Riassunto Articoli FOG

Fuser Alessandro

5 settembre 2017

Indice

1 Characterizing Freezing of Gait in Parkinsons's Disease: Models of an Episodic Phenomenon[1]

1.1 Abstract

The first aim was to provide a methodological and critical review of the most common research approach to understand FOG. The second aim was to summarize the literature on the potential mechanisms behind the episodic nature of FOG.

1.2 Article

We can use a decision tree to refine freezer/non-freezer classification by identifyng 3 categories:

1. A "self-reported freezer";
2. A "probable freezer" when FOG is confirmed by a third person (caregiver);
3. a "definite freezer" when freezing is actually observed during formal objective testing.

FOG is defined as a "brief, episodic absence or marked reduction of forward progression of the feet despite having the intention to walk". Freezing episodes never occur at rest but at "the wish to move". This intention to engage in voluntary action combined with the need to adjust movement to external circumstances or to internal motor commands seems to jam the system. Ther're four models of FOG:

1. **Threshold Model**, where we have accumulation of motor deficits until threshold is reached and freeze occurs, the prediction is involved in the increase motor cycle frequency, decrease amplitude, increase coordination complexity;
2. **Interference Model**, where we have competition for common central processing resources that induces breakdown, the prediction is involved in the increase number concurrent tasks, increase difficulty level tasks, increase load on executive function;
3. **Cognitive Model** where we have deterioration in processing of response conflict that induces block, the prediction is involved in increase incongruency level, increase response speed, increase load on executive model;
4. **Decoupling Model**, where the decoupling between motor programs and motor response induced block, the prediction is involved in increase strength/frequency stratle stimuli, increase postural load or instability.

The singole model is not satisfying, but, maybe, combining some of them the result could be better.

1.3 Conclusion

To conclude, we have presented four possible explanatory concepts of FOG, mostly of motor and cognitive origins, that are intertwined to a greater or lesser extent in different situations in which FOG occurs. These models need further validation and testing, but we suggest that this theoretical framework, as well as the precise measurement of FOG and its epiphenomena, will pave the way to a better understanding and characterization of the episodes.

2 The Clinical Spectrum of Freezing of Gait in Parkinson's Disease[2]

2.1 Abstract

Freezing of gait (FOG) is a common and very disabling symptom in Parkinson's disease (PD). It is usually observed in the advanced stage of the disease, although a mild form can be seen in the early stage. Although some studies have suggested that longer duration of dopaminergic treatment is associated with FOG, the disease progression alone may be responsible for the development of FOG. FOG can be experienced on turning, in narrow spaces, while reaching a destination, and in stressful situations. In PD, FOG is strongly associated with motor fluctuation. FOG is commonly observed in the "off" state and is observed less frequently in the "on" state. Dual tasking (cognitive load) aggravates FOG. Visual or auditory cues often resolve FOG. Analysis of gait revealed that the stepping rhythm suddenly jumps into high frequency (4 –5 Hz) in FOG (hastening), and that floor reaction forces are disregulated. Since the hastening phenomenon was also reported in patients with lesions in the striatum and/or the frontal lobe, fronto-basal ganglia projections are considered essential for FOG. Careful observation and gait pattern analysis may lead to a successful management of individual PD patients with FOG.

2.2 Article

The strongest provocative factor of FOG are:

- **Turning** (turning hesitation).Most patients have their favorite direction of turning. Usually, PD patients prefer to turn towards more affected side, but there are some exceptions, because each patient has his or her own strategy for turning;

- **Initiation of gait** (start hesitation),and when a patient is passing through a **narrow space** (tight quarters hesitation) or immediately before reaching a destination;
- Time pressure to execute walking;
- Distraction of the attention to walking;
- Cognitive load, such as verbal fluency and "serial calculation"
- Dual tasking, such as carrying a tray or bags.

Possible overcoming to FOG are:

- If a line is drawn on the ground in front of the foot of a patient, the patient can usually step over it (kinesia paradoxa);
- Providing verbal or auditory stimuli such as giving a marching command similar to that given to a soldier;
- Visual stimuli such as stepping over objects, including inverted walking sticks, another person's foot, and carpet patterns;

