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Highlights

• Cognitive workload is determined by performance, subjective ratings and effort. • Psychophysiological parameters reflect cognitive effort necessary to maintain performance. • Psychophysiological measures provide accurate information on cognitive workload during walking. • High cognitive workload induces a significant increase in cadence. • To optimize cognitive workload, psychophysiology could be 'fed back' to a biocooperative prosthesis.

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Psychophysiological response to cognitive workload during symmetrical, asymmetrical and dual-task walking

Kristel Knaepen[a,b], Uroš Marušič[c], Simona Crea[d], Carlos D. Rodríguez Guerrero[b,h], Nicola Vitiello[d,e], Nathalie Pattyn[a,f,g], Olivier Mairesse[f,g], Dirk Lefeber[b,h], Romain Meeusen[a,b,*]

[a] Department of Human Physiology, Vrije Universiteit Brussel, Pleinlaan 2, 1050 Brussels, Belgium
[b] Advanced Rehabilitation Technology and Science Research Group, Vrije Universiteit Brussel, Pleinlaan 2, 1050 Brussels, Belgium
[c] Institute for Kinesiology Research, Science and Research Centre of Koper, University of Primorska, Titovtrg 4, 6000 Koper, Slovenia
[d] The BioRobotics Institute, Scuola Superiore Sant'Anna, Viale Rinaldo Piaggio 34, 56026 Pisa, Italy
[e] Don Carlo Gnocchi Foundation, Via Di Scandicci 269, 50143 Firenze, Italy
[f] Vital Signs and Performance Monitoring Research Group, Belgian Royal Military Academy, Hobbemastraat 8, 1000 Brussels, Belgium
[g] Department of Biological Psychology, Vrije Universiteit Brussel, Brussels, Belgium
[h] Robotics and Multibody Mechanics Research Group, Vrije Universiteit Brussel, Pleinlaan 2, 1050 Brussels, Belgium

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Walking with a lower limb prosthesis comes at a high cognitive workload for amputees, possibly affecting their mobility, safety and independency. A *biocooperative* prosthesis which is able to reduce the cognitive workload of walking could offer a solution. Therefore, we wanted to investigate whether different levels of cognitive workload can be assessed during symmetrical, asymmetrical and dual-task walking and to identify which parameters are the most sensitive. Twenty-four healthy subjects participated in this study. Cognitive workload was assessed through psychophysiological responses, physical and cognitive performance and subjective ratings. The results showed that breathing frequency and heart rate significantly increased, and heart rate variability significantly decreased with increasing cognitive workload during walking ($p < .05$). Performance measures (e.g., cadence) only changed under high cognitive workload. As a result, psychophysiological

* Corresponding author at: Department of Human Physiology, Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel, Pleinlaan 2, 1050 Brussels, Belgium. Tel.: +32 2 6292222; fax: +32 2 6292876.

E-mail addresses: kknaepen@vub.ac.be (K. Knaepen), Uros.Marusic@zrs.upr.si (U. Marušič), crea.simona@gmail.com (S. Crea), carodrig@vub.ac.be (C.D. Rodríguez Guerrero), n.vitiello@sssup.it (N. Vitiello), npattyn@vub.ac.be (N. Pattyn), Omairess@vub.ac.be (O. Mairesse), dlefeber@vub.ac.be (D. Lefeber), rmeeusen@vub.ac.be (R. Meeusen).

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measures are the most sensitive to identify changes in cognitive workload during walking. These parameters reflect the cognitive effort necessary to maintain performance during complex walking and can easily be assessed regardless of the task. This makes them excellent candidates to feed to the control loop of a *biocooperative* prosthesis in order to detect the cognitive workload. This information can then be used to adapt the robotic assistance to the patient's cognitive abilities.

Q3

1. Introduction

Ambulating with a transfemoral prosthesis is not only associated with high metabolic costs (Hoffman, Sheldahl, Buley, & Sandford, 1997), it also requires a considerable larger amount of cognitive resources compared to individuals with intact limbs (Geurts & Mulder, 1994; Geurts, Mulder, Nienhuis, & Rijken, 1991; Heller, Datta, & Howitt, 2000; Hofstad et al., 2009; Williams et al., 2006). Some of these cognitive resources are devoted to compensate for the loss of motor control at the amputated joint(s). This loss requires new strategies, such as reliance on stump muscles and hip or trunk compensatory mechanisms, to control motor actions (Heller et al., 2000). Another part is lost due to the increased use of vision to compensate for the loss of somatosensory feedback from the amputated limb (Krewer et al., 2007; Williams et al., 2006; Witteveen, de Rond, Rietman, & Veltink, 2012). Consequently, walking with a transfemoral prosthesis involves higher cognitive demands, often leaving not enough cognitive capacity available to perform secondary information-processing tasks such as attending a conversation while walking (Heller et al., 2000; Williams et al., 2006). Additionally, increased cognitive workload can also endanger the primary motor task: for instance obstacle avoidance or uneven terrain negotiation during walking can be impeded. Moreover, some studies already showed that limping-like walking significantly increased the risk of falling in amputees (Duysens, Potocanac, Hegeman, Verschueren, & McFadyen, 2012).

A solution could be contained in recently developed physiological computing systems which 'sense, analyze and react' to the cognitive state of the user (Rodriguez Guerrero, Fraile Marinero, Perez Turiel, & Munoz, 2013). These systems are designed to promote the performance efficiency of the user and operate through a *biocybernetic* loop which monitors the users' cognitive state, reacts appropriately and tunes its functioning in an adaptive closed loop (Serbedzija & Fairclough, 2009). Such a *biocybernetic* control loop could also be incorporated in an active prosthesis in order to monitor and reduce the cognitive workload of the amputee during locomotor tasks (Deeny, Chicoine, Hargrove, Parrish, & Jayaraman, 2014). As for other physiological computing systems, it will allow the amputee and the prosthesis to interact in a collaborative symbiotic manner resulting in a higher motor performance at a lower cognitive workload (Serbedzija & Fairclough, 2009).

