Table 3. Continued.

CAS	Chemical name	log P Pred.	KATE class name	log (1/EC_{50} [mM]) Pred.	log (1/EC_{50} [mM]) Meas.	Domain log P^2	Domain C^3	"reactive"[4]
117–80–6	2,3-Dichloro-1,4-naphthoquinone	2.65	Halides1	3.06	4.13	O	X	Michael
1484–13–5	9-Vinylcarbazole	4.19	Conjugated systems1 (Clog P)	4.03	5.51	O	X	Michael
569–64–2	CI Basic Green 4	0.8	Amines aromatic or phenols5	0.56	3.45	X	X	Michael
101–20–2	3,4,4′-Trichlorodiphenylurea	4.9	Unclassified	2.71	4.3	O	X	acylating
89–40–7	4-Nitrophthalimide	1.12	Nitrobenzenes	0.45	0.84	X	X	acylating
86–73–7	Fluorene	4.02	Hydrocarbons aromatic	2.03	2.53	O	*C (1)*	
88–05–1	2,4,6-Trimethylaniline	2.72	Amines aromatic or phenols3	2.11	1.05	O	*C (1)*	
88–75–5	*o*-Nitrophenol	1.91	Amines aromatic or phenols4	1.06	0.7	O	*C (1)*	
91–17–8	Bicyclo[4.4.0]decane	4.2	Hydrocarbons aliphatic	2.22	2.78	O	*C (1)*	
91–17–8	Bicyclo[4.4.0]decane	4.2	Neutral organics	2.05	2.78	O	*C (1)*	
95–78–3	2,5-Dimethylaniline	2.17	Amines aromatic or phenols5	1.31	0.83	O	*C (1)*	
95–87–4	2,5-Xylenol	2.61	Amines aromatic or phenols4	1.46	1.37	O	*C (1)*	
100–63–0	Hydrazine, phenyl-	0.79	Hydrazines (Clog P)	2.14	3.83	O	*C (1)*	
108–87–2	Methylcyclohexane	3.59	Hydrocabons aliphatic	1.81	2.47	O	*C (1)*	
108–87–2	Methylcyclohexane	3.59	Neutral organics	1.63	2.47	O	*C (1)*	
111–78–4	1,5-Cyclooctadiene	3.73	Hydrocabons aliphatic	1.91	2.09	O	*C (1)*	
111–78–4	1,5-Cyclooctadiene	3.73	Neutral organics	1.73	2.09	O	*C (1)*	
129–00–0	Pyrene	4.93	Hydrocarbons aromatic	2.58	3.62	O	*C (1)*	
143–08–8	1-Nonanol	3.3	Alcohols or ethers aliphatic	1.06	1.4	O	*C (1)*	
143–08–8	1-Nonanol	3.3	Neutral organics	1.43	1.4	O	*C (1)*	
615–58–7	2,4-Dibromophenol	3.29	Amines aromatic or phenols4	1.85	2.08	O	*C (1)*	
634–93–5	2,4,6-Trichloroaniline	3.01	Amines aromatic or phenols3	2.15	1.66	O	*C (1)*	
716–79–0	1H-Benzimidazole, 2-phenyl-	3	Hydrocarbons aromatic	1.41	1.67	O	*C (1)*	
764–13–6	2,5-Dimethylhexa-2,4-diene	3.95	Hydrocabons aliphatic	2.05	1.42	O	*C (1)*	
764–13–6	2,5-Dimethylhexa-2,4-diene	3.95	Neutral organics	1.88	1.42	O	*C (1)*	
924–41–4	1,5-Hexadien-3-ol	1.48	Conjugated systems2	1.22	0.58	O	*C (1)*	
2219–82–1	6-*tert*-Butyl-*o*-cresol	3.97	Amines aromatic or phenols4	2.24	1.49	O	*C (1)*	
2243–62–1	1,5-Naphthalenediamine	1.34	Amines aromatic or phenols1	2.55	1.62	O	*C (1)*	
4798–44–1	1-Hexen-3-ol	1.61	Conjugated systems2	1.25	−0.32	O	*C (1)*	
3295–94–1	Allyl *n*-hexyl ether	3.37	Conjugated systems2	1.62	1.77	O	*C (1)*	
120–95–6	2,4-Di-*tert*-pentylphenol	6.31	Amines aromatic or phenols4	3.59	3.29	X	*C (1)*	
693–98–1	2-Methylimidazole	0.61	Hydrocarbons aromatic	−0.04	−0.39	X	*C (1)*	
1116–76–3	Tri-*n*-octylamine	10.35	Secondary and tertiary amines	1.58	4.13	X	*C (1)*	

4418–61–5	5-Aminotetrazole	–3.41	Hydrazines (Clog P)	1.34	0.72	X	*C (1)*
7212–44–4	1,6,10-Dodecatrien-3-ol, 3,7, 11-trimethyl-	5.68	Conjugated systems2	2.12	2.36	X	*C (1)*
16245–79–7	4-Octylbenzenamine	5.06	Amines aromatic or phenols3	2.42	3.84	X	*C (1)*
89–63–4	4-Chloro-2-nitroaniline	2.66	Amines aromatic or phenols3	2.1	1.61	O	*C (2)*
89–64–5	4-Chloro-2-nitrophenol	2.55	Unclassified	1.45	1.34	O	*C (2)*
96–96–8	2-Nitro-*p*-anisidine	2.1	Amines aromatic or phenols3	2.03	1.58	O	*C (2)*
101–80–4	4,4′-Diaminodiphenyl ether	2.22	Amines aromatic or phenols3	2.04	2.31	O	*C (2)*
827–52–1	Cyclohexylbenzene	4.81	Hydrocarbons aromatic	2.51	2.64	O	*C (2)*
843–55–0	1,1-Bis (4-hydroxyphenyl)-cyclohexane	5.48	Amines aromatic or phenols4	3.11	2.17	O	*C (2)*
2100–42–7	2-Chlorohydroquinonedimethylether	2.8	Unclassified	1.58	1.01	O	*C (2)*
78–51–3	Tri-*n*-butoxyethyl phosphate	3	Esters phosphate	4.02	1.08	X	*C (2)*
100–55–0	3-Hydroxymethylpyridine	–0.11	Hydrocarbons aromatic	–0.48	–0.79	X	*C (2)*
101–02–0	Triphenyl phosphite	6.62	Unclassified	3.63	2.84	X	*C (2)*
57–14–7	*N*,*N*-Dimethylhydrazine	–1.19	Hydrazines (Clog P)	1.76	1.66	O	X
374–25–4	1-Butene, 4-bromo-3-chloro-3,4,4-trifluoro-	3.78	Halides2	3.01	1.95	O	X
873–32–5	*o*-Chlorobenzonitrile	2.18	Amides and imides	1.05	0.88	O	X
948–65–2	2-Phenylindole	3.82	Hydrocarbons aromatic	1.9	2.81	O	X
2840–28–0	3-Amino-4-chlorobenzoic acid	1.6	Amines aromatic or phenols3	1.96	1.4	O	X
16691–43–3	3-Amino -5-mercapto-1H-1,2,4-triazole	0.31	Hydrazines (Clog P)	2.05	2.34	O	X
57500–00–2	Furfuryl methyl disulfide	2.95	Disulfides (Clog P)	2.35	2.71	O	X
63–74–1	Sulphanilamide	–0.55	Amines aromatic or phenols5	–0.19	1.12	X	X
90–30–2	1- (*N*-phenylamino)-naphthalene	4.47	Amines aromatic or phenols5	2.58	2.93	X	X
123–46–6	Ethanaminium, 2-hydrazino-*N*, *N*, *N*-trimethyl-2-oxo-, chloride	–5.29	Hydrazines (Clog P)	0.98	–0.24	X	X
462–08–8	3-Aminopyridine	–0.11	Amines aromatic or phenols5	0.05	1.12	X	X
497–18–7	Carbonohydrazide	–3.73	Hydrazines (Clog P)	1.28	0.98	X	X
504–24–5	4-Aminopyridine	–0.11	Amines aromatic or phenols5	0.05	0.8	X	X
504–29–0	2-Aminopyridine	0.53	Amines aromatic or phenols5	0.41	0.43	X	X
4418–61–5	5-Aminotetrazole	–3.41	Primary amines	–0.7	0.72	X	X
19715–19–6	3,5-Di-*tert*-butylsalicylic acid	6.06	Unclassified	3.33	1.89	X	X

Note: [1]When a chemical belongs to more than one QSAR class, all the predicted data are adopted.
[2]O: In-domain of log *P*-judgement, X: out-of-domain of log *P*-judgement.
[3]*C (1)*: In-domain of *C*-judgement, defined as: (1) all substructures of a test chemical are found in reference chemicals in the class.
C (2): In-domain of *C*-judgement, defined as: (2) all substructures of a test chemical are in reference chemicals in either *Neutral organics* or the class.
X: Out-of-domain of *C*-judgement.
[4]Names of the reactive mechanistic domains are given in the text.

