Motor control and olfaction – Influence of pleasant and disgusting odors on the Adaptive Force

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Research Article

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Abstract

The Adaptive Force (AF) characterizes the capability of the neuromuscular system to adapt to external forces. The aim was to measure the effects of different olfactory inputs on the AF of the hip and elbow flexors, respectively. The AF of 10 subjects was examined manually by experienced testers while smelling at sniffing sticks with neutral, pleasant or disgusting odors. The reaction force and the position of the tested limb were recorded by a handheld device. The results show, inter alia, a significantly lower maximal isometric AF and a significantly higher AF at the onset of oscillations with disgusting odor compared to pleasant or neutral odors ($p < 0.001$). The AF seems to reflect the functionality of the neuromuscular control, which can be impaired by disgusting olfactory inputs. An undisturbed functioning neuromuscular system appears to be characterized by a proper length-tension control and by an earlier onset of mutual oscillations during an external force increase under isometric conditions.

Introduction

The Adaptive Force (AF) is barely considered neither in health, sports and movement sciences nor in medicine. In general, it reflects the capability to adapt adequately to external forces with the intention to maintain a given position or motion[1,2]. The currently most relevant variant and definition for the present investigation is the execution of AF with the intention to maintain a given position in an isometric holding manner by adapting the muscular tension to comply with an increasing external force as good as possible. If the neuromuscular system is not able to match the increasing external force isometrically, the subject deviates from the quasi-static position. In case the external force exceeds the maximal isometric AF, the subject is forced to merge into eccentric muscle action, but still tries to counteract the increasing load as good as possible. Therefore, the AF as defined here can be realized during an isometric or an eccentric muscle action. The intention is to adapt the muscular tension with the aim to prevent or to decelerate at best a muscle lengthening. Thereby, the differentiation between a holding (HIMA) and a pushing isometric muscle action (PIMA) seems to be crucial, since the intention of the subject executing the AF is to adapt initially in a holding isometric manner. Some investigations showed that during HIMA the duration to maintain a defined force level is significantly briefer compared to PIMA[3–8]. It was hypothesized that HIMA is close to eccentric muscle action[7,8]. Enoka and Duchateau suggested a more complex neuronal control during eccentric muscle action compared to concentric contractions[9–12]. In case the neuromuscular system has to adapt to a varying external force in the described holding manner or during muscle lengthening, it is reasonable to assume that the requirements regarding the neuromuscular control could be even higher[13,14]. For the processing of AF, a mixed feed-forward and feedback control is assumed to be necessary. The mixed control was suggested by Caligiore et al.[15]. It is closely related to the “forward model”, which “predicts the behaviour of the motor apparatus for a motor command.”[15,16]. This requires an efference copy and direct somatosensory afferences[15,16]. For an optimal execution of AF, the muscle length and joint angle should stay constant for as long as possible during the external force increase. It is assumed, that the increasing external force causes an initial minimal deflection of the homeostasis of muscle length and limb position. The corresponding afferent signals, in turn, is supposed to lead to a mismatch in the responsible regulatory control loop. A compensatory increase of muscle tension would be necessary to maintain the homeostasis of length and position. However, at the moment of muscular response the external force has already increased further. This has to be predicted by the neuromuscular system to adapt optimally. Therefore, a forward model in the sense of a mixed feed-forward and feedback control[15] seems to be necessary to maintain the isometric position. If the maximal holding isometric AF is exceeded, the muscle is forced to lengthen. During the enforced subsequent eccentric muscle action, the motor system tries to further adapt to the external load as good as possible.

By executing the AF, the sensorimotor control is challenged in a specific way, because the motor output must be continuously adjusted regarding the sensory input triggered by the external force application. In case of varying forces an anticipatory feedforward control seems to be necessary. Therefore, it is hypothesized that the AF reflects the functionality of the complex sensorimotor control and its detection could particularly be suitable to identify interferences in these circuitries. The influences of nociception[17,18] or emotions[19,20] on motor control are well-known. Furthermore, the link between olfaction and the motor system was already proven[21]. However, the effect of olfaction on motor control is a rarely considered objectively in science. Primarily, odour induced changes of the cardiovascular system[22,23], psychophysiological brain activity[24], cognition and behaviour[25] or the influence of odours on the quality of life[26,27] are investigated. Motoric reactions to olfaction are considered, for instance, concerning the startle reflex with respect to pleasant, unpleasant or no odour[28]. Closer to motor control was an investigation showing that lavender odour could reduce falls in elderly nursing home residents[29]. Assessments concerning the influence of olfactory inputs on muscle function remain disregarded in research to our knowledge. Since the AF is considered as a special function of the sensorimotor control it seems to be conceivable that pleasant or disgusting odours might modulate that aspect of sensorimotor control. The cerebellum as well as the ventrolateral thalamus are, inter alia, involved in olfaction[30–32] and both structures are relevant for adaptive motor control. Additionally, olfaction and emotion are evolutionary strongly coupled[33–35]. And, as mentioned above, the effect of emotions on motor control are secured. Therefore, it seems reasonable to assume that the AF might be influenced by olfaction.

The assessment of AF can be performed manually (clinical, with or without a handheld device) or using an equipment system based on pneumatics[2,36]. In each case, the subject should adapt to the external increasing force application with the intention to maintain the position by holding isometrically for as long as possible. Thereby, the force profile differs depending on the test procedure. During the measurement with the pneumatic-based system, the participant will always be forced into eccentric muscle action after an isometric phase. Thereby, firstly it reaches its maximum isometric AF ($AFiso_{max}$), which indicates the highest force reached during isometric muscle action. If the individual $AFiso_{max}$ is exceeded, the muscle starts to lengthen and the subject merges into eccentric muscle action, but still should adapt to the increasing force. Thereby, the AF usually increases further on and the maximal eccentric AF ($AFecc_{max}$) is reached. During the manually assessed AF, the participant will not be forced into eccentric muscle action per se as described below. For scientific purposes, the kinematics and dynamics during execution of AF are recorded by a handheld device during manual muscle test (MMT) in the sense of a "break test"[36,37]. Since this has the advantages of a highly flexible and time saving objective assessment tool, it was used for the present investigation. The MMT in the sense of a "break test" is defined according to Conable and Rosner[37]: "The subject is asked to resist the tester`s gradually increasing pressure. If the muscle breaks away, there is also eccentric lengthening." The manually performed break test is usually conducted in submaximal intensity areas[37]. If the adaptation during the force increase is optimal, the muscle length will therefore stay quasi-isometric during the whole test until an oscillating force equilibrium on a considerably high force level is perceived by the tester[36]. Thus, the aim is not to force the subject into muscle lengthening and to perform a test of maximum strength thereby. A muscle lengthening would always occur if the tester applies a force that would exceed the maximal voluntary isometric contraction of the subject. However, the main focus during AF assessment using the MMT is to determine, if the subject is able to hold the position isometrically during the whole submaximal force rise up to an considerably high force level[36,37]. In case of a failing adaptation, the muscle would already start to lengthen ("breaking point") in submaximal areas clearly below the MVIC-level during force increase. Therefore, during the MMT the force maximum of the test (AFmax) can arise during isometric ($AFiso_{max}$) or during eccentric ($AFecc_{max}$) conditions. Thereby, the AFmax must not be equivalent to the MVIC of the participant but refers to the maximum force reached during the test either under isometric or eccentric behavior.

The aim of this pilot study was to investigate whether the AF in healthy participants shows different patterns in reaction to neutral, pleasant and disgusting odors. Since disgusting odours are linked to negative emotions (disgust), we assume a rather inhibiting effect on the motoric system. Because of the complex control processes during execution of AF suggested above, especially adjusting the muscular tension by maintaining constant muscle length and limb position, it is assumed that the $AFiso_{max}$ might be more vulnerable in reaction to probable influencing factors such as a disgusting odor compared to the $AFecc_{max}$, MVIC or the commonly assessed eccentric or concentric strength. We therefore hypothesize that disgusting odor will reduce the maximal isometric AF ($AFiso_{max}$) but will have no effect on the maximal eccentric AF ($AFecc_{max}$). Pleasant or neutral odors are assumed to have no reducing effect on the $AFiso_{max}$ or $AFecc_{max}$.

