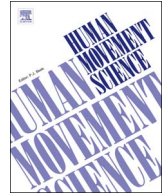




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Identification of specific gait patterns in patients with cerebellar ataxia, spastic paraplegia, and Parkinson's disease: A non-hierarchical cluster analysis

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A B S T R A C T

Background: Patients with degenerative neurological diseases such as cerebellar ataxia, spastic paraplegia, and Parkinson's disease often display progressive gait function decline that inexorably impacts their autonomy and quality of life. Therefore, considering the related social and economic costs, one of the most important areas of intervention in neurorehabilitation should be the treatment of gait abnormalities. This study aims to determine whether an entire dataset of gait parameters recorded in patients with degenerative neurological diseases can be clustered into homogeneous groups distinct from each other and from healthy subjects. Patients affected by three different types of primary degenerative neurological diseases were studied. These diseases were: i) cerebellar ataxia (28 patients), ii) hereditary spastic paraplegia (31 patients), and iii) Parkinson's disease (70 patients). Sixty-five gender-age-matched healthy subjects were enrolled as a control group. An optoelectronic motion analysis system was used to measure time-distance parameters and lower limb joint kinematics during gait in both patients and healthy controls. When clustering single parameters, step width and ankle joint range of motion (RoM) in the sagittal plane differentiated cerebellar ataxia group from the other groups. When clustering sets of two, three, or four parameters, several pairs, triples, and quadruples of clusters differentiated the cerebellar ataxia group from the other groups. Interestingly, the ankle joint RoM parameter was present in 100% of the clusters and the step width in approximately 50% of clusters. In addition, in almost all clusters, patients with cerebellar ataxia showed the lowest ankle joint RoM and the largest step width values compared to healthy controls, patients with hereditary spastic paraplegia, and Parkinson's disease subjects. This study identified several clusters reflecting specific gait patterns in patients with degenerative neurological diseases. In particular, the

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specific gait pattern formed by the increased step width, reduced ankle joint RoM, and increased gait variability, can differentiate patients with cerebellar ataxia from healthy subjects and patients with spastic paraplegia or Parkinson's disease. These abnormal parameters may be adopted as sensitive tools for evaluating the effect of pharmacological and rehabilitative treatments.

1. Introduction

Patients with degenerative neurological diseases such as cerebellar ataxia (CA), spastic paraplegia (SP), and Parkinson's disease (PD) often present a progressive gait function decline that inexorably impacts their autonomy, risk of falls, and quality of life (Bodranghien et al., 2016; Martinez-Martin, Rodriguez-Blazquez, Forjaz, & Kurtis, 2015; Pickering et al., 2007). For this reason, and considering the associated social and economic costs, one of the most important areas of intervention in neurorehabilitation should be the treatment of gait abnormalities. Consequently, evaluating gait to quantify and typify specific gait impairments in patients with degenerative neurological diseases is crucial when focusing on the specific factors in rehabilitation and thus for designing treatments tailored to individual needs. This need is further reinforced by the knowledge that gait outcomes are correlated with longevity (Studenski et al., 2011), cognitive decline (Verghese, Wang, Lipton, Holtzer, & Xue, 2007), and adverse events (Abellan van Kan et al., 2009).

Unfortunately, most descriptions of gait disorders are still largely based on qualitative clinical observations. Only recently have an increasing number of studies quantitatively evaluated gait disorders in degenerative neurological diseases, showing differences in spatio-temporal parameters and kinematic and kinetic variables when compared to healthy controls (Serrao et al., 2012, 2016; Sofuwa et al., 2005). However, the existence of more than a single gait pattern in healthy subject populations as well as in patients with the same neurological disease (Don et al., 2007; Ferrarin et al., 2012; Kinsella & Moran, 2008; Roche et al., 2014; Serrao et al., 2016; Toro, Nester, & Farren, 2007) could create heterogeneity and confound the results. For instance, in healthy subjects, Vardaxis, Allard, Lachance, and Duhaime (1998) found five distinct patterns based on 3-D peak muscle power. Simonsen and Alkjær (2012) showed that healthy subjects could be clustered into two groups based on ground reaction forces, and knee and ankle joint angles and moments in the sagittal plane. In addition, Mezghani and Fuentes (2013) recognized four different walking patterns according to knee frontal plane kinematics. Similarly, patients with the same neurological disease may be grouped according to joint kinematics (Don et al., 2007; Krzak et al., 2015; Serrao et al., 2016). Conversely, patients with different neurological diseases may show similar gait patterns in terms of spatio-temporal parameters and joint kinematics (e.g. step length and joint range of motion (RoM) reduction), making the gait analysis generic and not reflecting the wide clinical heterogeneity of gait disorders.

In evaluating gait function, it would be useful to measure which parameter or set of parameters are the most specific for a given disease. One approach to address this problem could be the use of cluster analysis techniques. Both hierarchical and non-hierarchical cluster analyses have been used to classify gait patterns among patients—either children or adults—with several neurological diseases (Ferrarin et al., 2012; Kinsella & Moran, 2008; Roche et al., 2014; Toro et al., 2007). However, these studies were not aimed at individuating the parameter (or set of parameters) specific for a given disease, identifying what was common rather than what was unique. The purpose of this study was to determine whether an entire data set of gait parameters recorded in patients with degenerative neurological diseases could be clustered into homogeneous groups distinct from each other and from healthy subjects. Our hypothesis was that specific gait patterns, for instance a widened base of support combined with other biomechanical variables for the ataxic gait, could be identified. Individuating specific gait patterns may be of value in determining the most meaningful gait features in the complexity of locomotion to recognize specific abnormalities and their impact on clinical decision-making, as well as to individualize rehabilitative treatment to better evaluate its effects over time. To achieve this aim, we investigated CA, SP and, PD, three neurodegenerative diseases that affect the three major systems of the central nervous system: the cerebellum, pyramidal, and extrapyramidal systems.

2. Materials and methods

2.1. Patients

This is a retrospective study based on gait analysis carried out in adult neurological patients and healthy subjects, who were recorded in the Motion Analysis Lab between October 2011 and May 2014 in Policlinico Italia, Rome, Italy.

Patients affected by three different types of primary degenerative neurological diseases were included: i) CA, ii) hereditary SP (HSP), and iii) (PD). All patients could walk without assistance or walking aids and did not show psychiatric, orthopedic, rheumatologic, or other diseases that could further alter their gait function. One hundred and ninety-four (194) participants were considered. Their composition was as follows. i) 28 patients had CA, ii) 31 patients had HSP, iii) 70 had PD and iv) 65 were healthy subjects. All 194 participants provided written informed consent before taking part in the study, which complied with the Helsinki Declaration, and was approved by the local ethics committee.

All patients were evaluated independently by two experienced neurologists (C.C. and F.P.) who assessed cognitive functions, cranial nerves, muscle tone, muscle strength, joint coordination, tendon reflexes, and sensory function.

At the time of the evaluation, all patients were undergoing physical therapy, which included lower limb and stretching exercises, balance, and gait training. Patients were required to remain on stable doses of all prescription and over-the-counter medications for

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