Table 4. Numbers (%[1]) of chemicals characterised by underestimation (Under-), overestimation (Over-) and acceptable criterion (Acceptable) for fish toxicity.

Reactive domain	*KATE domain*					
	all	*C(2)*	*C(1)*	*log P*	*log P & C(2)*	*log P & C(1)*
Reactive						
Under-	4 (14.8)	2 (16.7)	2 (20)	3 (15.8)	1 (11.1)	1 (14.3)
Over-	2 (7.4)	1 (8.3)	1 (10)	1 (5.3)	1 (11.1)	1 (14.3)
Acceptable	21 (77.8)	9 (75)	7 (70)	15 (78.9)	7 (77.8)	5 (71.4)
Non-reactive						
Under-	5 (13.5)	4 (12.5)	4 (15.4)	3 (10)	2 (6.9)	2 (8.7)
Over-	3 (8.1)	1 (3.1)	0 (0)	1 (3.3)	1 (3.4)	0 (0)
Acceptable	29 (78.4)	27 (84.4)	22 (84.6)	26 (86.7)	26 (89.7)	21 (91.3)

Notes: [1]For example, the proportion of 'Under-' is defined as [(Number of under-)/(Number of under- + over- + Acceptable in the same reactive and KATE domains)].
Under-: Numbers (%) of chemicals for which toxicity was underestimated. Underestimation was defined as [calculated log $(1/LC_{50})$ – measured log $(1/LC_{50})] < -1.0$.
Over-: Numbers (%) of chemicals for which toxicity was overestimated. Overestimation was defined as [calculated log $(1/LC_{50})$ – measured log $(1/LC_{50})] > 1.0$.
Acceptable: Absolute errors between predicted and measured toxicities were less than 1.0.
Columns *all*, *C(2)*, *C(1) and log P* are defined in the footnote to Table 1.

Table 5. Numbers (%) of chemicals characterised by underestimation (Under-), overestimation (Over-) and acceptable criterion (Acceptable) for *Daphnia* toxicity.

Reactive domain	*KATE domain*					
	all	*C(2)*	*C(1)*	*log P*	*log P & C(2)*	*log P & C(1)*
Reactive						
Under-	7 (24.2)	2 (15.4)	1 (11.2)	6 (31.6)	2 (25)	1 (16.7)
Over-	3 (10.4)	1 (7.7)	1 (11.2)	2 (10.6)	1 (12.5)	1 (16.7)
Acceptable	19 (65.6)	10 (77)	7 (77.8)	11 (57.9)	5 (62.5)	4 (66.7)
Non-reactive						
Under-	7 (12.3)	4 (9.8)	4 (13)	2 (5.2)	2 (6.3)	2 (8)
Over-	6 (10.6)	3 (7.4)	2 (6.5)	3 (7.7)	2 (6.3)	2 (8)
Acceptable	44 (77.2)	34 (83)	25 (80.7)	34 (87.2)	28 (87.5)	21 (84)

Notes: *Under-*: Numbers (%) of chemicals for which toxicity was underestimated. Underestimation was defined as [calculated log $(1/EC_{50})$ – measured log $(1/EC_{50})] < -1.0$.
Over-: Numbers (%) of chemicals for which toxicity was overestimated. Overestimation was defined as [calculated log $(1/EC_{50})$ – measured log $(1/EC_{50})] > 1.0$.
Acceptable: Absolute errors between predicted and measured toxicities were less than 1.0.
Columns *all*, *C(2)*, *C(1) and log P* are defined in the footnote to Table 1.

after application of the log *P*-judgement, but it did increase after use of the *C*-judgement. In contrast, the proportion of "non-reactive" chemicals meeting the acceptable criterion did not increase with the use of the *C*-judgement at the *C(1)* rather than the *C(2)* level, but it did increase after the log *P*-judgement was applied. Unlike the fish end-point, the log *P*- and *C*-judgements did not guarantee that the predicted values of *Daphnia* toxicity

Table 6. Root mean square errors (RMSEs) for chemical toxicities according to the KATE domains, with respect to the reactive mechanistic domains.

		KATE domain					
End-point	*Reactive domain*	*all*	*C(2)*	*C(1)*	*log P*	*log P & C(2)*	*log P & C(1)*
Fish	*Not considered*[1]	1.22	0.95	0.96	1.10	0.90	0.88
	Reactive	1.59	1.37	1.32	1.56	1.50	1.48
	Non-reactive	0.84	0.74	0.77	0.66	0.59	0.59
Daphnia	*Not considered*	0.97	0.86	0.82	0.77	0.72	0.73
	Reactive	1.12	0.71	0.68	0.93	0.83	0.73
	Non-reactive	0.89	0.91	0.85	0.67	0.69	0.73

Notes: [1] '*Not considered*' shows the RMSE without considering the existence of the reactive mechanistic domains ('*reactive*' + '*non-reactive*').
Columns *all*, *C(2)*, *C(1)* and *log P* are defined in the footnote to Table 1.9

met the acceptable criterion when the chemicals were classified by reactive domain (either "reactive" or "non-reactive"). Although there was a small difference between log *P* with *C(2)* and log *P* with *C(1)* domains, the RMSEs became less than 1.0 with the in-domain of the *C*-judgement when the chemicals were categorised in "reactive" or "non-reactive" domains (Table 6). In other words, when these judgements were considered, chemicals in the "reactive" group did not always have a higher RMSE than those in the "non-reactive" group.

Poor efficiency was revealed in the SB or pro-SB reactive domains (Figure 2). The predicted *Daphnia* toxicities [log $(1/EC_{50})$] of the chemicals that had these reactive substructures showed a difference of less than 1.0 from the measured toxicities. As shown in the case of the aldehyde substructure, –CH=O, in Figures 2(a)–(f), six SB chemicals were classified in the *aldehyde* class by KATE. The last of these, a pro-SB chemical (Figure 2(g)), was classified in the *secondary and tertiary amines* class by KATE. The pro-SB domains were thus inappropriate as additional information for *Daphnia* toxicity predictions for KATE. This was different from the fish toxicity prediction. One reason for the inconsistency between fish and *Daphnia* end-points is that *Daphnia* is a completely different organism from fish; consequently the "reactive" domain discussed is not always applicable to both *Daphnia* and fish.

3.3 *Outliers*

Our third focus is on the outliers among the "non-reactive" chemicals and the KATE log *P*- and *C(1)*-judgements (Figures 3 and 4). In the present article a chemical is considered to be an outlier if the KATE predicted toxicity differs by more than 1.0 log $(1/LC_{50})$ or log $(1/EC_{50})$ from the measured toxicity. The chemical structures of the outliers indicated that it was necessary to reconsider the fish and *Daphnia* toxicity predictions in the class that included aromatic amines and heterocyclics (Figures 3(a) and 3(b), and 4(a) and 4(b)). Additionally, the *Daphnia* toxicity predictions indicated that the presence of a pyrene structure (Figure 4(c)) was significant for its inclusion in the pro-S_N2 reaction mechanism, which for technical reasons is not defined by the current FITS. In addition, 1-hexen-3-ol (Figure 4(d)) was classified in the KATE *conjugated systems2* class, whose toxicity would not be predicted by only using log *P* descriptors [14].