Methods

Participants

The Adaptive Force (AF) of the hip flexors or the biceps brachii muscle, respectively, of n = 10 healthy participants was recorded by a handheld device during the manual muscle test (MMT) performed by two experienced testers (tester 1: female, 34 years, 168, 55kg; 8 yrs. of MMT experience; tester 2: male, 63 years, 185 cm, 87 kg; 25 yrs. of MMT experience). The anthropometric data of the healthy participants are given in Table 1 (detailed information are given in supplementary material Table S1). Exclusion criteria were any kind of health issues and an impaired neuromuscular function of the tested muscles assessed by the MMT prior to the measurements.

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of the University of Potsdam, Germany (protocol code 35/2018; 17.10.2018).

Table 1. Anthropometric data. Displayed are the arithmetic means and standard deviations (M ± SD) of age, height and body mass of the n = 10 participants.

Gender	Age (yrs.)	Height (cm)	Body mass (kg)
Female (n = 6)	36.00 ± 14.71	162.60 ± 7.96	65.20 ± 10.18
Male (n = 4)	31.75 ± 8.54	186.00 ± 2.45	79.00 ± 7.44

Handheld device for recording the dynamics and kinematics during manual assessment of Adaptive Force

The handheld device (development was funded by the Federal Ministry of economy Affairs and Energy; project no. ZF4526901TS7) consists of strain gauges (co. Sourcing map, model: a14071900ux0076, precision: 1.0 ± 0.1%, sensitivity: 0.3 mV/V) and kinematic sensor technology (Bosch BNO055, 9-axis absolute orientation sensor, sensitivity: ±1%) to record the reaction force, the accelerations and angular velocity (gyrometry) between tester and participant during the MMT. All data were buffered with a sampling rate of 180 Hz. The data were AD converted and sent via Bluetooth 5.0 to a notebook. A measuring software (based on National Instruments Lab-view) saved the transmitted data.

Manual muscle testing

The MMT is a clinical method of testing the AF as a marker of neuromuscular functioning[37]. For the present investigation, the so-called “break test” was applied (for description see introduction)[36,37]. Thereby, the tester applies an increasing force by pushing against the subject’s limb. On the tester’s side the maximally producible force is limited by the prescribed positioning to execute the test. The muscular strength of the tester would easily allow to generate a higher force, but it would lead to a displacement of the tester´s stance. Of course, individual anthropometric properties are additional factors which influence the maximum applicable force, but the testing position is the crucial limit. In preceding measurements, the two involved testers developed maximum forces around 280 N. With this amount one would normally not be able to overcome a well-functioning rectus femoris muscle or elbow flexor group, respectively, of young healthy subjects. Therefore, the MMT is not designed to measure the subject´s maximum strength. (This could be done using technical devices which could easily overwhelm the subject.) The MMT evaluates the submaximal stability of the muscle. On this account, the referred AFmax does not represent the subject´s maximum strength, but the force which is maximally applied to the subject during interaction.

The assessment of the MMT by the tester is differentiated into two conditions[36,37]: In case the limb of the subject maintains the isometric position during the whole force increase, the MMT is assessed as “stable”. In case it yields during the force rise on a submaximal force level (breaking point), the MMT is rated as “unstable”. Because of this manual approach, the test and its interpretation are subjective. By using the newly developed handheld device the force profile and the position of the tested limb can be objectified simultaneously during the MMT by recording the dynamics and kinematics. A recent investigation showed that experienced testers are able to reproduce the force application in a reliable way (see below), which is one prerequisite for the present investigation[36].

Characteristic and reproducibility of force profile

The applied force profile during the MMT was defined to have the progression as displayed in Figure 1[36]. During phase 1, the tester and the subject get in contact on a low force level for 1-2s. This is necessary to create a starting force level, so that the subject gets the opportunity to adapt to the external force of the tester at all, initially on a consistent and low force level. In phase 2, the tester increases the force smoothly in an exponential way. At the beginning, small steps of force rise are necessary, so that the subject gets a chance to adapt to the increasing force (for neurophysiological explanation see[36]). This second exponential phase merges into a linear force rise in phase 3. If an oscillating force equilibrium between tester and subject is reached, this should be maintained for a few seconds, whereby the maximal AF of the test is reached (phase 4) before the tester stops the interaction and the force decreases again. The duration of this whole force rise (phase 2 to 4) until the maximum reaction force should be within 4s. Of course, this force application depends especially on the tester. A sufficient reproducibility of the applied force profiles is a necessary precondition for valid data.

Prior to the study, both testers proofed their ability to test in a reproducible way by performing 10 repeated force increases against a stable resistance in the MMT setting of the hip flexors. The setting was equivalent to the here performed one (see below), except for a fixed leg of the participant to exclude its reaction as a second influencing factor[36]. The force profiles of both testers are illustrated in Figure 2. The coefficient of variation of the maximum force amounted 5.6% (tester 1) and 4.6% (tester 2), respectively. Both testers showed a reliable slope from start to maximum force comparing the 10 trials with an intraclass correlation coefficient of ICC(3,1) = 0.992 (tester 1) and 0.995 (tester 2), respectively. Furthermore, the inter-tester reproducibility of both testers is considered as high with ICC(3,1) = 0.989 and a Cronbach’s alpha of 1.0. Therefore, the force profiles of the two experienced testers, which performed the MMT here, can be considered as reliable. Group comparisons between experienced, little experienced and unexperienced testers showed significant differences in several parameters of force profile in a previous study[36].

Setting and procedure

Prior to the measurements, the participant was introduced to the procedure and gave its written consent to participate. Subsequently, the rectus femoris muscle was tested in a preliminary MMT. In case of full stability, the rectus femoris muscle was chosen for the investigation. If it did not fulfil this requirement, the biceps brachii muscle was used provided it was fully stable. Afterwards, the participants selected the most pleasant and most disgusting odor out of 12 standardized sniffing sticks (olfasense GmbH). Those sniffing sticks are normally used for testing the olfactory capacity in clinical circumstances for e.g., in Parkinson´s disease. After a break for neutralization of the olfactory sense, the AF of the participant was tested by the MMT performed by the same tester with the handheld device while smelling at different odors (single-blinded, randomized): 3 x neutral, 3 x pleasant, 3 x disgusting (in some subjects less than three trials per odor were performed; 1 trial had to be excluded because of technical problems; for further information see supplementary material Table S2). A double-blinded study is not possible since the participant will always smell the odor. However, the participants were instructed to not show any reaction with respect to the odors, so that the tester was not influenced by possible hints on which odor was presented. The order of stick presentation was randomized. An assistant gave the sticks to the participant and recorded the measurements. Tester 1 tested n = 6 subjects (1 x biceps brachii, 5 x hip flexors), tester 2 tested n = 4 subjects (1 x biceps brachii, 3 x hip flexors) (for further information see supplementary material Table S2).

The MMT was performed in the following way: The subject lay in supine position with a hip and knee angle of 90° for testing the rectus femoris muscle (Figure 3B). The tester had contact to the distal end of the thigh of the participant. The handheld device (Figure 3A) was located between the tester's palm and the participant's thigh to measure the dynamics and kinematics during the MMT. For testing the biceps brachii muscle, the participant was supine and flexed its elbow joint in 90° with a maximal supination (Figure 3C). The tester had contact with the handheld device at the distal forearm of the participant. In both settings, the exact placement of the device at the respective limb was marked to reproduce the position during subsequent measurements. The force rise was applied by the tester in direction of muscle lengthening of the participant's rectus femoris muscle (hip extension) or biceps brachii muscle (elbow extension), respectively.

The task of the participant was to maintain (hold isometrically) the respective starting position for as long as possible while adapting to the external force rise applied by the tester. The device detected the limb´s position during the force rise. After the test, the tester gave his or her judgement regarding the subjectively felt stability during the test. In case, the position of the limb stayed stable by maintaining the same muscle length and joint angle during the whole duration of force rise the MMT was assessed as "stable". If the participant merged into eccentric muscle action in the course of force increase the MMT was rated as "unstable".

Data processing and statistical analysis

For evaluation, the force and gyrometer signals were used. The csv-files were transferred to DIAdem 2017 (National Instruments). All signals were interpolated (linear spline interpolation) to ensure equidistant time channels (1000 Hz) and filtered (Butterworth, cut-off frequency 20 Hz, filter degree 5; for slope parameter to eliminate the oscillations: cut-off frequency 3 Hz, filter degree 10). The parameters of interest are the following:

The maximal Adaptive Force (AFmax)

This parameter refers to the maximal reached force value during the whole trial. AFmax (N) can be reached under two different circumstances. If the muscle length stayed stable over the whole force rise, AFmax was reached under isometric conditions ($AFiso_{max}$). In case of yielding during force increase, this value was obtained during eccentric muscle action ($AFecc_{max}$). The AFmax does not reflect the maximal strength of the participant, since it depends on the amount of force applicated by the tester (see above).

