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### ► To cite this version:

Tim Takken, Samantha Stephens, Astrid Balemans, Mark S Tremblay, Dale W Esliger, et al.. Validation of the Actiheart Activity Monitor for Measurement of Activity Energy Expenditure in Children and Adolescents with Chronic Disease.. European Journal of Clinical Nutrition, 2010, 10.1038/ejcn.2010.196 . hal-00580670

**HAL Id: hal-00580670**

**<https://hal.science/hal-00580670>**

Submitted on 29 Mar 2011

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**Validation of the Actiheart Activity Monitor for Measurement of Activity Energy Expenditure in Children and Adolescents with Chronic Disease.**

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*Funding source:* This study was funded by a grant from the Canadian Institutes of Health Research (# 167391/CIHR).

*Running head:* Validity of the Actiheart in children with Chronic Disease

*Keywords:* physical activity, measurement, indirect calorimetry, exercise, heart rate

*Conflict of Interest statement:* None of the authors had any conflicts of interest.

## **Abstract**

**Introduction:** The purpose of this study was to develop an activity energy expenditure (AEE) prediction equation for the Actiheart activity monitor (AH) for use in children with chronic disease.

**Methods:** 63 children, aged 8-18 years with different types of chronic disease (Juvenile Arthritis, Hemophilia, Dermatomyositis, neuromuscular disease, Cystic Fibrosis or Congenital Heart Disease) participated in an activity testing session which consisted of a resting protocol, working on the computer, sweeping, hallway walking, steps and treadmill walking at three different speeds. During all activities actual AEE was measured with indirect calorimetry (IC). During all activities the participants wore an Actiheart on the chest. Resting EE and resting heart rate were measured during the resting protocol and heart rate above sleep (HRaS) was calculated.

**Results:** Mixed linear modeling produced the following prediction equation:

Estimated AEE (J/kg/min) =  $-93.7 + (4.8 \times \text{HRaS}) + (0.04 \times \text{Accelerometer Counts}) + (39.8 \times \text{Gender [girls=0, boys=1]})$ .

This equation results in a non-significant mean difference of 2.1 J/kg/min (limits of agreement: -144.2 to 148.4 J/kg/min) for the prediction of AEE from the Actiheart compared to actual AEE.

**Conclusions:** The Actiheart is valid for the use of AEE determination when using the new prediction equation for groups of children with chronic disease. However, the prediction error limits the use of the equation in individual subjects.

## **Introduction**

Children with chronic disease are often sedentary and this behavior pattern can have various etiologies. For example in children with congenital heart disease (CHD) and hemophilia, hypoactivity might be caused by overprotection by parents and educators (Bar-Or 1987, Bergman and Stamm 1967), while in juvenile arthritis children might be hypoactive because of painful joints (Takken et al 2003).

There is an increasing body of literature showing that children with a chronic disease or condition are able to improve their physical fitness levels through an exercise training program (Edouard et al 2007, Johnson 2009, Klijn et al 2004, Takken et al 2007, Van Brussel et al 2008, Verschuren et al 2007). However, a frequently encountered problem is the deconditioning after the cessation of the structured exercise training program (Van Brussel et al 2008, Verschuren et al 2007). This may be caused by the fact that children with a chronic condition encounter many barriers in performing physical activities in their daily life. Many sport clubs are not equipped to have these children participate in their programs. Moreover, there may be perceived barriers to regular physical activity because of restriction in physical activity by parents, caregivers, health-care professionals, trainers and teachers as well as the child's own perception of the consequences of activity on their condition (Edouard et al 2007, Murphy et al 2008).

Increasing daily physical activity levels for children with a chronic disease or condition might be an effective method to maintain their physical fitness levels (Morris 2008). However, research in this area is limited because of a lack of robust direct measurement methods for assessing free-living physical activity in children with chronic disease. Activity monitoring seems to be a promising method to objectively assess and profile physical activity (de Graauw et al 2010, Esliger and Tremblay 2007, Hoos et al 2004), and seems to be more valid than indirect assessments (e.g. questionnaires and activity logs) (Adamo et al 2009).

