

**Title:** Measurement of sedentary behaviours or 'downtime' in Rett syndrome

**Running title:** Sedentary behaviours in Rett syndrome

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The authors have no conflicts of interests to declare.

## **Abstract (149/150)**

This study aimed to validate measures of sedentary time in individuals with Rett syndrome. Twenty-six individuals (median [IQR] age 16.0 (9.4-20.6) years) wore an activPAL accelerometer during video-taped activities and agreement was determined between sedentary time determined by the activPAL and observation. For 11 individuals (median [IQR] age 14.5 (11.5-25.6) years), linear regression was used to determine the relationship between sedentary time recorded on the modified Bouchard activity record (BAR) diary card and measured using the activPAL. In comparison to observation, the activPAL accurately measured duration of sedentary time with a mean difference (limit of agreement) of -1.0 (6.3) minutes. The duration of BAR downtime accounted for 73% of the variance of sedentary time measured by the activPAL (coefficient 0.762, 95%CI 0.413 to 1.111). These data provide clinicians and caregivers with capacity to investigate strategies that would aim to increase activity in the non-exercise component of the activity continuum.

## **Keywords**

Rett syndrome, sedentary behaviour, Bouchard activity record, ActivPAL™, psychometric testing

## Introduction

Rett syndrome (RTT) is a neurodevelopmental disorder mainly affecting females and caused by a mutation in the *MECP2* gene.<sup>1,2</sup> Functional abilities are severely impaired and comorbidities such as epilepsy and scoliosis occur frequently.<sup>3</sup> However, RTT can be seen as a model of disability with results applicable to other comparable severe disabilities. As articulated in the International Classification of Functioning, Disability and Health,<sup>4</sup> day to day living with severe disability is challenging and commonalities with other disorders include impairments such as altered muscle tone and poor coordination, activity limitations in relation to reduced gross motor functioning, and participation restrictions more generally in relation to involvement in community life. The Danish Center for Rett syndrome was established in 2007 providing clinical and molecular follow-up of and data collection for all individuals with RTT in Denmark.<sup>5</sup> Of those with a *MECP2* mutation (n=94), 58% walked independently or with assistance, 14% a few steps with substantial assistance and 28% were non-ambulant. A longitudinal investigation in the population-based Australian Rett Syndrome Database (ARSD) established in 1993 found that one third maintained the ability to walk independently, 13% maintained assisted walking, 14% had a deterioration in their skills and the remainder were unable to walk.<sup>6</sup> These findings suggest that approximately half will learn to walk but fewer maintain this skill.

There is growing recognition of the importance of physical activity for individuals with disability and clinicians are ideally placed to recommend services and support, and we have already developed measures to identify walking-based functional skill<sup>7</sup> and activity.<sup>8,9</sup> In individuals with capacity to walk, steps were accurately measured using the StepWatch Activity Monitor™ (SAM) compared with other accelerometer devices including the

activPAL™.<sup>8</sup> Using a modified Bouchard activity record (BAR),<sup>10</sup> the duration of standing and walking activities or 'uptime' was strongly associated with the number of daily steps.<sup>9</sup> However, given the difficulties with walking, individuals with a neurological condition typically accumulate substantial sedentary time,<sup>eg,11</sup> which is associated with deconditioning of muscle strength and fitness.<sup>12</sup> The intensity of physical activity can be conceptualised on a continuum through moderate to vigorous activity, light physical activity to sedentary behaviours.<sup>13</sup> In contrast with walking-based physical activity, especially activity undertaken at moderate or vigorous intensities, it may be more relevant to quantify sedentary time, as this may be a more feasible target to modify in those with this neurological condition.

In addition to counting steps, the activPAL is designed to record sedentary time. This is because the device attaches to the thigh and contains an inclinometer, which separates time in sedentary behavior (when the thigh is horizontal) from time in non-sedentary behavior such as standing and walking (when the thigh is vertical). Nevertheless, the capacity of activPAL to accurately record sedentary time has not been investigated in people with RTT. Combining data from Denmark and Australia, this study met two aims. In Part 1, we examined the accuracy of the activPAL to measure sedentary time, standing and walking. In Part 2, we compared sedentary time recorded on the modified BAR and sedentary time measured using the activPAL.