The maximal isometric Adaptive Force ($AFiso_{max}$)

This parameter refers to the maximal reached AF during holding isometric muscle action, thus no muscle lengthening occurred until this moment. The gyrometer signal was used to determine the breaking point indicating the starting of muscle lengthening. It oscillates around zero under isometric circumstances. In case the muscle lengthened the gyrometer signal decreased below zero. The force value at the moment of last zero crossing of the gyrometer signal was defined as $AFiso_{max}$ (N) indicating a deviation of the angle over time. In case the muscle did not lengthen, objectified by a gyrometer signal oscillating around zero over the whole MMT, the maximum force value AFmax = $AFiso_{max}$. The parameters $AFiso_{max}$ and the ratio of $AFiso_{max}$ to AFmax (%) were used for further considerations.

The Adaptive Force in the moment of onset of oscillations (AFosc)

The force signal showed an onset of oscillation in the course of force rise in some trials. Therefore, the oscillations of force signal were evaluated in NI DIAdem 2017. If three consecutive maxima with a time distance of < 0.15s were identified, this was defined as the onset of oscillations. The border of 0.15s was set since muscular oscillations occur in a low frequency range of 10 Hz[38–41]. The AF value at the first of those three oscillations referred to AFosc (N). If no onset of oscillation was present, AFmax = AFosc. The parameter AFosc and the ratio of AFosc to AFmax (%) were used for further considerations.

Slope of force rise

This parameter was evaluated to ensure the reproducibility of force rise comparing the trials with neutral, pleasant and disgusting odors. According to neurophysiological considerations and empirical experience, [36] the characteristic of the force rise might affect the outcome. To compare the slopes of neutral, pleasant and disgusting odor until the breaking point, the slope in phase 3 was calculated with reference to the breaking point in trials with unstable condition. For that, the arithmetic means of the $AFiso_{max}$ values of the trials assessed as unstable was used as reference for each participant ($AFiso_{unst}$). The slope of force curve was then calculated by the difference quotient from the time and force values at 60% of $AFiso_{unst}$ to 100% of $AFiso_{unst}$ for each trial and participant. Due to the exponential force rise, the decadic logarithm was taken from the slope values. The logarithmized slope is given by lg(N/s). In five as stable assessed trials, the 100% of $AFiso_{unst}$ was reached in the transition to phase 4. To avoid a distortion of slope results those trials were excluded from the analysis of slope.

The arithmetic means (M), standard deviations (SD) and 95%-confidence intervals (CI) of all parameters were calculated per participant separately for trials with neutral, pleasant and disgusting odors. All parameters were statistically compared between the three odors using IBM SPSS Statistics 27 to identify possible differences between the odors. For that, the normal distribution was checked with the Shapiro-Wilk test. In case normal distribution was not fulfilled the Friedman test was used. This was the case for both ratios (;). All other parameters were normally distributed and the ANOVA for repeated measurements was performed (RM ANOVA). In case, the sphericity was not fulfilled (Mauchly test), the Greenhouse-Geisser correction was applied. For post hoc test, Bonferroni correction was applied. The effect size eta squared (η^2) was calculated by SPSS. For pairwise comparisons between the odors, the effect size Pearson's r was calculated by for RM ANOVA and by r = for Friedman test. Significance level was set at $\alpha = 0.05$.

Results

Exemplary force and gyrometer signals during the MMT of the hip flexors of one female participant during neutral, pleasant and disgusting odors are displayed in Figure 4. As can be seen, the force rises are nearly identical for all three trials, especially in the first three phases (Figure 4 above). This illustrates the high reliability of the tester's force application during the MMT. Furthermore, the gyrometer signal (Figure 4, below) of disgusting odor decreases clearly, whereas during neutral (blue) and pleasant (green) odors, the gyrometer signal stays stable, oscillating around zero (defined as isometric behavior) until the maximal AF (AFmax) is reached. Thus, the values of AFmax correspond to $AFiso_{max}$ during neutral and pleasant odors. During disgusting odor, the $AFiso_{max}$ = 95.75 N, which amounts 60.5% of the $AFecc_{max}$ = 158.14 N, which is reached under muscle lengthening. The participant starts to lengthen her muscle at a considerably lower force level ($AFiso_{max}$) during disgusting odor, whereby a muscle lengthening does not occur during neutral or pleasant odors. It is important to mention that the $AFiso_{max}$ during disgusting odor arise at a 35% and 30% lower force level compared to the $AFiso_{max}$ during neutral and pleasant odors, respectively. During muscle lengthening (disgusting odor), the participant is able to produce an even slightly higher maximum force compared to the AFmax during neutral and pleasant odors. However, during neutral and pleasant odors, the AFmax of the test is reached under isometric conditions ($AFiso_{max}$) and under the appearance of oscillations. The oscillations during disgusting odor appear at a force level of 151.76 N, which amounts to 96% of the corresponding $AFecc_{max}$. The onset of oscillations (AFosc) during neutral and pleasant odors appears at a force level of 84.76 N and 95.06 N, respectively, which amounts 58% and 69% of the related $AFiso_{max}$ (Figure 4). The AFosc during neutral and pleasant odors amount to 56% and 63% of the AFosc during disgusting odor and appear at a lower force level than the $AFiso_{max}$ during disgusting odor.

This example illustrates the behavior of AF during different odors, which consistently appears in 73 of all 76 measurements (the three exceptions are described below). This is supported by the following statistical group comparisons (Table 2).

Table 2. Displayed are the arithmetic means (M), standard deviations (SD), lower and upper border of 95%-confidence intervals (CI) as well as the p-values and effect sizes η^2 of all parameters comparing the groups neutral, pleasant and disgusting odors.

Parameter	odor	M ± SD	CI	Significance p	η²
AFmax (N)	Neutral	189.58 ± 40.63	164.38; 214.75	0.051	
	Pleasant	201.70 ± 37.14	178.64; 224.72		0.334[1]
	Disgusting	219.85 ± 35.19	198.04; 241.66		
$AFiso_{max}$ (N)	Neutral	185.95 ± 40.80	160.66; 211.23	**< 0.001**	
	Pleasant	197.32 ± 34.52	175.92; 218.71		0.698[1]
	Disgusting	131.46 ± 30.03	112.85; 150.07		
Ratio $AFiso_{max}$ to AFmax (%)	Neutral	98.39 ± 3.39	96.29; 100.49	**< 0.001**[2]	
	Pleasant	98.04 ± 2.33	96.59; 99.48		-
	Disgusting	59.88 ± 10.26	53.52; 66.24		
AFosc (N)	Neutral	145.70 ± 46.76	116.71; 174.68	**< 0.001**	
	Pleasant	155.09 ± 31.87	135.34; 174.85		0.690[1]
	Disgusting	206.67 ± 38.03	183.10; 230.23		
Ratio AFosc to AFmax (%)	Neutral	75.22 ± 10.22	68.89; 81.55	**0.001**[2]	-
	Pleasant	77.04 ± 8.73	71.63; 82.45		
	Disgusting	93.86 ± 7.16	89.43; 98.30		
Slope lg(N/s)	Neutral	1.97 ± 0.13	1.89; 2.06	0.485	
	Pleasant	1.99 ± 0.09	1.94; 2.05		0.098[1]
	Disgusting	1.96 ± 0.12	1.89; 2.03		

[1] eta squared η² of RM ANOVA; [2]Friedman test. Significant results are displayed in bold.

Assessment of the manual muscle test by the tester

In total, 24 of 25 trials with neutral odor were rated as “stable” by the testers. One trial was assessed as “unstable” by tester 1. With pleasant odor, 25 of in total 26 trials were assessed as “stable” and one as “unstable” (tester 2), whereby the patient reported “sensing” her groin (no pain, appeared in no further measurement). 24 of in total 25 trials with disgusting odor were assessed as “unstable”, one trial was assessed as “stable” (tester 1). (For detailed information see supplementary material Table S2). Regardless of the testers’ subjective assessments, the following evaluation is only based on the grouping related to the presented odors.