Measuring cognitive workload has not yet been standardized in dynamic situations such as walking. A major challenge in these situations is that effects of the physical workload may overshadow effects of the cognitive workload (Novak, Mihelj, & Munih, 2010). Previous studies have mainly focused on performance and subjective parameters to assess cognitive workload in dynamic situations, mostly under dual-task paradigms (Al-Yahya et al., 2011; Kline, Poggensee, & Ferris, 2014; Q4 Nascimbeni, Minchillo, Salatino, Morabito, & Ricci, 2014; Patel & Bhatt, 2014). Yet, this could be inadequate, for example, walking performance of an amputee can be good, but this can come at a high cognitive effort, and thus a high cognitive workload. Or subjective measures can be intentionally manipulated or affected by subject characteristics (e.g., attitude, memory capacity, … etc.) and give a distorted picture of cognitive workload (Dirican & Göktürk, 2011; HFM-056/TG-008, 2004). Thus, to adequately assess cognitive workload, not only performance parameters and subjective ratings should be taken into account, but also the cognitive effort, i.e., the investment a subject puts in the task, will determine cognitive workload (Dirican & Göktürk, 2011; HFM-056/TG-008, 2004). Cognitive

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effort can be objectively measured through psychophysiological parameters (HFM-056/TG-008, 2004). A recent review presents the leading psychophysiological measures applied in human–computer interaction with their diagnosticity and sensitivity to assess the cognitive state of the user (Dirican & Göktürk, 2011). Yet, some of these measures are hard to assess in a dynamic environment (e.g., pupil diameter, eye movements) or are sensitive to artifacts and electrical noise (e.g., electroencephalography, electromyography). Therefore, based on the advantages and disadvantages presented in (Dirican & Göktürk, 2011), and taking into account that we want to assess cognitive workload during walking, we selected heart rate (HR), heart rate variability, breathing frequency (BF), skin conductance (SC) and skin temperature (ST). These are also the most recurrent parameters used in studies on cognitive workload in *biocooperative* rehabilitation robotics (Koenig, Omlin, et al., 2011; Novak, Mihelj, Ziherl, Olensek, & Munih, 2011; Rodriguez Guerrero et al., 2013). Next to that, psychophysiological measures display a unique characteristic, i.e., '*implicitness*' (Dirican & Göktürk, 2011): performance measures need to be customized to each task, while psychophysiological measures can be assessed in the same way regardless of the task (Ikehara & Crosby, 2010).

In this study we assessed the various aspects of cognitive workload (i.e., performance, subjective ratings and effort) in a dynamic dual-task situation. We manipulated cognitive workload by means of imposing a secondary spatial working memory task during a demanding (i.e., asymmetrical walking) and less demanding (i.e., symmetrical walking) walking condition. Asymmetrical walking corresponds to split-belt walking with different left and right belt speed and requires higher attentional resources than symmetrical walking, comparable to limping-like walking in amputees (Duysens et al., 2012; McFadyen, Hegeman, & Duysens, 2009). It influences physical as well as cognitive workload, as is a common situation for amputees engaged in walking. For the secondary task, we opted for a spatial working memory task as it activates similar brain areas (i.e., sensorimotor cortex) as motor tasks, and thus induces a high interference which will increase cognitive workload (Al-Yahya et al., 2011; Anguera, Reuter-Lorenz, Willingham, & Seidler, 2010; Nadkarni, Zabjek, Lee, McIlroy, & Black, 2010).

The goal of this study was to (1) examine whether changes in cognitive workload can be measured in dynamic conditions such as walking and (2) identify which parameters are the most sensitive to detect differences between walking conditions with different cognitive workload. We hypothesized that some psychophysiological parameters would be sensitive to detect changes in cognitive workload during walking. As such, we will know whether it is useful to integrate psychophysiological measures in the control loop of a *biocooperative* prosthesis and, if so, which parameters should be considered based on the ranking of the sensitivity analysis.

2. Materials and methods

2.1. Subjects

Twenty-four healthy male subjects (mean age 24.5 ± 2.9 years, height 1.79 ± 0.04 m, weight 69.6 ± 7.3 kg) participated in an experimental session comprised of two single- and two dual-task walking conditions (Table 1).

Table 1
Experimental protocol comprising two single- and two dual-task walking conditions with different cognitive workload.

Baseline
1. Symmetrical walking
Experimental conditions†
2. Asymmetrical walking*
3. Symmetrical walking + MRT
4. Asymmetrical walking + MRT

† Experimental conditions were randomized among subjects.
* Asymmetrical walking means that the left and right belts of the treadmill were set at a different speed.

2.2. Ethics statement

All experimental procedures were performed according to the standards set by the declaration of Helsinki for medical research involving human subjects and were part of a larger research project (i.e., http://www.cyberlegs.eu). Upon arrival in the lab, subjects signed a written informed consent form. This research has been approved by the medical ethics committee of the university hospital 'Universitair Ziekenhuis Brussel' in Brussels, Belgium.

2.3. Instrumentation and data acquisition

2.3.1. Assessment of cognitive effort

Cognitive effort was measured through the recordings of psychophysiological parameters. We used NeXus-10 (NeXus 10, Mind Media BV, The Netherlands) to assess skin conductance (SC), skin temperature (ST), electrocardiography (ECG) and breathing frequency (BF). SC was measured by two Ag–AgCl electrodes secured by velcro straps to the palmar surface of the middle phalanx of the left index and ring finger. For ST a thermistor point probe was placed on the palmar surface of the middle phalanx of the left middle finger. Three surface electrodes were used for recording of the ECG: one was affixed two centimeters below the right clavicle between the first and second rib, one was affixed at the fifth intercostal space on the left mid-axillary line, and a ground electrode was affixed to the right acromion. In order to measure BF, the relative expansion of the thorax was measured during in- and ex-halation by an elastic belt worn just below the chest.

2.3.2. Assessment of performance

Gait performance was assessed using a pair of pressure-sensitive insoles to detect relevant gait parameters such as stance time, swing time, cadence, ... etc. (Donati et al., 2013). A detailed description of the insoles and its accuracy to segment gait data can be found in (Crea, Donati, De Rossi, Oddo, & Vitiello, 2014; Donati et al., 2013; Novak et al., 2013).

Cognitive performance was assessed based by means of the scores (i.e., reaction time and accuracy) on the cognitive task.