## **Methods**

### *Participants*

At the time of recruitment in April 2014, the Danish population of girls and women with confirmed RTT was 108, 94 (87%) of whom had a pathogenic *MECP2* mutation. Individuals

living in the Capital Region of Denmark were invited to participate in Part 1 of this study. The population-based and longitudinal ARSD was the data source for Australian participants.<sup>6</sup> At the time of recruiting in December 2012, the ARSD included 392 girls and women with confirmed RTT born since 1976, of whom 64 (16.3%) had died since its inception in 1993. For Part 1 and 2, families from the ARSD were recruited if their daughter was able to walk independently or with assistance.

Approvals from the Human Research Ethics Committee were obtained from the Capital Regional Committee on Health Research Ethics, Denmark (H-6-2014-074) and the Human Research Ethics Committees Curtin University, Western Australia (HR 139/2011). Families provided written informed consent for their daughter to participate in the study.

### *Measures*

The activPAL (PAL Technologies, Glasgow, UK) was used to identify time spent in sitting, standing and walking. It is a uniaxial accelerometer including an inclinometer that attaches to the thigh using an adhesive pad.

The modified BAR<sup>9</sup> is a proxy-report diary card where each 15-minute epoch over a whole day is assigned one of five numbers which represents the dominant category of behaviour/activity as either lying, sitting, light activities in standing, walking at a slow intensity, and walking at a vigorous intensity.<sup>9</sup>

### *Part 1: Accuracy*

Families were visited at home or school in either Australia or Denmark. The activPAL was programmed using proprietary instructions and fitted to each participant. In Denmark, participants were videoed for a 2-hour period including periods of sitting, standing and walking. In Australia, participants were videoed during a 20 to 30 minute session during which they were encouraged to undertake physical activities that mostly included standing and walking.<sup>8</sup> Video data were coded to identify the start and finish of each epoch of sitting, standing (defined as feet still for at least 3 seconds) and walking. The first author coded or supervised two researchers in coding the videos. In the first instance, four randomly selected videos were coded by the two researchers and inter-observer reliability was good with high correlations for the durations of sitting (ICC=0.99), standing (ICC=0.98) and walking (ICC=0.76) activities. The total duration of each behaviour/activity (ie, sitting, standing, walking) in minutes was then determined for each participant.

### *Part 2: Whole day sedentary time*

As part of a larger study, parents in Australia were asked to fit their daughter with an activPAL over a seven-day period and to complete a modified BAR over 24-hours within this period, on a day that they were with their child all day. The BAR is a whole-day diary card in which each 15-minute period is labelled by the dominant activity selected from one of nine levels of intensity of physical activity.<sup>10</sup> We previously adapted these categories which were applicable to the general population (eg, intense sports) to categories that were applicable to those with severe disability, including lying, sitting, standing, walking at a slow intensity and walking at a vigorous intensity.<sup>9</sup> Parents categorised each 15-minute period by the dominant activity. Epochs of BAR data were excluded if one dominant activity had not been classified or if an activity such as horse riding was described for which the intensity could

not be assigned. A BAR variable labelled downtime was derived by merging the categories of lying and sitting during waking hours and the total duration of downtime was derived.

### *Data analyses*

For Part 1, intraclass correlation coefficients (ICC) were calculated to assess similarity of durations of sitting, standing and walking as recorded on the activPAL and observed on the video. Bland-Altman analyses were conducted to determine agreement (i.e. accuracy) for minutes in sitting, standing and walking, also derived from the video-tape and recorded by the activPAL. For Part 2, a linear regression model was calculated to determine whether the duration of downtime predicted the duration of sedentary time (sitting and lying) recorded on the activPAL. Data were analysed using STATA® (version 14, StataCorp, College Station, Texas).