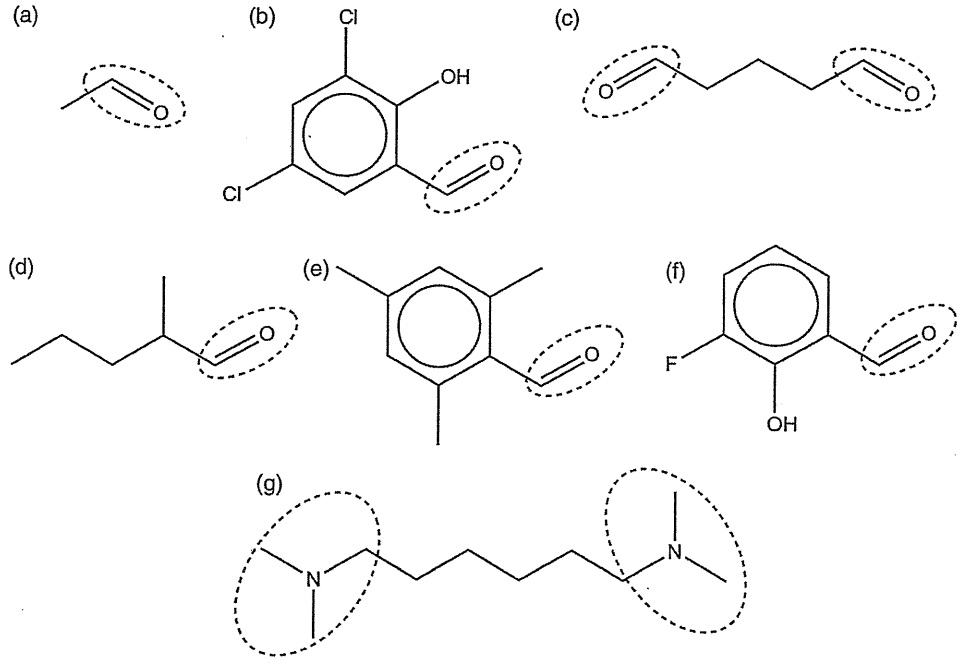

Figure 2. Chemical structure of (a) aldehyde, (b) 3,5-dichlorosalicylaldehyde, (c) glutaraldehyde, (d) methylvaleraldehyde, (e) 2,4,6-trimethylbenzaldehyde, (f) 3-fluoro-2-hydroxybenzaldehyde, and (g) *N,N,N′,N′*,-tetramethylhexamethylenediamine. The KATE predicted *Daphnia* toxicities, log ($1/EC_{50}$), had less than 1.0 difference from the measured toxicities. Reactive substructures are indicated by dotted lines: SB (a–f) and pro-SB (g) reactive mechanisms.

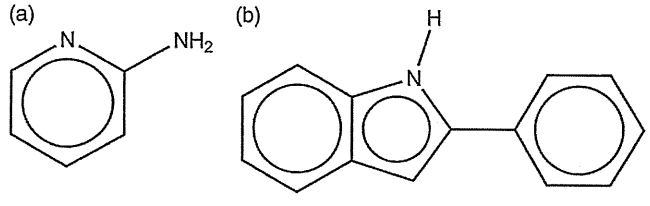

Figure 3. Outlier chemicals in the KATE fish toxicity prediction: (a) 2-aminopyridine, and (b) 2-phenylindole.

3.4 *Applicability to KATE*

Schultz and Cronin [48] have summarised both the essential and the desirable characteristics of ecotoxicity QSARs. They concluded that QSARs should be developed through the interaction of a group of multidisciplinary experts, since no single expert can construct a complete system to define toxicity in both fish and *Daphnia*. No one is able to categorise untrained or new chemicals, whose properties have yet to be established.

The QSAR models in KATE, even if they apply expert knowledge to the classification rules, have revealed certain drawbacks since their publication. For example, acrylonitrile is an alpha-beta unsaturated nitrile and due to the reactivity of other alpha-beta unsaturated

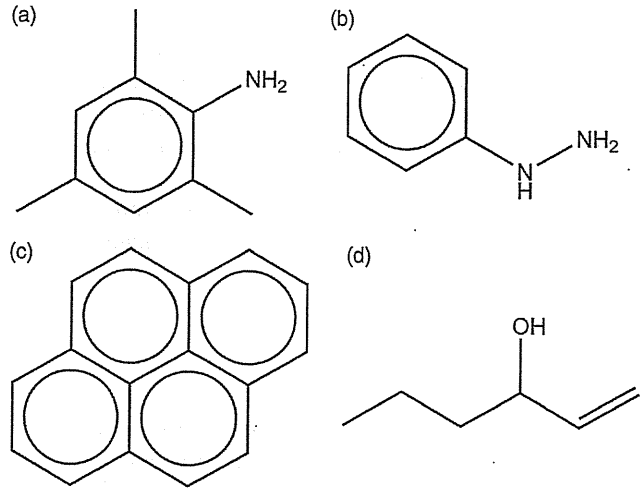

Figure 4. Outlier chemicals in the KATE fish toxicity prediction: (a) 2,4,6-trimethylaniline, (b) hydrazine, (c) pyrene, and (d) 1-hexen-3-ol.

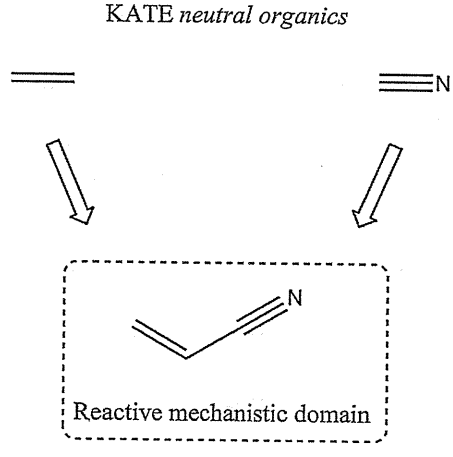

Figure 5. Acrylontrile (centre), including chemical substructures within the "reactive" mechanistic domain [18,19]. Due to the existence of the ethane (right) and hydrogen cyanide (left) structures, this chemical was classified in *neutral organics* in KATE.

compounds is therefore expected to be toxic to fish. However, acrylonitrile itself is an "untrained" substructure for the purposes of the current version of KATE and is categorised in the *neutral organics* class, since both ethylene (CH_2=CH_2) hydrogen cyanide (HCN) are categorised as *neutral organics* (Figure 5). Neither the KATE classification nor *C*-judgement can filter the reactive substructure, "acrylonitrile". The patterns introduced by Enoch et al. can thus reinforce chemical space information in the KATE system. This means that the classification rules of KATE can be reviewed and updated using information from other end-points. This procedure may play a corresponding role to QSAR development by the interaction of a range of multidisciplinary experts.

Moreover, SMARTS patterns may use a defined substructure to settle the *C*-judgement, especially for the fish end-point. But careful selection is required when the SMARTS patterns are applied to the *Daphnia* end-point. In such a situation the defined substructure seems to include the concept of "structural alerts". However, the structural alerts for aquatic toxicity QSARs [49] are normally defined in such a way as to discriminate between excess toxicity and narcotic effect levels [50,51]. The predicted toxicity discussed here was not from a QSAR for narcotic toxicity, and as a result of the KATE classification rules the QSAR models in the KATE system include discrimination from narcotic toxicity.

4. Conclusions

We have demonstrated the effectiveness of the reactive domains defined by skin sensitisation [16] applied to the ecotoxicity system, KATE. In predictions of fish toxicity, under identical judgements the group of chemicals with "reactive" substructures always had higher RMSEs than those with "non-reactive" substructures; this was confirmed by external validation of the current KATE system. The proposed reactive mechanism of skin sensitisation was valid for predicting fish toxicity using KATE. In the case of *Daphnia* on the other hand, the group of chemicals with "reactive" substructures did not always have higher RMSEs. One reason for this is that *Daphnia* organisms are very different in type from fish organisms: toxic action in *Daphnia* might not always correspond either to toxic action in fish nor to skin sensitisation potential. Even though there were some exceptions, the reactive domains discussed can be employed to improve the prediction accuracy in KATE. The presence of outliers in the test sets show, however, that the KATE classification needs to be reconsidered, especially in the case of chemicals containing nitrogen atoms.

