Longitudinal Variation in Volatile Organic Compound Levels in Whole Saliva

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Background

Volatile organic compounds (VOCs) are potential non-invasive biomarkers of disease. Variation in VOCs levels may reflect an individual's metabolic profile. Disease-specific VOCs have been reported in benign and malignant states; predominantly related to the oral cavity (halitosis, oral abscess and oral cancer). VOCs linked to the oral cavity include short chain fatty acids, polyamines, sulphur compounds. Before wider adoption of salivary volatolomics as a non-invasive diagnostic strategy, it is first important to establish the variation in VOC profiles both within and between healthy subjects.

Aim

To assess the intra- and inter- individual variability of VOC levels within whole saliva.

Methods

Unstimulated whole saliva was collected from participants after a minimum of 6 hours fasting on 5 mornings over a 3 week period (week 1: 3 samples, week 2: 1 sample, week 3: 1 sample). Exclusion criteria included: smokers, active oral disease, immunosuppression, clinically significant systemic disease. Triplicates of 500uL of saliva in 20mL glass headspace vials were incubated for 30 minutes at 37°C. Direct headspace analysis with the SIFT-MS (VoiceUltra200, Syft Technologies) was used to quantify VOCs with a targeted approach for short chain fatty acids (SCFA). Osmolality and production (flow) rates for each saliva sample was determined.

Results

Ten healthy participants (7 female) were recruited with a median age of 30 (IQR:25-32). Acetic-, butyric and propanoic acid demonstrated a wider variation within individuals. A single individual produced acetic acid levels ranging from 6.0 to 16ppbv (CV% 54), and butyric acid between 3.0 and 10ppbv (CV% 53). Hexanoic- and pentanoic acid remained the most consistent with low variability; CV% 14 (0.6 - 0.9ppbv) and CV% 11 (2.9 – 4.0 ppbv) respectively. The mean salivary flow rate for the cohort was 0.7ml/min (IQR: 0.5-0.9) and osmolality 77mOsm (IQR: 57-89). The inter-individual variability over the 3 weeks was minimal for butyric-, hexanoic- and pentanoic acid ($p>0.05$). Acetic acid ($p=0.03$) and propanoic acid ($p<0.001$) were statistically different.

Conclusion

Select VOCs within saliva can vary significantly within an individual. However, there is minimal inter-individual longitudinal variation with an acceptable coefficient of variation. It is important to define a normal range of VOCs in a healthy population to determine clinically significant disease-specific VOCs.

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