## **Results**

### *Part 1: Accuracy*

In Denmark, 19 families were contacted regarding participation in the accuracy study with 17 giving consent (recruitment fraction 89.5%). Due to technical problems, 1 video-recording had missing data providing 16 videos of Danish individuals with RTT. Twenty-nine Australian families were invited to participate and 28 provided consent (recruitment fraction 96.6%). The original purpose of the Australian study was to assess the accuracy of accelerometers to measure walking-based physical activity but 10 of the 28 videos also contained periods of sitting. A combined total of 26 videos were therefore available for analysis. The median (IQR) age at data collection was 16.0 (9.4 to 20.6) years and the distribution of genotype and walking ability is shown in Table 1. Each of the main mutation

groups are represented and half of the sample was able to walk independently. The median (IQR) duration of video footage was 105 (12 to 118) minutes.

There was strong consistency between the observed and recorded durations of sitting (ICC 0.996, 95%CI 0.993, 0.998), standing (ICC 0.979, 95%CI 0.928, 0.992) and walking (ICC 0.919, 95%CI 0.782, 0.966). There was close agreement between the video-tape observations and data derived from the activPAL for duration of sitting, with a mean difference (limit of agreement) of -1.0 (6.3) minutes (Figure 1). The activPAL recorded more time standing than was observed [mean difference (limit of agreement) 2.5 (7.0) minutes] (Figure 2), and less time walking than was observed [mean difference (limit of agreement) -1.6 (5.2) minutes] (Figure 3).

#### *Part 2: Whole day sedentary time*

Whole day activPAL™ data was available for 25 Australian participants and modified BAR data for 11 of those. This sample size was limited because the original purpose of activPAL wear was to measure walking-based physical activity and it was not used after its accuracy in measuring steps was demonstrated to be poorer than the SAM.<sup>8</sup> The median (IQR) age of these participants was 14.5 (11.5 to 25.6) years. Each individual walked independently and had a pathogenic mutation in *MECP2*.

The median (IQR) awake time was 11.8 (10.8 to 13.25) hours in which the median (IQR) downtime was 66% (51 to 69). The median (IQR) duration of downtime recorded on the modified BAR was slightly less than the sedentary time recorded on the activPAL [median difference -39 (-80 to 35) minutes]. Duration of downtime was strongly associated with



activPAL measured sedentary time accounting for 73% of the variance (coefficient 0.762, 95%CI 0.413, 1.111). As indicated by the coefficient, each additional minute of sedentary time recorded with the activPAL was associated with nearly one additional minute of downtime as classified on the modified BAR.

## **Discussion**

This study found that the duration of sedentary time can be quantified accurately in RTT using the activPAL accelerometer. Compared with the criterion measure of observation, the activPAL accurately recorded time in lying and sitting when the thigh was horizontal, also demonstrated in children in the general population.<sup>14</sup> Figure 1 revealed poor accuracy for one individual but inspection of the video showed that she was sitting on a kneeling chair with the line of her thigh midway between horizontal and vertical. On the other hand, the activPAL overestimated the duration of standing time and underestimated the duration of walking activities, consistent with its under-reporting of steps in RTT.<sup>8</sup> The device was nevertheless able to identify sedentary behaviors with good accuracy.

Subjective assessment has the benefits of convenience with reduced expense. We also found that modified BAR responses estimating downtime, a composite of lying and sitting activities and the mirror of uptime,<sup>9</sup> were strongly predictive of activPAL measured sedentary time. The modified BAR is a simple tool that can be readily used to understand the fundamental components of the physical activity continuum.

Strengths included using the criterion measure of observation to determine accuracy across a range of durations of observed sitting, standing and walking. There was potential for some

human error when identifying the time-points on the video that activities changed between sitting, standing and walking. We operationally defined standing as requiring at least 3 seconds during uptime when the feet were still, guided by the gentle nature of walking observed in many girls with RTT.<sup>8</sup> This definition could be modified in the future. We also acknowledge our small sample size when comparing accelerometer and proxy-reported data and that each could walk independently, but a variety of activities including substantial sedentary time were represented. Rating the modified BAR relies on approximation for each 15-minute epoch where the respondent records the dominant activity level and it can only provide an estimate of downtime.

