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KM developed the program, conceived and designed the study, performed the experiment and the analysis and drafted the manuscript. TY developed the program, conceived and designed the study, performed the analysis, and helped to draft the manuscript.

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Abstract

Heart rate (HR) and normalized pulse volume (NPV) are physiological indices that have been used in a diversity of psychological studies. However, measuring these indices often requires laborious processes. We therefore developed a new smartphone program, named iPhysioMeter, that makes it possible to measure beat-by-beat HR and \ln NPV using only a smartphone. We have examined its accuracy against conventional laboratory measures. Mental stress tasks were used to alter HR and \ln NPV in 12 participants. The Bland-Altman analyses revealed that there was negligible proportional bias for HR and \ln NPV, and for their change values expressed as Δ HR and $\Delta \ln$ NPV. However, there was a relatively large fixed bias for \ln NPV and a small one for $\Delta \ln$ NPV, though both were within the limits of agreement. These findings suggest that iPhysioMeter can yield valid measures of the absolute level of HR and relative changes in \ln NPV.

Keywords: electrocardiograph, finger photo-plethysmograph, iPhone, mobile health

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Heart rate (HR) and pulse volume (PV) are frequently used physiological measures in a wide range of psychological studies. Examples include the study of mental stress, health, mental disorders, emotion, and memory (e.g., Hamer, Tanaka, Okamura, Tsuda, & Steptoe, 2007; Matsumura, Yamakoshi, Noguchi, Rolfe, & Matsuoka, 2012; McNally et al., 2004; Sawada, Tanaka, & Yamakoshi, 2001). However, despite this widespread use, there are resource requirements and technical hurdles to be overcome before these indices can be reliably and conveniently measured. These include the setting up of laboratory or ambulatory sensors and instruments, the application of analysis software, and the provision of the associated technical expertise. These requirements are often outside the core expertise of the user groups, who wish to focus their skills and effort on the application sphere.

Of direct relevance to this situation has been the rapid evolution of compact yet powerful computing and communication devices, notably the emergence of the smartphone. In addition to allowing convenient mobile communication, the smartphone's processing power offers the possibility of measuring physiological indices using only the commercially available device itself (Jonathan & Leahy, 2010; Jonathan & Leahy, 2011; Scully et al., 2012). By using the light emitting diode (LED) of the inbuilt flash as a light source and the semiconductor (CMOS) camera as a light sensor, the smartphone can be configured as a photo-plethysmograph (PPG) and, among other things, then be used as a pulse wave recorder. Thus HR and normalized PV (NPV), reported to be a valid cardiovascular index of autonomic nerve activity (Sawada, et al., 2001), can be measured without using additional devices.

However, despite such progress, further significant developments are necessary. First, although the feasibility of calculating heart rate from the smartphone PPG has been

shown, its experimental validation has not yet been carried out. Second, to the best of our knowledge, there are no reported studies concerning the validation and use of the PV signal. Third, a beat-by-beat auto analysis program, to obviate the need for laborious manual analysis of the raw data, has not yet been made available for use with a smartphone. In this study, we therefore developed a smartphone program, named *iPhysioMeter*, equipped with all of the above-mentioned functions, and we then conducted an experiment in which HR and NPV were changed by psychological tasks. Our purpose was to examine the agreement of HR and NPV measurements derived from the *iPhysioMeter* and conventional laboratory equipment.

Method

Participants

A total of 12 university students (five women and seven men, age range: 21–24 years), recruited through flyers, participated in this study. The main aim of this study was not hypothesis testing but to determine the extent of agreement between two measurement techniques, we therefore used the same sample size as was used in the first published NPV study (Sawada, et al., 2001) under the condition that the number was even. The criteria for inclusion in the study were to be over 18 years of age, having no history of or current cardiovascular disease, and not taking any prescription medication. No participant declared either current or past history of being a smoker. Participants were asked in advance to refrain from any medication for 24 hours before laboratory testing and to avoid consumption of food and caffeine-containing substances, and intense physical activity for 2 hours before laboratory testing. They received about US\$2.5 for their participation. Written informed consent was obtained from participants after we had provided them with a complete description of the study. The ethical committee of Kanazawa University approved this study on May 18, 2011 (No. 9).