A recent report has called into question to use of methodologies established for children without chronic disease when predicting energy expenditure (EE) in children with chronic disease (Stephens et al 2009). Stephens and colleagues (2009) assessed the validity of prediction equations based on healthy subjects for measuring EE via accelerometry (Freedson et al 1998, Puyau et al 2002) for children with chronic disease (Stephens et al 2009). In this study, EE was measured by indirect calorimetry during seven activity tasks of variable intensities (Stephens et al 2009). Results showed significant differences between predicted EE and measured EE in children with chronic disease.

Therefore, the purpose of this study was to develop an AEE prediction equation for the Actiheart activity monitor for children with chronic disease and to assess the validity of the Actiheart to determine AEE in this population.

## **Methods**

### ***Participants***

Sixty-three participants with chronic disease were recruited from several clinics of the Wilhelmina Children's Hospital, University Medical Center Utrecht. Diagnostic distribution and descriptive characteristics of participants can be found in Table 1. Participants included children and adolescents in that ages ranged from 8-18 years. All participants' parents gave written informed consent and participants aged 12 years and older signed their own assent form. This study was approved by the Medical Ethics Committee of the University Medical Center Utrecht, the Netherlands. Participants were not included in the study if they used medications that interfered with heart rate response to exercise or if they were unable to ambulate and/or cooperate. One patient with a Fontan circulation had a rate responsive pacemaker. This cohort was a subsample of a larger multi-center study on accelerometry, using different activity monitors.

### ***Anthropometry***

Weight was determined using an electronic scale (Seca, Hamburg, Germany), and a wall-mounted stadiometer was used to measure height. Body mass index (BMI) was calculated by dividing body mass (in kg) by height squared (in meters).

### ***Testing protocol***

Participants participated in one testing session with a duration of ~1.5 hr, which consisted of three protocols:

*Resting Protocol:* Expired gas was collected using indirect calorimetry (IC) to determine resting metabolism over 20 minutes with the participant supine in a quiet room. Recordings were taken at 1-min intervals for the duration of the last 10 minutes of rest. The average values for heart rate (HR) and EE over the last 10 minutes was taken as resting HR (RHR) and resting EE (REE) since this provided steady-state values for RHR and REE.

IC measurements were made with the same equipment as the Activities protocol.

*Activities Protocol:* The participants completed a questionnaire on the computer while seated. In addition they performed a 6-minute cleaning task (sweeping), a 6-minute hallway walking task (at a self-selected comfortable walking pace) and a 6-minute stair stepping routine at a metronome-guided pace of 70 steps/min. A 6-minute duration was chosen to allow for a steady state oxygen uptake within the first 4 minutes of each activity.

Furthermore, participants were asked to walk or jog on a treadmill at three different speeds. The treadmill protocol selected depended on the walking speed chosen during the hallway walking task. For participants who walked with a self-selected walking speed of >3.5 km/h, a high function treadmill protocol was used (5 minutes at each of 3.5, 5 and 6.5 km/h, respectively). When the walking speed was <3.5km/h, a low function protocol was used (5 minutes each of 2.0, 3.5 and 5.0 km/h, respectively).

### ***Actiheart***

The Actiheart (AH2, CamnTech, Cambridge, UK) is a chest-mounted, combined-unit, synchronized heart rate monitor and accelerometer capable of storing time-sequenced data. Acceleration is measured by a piezoelectric element within the unit with a frequency range of 1-7 Hz. The Actiheart unit was clipped to two ECG electrodes (3M™ Red Dot™ 2271 Monitoring Electrodes, 3M Nederland BV, Zoeterwoude, the Netherlands) adhered to the child's chest. The Actiheart was positioned at the level of the third intercostal space (Brage et al 2006). Acceleration movement counts and heart rate from Actiheart were sampled every 15 seconds. The participants wore the Actiheart unit during the entire testing session. The existing AEE prediction equation developed on healthy children for the Actiheart used heart rate above sleep (HRaS) as a variable (Corder et al 2007). Accordingly, we converted resting HR to HRaS using the following formula from healthy children (Corder et al 2007):  $HRaS = 0.4195 \times RHR + 27.4$ .