Slope of force profiles

The slope is the main parameter to investigate the reproducibility of the testers’ force rises. As can be seen in Table 2, Figure 4 and 5, the slopes did not differ significantly between neutral, pleasant and disgusting odors ($F(2,14) = 0.762$, $p = 0.485$). Therefore, the following considerations of AF parameters are done based on the requirement of reproducible force profiles between the MMTs of the three odors.

Maximal Adaptive Force and maximal isometric Adaptive Force

The overall maximum AF (AFmax), which occurred under isometric or eccentric muscle conditions, is slightly but not significantly higher in measurements with disgusting odor compared to neutral ($p = 0.050$) or pleasant odors ($p = 0.086$), respectively (Figure 6A). The AFmax during neutral odor amounts averagely 93.95 ± 10.35% of the AFmax during pleasant odor and 87.20 ± 17.76% of AFmax during disgusting odor. The AFmax during pleasant odor amounts averagely 92.28 ± 12.97% of the AFmax during disgusting odor.

The maximal isometric AF ($AFiso_{max}$) is significantly lower in measurements with disgusting odor (131.46 ± 30.03 N) compared to neutral (185.95 ± 40.80 N; $p = 0.004$, $r = 0.79$) and pleasant odors (197.32 ± 34.52; $p < 0.001$, $r = 0.89$), respectively ($F_{Green}(1.285,11.536) = 20.790$, $p < 0.001$) (Table 2, Figure 6B). The $AFiso_{max}$ does not differ significantly between neutral and pleasant odors ($p = 0.105$, $r = 0.52$). In the trials with disgusting odor, the $AFiso_{max}$ amounts averagely 60 ± 10% of the related AFmax, whereas with neutral or pleasant odors, the ratio is significantly higher with around 98 ± 3% ($p_{adj} = 0.001$, $r = 0.52$) and 98 ± 2% ($p_{adj} = 0.008$, $r = 0.43$), respectively (Table 2, Figure 6C). Furthermore, the $AFiso_{max}$ during disgusting odor amounts averagely 73.23 ± 12.06% of the $AFiso_{max}$ with neutral and 67.62 ± 15.85% of $AFiso_{max}$ with pleasant odors, respectively. That indicates that during perception of a disgusting odor, the maximal isometric AF is significantly lower compared to neutral or pleasant odors. The participant is not able to appropriately resist the external increasing force in an isometric way under the perception of a disgusting odor; the muscle starts to lengthen at a substantially and significantly lower force level compared to neutral or pleasant odors, respectively, whereby the AFmax is statistical similar between all odors.

Adaptive Force at the onset of oscillations

The measurements with neutral or pleasant odors are characterized by an onset of oscillations during force rise at a submaximal force level. Those oscillations do not or only slightly occur at a high force level during perception of a disgusting odor. Significant differences with $p < 0.001$ arise comparing AFosc between neutral, pleasant and disgusting odors (Table 2). The pairwise comparisons reveal a significant difference between disgusting and neural odors ($t(9) = -4.952$, $p = 0.001$, $r = 0.86$) and between disgusting and pleasant odors ($t(9) = -4.432$, $p = 0.002$, $r = 0.83$) (Figure 7A). The AFosc does not differ significantly between neutral and pleasant odors ($t(9) = -1.579$, $p = 0.149$, $r = 0.47$).

Looking at the ratio of AFosc to AFmax, the significant difference is confirmed by the Friedman test ($\chi^2(9) = 15.20$, $p = 0.001$). The Bonferroni post-hoc test revealed p-values of $p_{adj} = 0.001$ comparing neutral and disgusting odors ($z = -3.578$, $r = 0.51$) and $p_{adj} = 0.005$ for pleasant and disgusting odors ($z = -3.130$, $r = 0.44$) (Figure 7B).

Discussion

The presented study investigated the dynamics and kinematics during the manually tested AF utilizing a handheld device in healthy participants under the influence of neutral, pleasant or disgusting odors, respectively. The evaluation of the slope of force rises reveal a non-significant difference between the three odors. Accordingly, the following discussion is based on reliable force applications of the testers. The main outcomes are:

The maximum AF (AFmax) does not differ significantly between the three odors. The main difference is that smelling neutral and pleasant odors, the AFmax was reached under isometric conditions ($AFiso_{max}$), whereas with disgusting odor, the AFmax was obtained during muscle lengthening ($AFecc_{max}$). The $AFiso_{max}$ was significantly lower by perceiving disgusting compared to pleasant and neutral odors, indicating that during disgusting odor, the participants merged into eccentric muscle action at a significantly lower force level (60% of $AFecc_{max}$), whereas under neutral or pleasant olfactory influence isometric stability was maintained almost until the maximum. That confirms the hypothesis that the maximal isometric AF, but not the AFmax, decreases during perception of a disgusting odor.

The AF at the oscillation onset is significantly lower for neutral and pleasant compared to disgusting odor, in which no or only poor oscillations occurred at a high force level. This indicates that the AF in healthy persons perceiving neutral or pleasant odors is characterized by oscillations, which emerge during force rise at 75% of the maximum.

Limitations

The testers' force profile application might be the main limitation in this investigation. As mentioned above, the force application must be reproducible and appropriate as suggested in[36]. A smooth start followed by a faster linear force increase might be suitable to test the adaptive capability of the neuromuscular system[36]. The testers proofed their ability to test reproducibly prior to the investigation and the slope was used as parameter to control the force increase. The slopes did not differ significantly in the present measurements between the MMTs with different odors. The slope prior to the breaking point is even slightly lower in measurement with disgusting compared to pleasant odor (-3%). This speaks against the frequently appearing criticism that an unstable MMT is due to a steeper force rise. Nevertheless, the slope might be one crucial parameter when applying the force rise and must be controlled. An assessment of the force application by recording the dynamics and kinematics during MMT should take place to verify reliable and valid results.

Furthermore, the reached maximum force of a stable muscle depends not only on the participant, but also on the tester. The force profile is a result of their interaction. Because the participant is only reacting in a holding way, the tester determines the course of force including its maximum when a stable muscle is tested. That is why it depends on the tester to what extend the participant´s holding capability is challenged under stable conditions. Due to biomechanical aspects, it is mostly not possible to overcome the here tested rectus femoris and biceps brachii muscles. However, if the tester applies a lower maximum force, the participant's response will naturally be lower, too. Therefore, the AFmax does not reflect the real maximum strength of the participant, since it depends on the amount of force applicated by the tester. As mentioned above, the "break test" is characterized by a force application in submaximal areas. However, the $AFiso_{max}$ under unstable conditions will refer to the maximal holding AF under the obviously impairing influence of a disgusting odor. The $AFecc_{max}$ monitors the maximal eccentric force of the participants under the given circumstances. Since the $AFiso_{max}$ under stable conditions and the $AFecc_{max}$ under unstable conditions are not differing significantly in the present study, it is assumable the applied force of the tester is close to the maximal force capacity of the participants; with the assumption that the $AFecc_{max}$ is not changed by the influence of disgusting olfaction. Since the MMT was performed in submaximal areas, no statement can be made concerning the behavior of $AFecc_{max}$ under the effect of neutral or pleasant odors. This investigation remains.

A tendency of a lower AFmax is visible for the tests under stable (neutral/pleasant) compared to unstable conditions (disgusting) (Figure 6A). This could be comprehended as a possible reason for the different muscle states. However, the decisive difference is that the breaking point ($AFiso_{max}$) in unstable conditions (disgusting) appeared at a substantially and significantly lower level compared to the maximum force the muscle reached under stable conditions (neutral/pleasant) without muscle lengthening.

Another limitation is the small sample size (n = 10). However, the significances and effect sizes are considerably high. That is why we regard these preliminary results as a valuable first consideration reflecting the neuromuscular control of healthy subjects. The sample size must, of course, be increased to verify the found results.

Eventually, there could be a concern regarding a possible confounding factor. Although the subjects were instructed to show no verbal or nonverbal reaction to the exposed odors and the tester avoided to get into visual contact with the subject prior to and during the test an unconscious influence cannot ruled out completely. In this case the tester involuntary could have changed his or her profile of force application and therefore influenced the outcome. An unaware sudden start and steeper course of force rise would have favored an unstable behavior of the tested muscle. This is one reason why the slope before the breaking point was considered. The results invalidate the concern about unconscious manipulations by the tester because there is no relevant difference between the odors.