95% of the patients experienced freezing on turning in the "off" state, but only 32% experienced freezing on turning in the "on" state. 13 Start hesitation, tight quarters hesitation, and destination hesitation are also less common in the "on" state than in the "off" state. In relation to leg motion, "small steps" and "trembling in place" types of freezing were manifested in both the "off" and "on" states. In contrast, the total akinesia type of freezing was observed only during the "off" state. 13 The duration of the freezing episode in the "on" state was significantly shorter than that in the "off" state. The EMGs of the thigh and leg muscles showed rhythmic contractions in normal walking. Reciprocity of muscular contractions between flexors and extensors was well maintained in shuffling gait. During freezing, these muscles contracted either simultaneously or reciprocally. Ankle flexors and extensors contract reciprocally at rates of 4 to 6 Hz during "trembling in place". A progressive decrease in stride length occurs with stable cadence just before freezing. Studies using an ambulatory gait analysis system with pressure sensitive insoles revealed that increased stride-to-stride variability, bilateral uncoordinated gait, and marked gait asymmetry are associated with FOG. Floor reaction force during forward locomotion in normal subjects showed two peaks corresponding to the increase in pressure on stepping in and kicking off from the floor. In contrast, shuffling gait showed a different pattern, in which the two peaks of vertical pressure in one step were replaced by a narrow, single peak. During freezing episodes, changes in foot pressure in alternating stepping behavior were extremely smaller than those in shuffling gait, and a complete shift of the center of pressure from one foot to the other was not observed. The frequency of this alternating stepping (trembling) ranges from 4 to 5 Hz.

3 Clinimetrics of Freezing of Gait[3]

3.1 Abstract

The clinical assessment of freezing of gait (FOG) provides great challenges. Patients often do not realize what FOG really is. Assessing FOG is further complicated by the episodic, unpredictable, and variable presentation, as well as the complex relationship with medication. Here, we provide some practical recommendations for a standardized clinical approach. During history taking, presence of FOG is best ascertained by asking about the characteristic feeling of "being glued to the floor." Detection of FOG is greatly facilitated by demonstrating what FOG actually looks like, not only to the patient but also to the spouse or other carer. History taking further focuses on the specific circumstances that provoke FOG and on its severity, preferably using stand- ardized questionnaires. Physical examination should be done both during the ON and OFF state, to judge the influence of treatment. Evaluation includes a dedicated "gait trajectory" that features specific triggers to elicit FOG (gait initiation; a narrow passage; dual tasking; and rapid 360 axial turns in both directions). Evaluating the response to external cues has diagnostic importance, and helps to determine possible therapeutic interventions. Because of the tight interplay between FOG and mental functions, the evaluation must include cog- nitive testing (mainly frontal executive functions) and judg- ment of mood. Neuroimaging is required for most patients in order to detect underlying pathology, in particular lesions of the frontal lobe or their connections to the basal ganglia. Various quantitative gait assessments have been proposed, but these methods have not proven value for clinical practice.

3.2 Article

The available methods to assess FOG are history taking, physical ex- amination, quantitative gait analysis and neuroimaging:

- **History Taking**: Ask about being 'glued to the floor'; Provide demonstration of FOG, including different subtypes: Shuffling forward with small steps, Trembling in place, Total akinesia; Interview spouse/other carer; Ask patient/carer to maintain a FOG diary; Ask about triggering circumstances: turning, starting, tight quarters, dual tasking, reaching destination; Ask about attenuating circumstances (e.g. external or internal cues); Differentiate between ON vs. OFF period FOG: ask about FOG immediately after waking up, ask about recent changes in medication; Falls that point to FOG: Forward falls, Falls during turning, 'Spontaneous' falls; Use the standardised FOG Questionnaire.

- **Physical Examination**: On and OFF (before first morning dose of medication or at 'end-of-dose'); Gait trajectory, including: Gait ignition, Crossing narrow passage (Doorway/Two chairs), (>) 360 axial turns in both directions, Voluntary stop; The trajectory should be repeated as quickly as possible and while performing a dual task (mental arithmic task); Videotape for objective assessment and future comparison; Physiotherapist to make home visit and assess effect of cues; Focus attention by cues: Auditory: metronome, Visual: stripes on the floor, Mental: counting, Divert attention using dual tasks; Differentiate FOG episode from normal stop: Preceded by decreased step length and increased cadence, Trembling/shuffling forward, Increased flexed posture with fixed flexion hip, knee, ankle; Ask about concurrent feeling of being 'glued to the floor';

- **Quantitative Gait Analysis**: Device using angular velocity sensors that can measure trunk motion in different planes; Goniometer and angular velocity sensor attached to the shank of one of the legs; An ambulatory gait analysis system with pressure sensitive insoles that continously record walking in freely moving subjects.

3.3 Conclusion

It is crucial to have a reliable definition of freezers versus nonfreezers, as misclassification can greatly affect the outcome of research studies. Currently, there is no such classifica tion system that can unambiguously separate freezers from nonfreezers. The main reason is that neither his tory taking nor physical examination is infallible, and gold standard laboratory measures are missing. We envision two possible approaches. The first would be an ordinal "black or white" classification, where patients would be defined as being a freezer when FOG is present according to at least one of the follow ing assessments: (a) subjectively (using a FOG ques tionnaire); (b) according to the carer (using video dem onstrations of FOG episodes); (c) during physical ex amination (using a standardized gait trajectory as S473 defined in Table 1); (d) "objectively" at home (using ambulatory gait assessment techniques); or (e) during formal experimental testing in a laboratory setting (e.g. kinematic gait analyses during treadmill walking). An alternative, and perhaps more reasonable approach, would acknowledge the inherent difficulties in making an absolute distinction between freezers and nonfreezers, and rather attempt to classify the severity of FOG, ranging from either absent to marked. Such a continuous rating scale should accommodate the frequency, severity and specific provoking circumstances of FOG, and could be used as a covariate in statistical analyses. Future studies are needed to develop and validate such classification systems, as these are an essential require ment to gain more insights into this curious gait abnormality.