Actiheart accelerometry counts and HRaS were converted to AEE using the established equation of Corder et al (Corder et al 2007) developed in healthy children:

$$AEE \text{ (J/kg/min)} = (5.17 \times HRaS) + (0.61 \times (\text{gender [0=girls, 1=boys]} \times HRaS)) + (0.07 \times \text{activity counts}) - (0.6 \times \text{gender}) - 74$$

### ***Indirect calorimetry (IC)***

During all tasks expired gas was collected through a face mask in order to measure oxygen uptake ( $VO_2$ , L/min) and carbon dioxide exhalation ( $VCO_2$ , L/min) breath-by-breath, to determine energy expenditure. Data were averaged over a 15-s epoch. A portable respiratory gas analysis system was used during all activities (Cortex Metamax, CORTEX Biophysik GmbH, Leipzig Germany). The Cortex Metamax was calibrated against ambient air and a

standard calibration gas mixture provided by the manufacturer (15% O<sub>2</sub>, 4% CO<sub>2</sub>), and volume calibrated prior to every exercise test session. VO<sub>2</sub> and VCO<sub>2</sub> data were converted to EE using the de Weir Equation (de Weir 1949):

$$EE \text{ (J/kg/min)} = (3.9 \times VO_2 + 1.1 \times VCO_2) \times 4184$$

Resting energy expenditure (REE) was determined from the average of the last 10 minutes of the resting protocol. AEE of the activities protocol were derived from the measured total EE of each task minus REE. The metabolic and activity data of the last two minutes of each task were averaged and used for analysis of actual AEE.

### *Statistical analysis*

In order to best predict activity energy expenditure from accelerometry counts and heart rate we used mixed linear modeling techniques using SAS 9.1 (SAS Institute, Cary, N.C. 2009). Mixed linear regression modeling is similar to simple linear regression only it allows for one to account for correlated data as well as non-constant variability. This difference in modeling techniques means that each subjects data contributes to the overall model as a random effect which allows for more accurate inferences to be made about the overall population effect rather than just being confined to making inferences about the existing data. Activity energy expenditure determined by indirect calorimetry was entered into the model as the main outcome. Heart rate above rest, accelerometer counts and gender were entered into the model as fixed effects. We also included random effects for heart rate above sleep and counts in order to account for the variation in each individuals response over the 7 different physical tasks. Further, as each subject was tested using 7 different tasks a repeated term was used to account for the within subject correlation (Singer 1998).

The difference between estimated AEE and actual AEE was analyzed using Bland-Altman plots and limits of agreement (Bland and Altman 1986). Moreover, Lin's concordance coefficient (LCC) and the corresponding 95% confidence interval were also used to determine the agreement between the two methods (Lin 1989). The LCC measures both precision (Pearson correlation) and accuracy (bias correction factor) to determine whether the observed data deviate significantly from the line of perfect concordance, which occurs at 45 degrees; that is, it assesses the linear relationship. The Bland-Altman plots and LCC were calculated

using MedCalc 10.0. (Medcalc BVBA, Mariakerke, Belgium). A P-value of  $< 0.05$  was considered as statistically significant.

## Results

The descriptive characteristics of the participants are provided in Table 1. The BMI Z-scores were significantly increased in the patients with JDM and Haemophilia and was significantly decreased in the patients with CF.

Five participants (1 CF, 1 JDM, 2 JIA and 1 HMSN) were not able to finish fast treadmill walking because of joint pain or exhaustion. Two participants with JDM stopped already at the start of slow treadmill walking because of exhaustion.