Measurements and Devices

Laboratory measurements. Beat-by-beat heart rate (HR) was derived from the R-R interval of the Electrocardiogram (ECG). Lead II of the ECG was obtained with disposal electrodes connected to standard bioamplifiers (John et al., 2009) built in the authors' laboratory.

Normalized pulse volume (NPV), an index of α -adrenalin mediated sympathetic activity (Sawada, et al., 2001), was calculated by dividing the AC, or pulsatile, component of the finger photo-plethysmogram (PPG) by the DC component. The finger PPG was measured in the transmittance mode using a 810 nm near-infrared light-emitting diode (LED) as the light source and a photodiode as the photo sensor, placed on opposite sides of the tip of the left middle finger. The sensors and an amplifier to which the sensors were connected were built in the authors' laboratory, as previously reported (2011). A logarithmic transformation was applied to the NPV values to normalize the distribution.

All signals were sampled at a rate of 1 kHz with a resolution of 16 bits using an A/D converter (National Instruments, USB-6218), and stored digitally in a computer (DELL, Latitude 5430).

iPhysioMeter. iPhysioMeter is a program that was developed using Xcode 4.3.3 developer tool (Apple), and designed to run on iPhone 4, 4S, or 5 smartphones with iOS 5.1 (Apple) and later.¹ The measurement principle is based on reflectance mode PPG, where the camera flash LED serves as the light source and a complementary metal oxide semiconductor (CMOS) image sensor (camera) as the photo sensor. In the present study the sampling rate was approximately 30 Hz (30 fps), which is the maximum speed allowed for iPhone 4 and

Footnotes

¹ The iPhysioMeter is available for free at the iTunes store where this program is distributed worldwide.

4S, and the resolution of light intensity detected by the CMOS camera was 8 bit each for red, green, and blue light on each of the 192×144 pixels (Apple., 2011). Although the pulse wave can be measured using any of the three light colors (red, green, or blue), we chose to use the green light, because previous studies have consistently shown its superiority over red and blue in terms of the relative freedom from motion artifacts and high signal/noise ratio (Jonathan & Leahy, 2011; Maeda, Sekine, & Tamura, 2011). Green light detected by the CMOS camera is averaged among all of the 192×144 pixels, and then artifacts are minimised by low-pass filtering implemented in software to produce the PPG DC component. The AC component is separated from the DC component using a software high-pass filter.

The application is run by tapping its icon on the iPhone's home screen. Then the flash LED and CMOS camera must be gently covered with the tip of the left index finger (Figure 1, A), whereupon measurement will start automatically after a 6-sec delay period during which time the CMOS camera is calibrated. This calibration was accomplished by using the camera calibration functions of iOS with the setting of white balance mode fixed. Once the measurement process is established, the detected pulse waves are displayed on the screen, and real-time beat-by-beat analysis is carried (Figure 1, B). HR is calculated from the peak-to-peak intervals in the pulse wave. NPV is subsequently derived by dividing the foot-to-peak amplitude of the AC component by the DC component; the latter is not seen on the display. Values departing significantly from the most recent 10-sec data trend, were treated as outliers. The 10-sec interval was determined on the basis of the 0.1 Hz characteristic frequency of Mayer waves (Julien, 2006). All beat-by-beat data were stored on the iPhone's memory. To stop or restart measurement, it is only necessary to touch the stop/start button displayed on the screen, or to press the stop/start hardware button of the wired headphone, normally provided with iPhone or third party product. Once finished measuring, stored data can be sent by e-mail *via* Wi-Fi or a Bluetooth wireless network.