Characterization of “stable” and “unstable” adaptation

Taken the above-mentioned results together, it is suggested to define a “stable” and an “unstable” adaptation to an increasing external force as follows. A stable adaptation can be characterized by two conditions: (1) the $AFiso_{max} \approx AFmax$ ($\geq$ 98% of AFmax), thus, the muscle length stays quasi-isometric during the whole force rise (slight muscle suspensions are acceptable); (2) Oscillations of force with about 10 Hz arise during force increase, thus, AFosc is significantly lower than AFmax. Based on the data a percentage of averagely 76 ± 9% of AFosc to AFmax can be expected. An unstable adaptation is characterized by the following two conditions: (1) $AFiso_{max}$ is considerably lower than AFmax. Thus, the muscle lengthens during the force rise in submaximal areas and the maximum is reached under eccentric conditions ($AFecc_{max}$). Based on the data a percentage of 60 ± 10% of $AFiso_{max}$ to $AFecc_{max}$ can be expected. (2) No or only poor oscillations on a high force level occur during the force rise, thus, AFosc is close to $AFecc_{max}$ with a ratio of 94 ± 7%.

It is suggested that the unstable behavior reflects an inadequate adaptation of muscle length and tension to external increasing force applications. In the present study, this emerged by presenting a disgusting odor. This obviously is impairing the muscle function in the sense of AF in the here investigated small sample size of 10 healthy participants. For a first cautious summary thereof, a well-functioning undisturbed neuromuscular adaptation to an external force increase seems to be characterized by a sufficiently adapted muscle tension maintaining muscle length and limb position as well as by the occurrence of mechanical oscillations.

Neurophysiological explanation of muscular adaptations with regard to perception of olfactory inputs

Based on the own research, there are no comparable investigations concerning the behavior of AF – or other motor functions – as reaction to different odors. Trying to understand the underlying mechanisms, the suggestion of neuromuscular AF processing should be regarded more detailed. During the manual assessment of AF, the tested participant receives sensory inputs due to the tester's contact and force application. Hereby, skin and joint receptors, muscle spindle cells and Golgi tendon organs are perceiving mechanical inputs. The sensory signals are forwarded through the posterior horn to other spinal and supraspinal structures[42–44] and provide the current muscle length, tension and joint status. Sighting the literature, one can assume that at least the thalamus, cerebellum, inferior olivary nucleus (ION), red nucleus, basal ganglia, cingulate cortex and the sensorimotor cortex are involved in the complex processing of adaptive motor control and are interconnected directly or indirectly[13–15,20,42–79]. The cerebellum is considered as one of the most relevant sensorimotor structures concerning the temporal-spatial processing[47,54]. Its anterior part seems to be especially relevant for sensorimotor functions and the posterior part for cognition and emotions[60]. However, the posterior cerebellum also seems to be involved in the "prediction of sensory events", especially for "timing perception and adjustment"[54]. Therefore, the cerebellum is relevant regarding the motoric adaptation[15,61], whereby it seems to be of particular importance in the beginning of an adaptation[61]. As mentioned in the introduction, a mixed mechanism of feedback and feedforward control is assumed to be involved in the adaptive process[15]. The cerebellum seems to work as the forward controller in cooperation with the ION, which provides the motoric time signal[45–48]. Thereby, the cerebellum can learn to predict the accurate timing of connected events and, thereby, intervenes in motor control[45,46,72]. This flows into the error processing of motor control and provides the rhythmic neuronal signal to enable temporal coordinated movements[45–47]. The cerebellum receives information of the muscle spindle, Golgi tendon organs and skin receptors[42]. Therefore, it might be essential for the target-actual comparison of muscle length and tension. Reafferences are compared with a copy of the initial motoric command[13]. Mismatches are then corrected by adjustments of the motor output. It was suggested that the cerebellum is a kind of "error-correcting machine", which compares the "expected and actual outcome of a sensory prediction or motor command"[51]. Also, other central structures seem to be relevant thereby. The parietal cortex was suggested as a central interface between sensory and motor processes concerning temporal processing[71]. Additionally, the thalamus is a central switching point for sensory and motor processes[64], with its main task of modulating and regulating the flow of information to the cortex[65]. Meanwhile, the involvement of the cingulate cortex in emotions, pain processing as well as in spatial and motor control is secured[14,20,57,68]. This area reacts to different sensory inputs, e.g. exteroception, proprioception and nociception, and has a wide interconnection to other central structures[20,57]. Additionally, the basal ganglia work as a kind of filtration station for the muscle tone, including temporal processing, by facilitating desirable and inhibiting undesired motoric programs[14,52,80]. Last but not least the motor cortex receives information of the thalamus, the cerebellum, the basal ganglia, the red nucleus and of the limbic system[54,58]. The premotor cortex as well as the supplementary motor area of the cerebral cortex are involved in the temporal processing of motor activity[71,73,81]. Therefore, all those networked structures seem to be relevant in controlling the muscle length and tension during adaptation to external forces. Jörntell suggests, that "the final motor command, i.e. the final spatiotemporal structure of the activation of the α-motoneurons and thereby the muscles, is a sum or a product of all the motor command signals issued and the pattern of sensory feedback”[53]. As mentioned above, the occurred oscillations of 10 Hz during stable conditions (neutral/pleasant odors) might indicate a relevance of mechanical muscle oscillations in interaction with external forces. Those did not or only sparsely arise during unstable status (disgusting odor). Oscillations are also found in the mechanical[38–41] as well as in electrical muscular activity[76,82–86] during isometric muscle actions. They also occur in central structures during muscular activity. The cerebellum shows great inhibitory postsynaptic potentials of 8-17 Hz, which were found in cats[50]. Also other vertebrates exhibit oscillatory activity of the olivocerebellar circuitry of 10 Hz[50,74]. Additionally, the thalamus and neurons of the motor cortex are characterized by discharge frequencies between 11-30 Hz[64] and 10 Hz[87–89], respectively. Furthermore, the long latency reflexes of proprioception are processed with 10 Hz[69,75]. If an external force is changing, the corresponding correction also takes place with latencies of 10-12 Hz[44,78]. It is hypothesized that the found oscillations during the MMT could represent the normal functioning of the complex neuronal network standing behind it. With this prospect, their absence could possibly indicate irritations.

If the regulative circuitries are working properly, the adaptation in the sense of AF ought to be performed adequately (“stable”). The neuromuscular system should be able to adapt appropriately to the external force increase in time and space if the force increases not too abrupt or intense. However, the present study showed that this neuromuscular adaptation might be impaired by perceiving disgusting odor. Olfactory inputs are not transferred to the thalamus[14]. Initially, the cingulate cortex was reported to be associated with olfaction[57]. Olfactory afferences, with latencies of around 300ms[90], are firstly transmitted to the olfactory bulb[91] and then are projected directly to the piriform cortex and the limbic system (amygdala, hippocampus)[91,92], which displays the close connection of olfaction and emotion[33–35,93,94]. Especially with perception of pleasant or disgusting odors, we assume the occurrence of positive or negative emotions, respectively. Therefore, it is likely that the here found reduced $AFiso_{max}$ and later occurred AFosc at a higher force level during perception of a disgusting odor might be related to a negative emotional component. A pilot-study investigating the AF under the influence of different emotions was performed and the results will be presented soon.

Characterization and specialty of the isometric Adaptive Force

The results strongly indicate that under particular circumstances a muscle can yield in length at a substantial submaximal force level. In this case the muscle loses its stability (ability to hold) despite of its further increase of tension. The maximum holding capacity ($AFiso_{max}$) changes within a few seconds depending on the influence of odor. Therefore, in contrast to $AFecc_{max}$, $AFiso_{max}$ it seems to be sensitive regarding a disgusting olfactory influence, which is interpreted as a possible disturbing factor. The arising oscillations 10 Hz under stable conditions suggest this could not only be a characteristic for maintaining muscular stability but perhaps a prerequisite. A loss of this function could be a sign of a disturbed sensorimotor processing characterized by a muscle lengthening at a considerably low AF. It is suggested that the $AFiso_{max}$, presumably depending on the onset of oscillations, seems to be the most vulnerable and, therefore, the possibly most relevant parameter in adapting to external forces. The immediate responses of $AFiso_{max}$ to the here investigated olfactory input strongly indicate to be based on regulatory mechanisms. Because of the close linkage of olfactory and emotional processing, the observed effect could possibly run via the influence of the limbic system on motor control[95,96]. However, the integration of the different central structures during adaptive motor processes leads to the conceivable and even likely assumption that also other internal and external inputs which enter the control circuitries might influence the adaptive motor control processes. The influence of health complaints on muscle function is reported for several indications, e.g. for infections as COVID-19[97], post-infectious diseases[98], CFS/ME[99,100], cancer[101], sarcopenia[102,103], hormonal dysfunctions[104,105] or fibromyalgia[106]. Thereby, possible nociception or other disturbing inputs might function as interferences in the complex motor control processes. We assume an impairment of the $AFiso_{max}$ thereby.