We have previously concluded that QSAR development for KATE should in future focus on the reactivity of the chemicals and include multi-regression analysis [14]. As regards the latter, Hidaka et al. [52] have tested quantum chemical parameters, such as dipole, HOMO and LUMO, for the ecotoxicity prediction by using multiple regression analysis (MLR) and partial least squares regression (PLS) analyses based on the *Daphnia* dataset gathered by the Japan MoE [33]. However Hidaka et al. were unable to exclude the unnecessary descriptors [52].

As regards reactivity, the present study has demonstrated that reaction mechanistic domains of toxic action in terms of skin sensitisation offer useful complementary information for prediction of acute aquatic ecotoxicity, particularly at the fish end-point. Ultimately, the reliability of toxicity prediction is improved by the refined *C*-judgement rule, which utilises the classification of the substructures for skin sensitisation. The results of the validation study will help to improve prediction accuracy in the next version of the KATE system.

Acknowledgements

KATE was researched and developed by the Research Centre for Environmental Risk at the National Institute for Environmental Studies (NIES) between 2004 and 2009 under contract to the Japan MoE.

We are grateful to the US EPA for permission to use KOWWIN in "KATE on PAS", the standalone version of the KATE system. We also wish to thank Drs S.J. Enoch and M.T.D. Cronin for providing the raw data for the SMARTS strings [25].

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TECHNICAL PAPER

ISSN:1047-3289 *J. Air & Waste Manage. Assoc.* 61:46–54
DOI:10.3155/1047-3289.61.1.46

Estimation of the Respiratory Ventilation Rate of Preschool Children in Daily Life Using Accelerometers

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ABSTRACT

Inhalation rate is an essential factor for determining the inhaled dose of air pollutants. Here, accelerometers were used to develop regression equations for predicting the minute ventilation rate ($\dot{V}_E$) to estimate the daily inhalation rate in young children. Body acceleration and heart rate were measured in 29 Japanese preschool children (6 yr of age) during nine different levels of activities (lying down, sitting, standing, playing with plastic bricks, walking, building with blocks, climbing stairs, ball tossing, and running) using the Actical omnidirectional accelerometer, the ActivTracer triaxial accelerometer, and a heart rate monitor. Measurements were calibrated against the $\dot{V}_E$ measured by the Douglas bag method. ActivTracer accelerometer measurements gave a strong correlation with $\dot{V}_E$ (Pearson's r = 0.913), which was marginally stronger than that for the Actical counts (r = 0.886) and comparable to the correlation between heart rate and logarithmic $\dot{V}_E$ (r = 0.909). According to the linear regression equation, the $\dot{V}_E$ for lying down, sitting, standing, playing with plastic bricks, walking, and running was overestimated by 14–60% by the Actical and by 14–37% by the ActivTracer. By comparison, for building with blocks, climbing stairs, and ball tossing, the $\dot{V}_E$ was underestimated by 19–23% by the Actical and by 13–18% by the ActivTracer. When these three activities were excluded, a stronger correlation was found between the $\dot{V}_E$ and ActivTracer measurements (r = 0.949); this correlation was 0.761 for the three excluded activities. Discriminant analysis showed that the ratio between vertical and horizontal acceleration obtained by the ActivTracer could discriminate walking from building with blocks, climbing stairs, and ball tossing with a sensitivity of 75%. The error in estimating $\dot{V}_E$ was considerably improved for the ActivTracer measurements by the use of two regression equations developed for each type of activity.

IMPLICATIONS

Respiratory ventilation rate is an essential factor for assessing the health risk from air pollutants because it allows the dose of air pollutants delivered to the respiratory system to be determined. When establishing standards or criteria related to the management of health risks from hazardous environmental pollutants, the particular vulnerability of young children to environmental pollutants and their pattern of exposure should be considered. However, there are limited data on the respiratory ventilation rate of young children in daily life. To help address this problem, accelerometers were used to develop regression equations for predicting the $\dot{V}_E$ to estimate the daily inhalation rate in young children.

INTRODUCTION

Respiratory ventilation rate is an essential factor for determining the daily inhaled dose of air pollutants, which is important information for the establishment of health criteria or guideline values for air quality. In recent years, the particular vulnerability of children to environmental pollutants and age-related differences in exposure have become a concern in health risk assessment and management.[1–3] In Japan, an inhalation rate of 15 $m^3 \cdot day^{-1}$ for a 50-kg adult is commonly used to estimate the daily inhaled dose of air pollutants.[4] However, no standard inhalation rate value has been established for children. To

adequately assess adverse health risks to children, the inhalation rate of young children in daily life needs to be determined.

The doubly labeled water (DLW) method and the time-activity-ventilation method are experimental approaches that have been used to estimate daily inhalation rates during the daily activities of free-living individuals.[5–11] The DLW method is the most accurate method to measure the average total energy expenditure (EE) of people over several days and is based on the rates of disappearance of a dose of water containing the stable isotopes ^{2}H and ^{18}O. Although the DLW approach provides an accurate estimation of the daily inhalation rate, it is an expensive method and requires the collection of urine samples for 2–3 weeks. By comparison, the time-activity-ventilation method estimates the volume of air inhaled by a person over a defined period of time as a time-weighted average of the minute ventilation rate (V_E) for each level of activity during the period. The daily inhalation rate using this approach is expressed by the following equation:

$$\text{Daily inhalation rate} = \left[\sum_{i=1}^{k} \dot{V}_{Ei} \times t_i\right] \times 10^{-3} \quad (1)$$

where *Daily inhalation rate* is the 24-hr inhalation rate ($m^3 \cdot day^{-1}$), $\dot{V}_{Ei}$ is the mean $\dot{V}_{Ei}$ for each activity i ($L \cdot min^{-1}$), t_i is the time spent at each activity i ($min \cdot day^{-1}$), i is activity during the day, k is the number of activities, and 10^{-3} is a conversion factor. The critical issue in this approach is the need to accumulate adequate data for $\dot{V}_E$ during short-term activities throughout the day. However, there have been quite limited experimental data on $\dot{V}_E$ for children, especially for moderate-to-vigorous levels of physical activity and the habitual activities of daily life. The absence of data for children has been a source of error in estimations of daily inhalation rate by the time-activity-ventilation method. For example, Brochu[12] reported that the time-activity-ventilation approach can lead to an overestimation of the daily inhalation rates in 5- to 12-yr-old children by 75% because of the lack of $\dot{V}_E$ data for children during different levels of activities in daily life.

Another limitation of the time-activity-ventilation method is the availability of suitable techniques to obtain the intensity and duration of physical activity of young children during daily life. Self-report activity diaries and heart rate monitoring are the traditional tools used to determine the level of physical activity for estimating the $\dot{V}_E$ of free-living people. The disadvantages of self-reporting are that it tends to be subjective and is not practical for the assessment of young children, who are unable to accurately self-estimate and record their physical activity levels.[13–15] Even if an observer records the activities of children, it is still not possible to accurately measure the intensity and duration of the activities of children, which can vary within a few seconds.[16,17] Heart rate is a valid predictor of $\dot{V}_E$,[18] but its limitations include interruption of heart rate measurement by electrode displacement and discomfort from the electrodes, which can reduce the compliance of children and their parents with the study requirements.[15] To overcome these issues in monitoring the activity of children, an accelerometer could be a practical alternative for measuring the intensity, frequency, and duration of physical activity of free-living people. The advantages of an accelerometer-based approach are that it is noninvasive, it is not affected by the wearing of clothes, and it can provide data on a second time scale over long periods of time without interfering with normal activities. Many studies have examined the reliability and validity of these devices in children under laboratory and field conditions and determined that they provide valid measures of EE and oxygen (O_2) consumption in children.[19–31]

The primary goal of this study was to develop a regression equation to predict $\dot{V}_E$ from accelerometer measurements to estimate the daily inhalation rate in young children. First evaluated was the validity of accelerometer measurements to predict $\dot{V}_E$ by calibrating the Actical omniaxial accelerometer and the ActivTracer triaxial accelerometer against the $\dot{V}_E$ measured at different levels of activity by the Douglas bag method. The performance of the accelerometers was also evaluated by comparing the accelerometer measurements with heart rate.