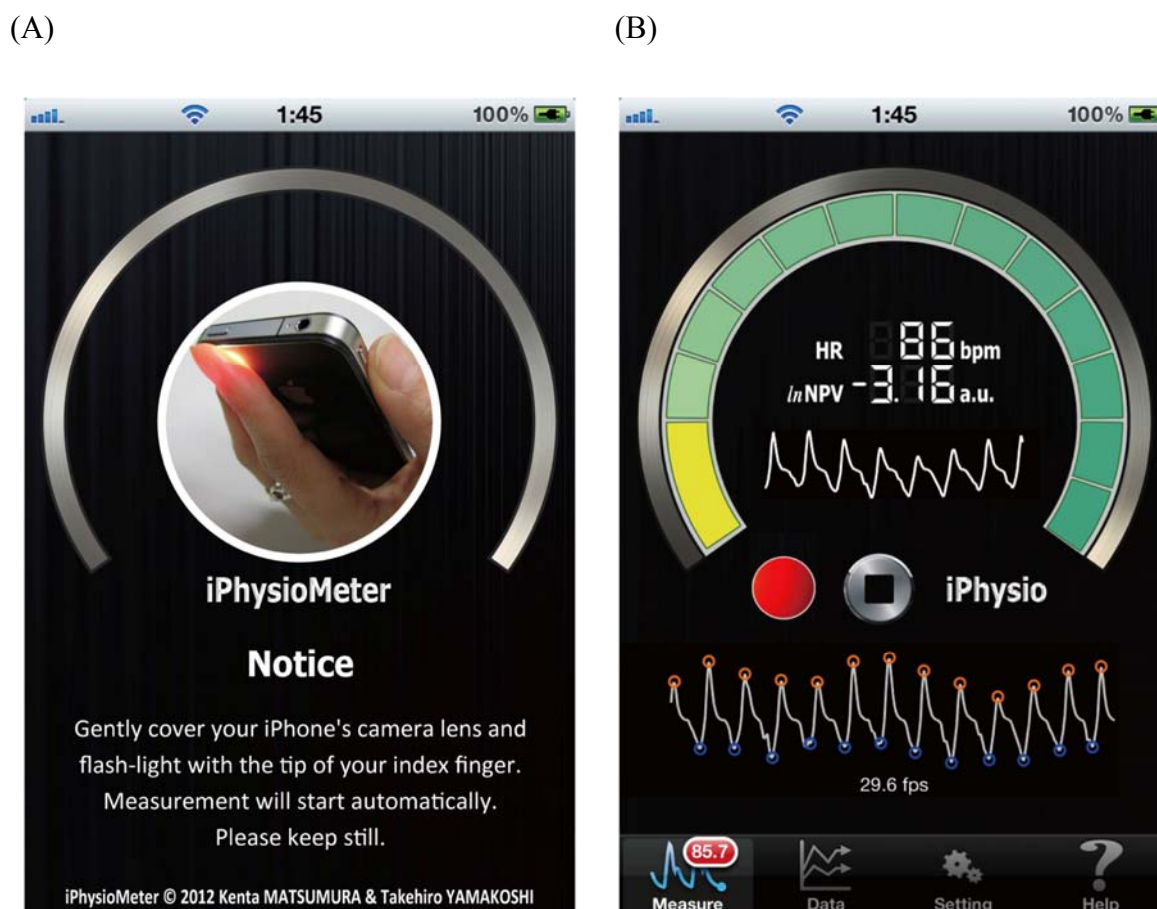


Figure 1. (A): An initial screen of iPhysioMeter. How to position the index finder on the iPhone is depicted with a brief description. (B): Typical example of the main screen of iPhysioMeter. The pulse wave measured is displayed in real-time across the screen. The numerical results of on-line beat-by-beat analysis of heart rate (HR) and normalized pulse volume (NPV) are displayed in the center and are also shown on the lower part. bpm = beats per minute, a.u. = arbitrary unit.