4 PERFORM: A System for Monitoring, Assessment and Management of Patients with Parkinson's Disease[4]

4.1 Abstract

We describe the PERFORM system for the continuous remote monitoring and management of Parkinson's disease (PD) patients. The PERFORM system is an intelligent closed-loop system that seamlessly integrates a wide range of wearable sensors constantly monitoring several motor signals of the PD patients. Data acquired are pre-processed by advanced knowledge processing methods, integrated by fusion algorithms to allow health professionals to remotely monitor the overall status of the patients, adjust medication schedules and personalize treatment. The information collected by the sensors (accelerometers and gyroscopes) is processed by several classifiers. As a result, it is possible to evaluate and quantify the PD motor symptoms related to end of dose deterioration (tremor, bradykinesia, freezing of gait (FoG)) as well as those related to over-dose concentration (Levodopa-induced dyskinesia (LID)). Based on this information, together with information derived from tests performed with a virtual reality glove and information about the medication and food intake, a patient specific profile can be built. In addition, the patient specific profile with his evaluation during the last week and last month, is compared to understand whether his status is stable, improving or worsening. Based on that, the system analyses whether a medication change is needed always under medical supervision and in this case, information about the medication change proposal is sent to the patient. The performance of the system has been evaluated in real life conditions, the accuracy and acceptability of the system by the PD patients and healthcare professionals has been tested, and a comparison with the standard routine clinical evaluation done by the PD patients' physician has been carried out. The PERFORM system is used by the PD patients and in a simple and safe non-invasive way for long-term record of their motor status, thus offering to the clinician a precise, longterm and objective view of patient's motor status and drug/food intake. Thus, with the PERFORM system the clinician can remotely receive precise information for the PD patient's status on previous days and define the optimal therapeutical treatment.

4.2 Article

The PERFORM system is an intelligent close-loop system that seamlessly integrates a wide range of wearable sensors constantly monitoring several motor signals of the PD patients. The information collected by the sensors (accelerometers and gyroscopes) is processed by several classifiers. Sensor

have been used as activity moitor or for the classification of different body postures. The system is composed of 3 sub-systems:

- **Wearable Multi-Sensor Monitor Unit**, that continous recordings of specific signals and is composed of 4 tri-axial accelerometers (one at each extremity), 1 accelerometer/gyroscope on the waist and 1 data acquisition;
- **Local Base Unit**, a touch screen computer responsible for downloading, storage and processing of the raw signals coming from the test devices and the WMSMU, the identification and quantification of motor symptoms, the UPDRS evaluation of the patient and the patient's diary keeping;
- **Centralized Hospital Unit**, responsible for processing all patient data and treating clinician in making appropriate treatment decisions (web-based application).

System includes intelligent modules for tremor, bradykinesia, LID and Fog; all of them have been developed using a database of short-term (15 mins) recordings and a long-term recording (4h). The FoG detection module methodology consists of three stages:

1. Preprocessing of the signals is performed and then the signals are analyzed using a sliding window of 1s length and 0.5s overlap;
2. The entropy of the signal for each axis of each sensor is extracted; these values formulate a feature vector which is used for the classification of each second of the recorded signals as FoG or not, base on a Random Forest classifier, which is a collection of tree-structured classifiers;
3. For the construction of each tree of the forest a subset of samples is selected from the dataset, using the bootstrap technique, while each tree is built to the maximum size without pruning.

4.3 Conclusion

In contrast with other diseases there is no treatment and therapeutic schema for PD. The dosage and the way of medication administration are totally personalized for every patient. When the PD disease appears the treatment seems very simple but in the course of time the treatment becomes complicated and requires more and more the patient's participation. During the short visit of PD patient the clinician must be informed for the patient's day motor status. This is required to configure the treatment strategy, drug time intake, drug doses, intervals between doses, combination of drugs depending on the food intake and other details. The clinician tries to retrieve information for patient's motor status for the previous days or weeks. This is almost

impossible since it is difficult for PD patients to describe their symptoms and they cannot assess exactly their reaction to the drug. Consequently, the clinician cannot receive proper information to define realistically the drug administration treatment. The PERFORM system offers daily assistance to the clinician neurologist who tries through conflicting information from the patients and their relatives to determine the optimal therapeutically schema. The PERFORM system is used by the PD patients and in a simple, safe, painless and non-invasive way to record patient motor status for long-time intervals. In this way, the clinician can have a precise, long-term and objective view of patient's motor status in relation to drug and food intake; all the aforementioned factors are directly involved in the drug absorption and action. With the PERFORM system the clinician can remotely receive precise information for the PD patient's motor status on previous days and define the optimal therapeutical treatment.