**Table 2** reports the regression coefficients of the prediction of AEE from activity counts, HRaS, and gender. The new regression equation for prediction of AEE was:

$$\text{AEE (J/kg/min)} = -93.7 + (4.8 \times \text{HRaS}) + (0.04 \times \text{Accelerometer Counts}) + (39.8 \times \text{Gender [girls=0, boys=1]})$$

The mean estimated AEE of the prediction equation of Corder et al. (Corder et al 2007) and the currently developed prediction equation for each task are shown in **Table 3** and **Figure 1**. The Corder et al. equation significantly over-predicted the AEE compared to the currently developed AEE prediction equation. In addition, the Bland-Altman plot analyzing the differences between actual AEE and estimated AEE is shown in **Figure 2**. The current equation gives a mean difference of 2.1 J/kg/min (Limits of Agreement: -144.2 to 148.4) for the overall estimation AEE compared with actual AEE, instead of a mean difference of 49.1 J/kg/min (Limits of Agreement; -89.3 to 187.5;  $P < 0.05$ ) using the model of Corder et al. developed in healthy children (Corder et al 2007). The LCC for the Corder et al. equation with IC-AEE was 0.81 (95% CI 0.78-0.84),  $r = 0.87$ , bias correction factor: 0.93. The LCC for the current AEE prediction with actual AEE was 0.81 (95%CI: 0.77 to 0.84),  $r = 0.82$ , bias correction factor 0.99.

## **Discussion**

The results of this study suggest that although activity monitors are regarded as an objective measure of physical activity, it remains a quite crude measure for estimating AEE in children with chronic disease. The derived prediction equation using both HR and activity counts accounted for 65% of the variance in actual AEE. The large range of the 95% CI in estimated AEE indicates that prediction equation seem to be more accurate for groups (e.g. research), than for individuals (e.g. clinical practice). The observed limits of agreement from the Bland-Altman plots were comparable to those reported in healthy adults using the Actiheart (Crouter et al 2008). The diversity of chronic conditions included in these analyses may have contributed to the individual variability. However, the derived prediction equation performs significantly better in children with chronic disease than a previously developed equation for healthy children (Corder et al 2007).

There are several potential explanations for why the equation of Corder et al. might be inaccurate for use in children with chronic disease. These include: delayed gross motor skill development among children with chronic disease; inefficiency of movement from disease complications; increased resting and activity energy expenditure associated with heart and lung function (Groen et al 2010, Hjeltnes et al 1984, Knops et al 1999); higher HR for a given  $VO_2$  because of deconditioning (Bar-Or and Rowland 2004); and altered movement patterns to reduce pain (Broström et al 2007). Each of these would increase HR and EE for a given activity which may explain why the equation of Corder et al. consistently over-estimated AEE (figure 1).

In our study a large group of children with different types of chronic diseases was tested to assess the validity of the Actiheart to determine AEE in this population. A strong overall correlation was found between estimated AEE from Actiheart with actual AEE for the complete exercise testing session. This suggests high overall criterion validity in measurement. The Actiheart showed no significant correlation with IC for working at the computer and a moderate to strong correlation for other activities. The correlations between predicted and measured AEE increased with higher intensity activities. From the current data it seems that the Actiheart becomes accurate starting from activities with an intensity of ~ 2.5 metabolic equivalents (METs).

The lack of correlation between Actiheart AEE estimation for working at the computer and IC can be explained by the fact that the activity monitor measures almost no acceleration of the chest during sedentary activities and low heart rates (Crouter et al 2008). In general, the Actiheart, and activity monitors, are better suited to predict EE during activity, rather than during sedentary activities (Crouter et al 2008, De Bock et al 2010)..

Since HRaS was a significant predictor of AEE in the mixed linear regression modeling (Table 2), AEE estimation in participants with a blunted HR response to exercise (e.g. chronotropic incompetence or beta-blocking medication usage (Thoren 1967) might impede the validity of this combined HR and activity counts prediction equation.