Procedure

The experiment was performed in a 2×5 -m, sound-attenuated experimental room, maintained at a temperature of 27–28°C. Although this temperature seems rather high, all the participants felt comfortable wearing light summer clothing. First, the participant sat in a reclining chair in front of an LCD monitor (EIZO, FlexScan S1721), keeping their left arm at heart level and the palm of the hand upward. The LCD monitor and a headphone (Sony, MDR-CD900ST) were used to present stimuli. Next, the sensors and instruments were attached to the participant, and they were then asked to hold the iPhone 4S (Apple) on which the iPhysioMeter was installed. The participant was then asked to keep as still as possible in order to minimize movement artifacts. Only one iPhone 4S was used in this study and, when measuring, no other applications were running in the background. The display of the iPhone was monitored by a further LCD monitor using a HDMI adapter. Finally, the left hand of the participant was covered with a black cloth to prevent them from looking at the iPhone's display.

The experimental procedure adopted in this study was essentially identical with that used in the first published NPV study (Sawada, et al., 2001). The experiment began with a 10-min rest period, the last 3-min of which was used as a baseline (BS). In this period, the participant was asked to sit still and observe the blank LCD screen where the stimulus would be shown. Next, they performed two kinds of mental stress task, one was a 3-min period of mental arithmetic (MA), and the other was a 3-min period of mirror tracing (MT). These two tasks were selected to evoke somewhat different physiological responses. In the MA task, the participants were required to subtract 13 sequentially from 5000 (to get 4987, 4974, 4961,...) as quickly and accurately as possible (e.g., Matsumura, et al., 2012). In the MT task, the participants were required to trace a narrow star-shaped track presented on the LCD clockwise as quickly and accurately as possible, without deviation using a cross-hair cursor on the LCD, which moved as the mirror image of a track pad (Apple, Magic Trackpad) (e.g.,

Sawada, Nagano, & Tanaka, 2002). These tasks were separated by a 5-min rest interval, and their order was changed and equalized across the participants. iPhysioMeter was rebooted between conditions.

Data Analysis

Beat-by-beat HR and \ln NPV values were averaged for each 1-min period. Then, delta change (Δ) values were calculated by subtracting the first 1-min BS value from the remaining two BS, three MA, and three MT values to conduct detailed analyses.

All 1-min average data were further averaged to produce single BS, MA, and MT values. These values were compared using a series of one-way repeated-measure analysis of variance (ANOVA) tests. The Greenhouse-Geisser correction was applied to the degree of freedom where appropriate. For post-hoc comparison, Tukey *HSD* was used to compare the differences among conditions.

To evaluate the correspondence between the two measurements, geometric mean regression (Ludbrook, 1997) and Bland-Altman analysis (Bland & Altman, 1986) were used. In the former, slope, intercept, and correlation coefficient (Pearson's r) were calculated, whereas in the latter, the mean of the differences (fixed bias) and correlation coefficient between the differences and averages were calculated. In each analysis, a total of 108 1-min data pairs, three conditions \times three 1-min periods \times 12 participants, were used. Analyses were carried out using IBM SPSS Statistics 19.0 (IBM) and Microsoft Excel for Mac 2011.

Results

HR and \ln NPV Values During BS, MA, and MT

The mean values of HR and \ln NPV during each period, together with the results of statistical analysis, are summarized in Table 1.

Table 1

Physiological Variables During Three Conditions Measured by Two Methods

Measures	Condition			Results of Statistical Test				
	BS	MA	MT	ANOVA				Tukey <i>HSD</i>
	<i>M (SD)</i>	<i>M (SD)</i>	<i>M (SD)</i>	<i>F</i> _(2, 22)	ϵ	<i>p</i>	η_p^2	
Laboratory device								
HR (bpm)	71.0 (9.6)	86.7 (14.7)	75.1 (12.3)	36.07	.56	< .001	.77	MA > MT, BS
<i>ln</i> NPV (a.u.)	-3.48 (0.47)	-4.44 (0.44)	-4.22 (0.47)	89.84		< .001	.89	MA < MT < BS
iPhysioMeter								
HR (bpm)	71.2 (9.8)	86.8 (14.6)	75.4 (12.1)	36.93	.56	< .001	.77	MA > MT, BS
<i>ln</i> NPV (a.u.)	-4.48 (0.44)	-5.26 (0.48)	-5.01 (0.48)	41.89		< .001	.79	MA < MT < BS

Note. HR = heart rate, *ln*NPV = *ln* normalized pulse volume, BS = baseline, MA = mental arithmetic, MT = mirror tracing. bpm = beats per minute, a.u. = arbitrary unit.