5 Freezing of Gait and Falls in Parkinson's Disease[5]

5.1 Abstract

Freezing of gait (FOG) and falls are common and disabling phenomena in Parkinson's disease (PD) and related disorders as they may lead to loss of independence. Both are usually observed in the advanced stage of the disease, although they can also be seen in the early stage. FOG and falls have similar risk factors, such as axial motor disability and cognitive impairment, and FOG is one of the most common causes of falls. The objective of this review is to address recent ideas about the underlying pathophysiology of FOG and falls, and discuss the similarities, differences, and relationships between FOG and falls. Recent advances in studies that elucidate physical and cognitive risk factors to predict future falls are also reviewed. In addition to the history of prior falls and disease severity, the presence of FOG and cognitive dysfunction are associated with falls in PD.

5.2 Article

FOG and falls have similar risk factors, such as axial motor disability and cognitive impairment, and FOG is one of the most common causes of falls. Absence of tremor, the presence of a gait disorder and the development of balance and speech problems are associated with the occurence of FOG. FOG predominantly occurd in the "off" state, whereas falls occur in the "on" state. Impaired automaticity would explain why FOG frequently occurs during performance of secondary cognitive or motor tasks (dual tasking). The most characteristic feature of FOG is knee trembling. Multiple anticipatory postural adjustments (APAs) produce knee trembling and that FOG associated with a forward loss of balance is caused by an inability to couple normal

APAs to the motor programs for stepping. A fall in the past year, abnormal axial posture , cognitive impairment and freezing of gait were indipendent risk factors for falls and predicted 75% of future falls within a year. The best prediction was reached by combining disease-specific measures, such as PD severity, freezing of gait severity and occurence of sympthomatic orthostatic hypotension, with balance measures, such as the Tinetti score and the extent of postural anterior-posterior sway. Freezers showed poor directional control during voluntary rhytmic weight shifting and FOG never occurs at rest but at "the wish to move" (whereas falls may happen spontaneously).

5.3 Conclusion

FOG and falls are common and disabling phenomena in PD and are interconnected. FOG and falls have similar risk factors, and FOG is one of the most common causes of falls. Many hypotheses on the pathophysiology of FOG have been presented; dysfunctions in central drive and automaticity, abnormal gait pattern generation, abnormality of rhythm forma tion and APAs, perceptual malfunction, and frontal executive dysfunction are proposed. Prospective studies on the prediction of future falls showed that previous falls, FOG, poor balance, disease severity, and cognitive dysfunction are risk factors for falls. Postural instability caused by a primary disease process and effects of interventions have been studied using static or dynamic posturography; levodopa and DBS improve some measures of balance but worsen others. A better understanding of the pathomechanisms underlying FOG and falls will improve strategies for their prevention and treatment.

6 Practical approach to freezing of gait in Parkinson's disease[6]

6.1 Abstract

Freezing of gait in Parkinson's disease and related disorders is common and very disabling. It usually occurs in the advanced stages, although mild forms may develop earlier. Freezing can occur on turning, in narrow spaces, immediately before reaching a destination, and in stressful situations. Dual tasking (motor or cognitive load) aggravates the problem. Freezing of gait in Parkinson's disease usually occurs in the 'off' rather than in the 'on' state. It is, therefore, not entirely drug-resistant; the first step in medical treatment is to ensure adequate dopaminergic stimulation to reduce the 'off' state. There is no good evidence for any specific drug to alleviate freezing. Visual or auditory cues are very helpful as behavioural therapy. Assistive devices, such as a wheeled walker sometimes help. Deep brain stimulation of the subthalamic nucleus may alleviate freezing in the 'off' state. Because of the complexi-

ty of freezing, individual patients need a careful assessment—particularly in relation to motor fluctuation—to optimise their treatment.

6.2 Article

There are three clinical patterns:

1. Trembling in place, with alternating rapid knees movements (knee trembling);
2. Shuffling forward, with very short, shuffling steps;
3. Complete (or total) akinesia, with no limbs or trunk movement.

Cause of Freezing:

- Turning (most provocative);
- Initiation of gait;
- Narrow space or immediately before reaching destination;
- Time Pressure;

Several methods to overcoming FOG:

- Verbal or auditory stimuli (soldier's marching command);
- Visual stimuli (another's person walk).