METHODS

Participants and Study Design

The study presented here was conducted from December 2006 through March 2007. The study population comprised 29 Japanese preschool children (16 boys and 13 girls) 6 yr of age (mean age, 6.5 ± 0.2 years) who were recruited from a single kindergarten class thanks to the cooperation of the administrative personnel. The children's mean height was 115.4 cm (SD, 5 cm; range, 103.4–124.6 cm) and mean body weight was 20.6 kg (SD, 2.4 kg; range, 17–26.3 kg); these data were obtained at the start of the experiment. The V_E associated with nine different levels of physical activity were measured in a laboratory setting. Body acceleration and heart rate were measured by using activity and heart rate monitors and these measures were calibrated against the $\dot{V}_E$ values. Written informed consent was obtained from the parents of each participant. The ethics committee of the National Institute (Tsukuba, Ibaraki, Japan) approved the experimental protocol for Environmental Studies.

Procedure

The experiment was conducted in a recreation room of the kindergarten from 2:00 to 6:00 p.m. Room temperature was set between 23 and 25 °C throughout the experiment to avoid the influence of cold temperature on the metabolism of the participants.[32,33] All participants had fasted for at least 2 hr before the experiment to avoid an increase in metabolic rate.[33] At the start of the experiment, participants first lay on a floor mat without movement for at least 30 min to allow their metabolic rate to stabilize. After this equilibrating period, expired breath was collected for the resting state over 10 min. The participants then sequentially performed eight activities: (1) sitting in a chair, (2) standing, (3) playing with plastic bricks, (4) building with blocks, (5) walking, (6) climbing stairs (up and down), (7) tossing a ball, and (8) running. When the participants were sitting or standing, they were

asked to keep calm and watch a cartoon video for 10 min. The children played for 15 min with the plastic bricks while sitting in a chair at a desk. When building with blocks, participants were allowed to move freely within a 1.9- by 2.4-m area of free space for 5 min; this activity included standing, squatting, walking, and lifting and carrying blocks. For climbing stairs, participants repeated climbing up and down four steps for 2 min. For ball tossing, a handball was thrown to the participant from a set distance every 7 sec for 3 min; participants were asked to catch the ball and throw it back. For walking, participants were instructed to walk continuously at their normal pace along a straight course of 10 m for 4 min. Running was performed for 3 min under the same conditions as walking, but participants were encouraged to maintain a speed of more than 100 $m \cdot min^{-1}$.[34] The average speed was 69 ± 6.4 $m \cdot min^{-1}$ for walking and 133 ± 17 $m \cdot min^{-1}$ for running. The activities were chosen because they are commonly performed by children and cover a wide range of activity levels on the basis of observations in the kindergarten and because they were thought not to interrupt the breath sampling described below.

The $\dot{V}_E$ during the nine different activities was measured by the Douglas bag method. During each activity, participants wore facemasks to collect expired breath. Expired breath was collected through tubes (2.5-cm inner diameter × 80-cm length) into the 50-L Douglas bag near the end of each activity, after O_2 consumption ($\dot{V}O_2$) had stabilized. Previous studies have reported that $\dot{V}O_2$ and heart rate almost reach a plateau 1–2 min after the start of a 5-min endurance run in children 5 yr of age.[35,36] The durations of the activities and sampling periods are summarized in Table 1.

Instruments

Body acceleration was recorded throughout the experiment by using an Actical accelerometer (27 × 28 × 10 mm, 17 g, Mini-mitter, Inc.) and an ActivTracer accelerometer (type AC-210A, 48 × 67 × 16 mm, 57 g, GMS, Inc.). These two acceleration monitors were selected because of superior technical support and the following reasons. The Actical was selected because it was small, lightweight, and was considered to be suitable for invasive monitoring of activities of young children. The ActivTracer was selected because triaxial accelerometers have been reported to capture the principal acceleration component, which varies considerably with type of activity (e.g., between arm work and walking)[21,22] and would thus more accurately measure the free-living activities of children than uniaxial accelerometers. This notion is supported by a previous report that the output from a triaxial accelerometer provides a stronger correlation with $\dot{V}O_2$ than that of a uniaxial accelerometer.[23]

Table 1. Time periods for performance of physical activity and sampling of exhaled breath.

Activity	Time for Performance (min)	Time for Breath Sampling (min)
Lying	30	10
Sitting	10	5
Standing	7	5
Playing plastic bricks	10	5
Building with blocks	5	2
Walking	4	2
Climbing stairs	3	1
Ball tossing	3	1
Running	3	1

The Actical accelerometer has an omnidirectional sensor that is sensitive to movements in all directions and is most sensitive to vertical movement when mounted on the hip. The sensor detects movements in the 0.5- to 3.2-Hz frequency range and generates an analog voltage. The voltage is amplified, filtered, and then digitized by an analog-to-digital converter to create a digital value. The process is repeated 32 times per second (32 Hz), or every 31.25 msec, and the 32 digitized values in 1 sec are summed. The resulting 1-sec value is divided by 4 and then added to an accumulated activity value for the time intervals (epoch) specified by the user. The Actical accelerometer provides the measurements in terms of activity counts.

The ActivTracer accelerometer contains a triaxial accelerometer that detects movements in the anteroposterior (*x*-axis), mediolateral (*y*-axis), and vertical (*z*-axis) directions. The sensor detects the movements in each of the three directions every 40 msec with a band-pass filter of 0.3–100 Hz. The measurement range of the sensor is 0 to ±4 G for the vertical direction and 0 to ±2 G for the anteroposterior and mediolateral directions, and the resolution is 0.002 G. The output measure of the ActivTracer is the average of absolute values for acceleration (mG) in each axis direction and a synthesis of acceleration in three directions (*xyz*, vector synthetic) for the time interval defined by the user. Note that the outputs of the two accelerometers are not comparable because each provides acceleration measurement through a different data processing algorithm.

During the experiment, participants wore the two accelerometers on the hip by using a belt (Figure 1). Heart rate was also monitored (ActiHR, Mini-mitter, Inc.) to compare the validity of the measurement for predicting $\dot{V}_E$ with the accelerometer measurement. The sensor and lead of the heart rate monitor were attached to the participant's chest using disposable electrode pads in accordance with the manufacturer's instructions. Acceleration and heart rate were monitored every 15 sec.

The volume of expired breath was measured with a dry gas flow meter (Shinagawa Company). To measure $\dot{V}O_2$ and carbon dioxide (CO_2) production by participants, the O_2 and CO_2 concentrations in expired breath were analyzed by using a portable gas analyzer (AR-1, ARCO System, Inc.), which was calibrated and verified with outdoor air before each sample analysis.

Data Analysis

The volume of expired breath measured at ambient temperature and pressure and saturated with water vapor (ATPS condition) was converted to the volume at standard temperature and pressure under dry conditions (STPD condition). With the exception of the data for running, if the respiratory quotient (which is expressed as the ratio between

Figure 1. Children wearing Actical and ActivTracer accelerometers on their hips with a belt. Heart rate was monitored at the same time using an ActiHR attached to the participant's chest. Dashed lines indicate the location of the sensor and lead of the heart rate monitor under the clothing.

CO_2 production [$\dot{V}CO_2$] and $\dot{V}O_2$) was outside of the range 0.75–0.99, the V_E data were excluded from the analysis because the participant was in a state of hyperventilation or the exhaled breath had leaked from the facemask during breath sampling. Mean height, body weight, and $\dot{V}_E$ values were compared between boys and girls by using the Student's t test. For comparison of acceleration among multiple activities, one-way analysis of variance (ANOVA) was conducted, followed by the Scheffe test for the individual comparison if the result of ANOVA was significant.

Linear regression analysis was performed to develop equations to predict $\dot{V}_E$ from the synthetic acceleration from the accelerometers and heart rates with all of the participants and activities combined. The regression equations were presented as follows:

$$y = a + b \times x \quad (2)$$

where y is $\dot{V}_E$ as an independent variable and x is the synthetic acceleration or heart rate as a dependent variable. The $\dot{V}_E$ for each activity and participant was estimated from the linear regression equation. To evaluate the validity, the $\dot{V}_E$ estimated from activity counts measured by the Actical and ActivTracer and from heart rate measurements were individually compared with the $\dot{V}_E$ measured by the Douglas bag method. The percentage differences were then calculated for each activity using a technique developed by Bland and Altman to assess the agreement between two methods of measurement.[37]

Using the vertical and horizontal acceleration measured by the ActivTracer, linear discriminant analysis was performed to identify variables that strongly discriminate between the different types of activities. This analysis was used to dichotomize the type of activity into two groups, group 0 and group 1, and group was included in the analysis as a categorical dependent variable. The vertical activity counts (z) and the ratio between vertical and horizontal acceleration ($z/[x^2 + y^2]^{0.5}$) were included as independent variables. The significance of the discriminant function was evaluated with Wilks' λ. All statistical analyses were performed using SPSS software version 15 for Windows (SPSS, Inc.). Statistical significance was set at $P < 0.05$.