Agreement of Two Measuring Methods

Scatter plots between paired measures of HR, Δ HR, *ln*NPV and Δ *ln*NPV, and their Bland-Altman plots are shown together in Figure 2. The outcomes of geometric mean regressions and Bland-Altman analyses were summarized in Table 2.

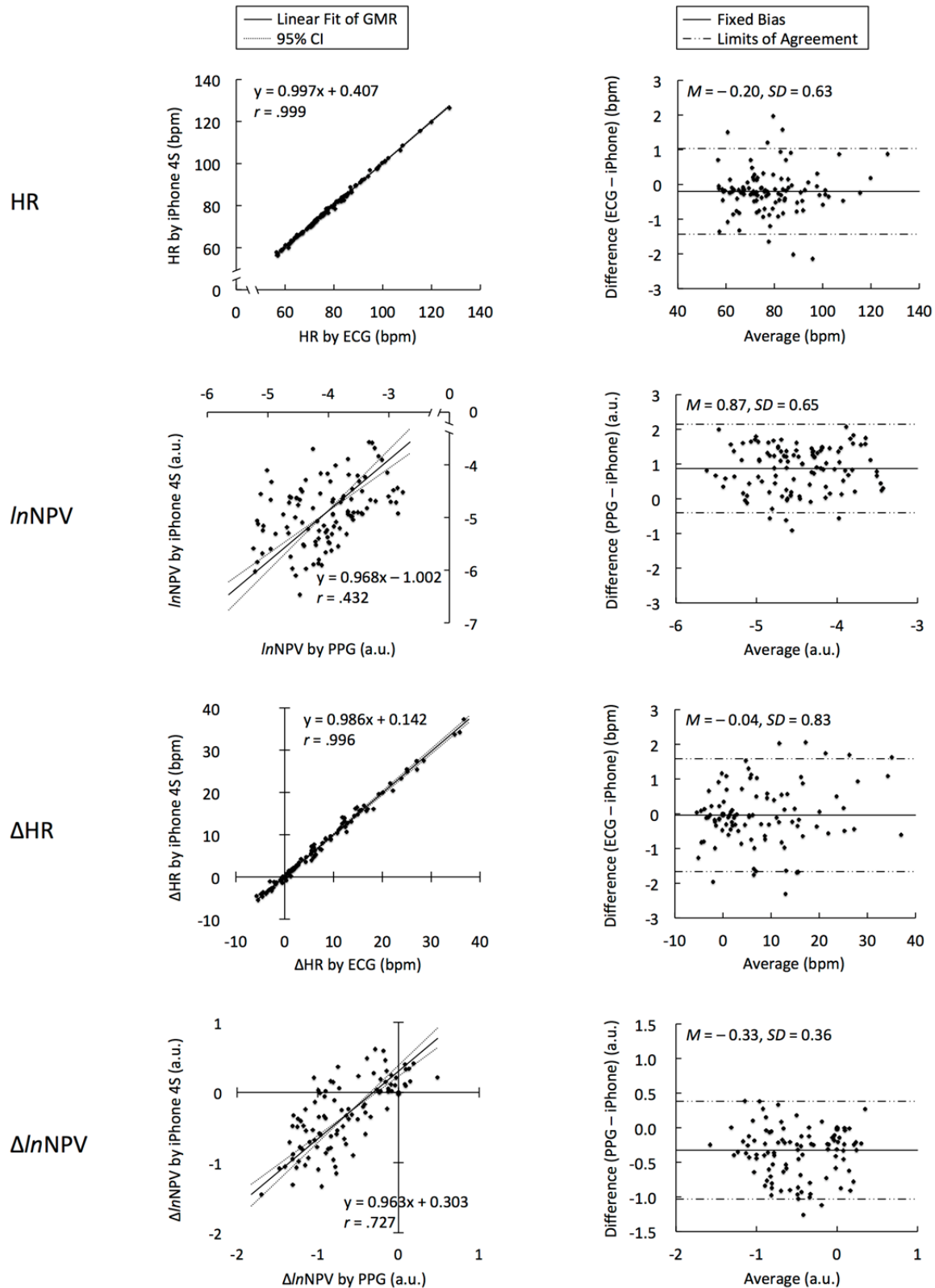


Figure 2. (Left): Scatter plots of each index measured by the iPhysioMeter against those measured by the corresponding conventional laboratory devices among all of the 108 data pairs (three conditions \times three 1-min periods \times 12 participants). (Right): Bland-Altman plots

of each index measured by the iPhysioMeter and the conventional laboratory devices. HR = heart rate, NPV = normalized pulse volume, Δ = delta change values, GMR = geometric mean regression, ECG = electrocardiograph, PPG = photo-plethysmograph, bpm = beats per minute, a.u. = arbitrary unit.

Table 2

Outcomes of geometric mean regression analyses and Bland-Altman plots

Measures	Geometric Mean Regression			Bland-Altman Plot		
	Slope [95% CI]	Intercept [95% CI]	<i>r</i> [95% CI]	<i>M</i> [95% LOA]	<i>SD</i>	<i>r</i> [95% CI]
HR	0.997 [0.989, 1.006]	0.407 [-0.261, 1.069]	.999 [.9985, .9993]	-0.20 [-1.43, 1.03]	0.63	.060 [-.131, .246]
Δ HR	0.986 [0.969, 1.002]	0.142 [0.027, 0.256]	.996 [.995, .997]	-0.04 [-1.67, 1.58]	0.83	.167 [-.023, .345]
<i>ln</i> NPV	0.968 [0.814, 1.150]	-1.002 [-1.623, -0.264]	.432 [.265, .574]	0.87 [-0.40, 2.14]	0.65	.037 [-.153, .224]
Δ <i>ln</i> NPV	0.963 [0.844, 1.099]	0.303 [0.230, 0.385]	.727 [.624, .805]	-0.33 [-1.03, 0.38]	0.36	.055 [-.135, .241]

Note. HR = heart rate, NPV = normalized pulse volume, Δ = delta change values, LOA = limits of agreement.

Discussion

In this study, we examined the agreement of physiological indices (HR and NPV) derived simultaneously from the newly developed iPhysioMeter smartphone program and from laboratory equipment, during the conduct of two mental stress tasks. As a result, the agreements of the two measurement methods for HR and Δ HR were found to be quite high. There were only negligible fixed and proportional biases and the ranges of limits of agreement in Bland-Altman plots were small. In addition, HR responses to mental stress tasks