2.3.3. Assessment of subjective workload

The National Aeronautics and Space Administration Task Load Index (NASA-TLX) was used to assess subjective workload (Hart & Stavenland, 1988). It is a multidimensional questionnaire comprising six subscales: mental, physical and temporal demand, frustration, effort and performance. The subscales are each rated on a twenty-step bipolar scale resulting in a score between 0 and 100 for each subscale. The average of these six subscales represents the total workload experienced by the subjects (Hart & Stavenland, 1988). Originally, a weighting procedure was applied to the raw test scores of each subscale to estimate the individual sources of workload (Hart & Stavenland, 1988). Yet, over the years many researchers have eliminated the weighting procedure and instead used the raw test scores (RTLX) for improved applicability (Hart, 2006). In this study we analyzed the six raw subscale ratings in addition to the total raw workload (i.e., average of the six subscales) (Hart, 2006; Hart & Stavenland, 1988).

2.4. Experimental design

Upon arrival in the lab, the purpose and procedure of the experiment were explained; subjects signed the written informed consent form and were equipped with the NeXus-10 and pressure-sensitive insoles. Next, a familiarization trial with the cognitive task and a baseline walking trial at 4 km/h were performed. This was followed by three experimental conditions (Table 1), which were randomized among subjects: 12 subjects started with the most difficult condition and the other 12 subjects started with the easiest condition. Each condition lasted for at least eight minutes (i.e., the time of completing the cognitive task) of which the last three minutes were analyzed to rule out any effects of task novelty. Time between conditions was as long as necessary for the heart rate (HR) and BF to return to the values measured during quiet standing in order to exclude order or

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carry-over effects. Walking consisted of either symmetrical or a symmetrical walking on a split-belt treadmill (Froce link BV, The Netherlands). Symmetrical walking corresponded to walking with both belt speeds set at 4 km/h. During asymmetrical walking the left belt speed was set at 2 km/h and the right belt speed at 6 km/h. The cognitive task comprised a computerized version of the Shepard and Metzler mental rotation of 3D objects (MRT) (Shepard & Metzler, 1971) generated from the stimulus library of Peters and Battista (2008). The MRT is an adaptive spatial ability test to assess the ability to perceive and transform spatial elements (Shepard & Metzler, 1971). Subjects were asked to compare 100 pairs of 3D objects displayed on a computer screen. They had to decide as quickly and accurately as possible whether each of these pairs were the same or mirrored.

2.5. Data analysis

2.5.1. Psychophysiological parameters

All signal processing was performed with the BioSig toolbox in MATLAB (The MathWorks; Natick, Massachusetts). Only the last three minutes of each condition were analyzed to ensure that steady-state had been reached. From the ECG, the intervals between two heartbeats (NN intervals) were extracted in order to calculate mean HR and a measure of heart rate variability (HRV): the square root of the mean squared differences of successive NN intervals (HRV_{rmssd}). In correspondence to the recommendations of Malik (Malik, 1996), the frequency analysis of HRV was performed using the quotient (HR_LFHF_{ratio}) of low-frequency components (i.e., the power in the low frequency range between 0.04 and 0.15 Hz) over high-frequency components (i.e., the power in the high frequency range between 0.15 and 0.40 Hz), after fast Fourier transform (Koenig, Omlin, et al., 2011). For SC two components were extracted: skin conductance level (SCL) and skin conductance response (SCR). The mean SCL, which is the baseline level of SC, was calculated for each condition. The SCR represents increases in SC followed by a return to the tonic level. SCR was detected from the SCL, when its amplitude changed by at least 0.05 microsiemens (μS) and the peak occurred less than five seconds after the beginning of the increase (Dawson, Schell, & Filion, 2000). From this, mean SCR amplitude (SCR_{ampl}) and SCR frequency (SCR_{freq}) were extracted (Novak et al., 2010). For BF the mean value with standard deviation (SD) over three minutes was calculated. ST changes relatively slowly in response to cognitive changes (Novak et al., 2010), therefore its mean value with SD was determined by averaging ST over the last five seconds of each time period. In that way we were certain to measure a stabilized ST for each condition.

2.5.2. Gait parameters

Recorded data from the pressure-sensitive insoles were processed offline by means of a custom routine that computed the vertical ground reaction force (vGRF). vGRF was then used to distinguish the stance and swing phases, by means of a simple threshold rule, expressed in Eq. (1).

$$\begin{cases} \text{vGRF} \leqslant -20\ N \rightarrow \text{phase} : \text{ST} \\ \text{vGRF} > -20\ N \rightarrow \text{phase} : \text{SW} \end{cases} \quad (1)$$

For each foot, the duration of the stance phase (namely, Δ^L_{ST} for the left foot, and Δ^R_{ST}, for the right foot) and the duration of the swing phase (Δ^L_{SW} for the left foot, and, Δ^R_{SW} for the right foot) were calculated based on the classification resulting from the threshold-based algorithm. Moreover, the duration of the double-support phase preceding a left-foot single support Δ^L_{DS} was computed as the time interval in which the left and the right feet were simultaneously in the stance phase, immediately after the left heel strike. Similarly, the duration of the double-support phase preceding a right-foot single support Δ^R_{DS} was computed as the time interval in which the left and the right feet were simultaneously in the stance phase, immediately after the right heel strike. Right and left step duration were computed as $\Delta^L_{Step} = \Delta^L_{ST} + \Delta^L_{SW}$, and $\Delta^R_{Step} = \Delta^R_{ST} + \Delta^R_{SW}$, while left and right step cadence were calculated as $C_L = 1/\Delta^L_{Step}$ and $C_R = 1/\Delta^R_{Step}$. Fig. 1 describes the extraction of temporal gait parameters, based on the identified gait phases.

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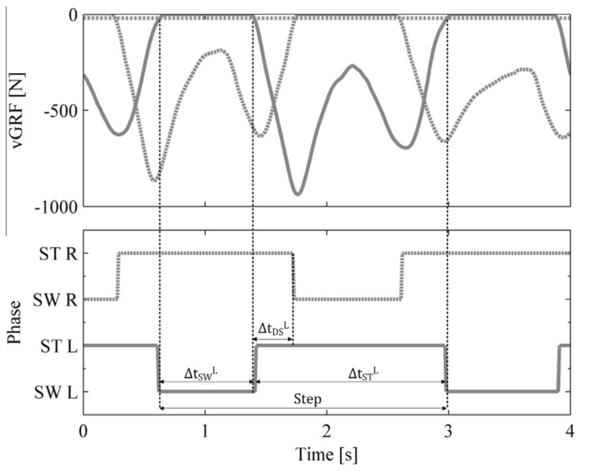

Fig. 1. Extraction of temporal gait parameters. The top panel depicts the VGRF profile from the left (solid gray line) and right (dashed gray line) pressure-sensitive insole. The bottom panel shows the results of the classification in gait phases (i.e., stance (ST) and swing (SW)) and the use of these phases to calculate temporal gait parameters for the left foot (L): Δt^{L}_{ST}, Δt^{L}_{SW}, Δt^{L}_{DS}. The same applies to the right foot (R): Δt^{R}_{ST}, Δt^{R}_{SW}, Δt^{R}_{DS}.