When a muscle gets unstable under certain circumstances this could lead to a destabilization of joints especially when they are under strain. A higher vulnerability regarding joint complaints or even injuries might arise in the process. In contrast to measure maximal forces as usual, the assessment of the special parameter $AFiso_{max}$ could provide a novel approach to understand injuries or orthopedic pathomechanisms.

Summarizing, the results highlight not only the suggested possibility of measuring a special adaptive neuromuscular control by the AF but might also deliver an approach for investigating the neuromuscular system regarding disturbances in the control circuits. The literature speaks for a complex control cascade as well as parallel working processes between the central areas characterized by oscillations which are involved in the control of the spatio-temporal structure of motor output. In an undisturbed, healthy neuromuscular system those complex control processes should enable the participant to adapt adequately to the external force stimuli.

In conclusion, the present study showed different adaptive motor outputs as a reaction to neutral, pleasant and disgusting odors in healthy persons. Assuming that the AF in reaction to neutral and pleasant odors reflect “normal” muscle function, the AF patterns during disgusting odor are interpreted as a disturbance of the neuromuscular control due to the unpleasant olfactory input. Based on the presented preliminary results, it is suggested that the length-tension control of muscles is affected thereby. Therefore, the isometric holding function including the peripheral mechanical muscle oscillations might be one or even the decisive parameter characterizing a well-functioning neuromuscular control of AF-action. It is hypothesized that measuring the AF, in particular the parameters $AFiso_{max}$ and AFosc, might be a suitable diagnostic tool to assess the functionality of neuromuscular control.

Based on the complex neuronal control, which is assumed to underlie the processing of AF, it is presumed that also other inputs as mental stress (negative emotions), nociception of joints or tissues or others might influence the AF as shown here for disgusting odors. If this hypothesis could be verified by further investigations, this might offer the possibility to use the measurement of AF as an individual diagnostic tool. The MMT is already used since decades[36,37]. However, due to the reasonable criticism of subjectivity, some skepticism concerning the AF tested by the MMT remains in different fields for which it might have potential. The acceptance could be improved by objectification using appropriate devices. The assessment and recording of the manually tested AF are necessary to secure a reliable and valid force profile of the tester. Because of the preliminary character of the present study further measurements with an enlarged data base are needed. In a next step, the AF in reaction to emotions and nociception should verify further evidence of the possible responses of the neuromuscular control to different inputs.

Declarations

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Author Contributions: LVS and FNB designed the study, SD and MA performed the measurements, LVS executed the data processing and analysis. FNB and LVS supervised the study. LVS wrote the main manuscript text and prepared the figures. All authors reviewed the manuscript.

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Figures

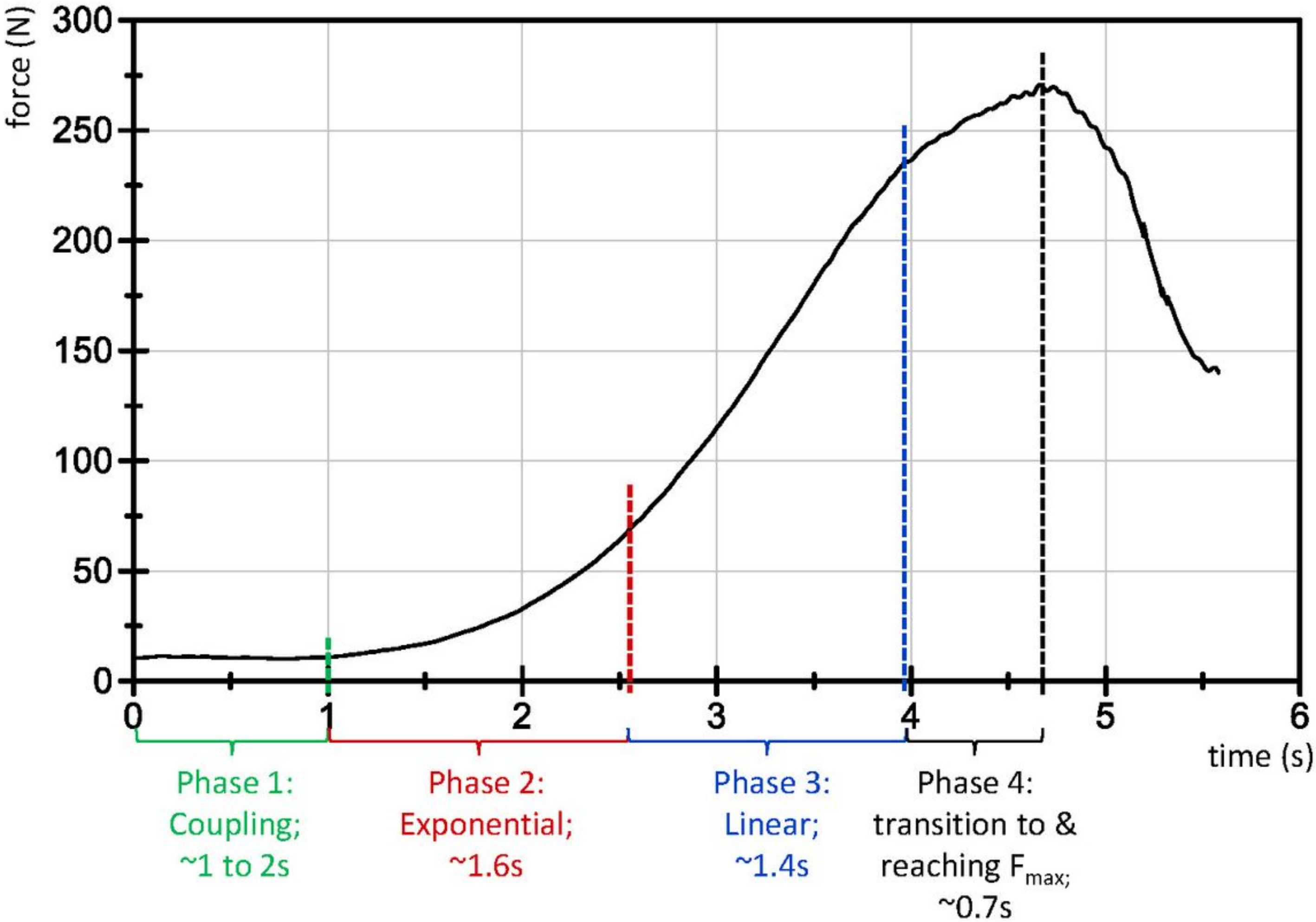

Figure 1

Schematic force profile. The force increase applied externally by the tester during the MMT consists of the four illustrated phases. (according to Bittmann et al. 36).