Our results indicate that other approaches should be explored to improve the estimation of AEE for individual subjects. A study with adults with acquired brain injury suggested an individual calibration of the activity monitor output (e.g. activity counts) with actual AEE (Tweedy and Trost 2005). Moreover, our Actiheart prediction equation was developed using the mean HR response in a group of subjects; which compromises the accuracy at the individual level (Brage et al 2005). Future studies should examine approaches that take into account individual HR response at known exercise intensities to improve the accuracy of the prediction of AEE.

An other approach to improve accuracy might be more advanced mathematical modeling. Zakeri et al have recently used multivariate adaptive regression splines (MARS) modeling in healthy children and adolescents to predict EE using the Actiheart activity monitor (Zakeri et al 2010).

This study has a number of strengths. It is the first study to validate an objective measure of physical activity (Actiheart) in children and adolescents with chronic disease using actual energy expenditure (indirect calorimetry) as a criterion measure. The use of several different activities with both self-selected exercise intensities as well as a standardized treadmill protocol, allows our findings to be generalizable to free living activities.

This study had a few important limitations. We defined chronic disease using a non-categorical approach that considers chronically-ill young people as one population rather than specific disease classes (Stein and Jessop 1982). The current sample size prohibited a subgroup analysis in specifying the disease classes, however a secondary analysis revealed no significant effects between groups. Furthermore, it is unclear whether this equation is also valid for other pediatric patient groups including younger children.

In addition, the HRaS was calculated using an equation developed in healthy 12 year old children (Corder et al 2007). Unfortunately, we do not have overnight HR data of the participants to confirm this equation. Lastly, the derived prediction equation should be confirmed in a cross-validation study using similar and different activities; we only measured AEE during structured activities and did not measure AEE during free play activities of the participants.

A limitation of the practical use of the current prediction equation is the necessity of the determination of RHR. However, if overnight data are obtained, HRaS can be directly obtained from the data when the monitors are worn during sleep.

In conclusion, these results demonstrate that the Actiheart is valid for determining AEE when using the new prediction equation for groups of children with chronic disease. However, the prediction error limits the use of the equation in individual subjects.

Future research should determine the need for disease-specific AEE prediction equations and the applicability of the new prediction equation in other patient groups. Moreover, additional approaches should be explored to improve the prediction of AEE for individual subjects.

## **Acknowledgements**

This study was funded by a grant from the Canadian Institutes of Health Research (# 167391/CIHR). We would like to thank Fypro BV, Amsterdam, the Netherlands for their unconditional support with the Actiheart. We want to thank Preeya Govan, and Danial Ingas for their assistance in this project.

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## **LEGEND TO FIGURES**

**Figure 1.** Scatter plot of actual AEE as measured by indirect calorimetry and estimated by two Actiheart prediction equations (according to Corder et al (Corder et al 2007) and the current study).

**Figure 2.** Bland-Altman plot of actual AEE (in J/kg/min) as measured by indirect calorimetry and AEE estimated using the Actiheart (current prediction equation).