were comparable between the two methods. Therefore, these findings suggest that iPhysioMeter yields valid measures of HR and Δ HR.

In contrast, the agreements for \ln NPV and $\Delta \ln$ NPV were not as consistent as those for HR and Δ HR. Although there were only negligible proportional biases, there was relatively large fixed bias for \ln NPV, though within the limits of agreement. First, this systematic error most likely arose from the difference in measuring configurations such as wavelength (near-infrared vs. green light) and measuring mode (transmittance vs. reflectance). It is known that these configurations can have a substantial influence on \ln NPV via the differences in absorption coefficient of hemoglobin and melanin pigment and those in the pathway of light from light source to sensor (Giltvedt, Sira, & Helme, 1984; Sawada, et al., 2001). Second, it is possible that this systematic error could have arisen from the adverse effect of finger-iPhone contact pressure during measurement. A certain degree of contact pressure is a prerequisite for smartphone measurements, including iPhysioMeter, but this pressure is practically negligible for laboratory measurements where the sensors are attached directly to the finger. It has been reported that arterial pressure can have a substantial effect on \ln NPV (Tanaka, et al., 2011) and it also seems plausible that finger-iPhone contact pressure could affect arterial pressure at the measuring site. Therefore, we might reasonably conclude that finger-iPhone contact pressure, via subsequent arterial pressure change, can exert an influence on \ln NPV that is by no means negligible. Taken together, the origin of the fixed bias is an inherent feature of smartphone measurements, and thus is inevitable for iPhysioMeter.