The physical activity ratio (PAR), which is the energy cost of an activity per unit time, was calculated to classify V_E according to the intensity of physical activity on the basis of energy consumption. The PAR was calculated by dividing the EE (kcal · min^{-1}) for a specific activity by the estimated basal metabolic rate (BMR).[38,39] EE was calculated from the $\dot{V}O_2$ (L · min^{-1}) and $\dot{V}CO_2$ (L · min^{-1}) as described previously.[40] BMR was calculated by dividing the EE during the resting state by 1.1 on the assumption that the thermic effect of food is 10% of the BMR.[32] PAR was categorized as sedentary (PAR < 1.5), light (1.5 ≤ PAR < 3), moderate (3 ≤ PAR < 6), and vigorous (6 ≤ PAR) according to values given in the literature for the energy cost of physical activities.[26] All data in the text, tables, and figures are presented as mean ± 1 SD.

RESULTS

The $\dot{V}_E$ (STPD), $\dot{V}O_2$ (STPD), accelerometer measurements, and heart rates of participants during the nine physical activities are summarized in Tables 2 and 3. The $\dot{V}_E$ ranged from 0.18 ± 0.02 L · kg^{-1} · min^{-1} when the participant was lying down to 1.07 ± 0.29 L · kg^{-1} · min^{-1} during running. There were no gender-associated differences ($P > 0.05$, t test) in the height or weight of participants or in $\dot{V}_E$ during the various activities.

Table 2. Summary of $\dot{V}_E$ and $\dot{V}O_2$ at STPD and PAR during nine different activities.

		$\dot{V}_E$ (STPD)			
Activity	***n***	**L · min^{-1}**	**L · kg^{-1} · min^{-1}**	**$\dot{V}O_2$ (STPD) L · kg^{-1} · min^{-1}**	**PAR**
Lying	27	3.9 ± 0.5	0.18 ± 0.02	0.006 ± 0.001	–
Sitting	24	4.4 ± 0.6	0.21 ± 0.02	0.007 ± 0.001	1.15 ± 0.77
Standing	25	4.5 ± 0.6	0.22 ± 0.03	0.007 ± 0.001	1.19 ± 0.21
Playing plastic bricks	28	5.1 ± 0.7	0.25 ± 0.03	0.008 ± 0.001	1.37 ± 0.36
Building with blocks	28	10.5 ± 1.7	0.51 ± 0.09	0.017 ± 0.003	2.98 ± 0.68
Walking	24	9.7 ± 1.5	0.47 ± 0.06	0.016 ± 0.002	2.80 ± 0.48
Climbing stairs	28	16.5 ± 3.3	0.81 ± 0.12	0.028 ± 0.004	4.79 ± 0.83
Ball tossing	28	15.4 ± 3.1	0.75 ± 0.12	0.026 ± 0.004	4.55 ± 0.89
Running	28	22.8 ± 4.8	1.07 ± 0.29	0.032 ± 0.005	5.74 ± 0.23

Table 3. Summary of accelerometer measurements and heart rate during nine different activities.

	Accelerometer Measurements							
	Actical (counts · 15 sec^{-1})		ActivTracer (mG · 15 sec^{-1})				Heart Rate (beats · min^{-1})	
Activity	*n*	Synthetic	*n*	Synthetic	Vertical	Horizontal	*n*	
Lying	27	2 ± 4	27	7 ± 5	2 ± 2	6 ± 4	27	98 ± 9
Sitting	27	1 ± 3	28	15 ± 7	3 ± 2	11 ± 6	28	101 ± 10
Standing	29	5 ± 9	29	19 ± 11	6 ± 5	15 ± 8	29	102 ± 22
Playing with plastic bricks	27	23 ± 38	27	38 ± 16	7 ± 4	31 ± 13	25	111 ± 9
Building with blocks	26	217 ± 133	26	205 ± 57	116 ± 49	128 ± 26	26	134 ± 16
Walking	24	523 ± 176	24	341 ± 70	241 ± 62	179 ± 31	25	131 ± 13
Climbing stairs	24	772 ± 160	24	441 ± 78	321 ± 69	217 ± 34	24	162 ± 12
Ball tossing	26	673 ± 210	26	426 ± 94	293 ± 91	223 ± 29	26	161 ± 16
Running	26	1960 ± 370	25	1024 ± 126	855 ± 118	386 ± 70	27	177 ± 14

Synthetic acceleration ranged from 1 ± 3 counts · sec^{-1} during sitting to 1960 ± 370 counts · sec^{-1} during running when measured with the Actical accelerometer and from 7.4 ± 5.2 during lying down to 1024 ± 126 mG · sec^{-1} during running with the ActivTracer accelerometer. The ActivTracer detected body acceleration in all participants during all nine activities. By comparison, the Actical detected body acceleration in only 78% of participants when lying down, 61% during sitting, 90% during standing, 75% while playing with plastic blocks, and in 100% of participants during all other activities. A significant difference was observed among the accelerations for resting, sitting, standing, and building with blocks when measured with the ActivTracer, whereas no significant difference was observed among the accelerations for these four activities when measured with Actical (ANOVA, $P < 0.05$). Heart rates ranged from 98 ± 9 beats · min^{-1} when the participant was lying down to 177 ± 14 beats · min^{-1} during running.

Calibration

There was a strong correlation between the experimentally measured $\dot{V}_E$ using the Douglas bag method and the synthetic acceleration measured by the Actical and ActivTracer; Pearson's correlation coefficients were r = 0.886 ($n = 223$, $P < 0.001$) for the Actical and 0.913 ($n = 222$, $P < 0.001$) for the ActivTracer. Heart rates showed a high linear correlation with the logarithmic $\dot{V}_E$ (r = 0.909, $n = 223$, $P < 0.001$).

The mean percentage differences between experimentally measured $\dot{V}_E$ and that estimated from synthetic acceleration and heart rates were calculated using linear regression models (Table 4). The synthetic acceleration overestimated $\dot{V}_E$ from lying down through playing with plastic bricks by 24–60% for the Actical and by 14–37% by the ActivTracer. $\dot{V}_E$ values for walking and running were overestimated by 11–20% for the Actical and by 11–24% for the ActivTracer. By comparison, the Actical underestimated the $\dot{V}_E$ values for building with blocks, ball tossing, and stair climbing by 19–23%, and the ActivTracer underestimated these values by 13–18%. When predicted from heart rates, $\dot{V}_E$ for lying down through to playing with plastic bricks was overestimated by 14–19%, whereas that for walking through to running was underestimated by 2–11%, with the exception of ball tossing, which was within an overestimation of 1%. The overall mean differences between the observed and predicted $\dot{V}_E$ were greater for the Actical (13% ± 33%) and ActivTracer (9% ± 24%) than for those calculated from heart rates (4% ± 26%).

Table 4. Difference between observed and estimated $\dot{V}_E$ from Actical and ActivTracer accelerometer measurements and heart rate using a single regression equation.