There has been increasing focus on the non-activity component of the activity continuum because of the deleterious effects of excessive daily sedentary time and the challenges individuals with neurological conditions face in order to overcome this.<sup>15</sup> The literature consistently shows that individuals with a neurological disability accumulate large amounts of sedentary time,<sup>eg 11</sup> which is of concern because of implications for muscle weakness<sup>12</sup> and bone density<sup>16</sup> and quality of life.<sup>17</sup> Because of variable gross motor skills, activity plans with appropriate supervision to protect against falls and fracture<sup>16</sup> could provide short and long term health benefits. The proxy-report modified BAR provides capacity to map day-to-day activities in developing these plans: to inform caregivers and professionals when and how often to intervene, using strategies that might include breaks in sedentary time and replacement with light-intensity activities.<sup>15</sup> This study also validates the activPAL to provide precise information on the duration of sedentary time for more formal evaluative studies. The physical activity continuum is of fundamental importance to health and wellbeing and this validation study provides improved capacity to increase activity in RTT.

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Table 1: Distribution of genotype and walking ability for Danish and Australian individuals in the accuracy study (N=26)

		N (%)
Mutation group	C-terminal	2 (7.7)
	Early truncating	1 (3.8)
	Large deletion	2 (7.7)
	p.Arg106Trp	1 (3.8)
	p.Arg133Cys	2 (7.7)
	p.Arg168*	2 (7.7)
	p.Arg255*	1 (3.8)
	p.Arg270*	2 (7.7)
	p.Arg294*	5 (19.2)
	p.Arg306Cys	1 (3.8)
	p.Thr158Met	4 (15.4)
	Other	2 (7.7)
	Negative	1 (3.8)
	Walking ability	Unable
Walks with assistance		10 (38.5)
Walks independently		13 (50.0)

## FIGURE LEGENDS

Figure 1: Bland-Altman plot showing agreement between the duration of sitting measured using the activPAL and from direct observation (n=26). The solid line represents bias (-1.0) and the dashed lines represent the limits of agreement (6.3) in minutes.

Figure 2: Bland-Altman plot showing agreement between the duration of standing measured using the activPAL and from direct observation (n=26). The solid line represents bias (2.5) and the dashed lines represent the limits of agreement (7) in minutes.

Figure 3: Bland-Altman plot showing agreement between the duration of walking measured using the activPAL and from direct observation (n=26). The solid line represents bias (-1.6) and the dashed lines represent the limits of agreement (5.2) in minutes.





FIGURE 2:

