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# Walking on treadmill with Rett syndrome—Effects on the autonomic nervous system

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ABSTRACT

People with Rett syndrome have deficient central autonomic control, which may interfere with walking. We have limited knowledge regarding the effects of exertion during physical activity in Rett syndrome. The aim was to investigate the autonomic responses during walking on a treadmill in Rett syndrome. Twenty-six females, 12 with Rett syndrome and 14 healthy females were included. All individuals started on the treadmill by standing still, followed by walking slowly with progressive speed until reaching maximum individual speed, which they kept for 6 min. Heart rate (HR), systolic (SBP), diastolic (DBP), mean arterial blood pressures (MAP), cardiac vagal tone (CVT), cardiac sensitivity to baroreflex (CSB), transcutaneous partial pressures of oxygen ($pO_2$), carbon dioxide ($pCO_2$), and breathing movements were recorded simultaneously and continuously. Autonomic responses were assessed by MAP, CSB and CVT during walking at 3 and 6 min. The changes in CSB and CVT in people with Rett syndrome compared to controls indicated more arousal, but only when the treadmill was started; as they continued walking, the arousal dropped to control level. People with Rett syndrome exhibited little changes in $pCO_2$ whereas the controls showed increased values during walking. This suggests poor aerobic respiration in people with Rett syndrome during walking. Five people with Rett syndrome had Valsalva type of breathing at rest, three of those had normal breathing while walking on the treadmill while the remaining two started but soon stopped the Valsalva breathing during the walk. Our results show that individuals with Rett syndrome can walk for up to 6 min at their own maximum sustainable speed on a treadmill. Energy production may be low during walking in Rett syndrome, which could cause early tiredness. A treadmill can be used in people with Rett syndrome, but must be introduced slowly and should be individually tailored. We propose that walking promotes regular breathing in Rett syndrome.

*Abbreviations:* CP, cerebral palsy; HR, heart rate; BP, blood pressure; DBP, diastolic blood pressure; ECG, electrocardiogram; EEG, electroencephalogram; ISS, international severity score; LVS, Linear Vagal Scale; MAP, mean arterial pressure; $pO_2$, partial pressure of oxygen; $pCO_2$, partial pressure of carbon dioxide; RTT, Rett syndrome; SBP, systolic blood pressure; WHO, World Health Organization

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## 1. Introduction

Rett syndrome is an X-linked neurodevelopmental disorder mainly affecting females. In its classical form the prevalence in the world ranges from 1:10 000 to 12 000 born girls (Hagberg & Witt-Engerstrom, 1987; Kerr, 1995). Diagnosis is based on clinical criteria and may nowadays be supported by a mutation in the MECP2 gene. The severity of the clinical picture varies considerably but is characterized by a baby's uneventful start and later a regression with loss of achieved skills such as words or babble and voluntary use of the hands. Gross motor skills are also affected with delayed walking and gait abnormalities. After the regression the disorder is mainly stable but the clinical picture can be severe with multiple disabilities that may include epilepsy, autonomic disturbances with breathing irregularities and gastro-intestinal complications. The associated intellectual disability is difficult to define. Eye gaze is a means of communicating in Rett syndrome according to a study using pictures and objects, lately using computers with eye gaze access (Wandin, Lindberg, & Sonnander, 2014).

Motor disability is prominent in Rett syndrome. About 73% would learn to walk but 20% of these will stop walking all together and in 27% of those who continue walking, the walking abilities will deteriorate (Larsson, Lindstrom, & Witt Engerstrom, 2005). These authors also suggest that some people with Rett syndrome can regain the walking ability previously lost, but no information was given about the intervention that was made to keep or improve walking. It is however known that poor gait due to dyspraxia, ataxia, rigidity, dystonia, spasticity and sometimes aging, often affect walking in Rett syndrome causing them to walk slowly without rhythm (Kerr & Witt Engerstrom, 2001). A lack of accurate tuning of the initiation and feedback control of movements together with poor gait control has been suggested to cause the lateral steps or back steps observed in Rett syndrome, leading to a dysrythmic way of walking (Isaias et al., 2014).

Dysautonomia and breathing dysrhythmia are common and may interfere with walking in Rett syndrome. People with Rett syndrome have inadequate central parasympathetic control, a condition that causes them to frequently end up in a state of stress (Armstrong & Kinney, 2001; Bieber Nielsen, Friberg, Lou, Lassen, & Sam, 1990; Halbach et al., 2016; Julu, 2001; Julu et al., 2001; Kerr & Witt Engerström, 2001; Nomura, Kimura, Arai, & Segawa, 1997; Weese-Mayer et al., 2006, 2008; Witt-Engerstrom, 1990). Regular exercises have been proposed to ameliorate and improve stress in people who have low stress thresholds (Brown & Siegel, 1988; Norris, Carroll, & Cochrane, 1992; von Haaren et al., 2016). There is increasing knowledge of the importance of and the need for activity in people with disabilities. However, it is still rare for professionals and carers to advise and encourage increased physical activity in people with multiple disabilities due to the lack of firm evidence of the advantages, particularly in people with Rett syndrome.

The Swedish National Rett Center in Frösön has been studying the central control of many functions of the autonomic nervous system in people with Rett syndrome since 1998. Various breathing dysrhythmia have been observed and reported in these studies including the variations of blood pressure, tissue oxygenation and heart rhythm (Julu & Witt Engerström, 2005; Julu, 2001; Julu et al., 2001; Smeets, 2005). To our knowledge, there are no previous studies of the autonomic reactions to physical activity in a group of females with Rett syndrome compared to a group of normally developed females. It is therefore important to fill in this knowledge gap. We hypothesize that since there is poor parasympathetic integrative inhibition in Rett syndrome, their general autonomic reaction to physical activity will be different compared to healthy controls. We also hypothesize that mental concentration during walking on treadmill will decrease Valsalva breathing due to lack of ability to multi-task in Rett syndrome. The overall aim of this study is therefore to investigate the autonomic responses to walking on a treadmill in females with Rett syndrome compared to age and sex matched controls. We also investigated whether the involuntary Valsalva manoeuvres in Rett syndrome would be affected by the mental concentration during walking.

## 2. Method

### 2.1. Participants

#### 2.1.1. The Rett syndrome population sampled

All females with Rett syndrome referred to the Swedish National Rett Center between 2009 and 2011 for assessment of the central control of the autonomic nervous system were asked to participate in this particular study if they were able to walk by themselves or with minor support. All the 12 persons we asked accepted to participation in the study. They had been diagnosed with Rett syndrome either earlier by our co-author Ingegerd Witt Engerström (IWE), a Specialist in Paediatrics and Paediatric Neurology, who was also the responsible physician at the Swedish Rett Center, or by their local physician, or by a paediatrician. It was later confirmed by IWE at the Swedish Rett Center.

#### 2.1.2. Inclusion criteria from the Rett population

Participants with Rett syndrome had to be able to walk independently or with some support. They were observed prior to walking on the treadmill by GL in order to gather information about mobility, walking ability, balance, walking rhythm on the floor, and mood when walking. In addition, parents or guardians were interviewed on these topics.

#### 2.1.3. The control population

Controls were recruited locally through colleagues and friends and on the basis that they were females who did not suffer from any medical complaints that could interfere with the investigation.

Informed and written consents were used for all participants. Children and participants with Rett syndrome had informed written