2.5.3. Cognitive performance

The reaction time and accuracy on the MRT were calculated using E-DataAid by E-Prime® 2.0 software (Psychology Software Tools, Pittsburgh, PA) (Schneider, Eschman, & Zuccolotto, 2012).

2.5.4. Subjective workload

The raw scores on each of the subscales of the NASA-RTLX as well as the raw averaged total workload were manually analyzed.

2.5.5. Sensitivity index

A unitless ordinal sensitivity index (SI) was calculated in order to distinguish more from less important psychophysiological and subjective parameters. Balkin et al. (2004) defined sensitivity as the ratio of the effect size of an outcome variable to its 95% confidence interval (CI) (Balkin et al., 2004). Analogously, we defined sensitivity to cognitive workload as the proportion of the magnitude of the effect of each condition in a within-subject ANOVA and the magnitude of the effect size variability. Bias-corrected accelerated bootstrapped CIs (BC_{α}CIs) account for both skewness in the distribution and scale transformations and are therefore the method of choice for estimating CIs. Based on Mairesse et al. (2009), Balkin et al. (2004) the SI reads as: SI = (partial η^2)/(upper BC_{α}CI – lower BC_{α}CI).

2.6. Statistical analysis

Data are presented as mean with SD. Statistical significance was accepted at $p < .05$. Distributions were checked for normality with a one-sample Kolmogorov–Smirnov test. A two-way repeated measures analysis of variance (i.e., REPANOVA) using walking condition (i.e., symmetrical versus asymmetrical) and cognitive task (i.e., walking with or without cognitive task) as main factors, was used to find significant differences in psychophysiological parameters and subjective ratings of workload between the four conditions (Table 1). If the interaction effect was significant, a one-way REPANOVA and post hoc paired *t*-tests with Bonferroni correction were applied to identify pairwise differences. If the interaction effect was not significant, pairwise comparisons with Bonferroni corrections among the levels of the significant factors were performed. For SCL, SCR_{ampl}, SCR_{freq} and ST, the difference in room temperature before and after the experiment was taken into account as a covariate (i.e., REP-ANCOVA). A Friedman's ANOVA and a post-hoc Wilcoxon signed rank test with Bonferroni correction were used for not normally distributed data. Differences in gait parameters between walking with and without cognitive task and differences in reaction time and accuracy on the MRT between symmetrical and asymmetrical walking were tested by means of a paired *t*-test.

3. Results

3.1. Physiological measures

Table 3 shows the mean values with SD and significant differences ($p < .05$) between the physiological parameters for each condition. A significant interaction effect could be found for HR, HRV_{rmssd} and BF (HR: $F(1, 23) = 9.14$, $p = .006$; HRV_{rmssd}: $F(1, 23) = 13.93$, $p = .001$; BF: $F(1, 23) = 6.07$, $p = .022$). Post-hoc Bonferroni corrected pairwise comparisons showed a significant higher HR during asymmetrical walking + MRT (MHR = 109.4, SD = 14.7) compared to symmetrical walking + MRT (MHR = 100.4, SD = 12.7), asymmetrical (MHR = 102.2, SD = 14.0) and symmetrical walking (MHR = 88.5, SD = 10.5) ($p < .05$). HR was also significantly higher during symmetrical walking + MRT compared to symmetrical walking but not compared to asymmetrical walking and asymmetrical walking showed to be associated with a significantly higher HR compared to symmetrical walking ($p < .05$). Heart rate variability (i.e., HRV_{rmssd}) was significantly decreased during asymmetrical walking + MRT ($MHRV_{rmssd} = 13.4$, SD = 6.6) compared to asymmetrical walking ($MHRV_{rmssd} = 16.6$, SD = 9.2) and symmetrical ($MHRV_{rmssd} = 24.5$, SD = 10.5) walking ($p < .05$), but not compared to symmetrical walking + MRT ($MHRV_{rmssd} = 15.6$, SD = 7.6). Symmetrical walking + MRT only showed a significantly lower heart rate variability compared to symmetrical walking and asymmetrical walking also showed a significantly lower HRV_{rmssd} compared to symmetrical walking ($p < .05$). BF was significantly higher during asymmetrical walking + MRT (MBF = 27.3, SD = 4.5) compared to symmetrical walking + MRT (MBF = 25.4, SD = 4.0), asymmetrical (MBF = 24.8, SD = 3.8) and symmetrical walking (MBF = 22.1, SD = 3.3) ($p < .05$). BF was also significantly higher during symmetrical walking + MRT compared to symmetrical walking but not compared to asymmetrical walking and asymmetrical walking showed to be associated with a significantly higher BF compared to symmetrical walking ($p < .05$).

3.2. Subjective workload

Fig. 2 shows the results of the two-way REPANOVA and the subsequent Bonferroni corrected pairwise differences for subjective workload and its subscales between all conditions. The condition with the highest overall subjective workload was asymmetrical walking + MRT ($M_{workload} = 56.9$, SD = 12.6). Subjects experienced a significantly higher subjective workload compared to all other conditions ($p < .05$). The second highest subjective workload was reported for symmetrical walking + MRT ($M_{workload} = 48.8$, SD = 10.9) which was significantly higher compared to asymmetrical walking ($M_{workload} = 38.8$, SD = 14.9) and symmetrical walking ($M_{workload} = 22.0$, SD = 14.5) ($p < .05$). The condition with the lowest subjective workload was thus, as expected, symmetrical walking, it showed a significant lower subjective workload compared to all other conditions ($p < .05$).