7 Characterization and quantification of freezing of gait in Parkinson's disease: Can detection algorithms replace clinical expert opinion?[7]

7.1 Abstract

Freezing of gait is a paroxysmal phenomenon that is frequently reported by the parkinsonian patients or their entourage. The phenomenon significantly alters quality of life but is often difficult to characterize in the physician's office. In the present review, we focus on the clinical characterization and quantification of freezing of gait. Various biomechanical methods (based mainly on time-frequency analysis) can be used to determine time-domain characteristics of freezing of gait. Methods already used to study non-gait freezing of other effectors (the lower limbs, upper limbs and orofacial area) are also being developed for the analysis of freezing in functional magnetic resonance imaging protocols. Here, we review the reliability of these methods and compare them with reliability of information obtained from physical examination and detailed analysis of the patient's medical history.

7.2 Article

Freezing occurs most of the times when turning, step initiation, space constraints and stress or distraction. Duration of FOG could be between 2s to several minutes and the ctegory of FOG is related to its duration:

1. <10s;
2. 10s<d<30s;
3. >30s.

The most common data is referred to Percent Time [#/time]. The events immediately before FOG could be:

- Cadence of gait rise;
- Incomplete shifting of the centre of pressure from one foot to the other;
- Decrease stride length;
- Start hesitation in the first three steps;
- Cognitive overload during concomitant cognitive and motor tasks.

Automatic detection can be lead using time-frequency methods and pathological threshold.

7.3 Conclusion

Clinical expert opinion remains the gold standard for characterizing FoG. Quantification now tends to be based on percent time frozen rather than the number of episodes, although a combination of the two metrics can be used. Automatic detection (based on time-frequency methods) is highly sensitive and specific, although determination of a pathological threshold is sometimes difficult. Models of FoG (such as stepping in place) could facilitate threshold determination, and might easily and rapidly provide a freezing index for a given patient. Furthermore, these methods can be applied in an ambulatory environment (to test a supposed therapeutic effect under ecological conditions, for instance). Various sensors (accelerometers, goniometers, force-measuring insoles, etc.) have been used to determine kinematic variations. These wearable sensors can be useful to detect FoG phenomenona but also abnormalities of continuous gait excluding FoG. Other approaches are based on variability in time and/or amplitude signals. FoG has similarities with perturbations of rhythmic movements of the upper limbs, lower limbs and orofacial area. However, these equivalents of FoG are mainly used to study the pathophysiological basis of the phenomenon, rather than to clinically characterize FoG.

8 Measurement Instruments to Assess Posture, Gait, and Balance in Parkinson's Disease: Critique and Recommendations[8]

8.1 Abstract

A literature review was conducted. Identified instruments were evaluated systematically and classified as "recommended," "suggested," or "listed." Inclusion of rating scales was restricted to those that could be used readily in clinical research and practice.

8.2 Article

Scoring is obviously subjective, but we recognize 12 rating scales, but only 3 of them are recommended or suggested:

- **PIGD**: base on 5 UPDRS items relevant and postural instability, not include an adequate rating of freezing of gait;
- **RSGE**: 21 items in subgroups, high internal consistency and is recommended to use subscale scores;
- **TINETTI**: has 2 subscales: balance and gait tests.

Specific task delivery vary between scales and all of them have lack sufficient details because they are primarily address to non PD-specific constructs. No scale for all purpoes (gait, balance, posture): need for assess them simultaneously, but different score obtained for construct of tests. For freezing, therś only one questionnaires acceptable: NFOGQ.

8.3 Conclusion

We identified several questionnaires that adequately assess freezing of gait and balance confidence in PD and a number of useful clinical tests. However, most clinical rating scales for gait, balance, and posture perform suboptimally or have been evaluated insufficiently. No instrument comprehensively and separately evaluates all relevant PD-specific gait characteristics with good clinimetric properties, and none provides separate balance and gait scores with adequate content validity for PD. We therefore recommend the development of such a PD-specific, easily administered, comprehensive gait and balance scale that separately assesses all relevant constructs.

9 Free-Living Monitoring of Parkinson's Disease: Lessons From the Field[9]

9.1 Abstract

Wearable technology comprises minia- turized sensors (eg, accelerometers) worn on the body and/or paired with mobile devices (eg, smart phones) allowing continuous patient monitoring in unsupervised, habitual environments (termed free-living). Wearable technologies are revolutionizing approaches to health care as a result of their utility, accessibility, and afford- ability. They are positioned to transform Parkinson's disease (PD) management through the provision of individualized, comprehensive, and representative data. This is particularly relevant in PD where symptoms are often triggered by task and free-living environmental challenges that cannot be replicated with sufficient veracity elsewhere. This review concerns use of wearable technology in free-living environments for people with PD. It outlines the potential advantages of wearable technologies and evidence for these to accurately detect and measure clinically relevant features including motor symptoms, falls risk, freezing of gait, gait, functional mobility, and physical activity. Technological limitations and challenges are highlighted, and advances concern- ing broader aspects are discussed. Recommendations to overcome key challenges are made. To date there is no fully validated system to monitor clinical features or activities in free-living environments. Robust accuracy and validity metrics for some features have been reported, and wearable technology may be used in these cases with a degree of confidence. Utility and acceptability appears reasonable, although testing has largely been informal. Key recommendations include adopting a multidisciplinary approach for standardizing definitions, protocols, and outcomes. Robust validation of developed algorithms and sensor-based metrics is required along with testing of utility. These advances are required before widespread clinical adoption of wearable technology can be realized.