## **TABLES**

**Table 1.** Characteristics of the participants (mean  $\pm$  SD).

Group	Age (years)	Height (cm)	Weight (kg)	BMI (kg/m <sup>2</sup> )	BMI for age (Z-score)	HR <sub>rest</sub> (bpm)	REE (J/kg/min)
CF (N=9)	13.3 $\pm$ 3.53	155.7 $\pm$ 15.7	43.3 $\pm$ 12.8	17.5 $\pm$ 2.03	-.55 $\pm$ .55*	74.1 $\pm$ 14.4	173.9 $\pm$ 44.8
JDM (N=9)	13.9 $\pm$ 1.96	159.0 $\pm$ 9.0	55.1 $\pm$ 10.5	21.6 $\pm$ 2.42	.89 $\pm$ .97*	74.9 $\pm$ 14.4	113.6 $\pm$ 20.9
JIA (N=10)	11.7 $\pm$ 2.58	152.5 $\pm$ 11.5	41.2 $\pm$ 12.1	16.2 $\pm$ 6.19	-.43 $\pm$ 1.55	78.8 $\pm$ 8.77	153.7 $\pm$ 43.8
Hemophilia (N=10)	12.5 $\pm$ 3.31	166.0 $\pm$ 17.6	59.3 $\pm$ 22.5	20.7 $\pm$ 4.73	.94 $\pm$ .98*	70.5 $\pm$ 5.15	129.3 $\pm$ 33.5
CHD (N=8)	14.4 $\pm$ 3.20	159.1 $\pm$ 13.2	49.8 $\pm$ 10.8	19.7 $\pm$ 2.62	-.02 $\pm$ 1.68	71.2 $\pm$ 10.3	128.0 $\pm$ 29.9
NMD (N=17)	13.3 $\pm$ 3.41	159.9 $\pm$ 15.4	48.8 $\pm$ 13.0	20.1 $\pm$ 6.34	-.12 $\pm$ 1.25	75.4 $\pm$ 8.99	137.2 $\pm$ 36.0

Abbreviations: CF: Cystic Fibrosis, JDM, Juvenile Dermatomyositis, JIA: Juvenile Idiopathic Arthritis, CHD: Congenital Heart Disease, NMD: Neuromuscular Disorders, REE: Resting Energy Expenditure, HR<sub>rest</sub>: Resting Heart Rate, BMI: Body Mass Index; \*=significantly different from Dutch growth charts.

**Table 2.** Results from the mixed linear regression modeling for the prediction of Activity Energy Expenditure (AEE) in children with chronic disease using the Actiheart heart rate and activity counts.

Model <sup>a</sup>	Estimate	Standard error	T-value	Sig.
(Constant)	-93.7	14.078	-6.66	<.0001
Counts	0.039	0.0142	20.36	<.006
HRaS	4.776	0.235	2.76	<.0001
Gender (girl=0, boy=1)	39.79	13.34	.2.98	.0042