Only the subscales mental demand ($F(1, 23) = 8.64$, $p = .007$) and effort ($F(1, 23) = 6.16$, $p = .021$) showed a significant interaction effect following the two-way REPANOVA (Fig. 2). Post-hoc pairwise comparisons showed that mental demand during asymmetrical walking + MRT ($M_{mental} = 69.8$, SD = 13.7) was rated significantly higher compared to asymmetrical ($M_{mental} = 35.8$, SD = 26.0) and symmetrical ($M_{mental} = 15.6$, SD = 15.3) walking but not compared to symmetrical walking + MRT ($M_{mental} = 64.8$, SD = 13.4) ($p < .05$). The mental demand during symmetrical walking + MRT on its turn was significantly higher compared to that of asymmetrical and symmetrical walking ($p < .05$). Subjects experienced a significantly higher effort during asymmetrical walking + MRT ($M_{effort} = 71.5$, SD = 14.9) compared to the other three conditions ($p < .05$). The effort during symmetrical walking + MRT ($M_{effort} = 60.0$, SD = 14.1) did not differ significantly from that of asymmetrical walking ($M_{effort} = 50.2$, SD = 19.0) but was significantly higher compared to that of symmetrical walking ($M_{effort} = 25.8$, SD = 20.3) and also asymmetrical walking was associated with a significantly higher subjective effort compared to symmetrical walking (Fig. 2, $p < .05$). Next to that, there was a significant main effect of

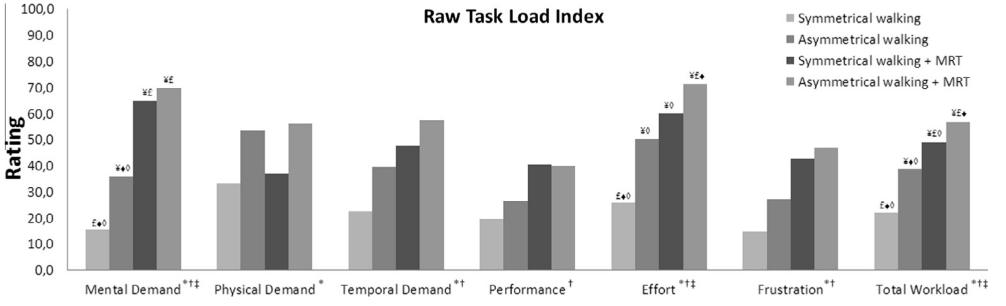

Fig. 2. Subjective ratings of total workload and subscales (with standard error) for the four conditions. Results of the two-way REPANOVA: *significant main effect of walking condition; †significant main effect of cognitive task; ‡significant interaction effect of walking condition x cognitive task. Results of the post hoc pairwise Bonferroni corrected comparisons: ¥significantly different from symmetrical walking; £significantly different from asymmetrical walking; ♦significantly different from symmetrical walking + MRT; ◇significantly different from asymmetrical walking + MRT; $p < .05$.

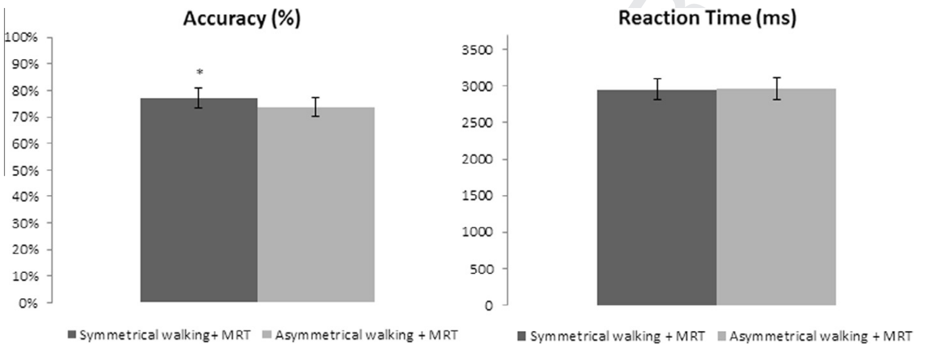

Fig. 3. Significant differences in accuracy and reaction time on the MRT between symmetrical and asymmetrical walking. *$p < .05$.

walking condition on the subscale physical as well as on mental demand ($p < .05$), indicating that asymmetrical walking induced both an increased physical as well mental demand.

3.3. Mental rotation task

Fig. 3 shows the results of accuracy and reaction time on the MRT. Subjects were significantly more accurate ($M_{accuracy} = 77.0\%$, SD = 0.10%) on the MRT during symmetrical compared to asymmetrical walking ($M_{accuracy} = 73.8\%$, SD = 0.10%) ($p = .017$). Reaction time on the MRT during asymmetrical walking was higher ($M_{reaction\ time} = 2965.2$ ms, SD = 619.8 ms) than during symmetrical walking ($M_{reaction\ time} = 2955.4$ ms, SD = 549.5 ms), yet this difference was not significant ($p = .89$).

3.4. Gait performance

Although slight differences in most gait parameters can be seen between symmetrical walking with and without performing a cognitive task, no statistically significant differences were found (Table 2). Only during asymmetrical walking significant differences between walking with and without performing a cognitive task were seen: decreased left stance time ($p = .037$), decreased right swing time ($p = .029$), decreased left and right step duration (left: $p = .031$; right: $p = .030$), increased left and right cadence (left: $p = .030$; right: $p = .030$). Table 2 shows the mean values with SD for all parameters.

Table 2
Temporal gait parameters during symmetrical and asymmetrical walking with and without completing a cognitive task.

Gait parameters	A		B	
	Symmetrical walking	Symmetrical walking + MRT	Asymmetrical walking	Asymmetrical walking + MRT
Stance L (s)	.744 ± .045	.733 ± .039	.850 ± .105	.784 ± .085*
Stance R (s)	.701 ± .049	.691 ± .061	.547 ± .064	538 ± .068
Swing L (s)	.440 ± .047	.443 ± .037	.330 ± .039	.326 ± .049
Swing R (s)	.483 ± .045	.485 ± .057	.634 ± .096	.573 ± .096*
Step duration L (s)	1.184 ± .071	1.176 ± .065	1.180 ± .116	1.110 ± .106*
Step duration R (s)	1.184 ± .071	1.176 ± .065	1.181 ± .116	1.111 ± .105*
Cadence L (step/s)	.848 ± .050	.853 ± .047	.856 ± .082	.910 ± .090*
Cadence R (step/s)	.848 ± .050	.853 ± .047	.856 ± .082	.909 ± .090*
Double support L (s)	.120 ± .026	.113 ± .038	.101 ± .033	.101 ± .037
Double support R (s)	.147 ± .030	.134 ± .032	.126 ± .026	.123 ± .029

* Significantly different from asymmetrical walking; $p < .05$.

