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Analysis of Vis–NIR spectra changes to measure the inflammatory response in the nasal mucosal region of influenza A and B virus-infected patients

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ABSTRACT

Background: Human influenza A and B viruses cause severe seasonal respiratory tract infections, especially in infants and young children. Influenza A and B viruses have been reported to produce different symptoms and/or severity in infected patients, although these remain inconclusive.
Objectives and study design: In this study, non-invasive visible and near-infrared (Vis–NIR) spectroscopy was used for comparative analysis of the inflammatory response to influenza A and B virus infections, by measuring changes in water peak (970 nm) spectra collected from patient nasal mucosal regions.
Results: The results suggested that infection with influenza B virus induced more severe inflammatory responses in the nasal mucosal region than influenza A virus.
Conclusions: These are the first data showing different inflammatory responses to influenza A and B viruses at the sites of virus infection.

1. Background and objectives

Temperature is an important indicator of circadian rhythms, and physical and mental activities. Body temperature can reflect an abnormality in blood flow or fever as a result of an inflammatory response, and provide useful diagnostic information. For example, breast cancer screening can be performed by detection of differential temperatures of 1 °C[1] or 2.5 °C.[2] Malignant tumors show a 1–2 °C increase in temperature compared to the temperature of arterial blood.[3] In contrast, a high temperature of about 43 °C is essential for cancer therapy.[4]

Thermography can be used to analyze surface and body temperature, but cannot quantify body temperature due to its low accuracy. Nuclear magnetic resonance (NMR) spectroscopy, microwave radiometry,[5] and ultrasound thermometry[6] can also detect temperature change. However, none of these methods is applicable to local or regional temperature changes. In contrast, near-infrared radiation (NIR) transmitted through the body can be used for determining temperature changes in a small body region.

Recently, the potential of visible and near-infrared (Vis–NIR) spectroscopy for virus diagnosis has been reviewed.[7] Vis–NIR spectroscopy measures absorption of near-infrared radiation. Oxyhemoglobin, deoxyhemoglobin, cytochrome c oxidase, and water are the major biological molecules absorbed by Vis–NIR radiation.[7] Water is especially sensitive to temperature changes, showing an increase in Vis–NIR absorption and a peak shift. In this study, Vis–NIR spectra was analyzed to investigate the inflammatory response in the nasal mucosal region of patients with non-influenza virus, influenza A virus, and influenza B virus infections.

2. Study design

2.1. Patients and nasal fluid collection

Clinical nasal aspirates were collected from 244 pediatric patients at the Baba pediatric clinic during the 2006–2007 influenza season (December 26, 2006 to March 31, 2007). The collection method was described previously.[8] Briefly, saline was introduced into the nasal cavity, and fluid was collected using a Belvital nasal aspirator (Melisana, Nogent-sur-Marne, France). To remove cell debris, the nasal fluid was filtered using a stainless steel mesh with 200 grids per inch (25.4 mm). The filtered nasal aspirates were analyzed by immunochromatography for influenza A and B viruses as described below.

Abbreviations: NA, neuraminidase; NIR, near-infrared; NMR, nuclear magnetic resonance; PCA, principal component analysis; SNV, standard normal variate; Vis–NIR, visible and near-infrared.

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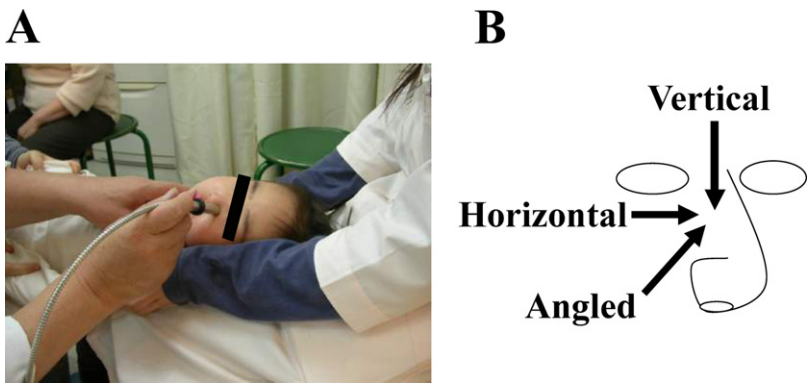

Fig. 1. Directions of Vis–NIR spectra collection from the nasal mucosal region. (A) Picture of representative patient during Vis–NIR spectra collection at the angled direction. (B) Schematic showing the three directions for Vis–NIR spectra collection: angled, vertical, and horizontal.

An axillary electric thermometer C202 (Thermo Corp., Tokyo, Japan) was used for measurement of patient central core temperature.

This research project was approved by the Ethics Committee of the Research Institute for Microbial Diseases of Osaka University and written informed consent was obtained from all children's parents.