9.2 Article

Application of passive single sensor-based devices for PD. Clinical assessment are challenging and restristive, so WTCD may obtain optimal management (variation and stress reduced) and lead to comprehensive picture of patient with 1 assessment. Motor symptoms measurements are accurated and sleep is correlated with movements and the accuracy of the relevation are near to 80%. Micro features are better than Macro features for predicting falls (short survey > long survey). Free-living assessment appears to discriminate pathology better than testing in laboratory (because of stress of tests). We could use WTCD monitoring as ambulatory activity (in fact, a diary), but need for attention to threshold (# of steps or time of walking) and to sensor

configuration (it is subjective). We use the micro-level to enhance diagnostics, measure efficacy of intervention and prediction, the macro-level to reflect the global burden of disease and impact of theraphy.

9.3 Conclusion

There is no doubting the possibilities and potential of real-world monitoring and assessment of clinical features for people with PD. It is conceivable to imagine a future where micro-level data are used to enhance diagnostics, measure efficacy of intervention, monitor disease progression, and predict the risk of disease, falls, and cognitive decline. Macro-level data, on the other hand, reflect the global burden of disease and the mpact of therapy. Both sources of data pro- vide insights into personalized treatment. As this special issue in the journal indicates, this is a rapidly developing field. However, much work remains before widespread clinical adoption is a reality. We highlight key recommendations and some practical solutions to move this field forward. These challenges are likely to be met most effectively by adopting a multidisciplinary approach between key stakeholders such as clinicians, patients, engineers, computer scientists, and statisticians.

10 deFOG – a Real Time System for detection and unfreezing of Gait of Parkinson's Patients[10]

10.1 Abstract

Freezing of gait (FOG) is a common complication in movement disorders, typically associated with the advanced stages of Parkinson's disease. Auditory cues might be used to facilitate unfreezing of gait and prevent fall related injuries. We present a wearable, unobtrusive system for real-time gait monitoring, which consists of an inertial wearable sensor and wireless headset for the delivery of acoustic cues. The system recognizes FOG episodes with minimum latency and delivers acoustic cues to unfreeze the gait. We present design of a system for the detection and unfreezing of gait (deFOG), and preliminary results of the feasibility study. In a limited test run of 4 test cases the system was able to detect freezing of gait with average latency of 332 ms, and maximum latency of 580 ms.

10.2 Article

Akinesia usually denotes the sudden inability to initiate movement, which can lead to falls and injuries. It can occur as start-hesitation or during walking, and could be initiated by visual patterns on the path or by approaching narrow spaces, such as thresholds and doorways. There are several devices on the market that specifically target the ability to break the FOG. One group

of devices uses a visual stimulus for breaking the freeze. Another group of devices use both visual and audio stimuli, this is accomplished by a wearable device that monitors the movement and learns the users walking pattern. Existing research projects mostly use spectral analysis of signals from three axis accelerometers placed on various parts of the lower body to record movement patterns at varying sampling rates: normal gait frequency was close to 2Hz while the frequencies of a freeze gait ranged between 6-8Hz. Morrea experiments said that The 'locomotor' (or normal movement) band includes the frequency components between 0.5 and 3 Hz. A freeze band has a higher frequency component ranging from 3 to 8 Hz. Comparing these two bands allows for a **freeze index** (FI) to be calculated for a specific time. Using a window of 6 seconds they used the square of the freeze band area and divided it with the square of the area under the power spectra of the locomotor band. This calculation of the FI compensates for high frequency harmonics caused by normal walking that could potentially be perceived as a freeze condition. A FI threshold can be determined to signify the beginning of a FOG. However, existing gait analysis algorithms did not provide the ability to detect freezing gait in real-time using spectral methods. A global threshold detected 78% of FOG events and 20% of stand events were incorrectly labeled as FOG. Individual calibration of the freeze threshold improved accuracy and sensitivity of the device to 89% for detection of FOG with 10% false positives. The system consists of an inertial sensor and a wireless headset, the inertial sensor can be worn on several locations on the body, such as pager like attachment to the belt, knee, ankle, or a shoe. The board features an ARM7 processor with 58kB RAM and 512KB of flash, it can operate at up to 72MHz at 62mA/90mA. Three main power modes: idle, sleep and power-down. In Idle we have a 60µm wake up to execute in RAM and another 100µm is necessary if we operate off RAM. The on-board accelerometer is the Bosch SMB380 with configurable acceleration ranges ±2g, ±4g, and ±8g but signals were very often exceeding 5g during freezing gait events. The Bluetooth interface is integrated module WT32 by Bluegiga that allows integration with embedded systems through serial interface. The processor reads input signals from accelerometer and gyroscope with the sampling frequency of 200 Hz. All five signals (3 axis of the accelerometer and 2 rotational signals from the gyroscope) are filtered to eliminate the DC baseline, and processed in time and frequency domain. Choice of the spectral processing and the size of window determine the performance of the algorithm, frequency resolution, and latency of the processing algorithm: 64 simple window that introduces laency of 160ms, while the spectral analysis was performed every 10 samples, which determines time resolution of our algorithm to 50ms (time where we calculate FI). The primary technique used for detection of the freezing gait calculates the ratio of two spectral bands. The ratio of the energy in bands provides good indication of the freezing gait. Statistical analysis of the ratio provides a threshold that is relatively inde-