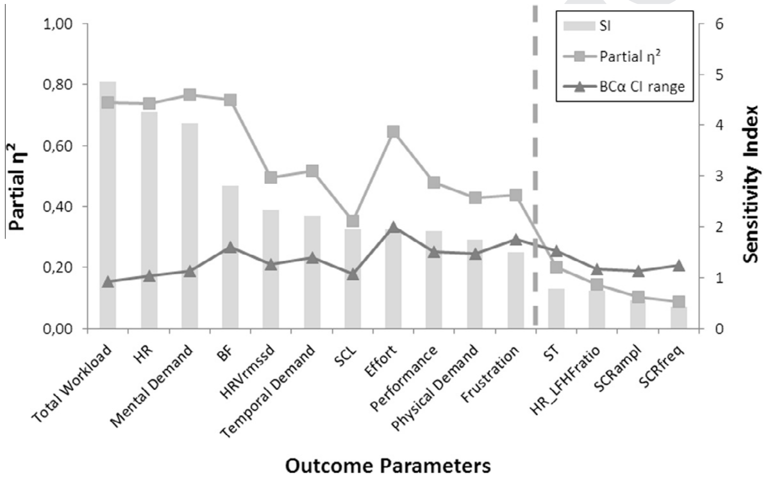

Fig. 4. The ranking of psychophysiological and subjective parameters based on the sensitivity index (SI) and the relation between effect size and effect size variability. Effect size and bias-corrected accelerated confidence intervals for the outcome variables are plotted against the left *Y*-axis. The light gray line represents the size of the effect (partial η^2) and the dark gray line the range of the confidence intervals. Gray bars represent the SI of the different outcome variables plotted against the right *Y*-axis in decreasing sensitivity from left to right. Variables left from the vertical dashed line represent a positive ratio of effect size over effect size variability (SI > 1.00).

3.5. Sensitivity index

Results of the sensitivity analysis are displayed in Fig. 4. The figure combines the SIs of the physiological and subjective parameters. Ranking based on the SIs shows that total workload ($SI_{total\ workload}$ = 4.85) is the most sensitive outcome variable, closely followed by HR (SI_{HR} = 4.27). Next in line is mental demand (SI_{mental} = 4.05). Other parameters in the top five are, from high to low, BF (SI_{BF} = 2.80) and HRV_{rmssd} ($SI_{HRV_{rmssd}}$ = 2.33). All other parameters indicate a positive ratio of effect size over effect size variability (SI > 1.00, left of dashed line), except for ST, HR_LFHF_{ratio}, SCR_{ampl} and SCR_{freq} (Fig. 4, right of dashed line). Parameters with a SI below a threshold of one mostly display very low effect sizes.

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Table 3
Changes in physiological parameters between all four conditions.

Physiological parameters	Symmetrical walking	Asymmetrical walking	Symmetrical walking + MRT	Asymmetrical walking + MRT
HR (bpm)[*†‡]	88.5 ± 10.5[£♦◇]	102.2 ± 14.0[¥◇]	100.4 ± 12.7[¥◇]	109.4 ± 14.7[¥£♦]
HR_LFHF_{ratio}[*]	3.8 ± 3.0	5.8 ± 3.3	4.5 ± 2.2	5.5 ± 3.1
HRV_{rmssd} (ms)[*†‡]	24.5 ± 10.5[£♦◇]	16.6 ± 9.2[¥◇]	15.6 ± 7.6[¥]	13.4 ± 6.6[¥£]
SCL (µS)[*†]	3.3 ± 1.3	4.0 ± 1.4	4.1 ± 1.7	4.2 ± 1.7
SCR_{ampl} (µS)[*†]	3.8 ± 1.1	4.4 ± 1.2	4.7 ± 1.7	4.7 ± 1.7
SCR_{freq}[*]	2.5 ± 2.1	4.9 ± 3.1	4.8 ± 4.1	5.7 ± 4.4
ST (°C)[*]	24.2 ± 3.9	27.9 ± 5.6	27.2 ± 5.2	27.5 ± 5.3
BF (cpm)[*†‡]	22.1 ± 3.3[£♦◇]	24.8 ± 3.8[¥◇]	25.4 ± 4.0[¥◇]	27.3 ± 4.5[¥£♦]

Results of the two-way REPANOVA:
* Significant main effect of walking condition.
† Significant main effect of cognitive task.
‡ Significant interaction effect of walking condition x cognitive task; Results of the post hoc pairwise Bonferroni corrected comparisons.
¥ Significantly different from symmetrical walking.
£ Significantly different from asymmetrical walking.
♦ Significantly different from symmetrical walking + MRT.
◇ Significantly different from asymmetrical walking + MRT, $p < .05$; bpm = beats per minute; cpm = cycles per minute.

4. Discussion

In this study we wanted to examine whether changes in cognitive workload can be measured during walking and which parameters are the most sensitive to detect differences between walking conditions with different cognitive workload. We hypothesized that psychophysiological parameters would be sensitive to detect even small changes in cognitive workload during walking.

4.1. Psychophysiological measures

Correspondingly to what has been found in previous studies (Koenig, Omlin, et al., 2011; Neumann & Waldstein, 2001; Novak, Mihelj, & Munih, 2012; Roth, Bachtler, & Fillingim, 1990), we found that HR and BF increased significantly with increasing cognitive demand of the walking task. HR and BF were indicators of changes in cognitive workload during walking: both during symmetrical and asymmetrical walking, the additive effect of a cognitive task can clearly be pointed out through the change in HR and BF. This is confirmed by Roth et al. (1990), Mihelj et al. (2011) and Mehler et al. (2012). The significant increase in HR and BF between symmetrical and asymmetrical walking (both with and without cognitive task), possibly reflects in part an increase in physical demand, as the subjective physical demand showed a significant main effect for walking condition (Fig. 2). Yet, the subjective questionnaire also showed a significant difference in mental demand between symmetrical and asymmetrical walking. This supports the hypothesis that asymmetrical walking also demands a higher cognitive effort compared to symmetrical walking (McFadyen et al., 2009). Next to that, there was no difference in HR and BF between asymmetrical walking and symmetrical walking + MRT, suggesting that the increase in physical demand of asymmetrical walking has less or at the most the same effect on HR and BF as the increase in mental demand of symmetrical walking + MRT.

