then grouped into clusters.

Data collection method

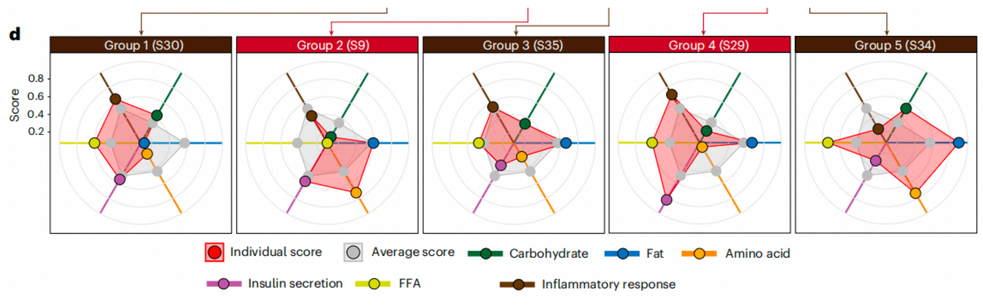


RESULTS

- When using the microsampling approach, proteins are the most stable analytes (median CV 0.397), followed by metabolites (median CV 0.378) then lipids (median CV 0.335).
- Blood samples collected via microsampling closely resembled those from traditional venous blood draws. Spearman correlations were 0.81 for metabolites and 0.94 for lipids, demonstrating high similarity. Metabolites and lipids that were not well correlated (Spearman correlation <0.5) were enriched with amino acids and triglycerides respectively.
- Variability in kinetics of metabolic responses between individuals. 2 distinct clusters of individuals were identified - group 1 participants showed faster, more pronounced changes in their metabolic profiles after consuming the shake. Whereas group 2 participants exhibited slower or more gradual metabolic responses.

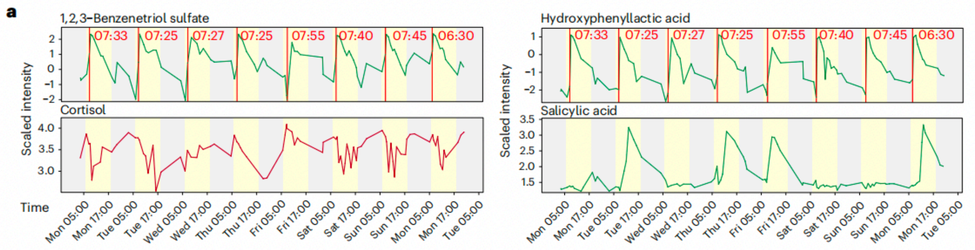


- For each participant, there is a consistent distribution pattern of the molecular species within each metabolic score. However, those patterns differed greatly across subjects demonstrating high inter-individual variability in the metabolism of nutrients.



- Two major clusters of molecules followed circadian patterns. Cluster 4 mainly containing metabolites peaked in the daytime whereas cluster 11 mainly containing lipids peaked at night.

- Within-day cortisol levels may not represent accurate inter-day cortisol patterns for an individual.



- Identification of a subclinical event which may represent an asymptomatic infection or stress event. Detected due to a rise in both inflammatory cytokines (for example, TNFα and CD40L) and as well as several others that decreased (for example, eotaxin).
- It is plausible that circadian lipids were driven by individual rhythmic kinetics or gut microbes.
- Using the random forest model, 24 wearable features were able to accurately predict the changes in 447 molecules out of 2,223 molecules. ($R^2 > 0.3$). Lipids and cytokines, especially triglycerides, were strongly correlated with wearable features.
- High degree of association between wearable and multi-omics data that coincides with previous studies conducted. New insights include the blood coagulation pathway positively correlates with HR and the neutrophil degranulation pathway negatively correlates with HR.

DISCUSSION

- The multi-omics microsampling approach is able to measure thousands of biological molecules with high reliability and stability.
- Compared to the traditional dried blood spot (DBS) sampling, this method allows for minimally invasive, user-friendly and frequent sampling.
- However, this study is limited by potential biomolecule degeneration under certain storage conditions and restriction to measuring specific biomolecules like proteins, lipids, metabolites and cytokines. Such limitations can be overcome by expanding the cohort size and measuring additional biomolecules like DNA, RNA, and epigenomes.
- Another possible research topic that can be explored is whether the microsampling approach can be used in hospitals for therapeutic drug monitoring.
- To summarise, multi-omics microsampling has great potential for biomarker discovery and personalised health monitoring. It offers an accessible, scalable, and efficient solution to advance precision medicine.