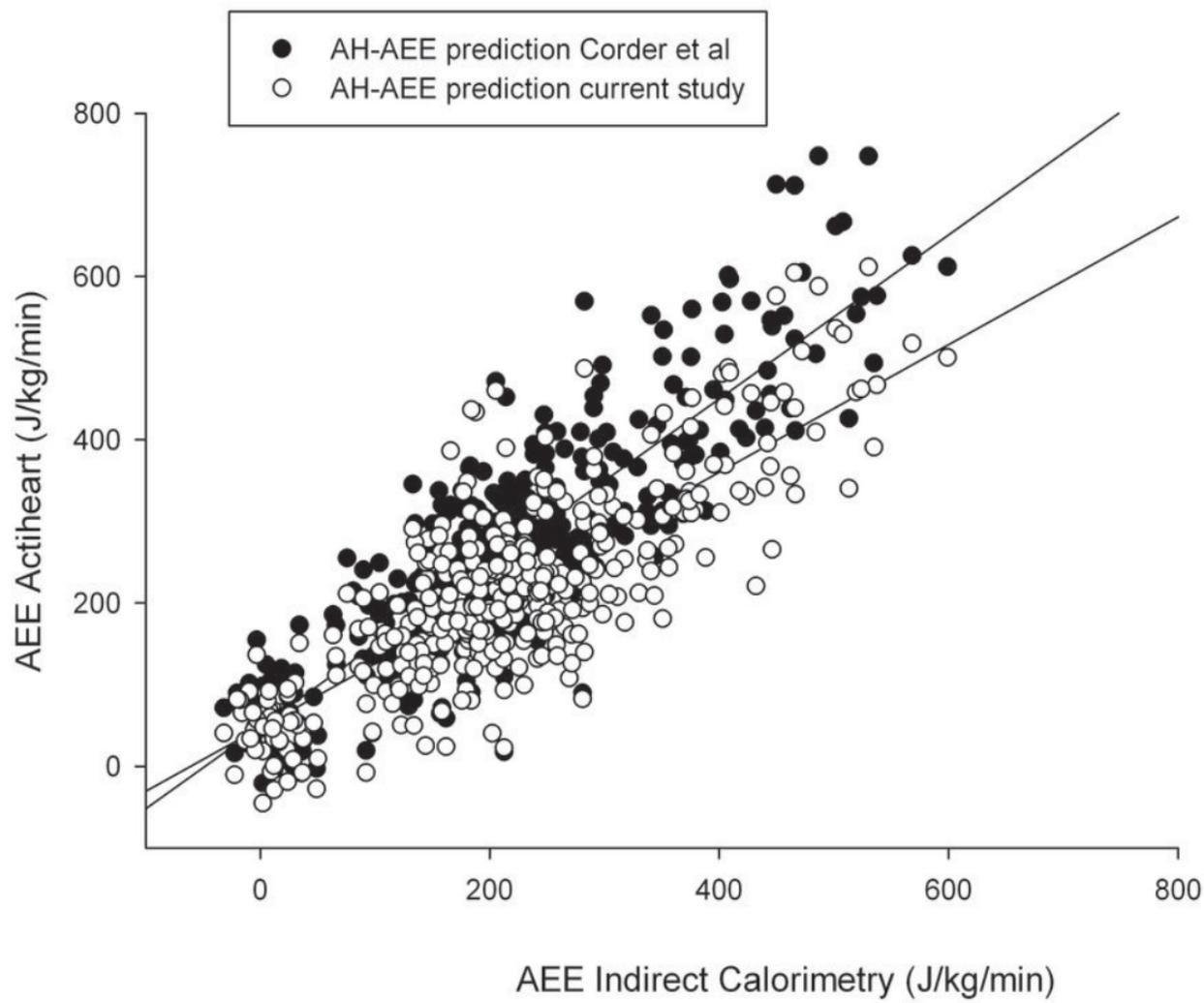
*Abbreviations: a Dependent Variable: AEE (J/kg/min); HRaS: heart rate above sleep.*

**Table 3.** Comparison of the actual AEE with the estimated AEE from Actiheart using the prediction equation of Corder et al and the currently developed prediction equation.