Besides the fixed biases, there were larger variations in \ln NPV and $\Delta \ln$ NPV than in HR and Δ HR. Although, in general, such random error could arise from one or more unknown sources, especially for this case, finger-iPhone contact pressure was probably one of the main causes here, too. That is, the contact pressure served as a random error in that it

would not be constant across participants. It is likely that some users press the iPhone firmly whilst others do so lightly, but it is difficult to control this. Interestingly, random error was still evident in $\Delta \ln \text{NPV}$ even after canceling out this kind of variation by conducting the delta change calculation. This is likely to be due to the fact that the participants could not maintain constant contact pressure throughout the measurement process. Meanwhile, HR is free from such a problem because this chronometric index can be calculated regardless of PV amplitude so long as the finger-iPhone pressure does not occlude the arteries completely.

Despite the existence of fixed bias and random error, this does not necessarily negate the usefulness of $\ln \text{NPV}$ measured by iPhysioMeter. This is because physiological indices may often exhibit absolute level inaccuracies and/or large individual differences that are irrelevant to psychological factors. Thus psychologists examining condition differences or condition \times group interactions using physiological indices prefer to adopt within-subjects design or mixed-design and/or to use change value, namely reactivity, to avoid this problem in advance (e.g., Hamer, et al., 2007; Matsumura, et al., 2012; McNally, et al., 2004). This supports the view that the existence of fixed biases is not detrimental in many cases and, on balance, $\ln \text{NPV}$ measured by iPhysioMeter actually fulfills the necessary requirements. In fact, as shown in Table 1, $\ln \text{NPV}$ responses to mental stress tasks were comparable between the two methods, which is probably due to there being only negligible proportional biases in $\ln \text{NPV}$ and $\Delta \ln \text{NPV}$. Moreover, even though the variation in $\ln \text{NPV}$ was larger than that in HR, the sensitivity of $\ln \text{NPV}$ by iPhysioMeter to these tasks ($\eta_p^2 = .79$) was comparable to that of HR by conventional laboratory devices ($\eta_p^2 = .77$). This is consistent with the opinion of Sawada et al. (2001) that PV is quite sensitive to a wide range of psychological stimuli. In normal situations, large sample sizes or the averaging of repeated measurements are necessary to reduce such random error, but NPV's high sensitivity to tasks obviates this necessity. Therefore, when an absolute level of $\ln \text{NPV}$ measurement is not necessary, which

is true in the majority of cases, iPhysioMeter yields valid measures of $\ln\text{NPV}$ and $\Delta\ln\text{NPV}$.

In addressing the limitations of the iPhysioMeter, two issues should be noted. First, the iPhysioMeter program calculates HR on the basis of pulses detected on the finger and therefore, in the case of arrhythmias, it may not yield accurate results. For example, in the case of pulse deficit, the HR derived from the iPhysioMeter would be lower than that from the ECG. However, a careful examination of the beat-by-beat data helps detect such problems. Second, our experiment was conducted on a limited population and a small number of situations, so further studies dealing with more diverse populations and situations are needed. Despite these limitations, iPhysioMeter can provide researchers with a measurement environment for accurate absolute level HR and relative change level $\ln\text{NPV}$, and we hope it will make a positive contribution to a wide range of psychological studies.

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