2.2. Immunochromatography

Immunochromatography for influenza A and B virus nucleoprotein was performed using a Quick-S Influ A/B kit (Denka Seiken Co. Ltd., Tokyo, Japan) or a Capilia Flu A+B kit (Alfresa Pharma Corporation, Osaka, Japan). The sensitivity and specificity of these commercial antigen detection kits for influenza A in Japan were

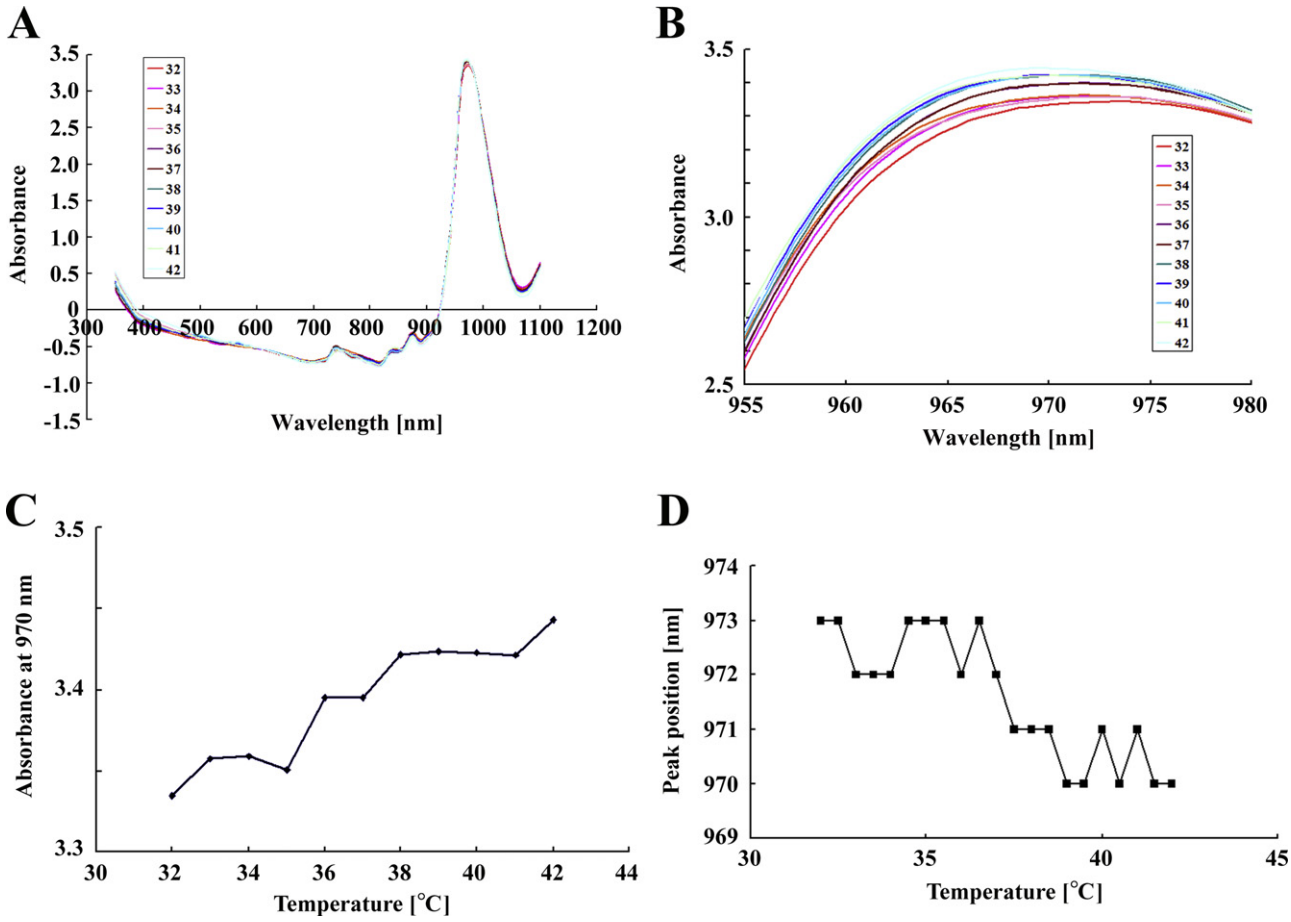

Fig. 2. Temperature dependence of the water Vis–NIR spectra. Water spectra were measured as a function of temperature, with the water temperature controlled by a water bath. The collected spectra were transformed by smoothing and SNV correction in wavelength region (A) 350–1100 nm and (B) 955–980 nm. A sharp peak around 970 nm was observed in the spectra. Temperature-dependent increased absorbance of the peak around 970 nm (C) and blue-shift of this peak (D) was observed.