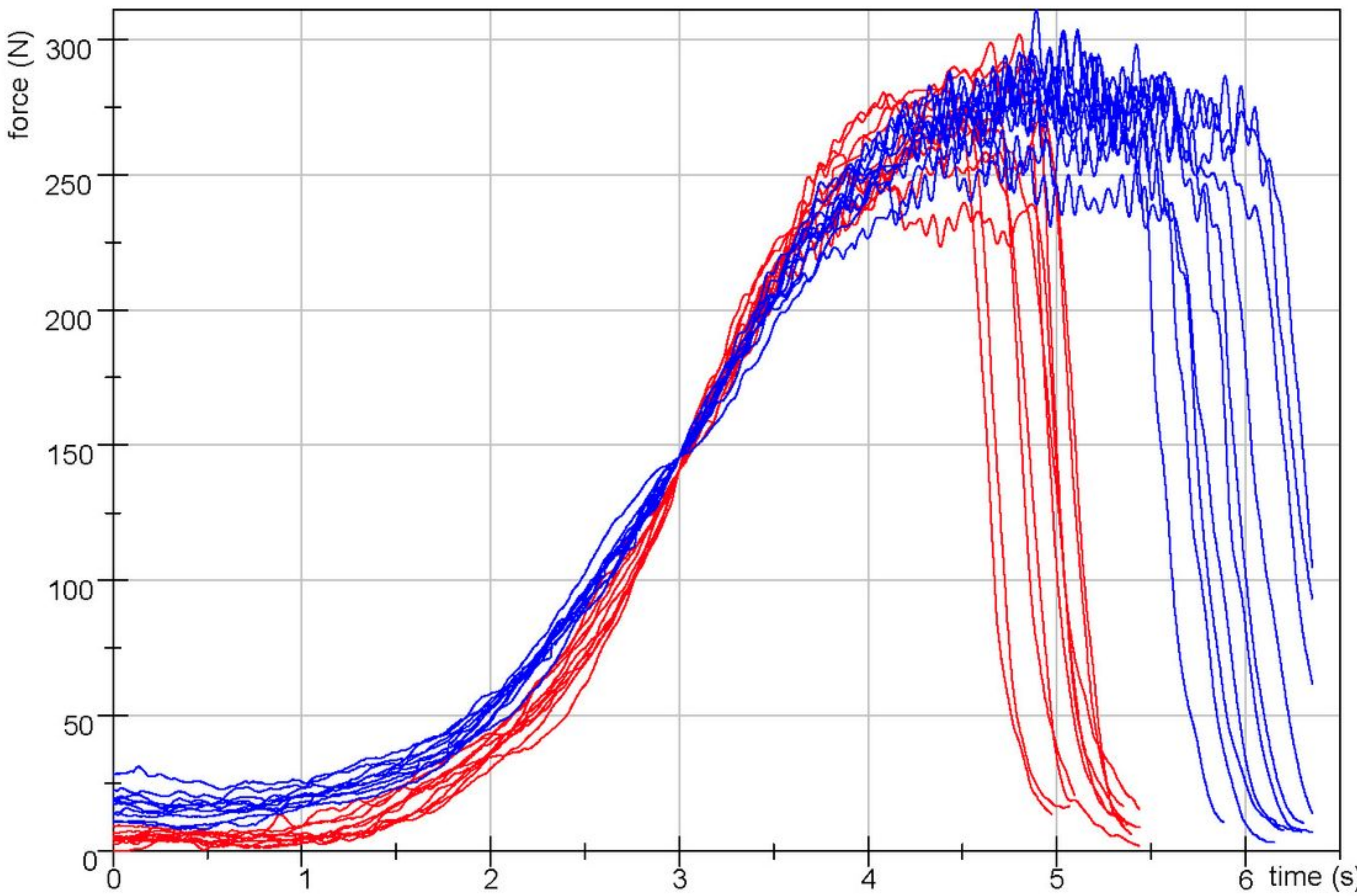

Figure 2

Repeated force profiles against stable resistance. Ten repeated force profiles of tester 1 (female, red) and tester 2 (male, blue) against a stable resistance in the MMT setting of the hip flexors (filtered with Butterworth, cut-off frequency 20 Hz, filter degree 5). (according to Bittmann et al. 36)

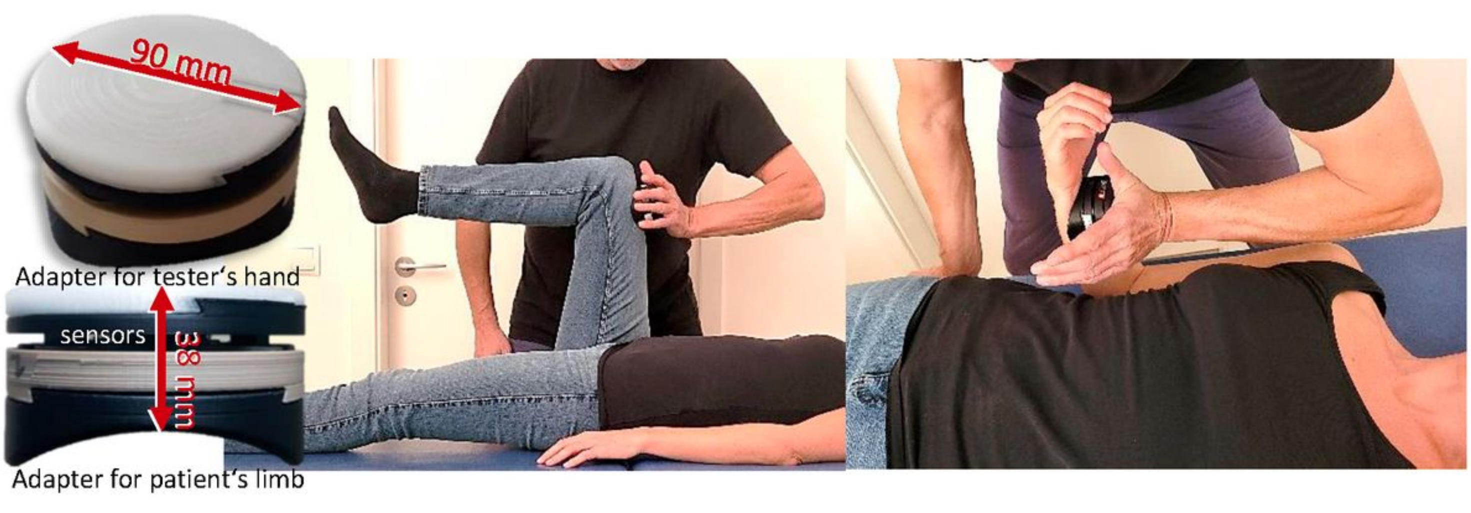

Figure 3

Setting of the manual AF measurements. The handheld device (A) is placed between the palm of the tester and the limb of the participant; (B) Manual muscle test (MMT) of the rectus femoris muscle; (C) MMT of biceps brachii muscle. The sniffing stick (olfasense) is held by the participant to his or her nose to smell the odor during the MMT.

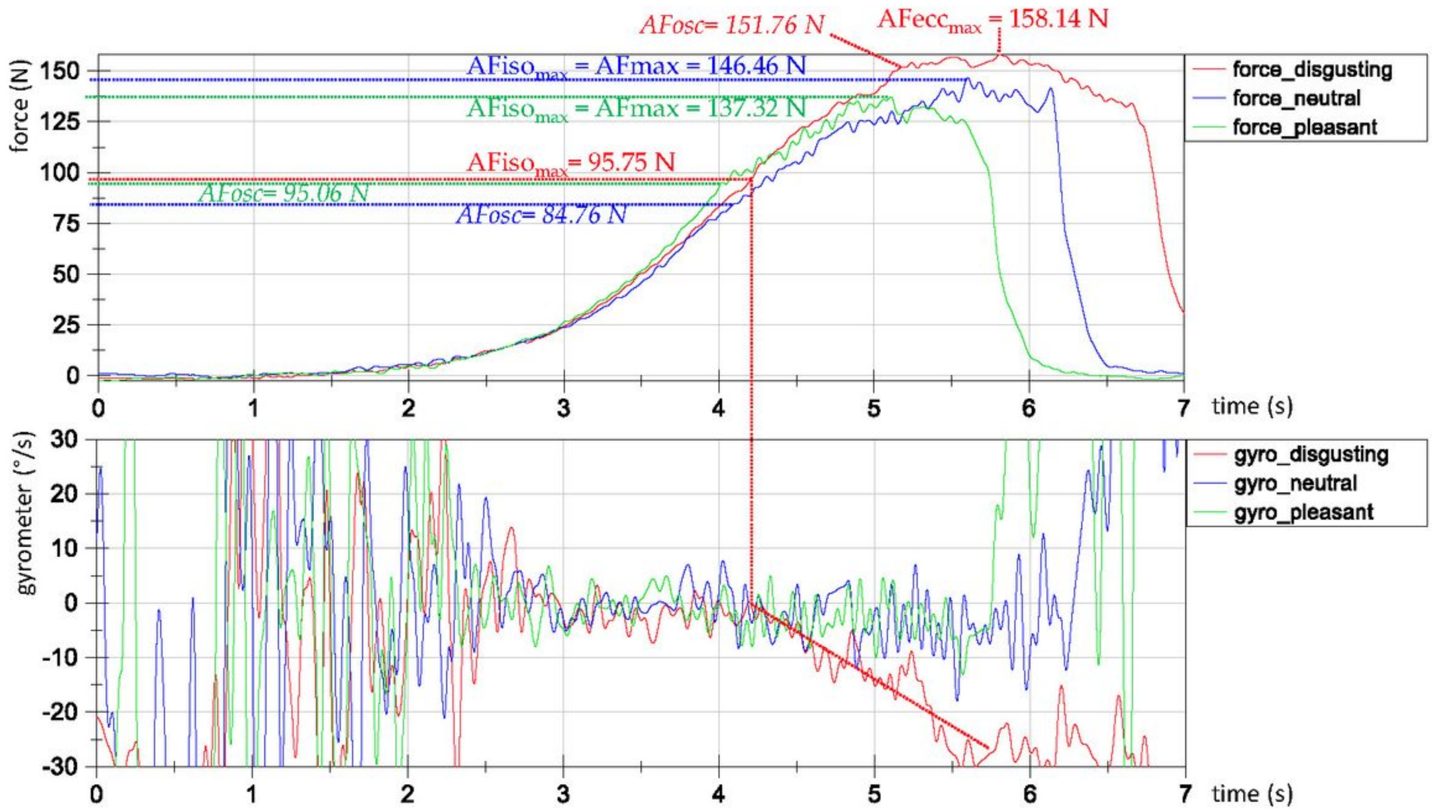

Figure 4

Exemplary signals. Displayed are the force rises (N) (above) and gyrometer signals (°/s) (below) during manual muscle test (MMT) of tester 1 testing the same female participant (age: 44 yrs., height: 173 cm, body mass: 77 kg) during disgusting (red), neutral (blue) and pleasant (green) odors. Marked are the parameters AFmax, AFeccmax, AFisomax and AFosc. (according to Figure 12 in 36).