	Actical		ActivTracer[a]		Heart Rate	
Activity	Difference (L · kg^{-1} · min^{-1})	Percent Difference	Difference (L · kg^{-1} · min^{-1})	Percent Difference	Difference (L · kg^{-1} · min^{-1})	Percent Difference
Lying	0.11 ± 0.02	60.0 ± 22.5	0.06 ± 0.02	36.6 ± 19.0	0.03 ± 0.04	18.7 ± 23.5
Sitting	0.09 ± 0.02	43.0 ± 17.6	0.05 ± 0.02	24.6 ± 15.3	0.03 ± 0.05	13.8 ± 25.1
Standing	0.08 ± 0.03	37.3 ± 19.8	0.04 ± 0.03	21.8 ± 17.6	0.04 ± 0.06	19.7 ± 32.6
Playing plastic bricks	0.05 ± 0.03	24.1 ± 17.1	0.03 ± 0.03	14.1 ± 14.1	0.03 ± 0.04	13.9 ± 17.4
Building with blocks	−0.13 ± 0.04	−22.7 ± 13.9	−0.09 ± 0.07	−15.0 ± 12.1	−0.06 ± 0.10	−11.4 ± 19.4
Walking	0.06 ± 0.07	14.1 ± 14.4	0.09 ± 0.07	20.4 ± 15.1	−0.05 ± 0.10	−10.2 ± 20.3
Climbing stairs	−0.16 ± 0.11	−18.7 ± 11.0	−0.15 ± 0.11	−17.5 ± 12.3	−0.02 ± 0.16	−2.2 ± 20.9
Ball tossing	−0.15 ± 0.11	−18.7 ± 12.4	−0.11 ± 0.12	−13.5 ± 13.9	0.01 ± 0.19	0.6 ± 24.3
Running	0.08 ± 0.25	10.7 ± 24.9	0.08 ± 0.21	10.9 ± 20.9	−0.04 ± 0.27	−3.1 ± 23.9

Notes: [a]Results of estimation using a single regression equation are presented.

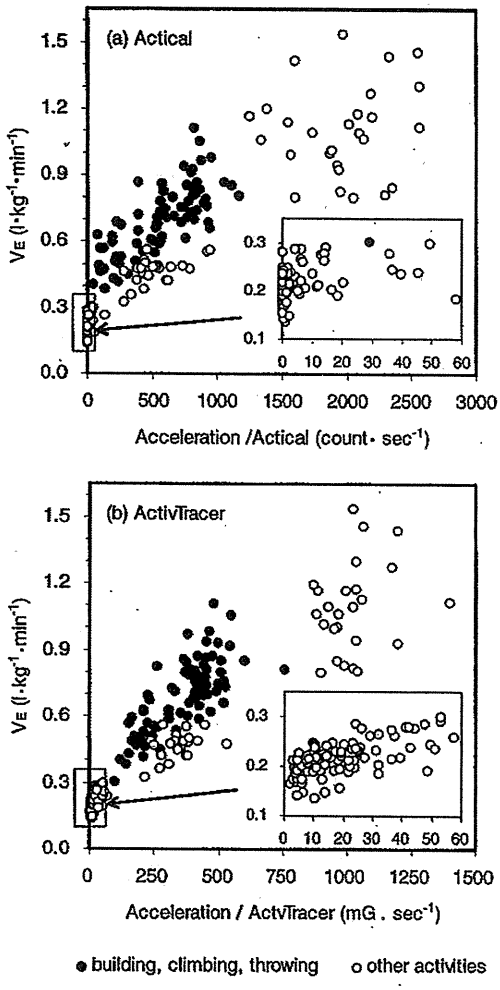

Figure 2. Scatterplots of $\dot{V}_E$ vs. accelerometer measurement (vector synthesis): (a) Actical and (b) ActivTracer. Activities were divided into two groups: (1) building, climbing, and throwing and (2) all other activities.

Additional regression analysis showed that when building with blocks, ball tossing, and stair climbing were excluded, the correlation between $\dot{V}_E$ and synthetic acceleration was improved, with r = 0.949 (n = 146, $P < 0.001$, $y = 0.0004x + 0.22$) for the Actical and r = 0.962 (n = 145, $P < 0.001$, $y = 0.00086x + 0.20$) for the ActivTracer. For the group of activities including building with blocks, ball tossing, and stair climbing, the correlation between $\dot{V}_E$ and synthetic acceleration was r = 0.781 (n = 77, $P < 0.001$, $y = 0.0004x + 0.44$) for the Actical and r = 0.761 (n = 77, $P < 0.001$, $y = 0.00094x + 0.35$) for the ActivTracer (Figure 2).

Activity Type by Using Vertical and Horizontal Activity Counts

The linear discriminant analysis showed a significant difference between walking and the group of activities comprising building with blocks, stair climbing, and ball tossing (Wilks' λ = 0.897, $P < 0.005$). The discriminant function obtained was

$$f = -3.31 + 5.98 \times (z/[x^2 + y^2]^{0.5}) - 0.017 \times z \quad (3)$$

The standardized canonical coefficient was greater for the ratio between vertical and horizontal acceleration than for vertical acceleration alone, indicating that the ratio was a more significant discriminator than the vertical acceleration. The sensitivity of discrimination was 75% for group 1 (walking) and 70% for group 0 (other activities). The correct classification rate was 75% for walking, as category 1, and was 60, 64, and 89% for the category 0 activities building with blocks, stair climbing, and ball tossing, respectively.

The $\dot{V}_E$ for each activity was recalculated in two steps for data obtained with the ActivTracer. When the synthetic acceleration of a given activity was between 96 and 754 mG · sec^{-1} (the range of accelerometer measurements by the ActivTracer from building with blocks through to ball tossing), the activity was classified as walking or other activities using the previously described discriminant function. The $\dot{V}_E$ then was estimated from the synthetic acceleration measured by the ActivTracer using the regression equation developed for the group of activities to which the activity of interest was classified. As a result, the mean difference between observed and estimated $\dot{V}_E$ was +10% for lying down, +1% for sitting, −1% for standing, −6% for playing with plastic bricks and building with blocks, +16% for walking, −12% for stair climbing, −0.3% for ball tossing, and +1% for running (Figure 3). The overall mean percentage difference was 0.2% ± 19% (−0.01 ± 0.12 L · kg^{-1} · min^{-1}).

Classification of $\dot{V}_E$

The mean PAR was 1.16 ± 0.07 for sitting, 1.20 ± 0.11 for standing, 1.38 ± 0.20 for playing with plastic bricks, 2.79 ± 0.48 for walking, 3.00 ± 0.56 for building with

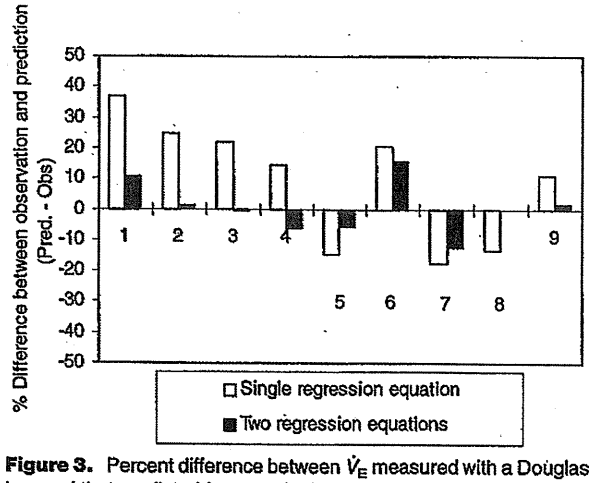

Figure 3. Percent difference between $\dot{V}_E$ measured with a Douglas bag and that predicted from synthetic accelerometer measurements by the ActivTracer during nine different activities. Percent differences using the two regression equations were compared with those using the single regression equation. Activity: 1 = lying down, 2 = sitting, 3 = standing, 4 = playing with plastic bricks, 5 = building with blocks, 6 = walking, 7 = stair climbing, 8 = ball tossing, and 9 = running.

blocks, 4.84 ± 0.68 for climbing stairs, 4.54 ± 0.91 for ball tossing, and 5.79 ± 1.05 for running. The PAR indicates a sedentary state for sitting, standing, and playing with plastic bricks; a light-to-moderate level of physical activity for building with blocks and walking; moderate physical activity for stair climbing and ball tossing; and moderate-to-vigorous physical activity for running. The thresholds corresponding to PAR values of 1.5, 3, and 6, which are the cutpoints between sedentary-to-light, light-to-moderate, and moderate-to-vigorous levels of physical activity intensity were 132, 478, and 1783 counts · sec^{-1} for the Actical measurements and 71, 412, and 1093 mG · sec^{-1} (category 1) and 31, 218, and 593 mG · sec^{-1} (category 0) for the ActivTracer measurements.