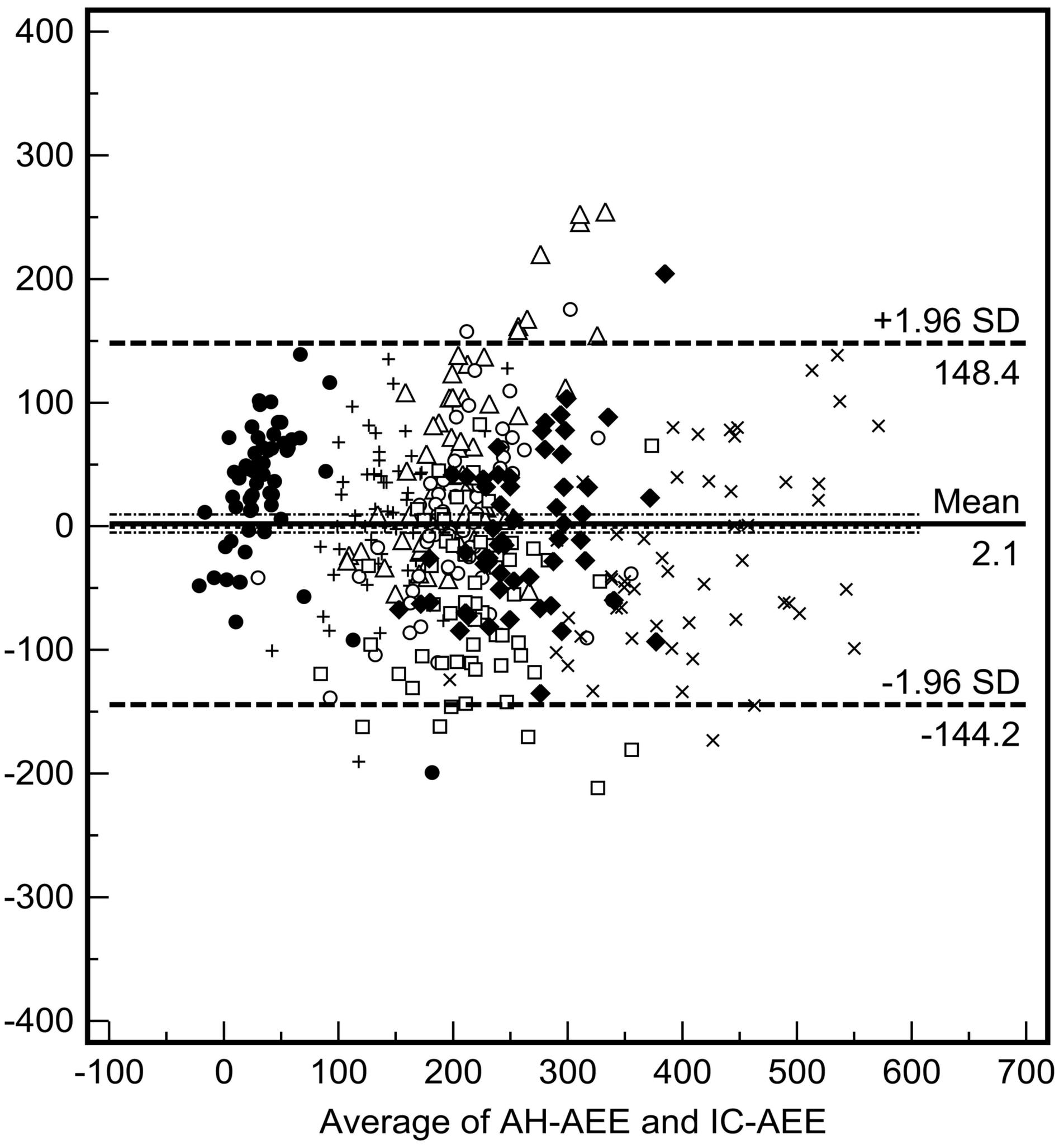
<b>Task</b>	<b>Actual AEE (J/kg/min)</b>	<b>Estimated AEE Corder prediction (J/kg/min)</b>	<b>Actual AEE – AEE Corder prediction (correlation, r)</b>	<b>Estimated AEE current AH prediction (J/kg/min)</b>	<b>Actual AEE -current AH prediction (correlation, r)</b>
Computer	19.2 ± 43.8	63.3 ± 40.0	0.07	48.3 ± 39.5	0.11
Sweeping	139.6 ± 42.9	182.8 ± 63.0	0.25*	150.2 ± 55.0	0.27*
Hallway walking	249.7 ± 78.6	293.3 ± 99.0	0.71*	232.9 ± 81.3	0.31*
Steps	202.9 ± 50.8	254.7 ± 82.1	0.50*	209.6 ± 71.7	0.51*
Slow TW	178.9 ± 36.3	231.5 ± 68.4	0.32*	187.3 ± 61.6	0.42*
Moderate TW	263.7 ± 47.6	318.6 ± 76.9	0.47*	257.9 ± 66.3	0.47*
Fast TW	424.5 ± 72.9	487.2 ± 125.0	0.69*	393.7 ± 102.8	0.69*
All activities	206.0±125	257.83±143.2	0.87*	208.4 ± 118.2	0.81*

*Abbreviations: AEE: Activity Energy Expenditure, TW: Treadmill walking, AH: Actiheart, \* Significant (P<0.05).*





Difference AH-AEE and IC-AEE



Tasks

- Computer
- + Sweeping
- △ Hallway walk
- Steps
- Slow treadmill
- ◆ Moderate treadmill
- × Fast treadmill