Heart rate variability (i.e., HRV_{rmssd} and HR_LFHF_{ratio}), has previously shown to be an important marker of cognitive workload. We found that HRV_{rmssd} differs significantly between walking tasks with and without cognitive workload, both for symmetrical and asymmetrical walking and also between symmetrical and asymmetrical walking but not between the other conditions. Also Koenig, Omlin, et al. (2011) did not find significant differences in HRV between all levels of a cognitive challenge while walking (Koenig, Novak, et al., 2011). It is possible that for small changes in cognitive workload, the physical workload of walking occludes the effect of a cognitive load on HRV (Novak et al., 2010; Perini & Veicsteinas, 2003). This could explain why HR_LFHF_{ratio} in our study only differed significantly between symmetrical and asymmetrical walking and not between walking with and

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without cognitive task. Taelman et al. (2011) agree that the LF/HF ratio could be less accurate in measuring sympathetic modulations (Taelman, Vandeput, Gligorijevic, Spaepen, & Van Huffel, 2011; Taelman, Vandeput, Vlemincx, Spaepen, & Van Huffel, 2011). Nevertheless, the decrease in HRV_{rmssd} which we see with increasing task difficulty assumingly corresponds to the increase in stress (i.e., affective load) and the increasing demand on executive functions (i.e., cognitive load) located in the prefrontal cortex (Hovland et al., 2012; Thayer, Ahs, Fredrikson, Sollers, & Wager, 2012). Displaying brain activations patters during the different task conditions would be interesting in order to see whether activity in the prefrontal cortex indeed decreases with increasing task difficulty and whether this is linked to changes in HRV.

Changes in SC observed in this study were very small: a gradual increase of SCL, SCR_{freq} and SCR_{ampl} with increasing cognitive demand could be observed yet there was a lack of significant interaction effects indicating that this parameter is less robust in detecting responses to cognitive workload during walking. According to Novak et al. (2010) SC is predominantly affected by physical load (Novak et al., 2010). Thus, for SC the metabolic effect of walking might have been sufficiently high to overrule the effect of an additional cognitive load in our study.

Although ST has been put forward as a good marker for cognitive workload (Mihelj et al., 2011; Novak et al., 2012; Ohsuga, Shimono, & Genno, 2001), this could not be confirmed in our study: ST only differed significantly between symmetrical and asymmetrical walking. Our results are similar to those of Rodriguez Guerrero et al. (2013) who reported no meaningful variability for ST during a reaching task in a virtual environment (Rodriguez Guerrero et al., 2013). Novak et al. (2010) proposes that a certain threshold of cognitive workload must be exceeded before ST decreases (Novak et al., 2010). It might be that in our study this threshold was not achieved during the most challenging walking condition or that the metabolic cost of walking occluded the effect of the added cognitive workload. The NASA-RTLX showed a maximal mental demand of 69.8/100 during what we had designed to be the most challenging condition, which means that subjects did not feel completely overloaded (i.e., 100/100).

The results of the sensitivity analysis support the previous findings. The most sensitive psychophysiological parameters to cognitive workload during walking are: HR and BF, followed by HRV_{rmssd} and SCL. This ranking offers the opportunity to justify the in- or exclusion of sensors from a biocooperative device. This could be important in order to simplify biocooperative control and to avoid overloading the subject with sensors.

4.2. Subjective ratings

The overall score and scores on some subscales (i.e., mental demand and effort) of the NASA-RTLX indicated that the highest subjective workload is experienced for asymmetrical walking + MRT, followed by symmetrical walking + MRT, asymmetrical and symmetrical walking. The sensitivity analysis revealed that the subjective scores on the mental demand subscale and the total workload of the NASA-RTLX are very sensitive to the effect of cognitive workload during walking. This means that not only objective measurements can contribute to estimating the cognitive workload of the subject, but also subjective measurements are important. This may seem trivial, however, when working with automated indirect measurements, this is an important reminder. These results support the idea that, in HRI, automated interaction between human and robot should be possible, but the human should also have the possibility to take over the control. This could be done by introducing a simple manual control button into the robotic system which allows the subject to decide on the amount of assistance. On the other hand, manual control alone could have disadvantages as well: it could be slower than automated control, it could be more demanding (i.e., increase the cognitive workload) or as Novak et al. (2012) pointed out, a discrepancy can occur between objective and subjective measures of workload, leading to incorrect feedback and thus control (Novak et al., 2012). Moreover, the ultimate goal of HRI is that robotic devices become an extension of the human body, as for example in a *biocooperative* lower-limb prosthesis, making the argument for automated over manual control even stronger. If amputees continuously have to think about the amount of control they want, the cognitive workload of walking will become too high. Therefore, automated control should be preferred over manual control when aiming for a high performance at a low effort.

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4.3. Performance measures

In our study, some gait parameters differed significantly between asymmetrical walking with and without a cognitive task: performing a cognitive task during asymmetrical walking significantly decreased stance time and step duration and increased cadence. A recent review of Al-Yahya et al. (2011) showed that in different populations and for the majority of cognitive tasks, dual-task walking induces a reduction in gait speed (Al-Yahya et al. (2011)). Yet, in our study the treadmill speed was held constant. The increase in cadence and the decrease in stance time and step duration which we observed, represent alternative strategies to maintain gait stability under high cognitive workload. This has been demonstrated by Hak et al. (2012), Hak, Houdijk, Beek, and van Dieen (2013), Hak, Houdijk, Steenbrink, et al. (2013) who explain that these adaptations increase the margin of stability in the medio-lateral direction, and therefore decrease the risk of falls in this direction (Hak, Houdijk, Beek, et al., 2013; Hak et al., 2012; Hak, Houdijk, Steenbrink, et al., 2013; Hof, van Bockel, Schoppen, & Postema, 2007). Hof, Gazendam, and Sinke (2005) stated that, based on the inverted pendulum behavior of the human body while walking, an increase in cadence is indeed expected to increase the medio-lateral margin of stability (Hof et al., 2005).