DISCUSSION

In the study presented here, mean $\dot{V}_E$ values were obtained for Japanese preschool children 6 yr of age during the resting state and during sedentary through to vigorous physical activity. The weight and height of the participants in this study were similar to those reported for 6-yr-old children by the Ministry of Health, Labor, and Welfare, Japan.[41] The $\dot{V}_E$ values presented here for sitting and standing, which were equivalent to 5.00 ± 0.64 and 5.23 ± 0.67 L · min^{-1}, respectively, at body temperature, ambient pressure, and saturated with water vapor (BTPS) were consistent with the $\dot{V}_E$ values of 4.98 ± 0.56 and 5.48 ± 0.44 L · min^{-1} (BTPS) in children 4–6 yr of age reported by Honda.[42]

The accelerometer measurements were also validated for estimating the $\dot{V}_E$ of young children during daily life. To the authors' knowledge, this study is the first to use accelerometer-based activity measurements to estimate $\dot{V}_E$ for different levels of activity. There was a strong positive linear correlation between synthetic acceleration from the accelerometers and $\dot{V}_E$ from the resting state through to vigorous physical activity, indicating that accelerometers can be used to estimate $\dot{V}_E$.

The comparison between the Actical and ActivTracer accelerometers presented here revealed smaller percentage differences between observed and predicted values with the ActivTracer, especially from resting through to light levels of physical activity. This result suggests that the ActivTracer more accurately measures physical activity and hence $\dot{V}_E$ than does the Actical. This difference is largely because of the differences in the ability of the Actical and ActivTracer to sense body acceleration. The ActivTracer detected body acceleration during resting and sedentary activities in all participants and revealed significant differences among the accelerations for resting, sitting, standing, and building with blocks. In contrast, the Actical failed to detect body movement in all participants during these activities and could not detect differences in acceleration among the activities. On the basis of the correlation coefficients for the single linear regression model, heart rate was a better predictor of $\dot{V}_E$ than the synthetic acceleration measurements from the accelerometers, but there was poor agreement between observed and predicted $\dot{V}_E$ from the resting state through to light levels of activity.

The primary limitation of accelerometers for estimating $\dot{V}_E$ is that a single regression model does not accurately predict the $\dot{V}_E$ associated with activities during daily life. This study showed that the $\dot{V}_E$ for building with blocks, stair climbing, and ball tossing was underestimated by using the synthetic acceleration from the Actical and ActivTracer accelerometers. The experimentally observed $\dot{V}_E$ was significantly higher for these three activities than for walking, although activity counts for all of these activities varied similarly. This variability in the relationship between $\dot{V}_E$ and synthetic acceleration resulted in marked differences between observed data and estimated values derived using the single regression model. Similar results have been reported in studies validating the use of accelerometer-based activity monitors for determining EE.[43,44] The underlying explanation is that static work or upper body activities such as lifting, carrying, and throwing objects results in increased EE or $\dot{V}O_2$,[45–49] and thus an increase in $\dot{V}_E$, without a proportional increase in body movement. This discrepancy cannot be captured by synthetic acceleration alone.

It was shown that the type of activity can be discriminated by using three-dimensional motion data obtained from a triaxial accelerometer. Discriminant analysis revealed that the ratio between vertical and horizontal acceleration and vertical acceleration alone were reasonably effective in discriminating walking from playing with plastic bricks, climbing stairs, and ball tossing as a group but were less effective in discriminating between playing with plastic bricks and climbing stairs. The study presented here also demonstrated that prediction of $\dot{V}_E$ can be improved through discrimination of the type of activity using the three-dimensional motion data and use of one of two regression models specific for the type of activity. Using this approach, the percentage difference between observed and predicted $\dot{V}_E$ was improved for each activity by an average of 14% and was even smaller than those predicted from heart rate (Table 4 and Figure 3).

This approach for improving the accuracy of estimating $\dot{V}_E$ is essential for the more accurate assessment of the short-term or daily dose of air pollutants through inhalation, especially from the resting state through to light physical activity, because people tend to spend the greatest proportion of time at these levels of activity.[50,51] For example, for lying down, the 37% overestimation in $\dot{V}_E$ resulting from the single regression equation with all activities combined is estimated to result in an overestimation of 8.6% in daily inhalation volume given the assumption that in 1 day children spend 10.2 hr in a resting state; 4 hr in a sedentary state; and 8.3, 1.3, and 1.2 hr in light, moderate, and vigorous levels of physical activity, respectively.[52] By comparison, the 10% overestimation in $\dot{V}_E$ for lying down calculated by the two regression equations is estimated to result in only a 2% overestimation in daily inhalation volume using the same assumptions.

Misclassification of the activity type by the discriminant function still leads to inaccurate estimations of $\dot{V}_E$ for walking and climbing stairs. Using the assumption described above, a 16% error in the estimation for light-level activities (e.g., walking) is roughly equivalent to 7%

of the total daily inhalation volume. However, an overestimation of $\dot{V}_E$ can be canceled out, at least in part, by underestimation of V_E for other light-to-moderate activities (e.g., building with blocks and stair climbing). Underestimation of $\dot{V}_E$ for climbing stairs will not cause considerable error because generally people spend only brief amounts of time in this type of activity during daily life.

The study presented here demonstrates that accelerometer measurements are a valid predictor of $\dot{V}_E$ in children and overcome some of the limitations of traditional approaches. The traditional approach using self-report activity diaries has limited objectivity and accuracy in quantifying the intensity of physical activity of free-living people. For example, Bender[16] conducted a study of 65 children aged 10–16 yr together with their parents and reported a poor correlation between proxy records of children's physical activity by parents and the metabolic equivalent value on the basis of accelerometer measurements as an objective measure of physical activity ($r \leq 0.383$). In another study, Lichtman[53] reported that the actual daily EE, measured by the DLW method, was overestimated by 50% in self-report activity diaries for adults. The inherent inability of self-reports to accurately quantify the intensity of physical activity could thus result in errors in estimating the daily inhalation rate. The validity of accelerometers in estimating $\dot{V}_E$ was estimated by comparing measurements from them with measurements from the Douglas bag method, and it was found that the correlation between accelerometer measurement and $\dot{V}_E$ is strong and that the error in estimating $\dot{V}_E$ using the regression equations derived from ActivTracer measurements is between −12% and +16% depending on the activity. Also, this difference was smaller than those estimated from the heart rate measurements.

Standards for categorizing $\dot{V}_E$ have not been defined for children. Here, $\dot{V}_E$ was classified in relation to the level of physical activity for children in terms of the PAR. Differences in this classification structure between studies might lead to differences in the $\dot{V}_E$ corresponding to the activity level of interest and the estimates of the time spent in activities of different intensity categories. A previous study[54] presented V_E corresponding to the level of physical activity intensity described in terms of metabolic equivalents (METs), which are expressed as a multiple of the resting metabolic rate for an activity. One MET is generally considered equivalent to the resting $\dot{V}O_2$ of 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$ in adults. However, in children, the resting metabolic rate is known to exceed 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$.[26,55] Puyau et al.[24] reported that use of the adult default value resulted in significant differences between the observed PAR and estimated MET and that this difference was greater in younger children and at higher levels of EE. Thus, use of the adult default value would inaccurately reflect the level of intensity of physical activities in young children.

One of the shortcomings of this study is the small number of subjects. Further studies with a larger study group would more accurately represent the population of 6-yr-old children in Japan. Repeated measurements of $\dot{V}_E$ are also needed to obtain a more reliable assessment of $\dot{V}_E$ in young children. The conclusions presented here are based on nine different levels of physical activity in a laboratory setting and provide strong groundwork for further analysis and research. Additional studies covering a more comprehensive range of activities are needed to confirm the validity of this approach for prediction of $\dot{V}_E$ and to better understand the factors that contribute to variability in accelerometer measurements.

ACKNOWLEDGMENTS

The authors thank Seiko Yamaguchi for her technical advice on V_E measurements and Naoko Yoshida, Mai Yamanishi, Makiko Yamamoto, Mamiko Iwasaki, and Satomi Hara for their assistance with the laboratory work. The authors thank all of the participants, their parents and teachers, and the administration of the kindergarten for their kind participation and support. The Ministry of Environment of Japan supported this study from 2005 through 2006. The contents of this article are solely the responsibility of the authors and do not necessarily represent official views of the ministry. The peer reviewer provided excellent comments that resulted in an improved paper.

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