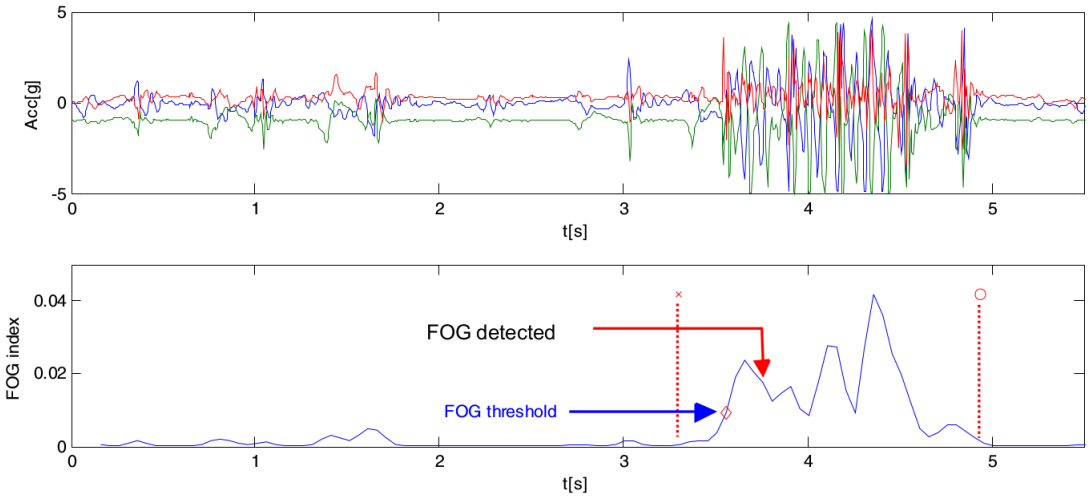

Figura 1: Detection of freezing gait with sensor on knee; a) raw accelerometer signals; b) freezing gait index (FOG); dotted lines denote manually annotated freezing gain event.

pendent of inter-user variability. We improved the algorithm by providing a correlation with the total power in the window. This approach effectively eliminates false detection during quiet periods.

10.3 Conclusion

We present a novel approach to detection and unfreezing of gait of Parkinson's patients. Initial estimation proves the feasibility of the proposed concept for real-time unfreezing of gait. Future work will include clinical experiments on the larger set of patients at Rush University. Longer periods of monitoring and observations of a larger number of patients will provide the ability to more effectively analyze freeze of gait and the effects of our proposed solution. In addition to the further refinement of the algorithm, we plan to experiment with different time-frequency analysis approaches to reduce delay caused by FFT-based block processing of sampled data. Possibilities include time domain band pass digital filters for band separation, or wavelet based spectral estimation.