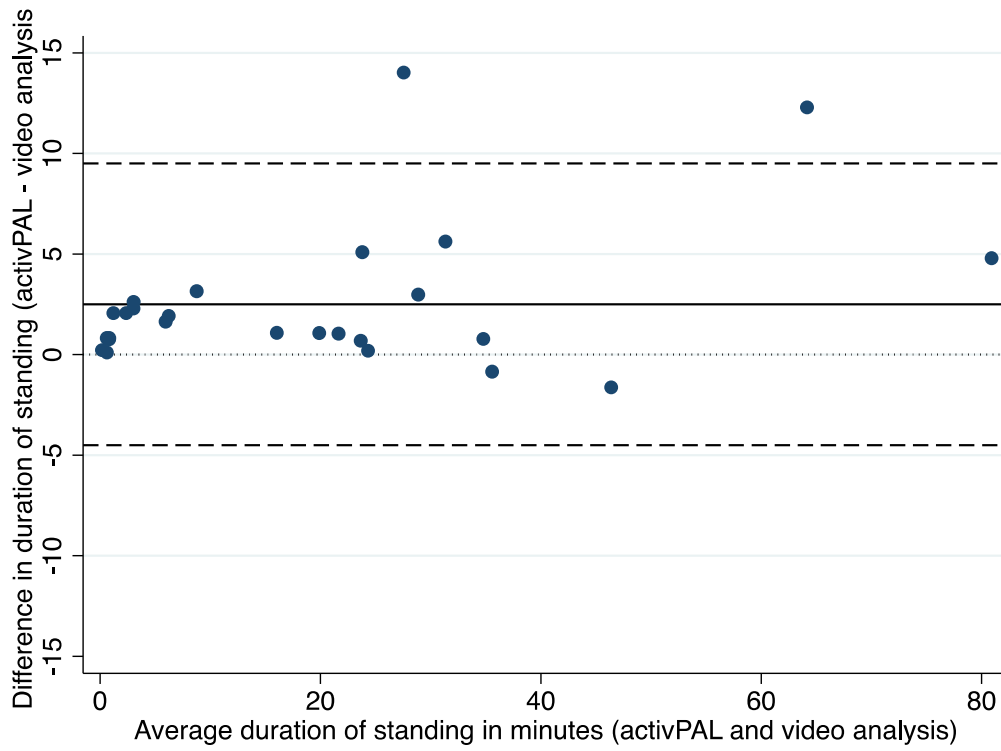


Figure 2: Bland-Altman plot showing agreement between the duration of standing measured using the activPAL and from direct observation (n=26). The solid line represents bias (2.5) and the dashed lines represent the limits of agreement (7) in minutes.

FIGURE 3:

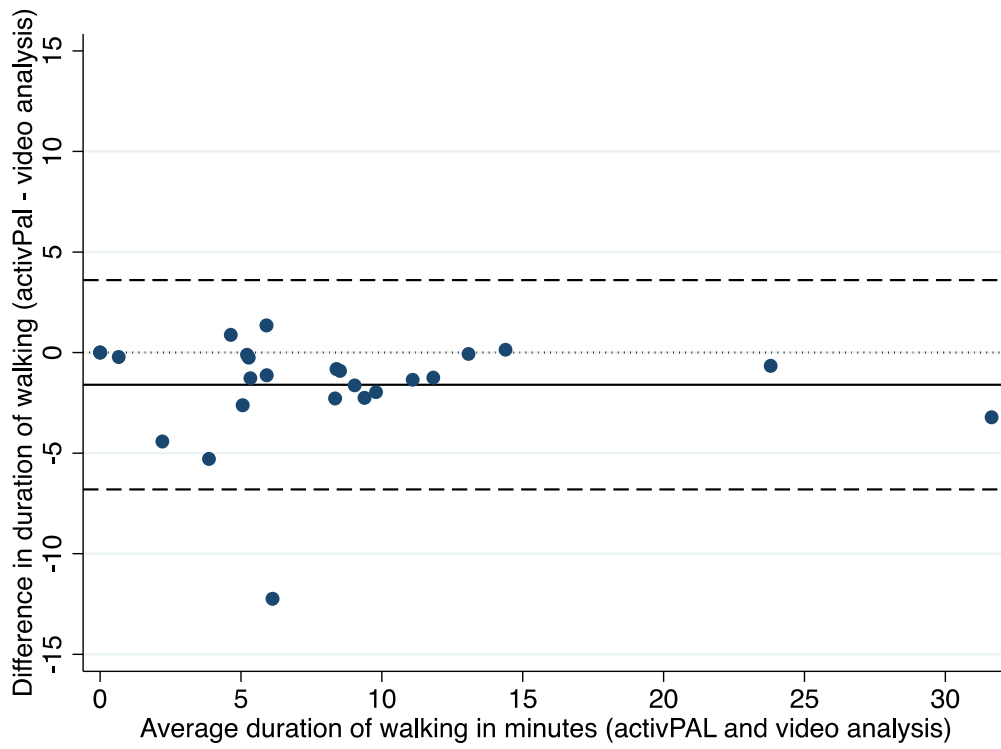


Figure 3: Bland-Altman plot showing agreement between the duration of walking measured using the activPAL and from direct observation (n=26). The solid line represents bias (-1.6) and the dashed lines represent the limits of agreement (5.2) in minutes.