The lack of significant differences in gait parameters during symmetrical walking with and without cognitive task may be due to the limited cognitive workload of symmetrical walking: subjects still have enough information processing capacity available to complete the MRT. Yogev, Hausdorff, and Giladi (2008), Al-Yahya et al. (2009) confirm that attentional resources for gait control increase when the motor task becomes challenging. McFadyen et al. (2009) showed that the cognitive workload of asymmetric stepping is increased because of the increased dynamic balance requirements associated with asymmetric loading and unloading of the limbs (McFadyen et al., 2009). This can also be concluded from the scores on the MRT, where the accuracy significantly decreased during asymmetrical walking. Next to that, the mean age of our subjects was 24.5 ± 2.9 years: previous studies pointed out that temporal gait parameters of younger subjects might be stable under moderate dual-task conditions (Lajoie, Teasdale, Bard, & Fleury, 1996; Li, Abbud, Fraser, & DeMont, 2013; Regnaux, Roberston, Smail, Daniel, & Bussel, 2006).

4.4. Cognitive workload and biocooperative control

In this study we have assessed all aspects of cognitive workload: performance, subjective ratings and cognitive effort (Dirican & Göktürk, 2011). If we only would have measured performance, we would have got an incomplete picture of the cognitive workload associated with symmetrical, asymmetrical and dual-task walking. For example, we found no significant difference in gait performance between symmetrical walking and symmetrical walking with a simultaneous cognitive task, meaning that there would be no difference in cognitive workload between these conditions based on performance measures alone. Yet, our healthy young subjects indicated that walking while completing a cognitive task was significantly more demanding compared to walking alone (i.e., significant increase of subjective mental demand, effort and total workload in Fig. 2). This increase in cognitive workload, which does not affect performance, should thus increase cognitive effort in order to maintain performance (HFM-056/TG-008, 2004). Cognitive effort is indeed increased in our study which is reflected in the significant changes in psychophysiological parameters (i.e., HR, BF and HRV_{rmssd}). It seems that performance measures are sensitive to detect high cognitive workload, but are not sensitive enough to detect smaller changes in cognitive workload.

In patients such as amputees, increases in cognitive workload without affecting performance can influence their mobility, safety and independency. Amputees might be able to walk safely, and thus perform well, but when this comes at a high effort and thus a high workload, they risk to be stressed and discouraged to ambulate with their prosthesis (Bussmann, Grootscholten, & Stam, 2004; Miller, Deathe, Speechley, & Koval, 2001). This has also been found in studies on operator functional state: an increased cognitive effort will decrease the acceptance and use of automated devices/systems (Brookhuis, van Driel, Hof, van Arem, & Hoedemaeker, 2009; Smith, Conway, & Karsh, 1999). Next to that, for a prosthesis it will be almost impossible to rely only on performance measures to adjust its amount of assistance as tasks performed with the prosthesis can vary widely during ADL and thus it might be difficult to find an accurate performance measure (Ikehara & Crosby, 2010). Also, relying on a change in performance might be unsafe in patient populations, for example in the case of obstacle avoidance (Duysens et al., 2012). The previous points stress the importance of including psychophysiological measures when assessing cognitive workload in the context of assistive robotic devices for ADL.

To progress from these results (i.e., identifying parameters to determine cognitive workload during walking) to an actual *biocooperative* prosthesis which is able to influence cognitive workload a few important steps are necessary. First of all, an adaptive classifier (e.g., artificial neural networks (ANN), linear discriminant analysis (LDA) classifier, ... etc.) should be trained with psychophysiological and performance data (i.e., input) from open loop experiments with amputees to automatically classify cognitive workload (i.e., output: low, moderate, high cognitive workload) (Koenig, Novak, et al., 2011). Following, the accuracy of this classifier should be verified by training it on a part of the data and performing a classification on another part of the data (Wilson & Russell, 2003). Next, real-time data acquisition and classification should be tested (Ting et al., 2010). If the classifier works properly, the prosthetic properties that might influence cognitive workload (i.e., timing or amount of assistance, ... etc.) should be identified (Serbedzija & Fairclough, 2009). Finally, information between the user and the assistive device should be exchanged through a *biocooperative* control loop in order to perform automated control of cognitive workload during walking (Fairclough, 2009).

4.5. Study limitations

In our test protocol we always started with symmetrical treadmill walking and randomized the other three conditions (Table 1). The lack of complete randomization can possibly cause an order effect which might influence the data (Pattyn, Neyt, Henderickx, & Soetens, 2008). However, our results are not consistent with an order effect, meaning that there are not only differences between the baseline and any other condition, but also within the three conditions which were randomized. Also, we introduced a resting period between each condition. During this resting period HR and BF had to return to the same level as measured during quiet standing. This was done to eliminate order, carry-over or possible effects of fatigue. With regard to the MRT, all conditions were randomized because the learning effect on the cognitive task was a real risk which we needed to control for. Whereas we acknowledge that this design does not reach the standards of a full factorial, which would be used in fundamental research, we are convinced it allows answering the research question, being the identification of parameters that would allow differentiating between different cognitive loads during physical activity, with the potential application of adaptable automation.

5. Conclusion

In this study we have assessed the different aspects of cognitive workload during symmetrical, asymmetrical and dual-task walking. We found that psychophysiological measures provide the most accurate information on changes in cognitive workload during walking and are representative of the cognitive effort that is necessary to maintain performance. Performance measures such as increased cadence and decreased accuracy on the cognitive task, could accurately identify high cognitive workload, but not small changes in cognitive workload. The sensitivity of psychophysiological parameters is also reflected in the ranking of the sensitivity analysis: HR and BF are the most sensitive parameters, followed by HRV_{rmssd} and SCL to detect cognitive workload. This ranking offers the opportunity to justify the in- or exclusion of sensors from a *biocooperative* control loop of an auto-adaptive prosthesis. Based on these results, psychophysiological measures are the most suitable to feed to the control loop of an assistive device in order to adapt the cognitive workload of daily activities where the lower limbs are involved (i.e., walking, dancing, standing, ... etc.). Moreover, psychophysiological parameters can be assessed in the same way regardless of the task while performance measures need to be adjusted to each task (e.g., performances measures will be different for walking compared to dancing).

This study is a first step in the direction of the development of a prosthesis with *biocooperative* control which is able to detect the cognitive workload of walking in amputees. This information can then be used to adapt the robotic assistance to the patient's cognitive abilities. Auto-adaptive assistance

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from a *biocooperative* prosthesis should help amputees in achieving a high walking performance at a low cognitive effort to maximize mobility, safety and independency.

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