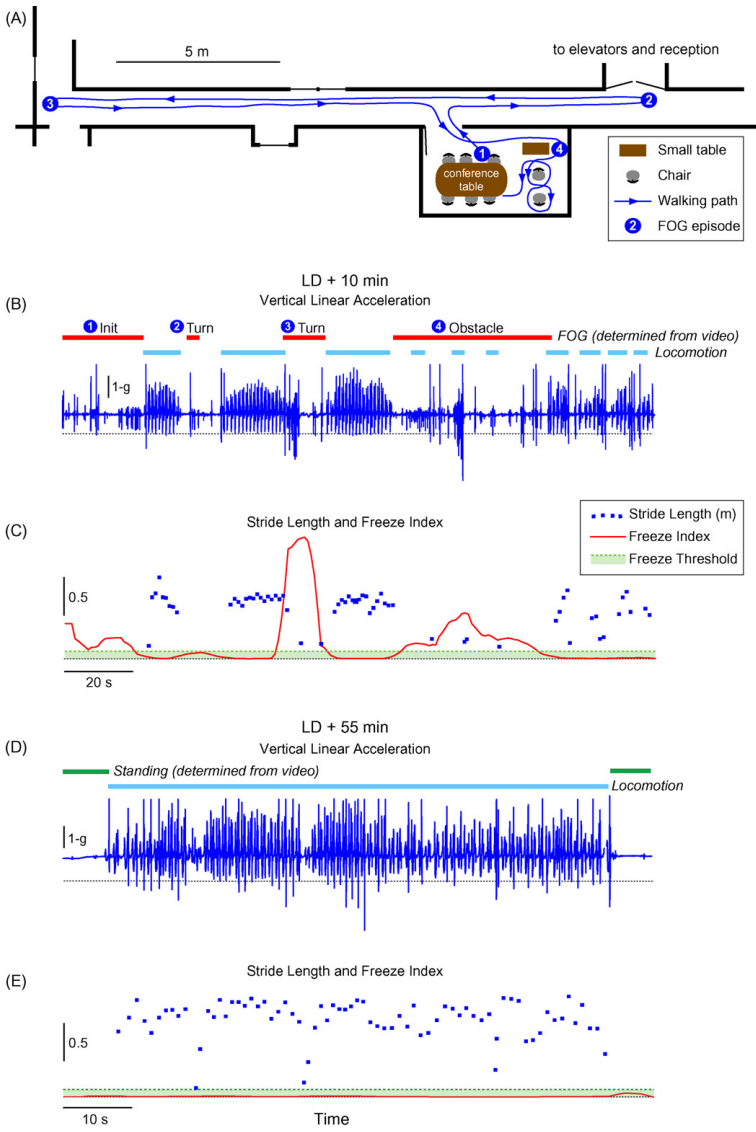

Figura 2: Data from a patient with advanced PD (subject 6) demonstrates the FOG detection algorithm. (A) Approximate path taken by the subject 10-min post levodopa administration. This subject had four FOG events; when initiating gait, at each 180 ◦ turn in the corridor, and when negotiating an obstacle (small table). (B) Vertical linear acceleration of the left shank during the trial shown in (A). Red bars above the data indicate freezing episodes as determined from video recordings; light blue bars indicate periods of walking (determined from vertical acceleration). During FOG there was a high-frequency 'trembling' of the leg apparent in the acceleration data. (C) The freeze index (FI—red trace) was calculated from the power in the freeze band (3–8 Hz) divided by power in the locomotor band (0.5–3 Hz). Large peaks occurred during FOG. A 'freeze' threshold could distinguish between FOG and periods of volitional standing. Stride length (blue squares) was also calculated from angular velocity and linear acceleration of the leg. (D) Vertical linear acceleration of the leg when following a similar trajectory as in (A) 55-min after levodopa administration. Green bars above the data indicate periods of volitional standing (not FOG) identified from the video recording. (E) FI during locomotion and standing was below the freeze threshold.

Riferimenti bibliografici

[1] Alice Nieuwboer, Nir Giladi (2013), *Characterizing Freezing of Gait in Parkinson's Disease: Models of an Episodic Phenomenon*

[2] Yasuyuki Okuma, Nobuo Yanagisawa (2008), *The Clinical Spectrum of Freezing of Gait in Parkinson's Disease*

[3] Anke H. Snijders, Maarten J. Nijkrake, Maaike Bakker, Marten Munneke, Carina Wind, Bastiaan R. Bloem (2008), *Clinimetrics of Freezing of Gait*

[4] Alexandros T. Tzallas, Markos G. Tsipouras , Georgios Rigas, Dimitrios G. Tsalikakis, Evaggelos C. Karvounis, Maria Chondrogiorgi, Fotis Psomadellis, Jorge Cancela, Matteo Pastorino, María Teresa Arredondo Waldmeyer, Spiros Konitsiotis and Dimitrios I. Fotiadis (2014), *PERFORM: A System for Monitoring, Assessment and Management of Patients with Parkinson's Disease*

[5] Yasuyuki Okuma, *Freezing of Gait and Falls in Parkinson's Disease*

[6] Yasuyuki Okuma (2014), *Practical approach to freezing of gait in Parkinson's disease*

[7] A. Delval, C. Tard, M. Rambour, L. Defebvre, C. Moreau (2015) *Characterization and quantification of freezing of gait in Parkinson's disease: Can detection algorithms replace clinical expert opinion?*

[8] Bastiaan R. Bloem, Johan Marinus, Quincy Almeida, Lee Dibble, Alice Nieuwboer, Bart Post, Evzen Ruzicka, Christopher Goetz, Glenn Stebbins(2016), Pablo Martinez-Martin, MD, PhD, 8 Anette Schrag *Measurement Instruments to Assess Posture, Gait, and Balance in Parkinson's Disease: Critique and Recommendations*

[9] Silvia Del Din, Alan Godfrey, Claudia Mazzà, Sue Lord PhD, Lynn Rochester(2016), *Free-Living Monitoring of Parkinson's Disease: Lessons From the Field*

[10] E. Jovanov, E. Wang, L. Verhagen, M. Fredrickson, R, Fratangelo (2009), *deFOG – a Real Time System for detection and unfreezing of Gait of Parkinson's Patients*, 31st Annual International Conference of the IEEE EMBS