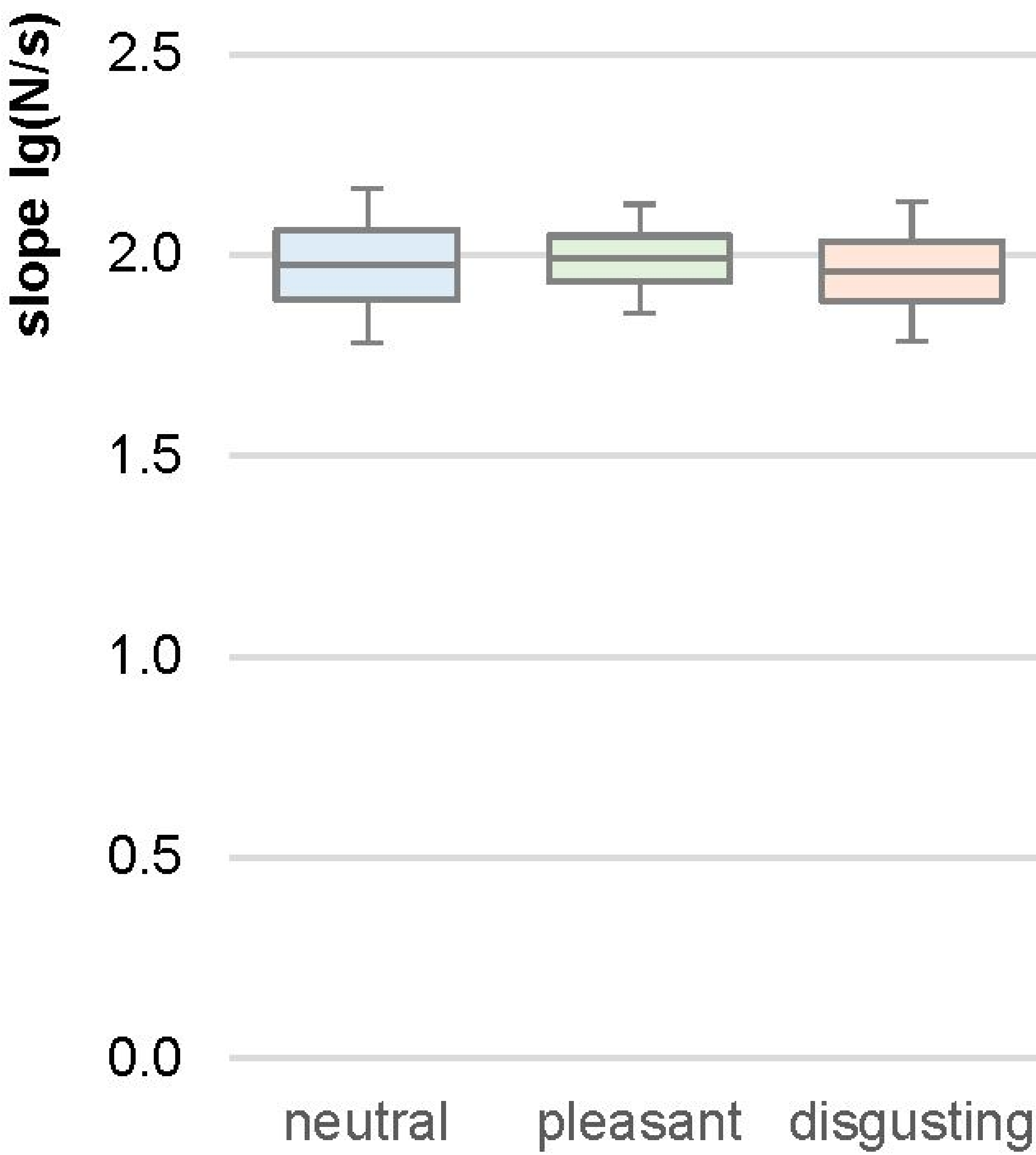

Figure 5

Slope. Displayed are the arithmetic means, standard deviations (error bars), 95%-CIs of the decadic logarithmus of slope from 60% to 100% of AFisounst lg(N/s) comparing the different odors neutral (blue), pleasant (green) and disgusting (orange). The statistical comparisons turned out to be non-significant ($p > 0.05$).

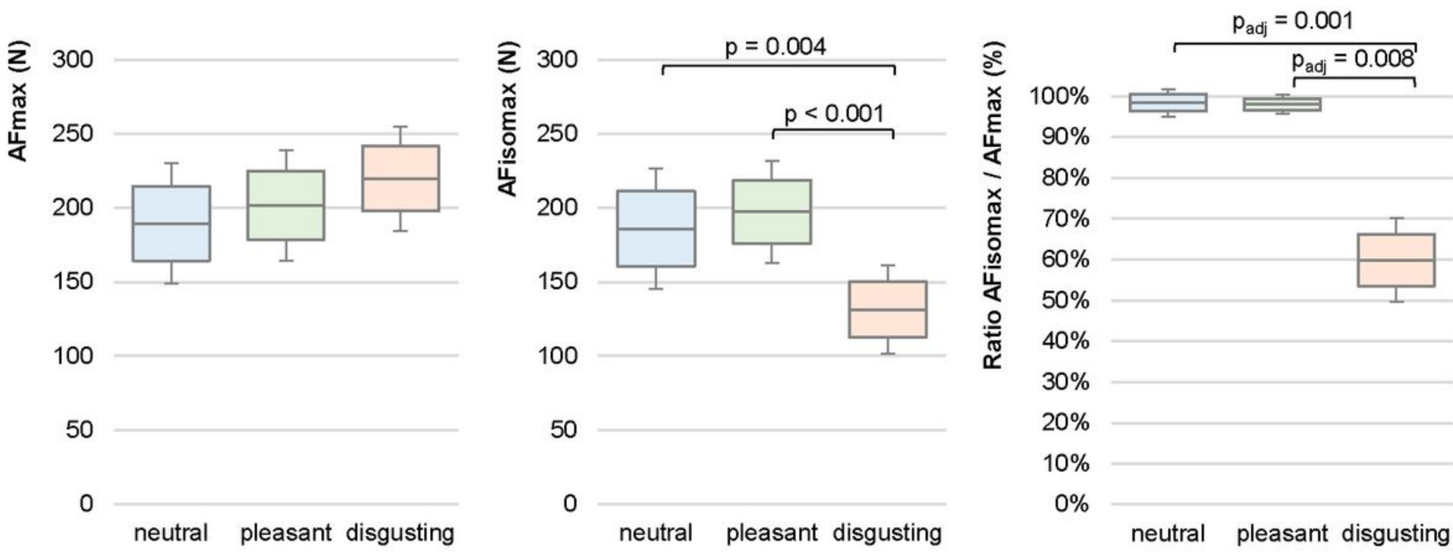

Figure 6

Maximum Adaptive Force and maximum isometric Adaptive Force. Displayed are the arithmetic means, standard deviations (error bars) and 95%-CIs of (A) the maximum Adaptive Force (AFmax), (B) the maximal isometric Adaptive Force (AFisomax) and (C) the ratio of AFisomax to AFmax comparing the odors neutral (blue), pleasant (green) and disgusting (orange). The p-values of significant comparisons are given.

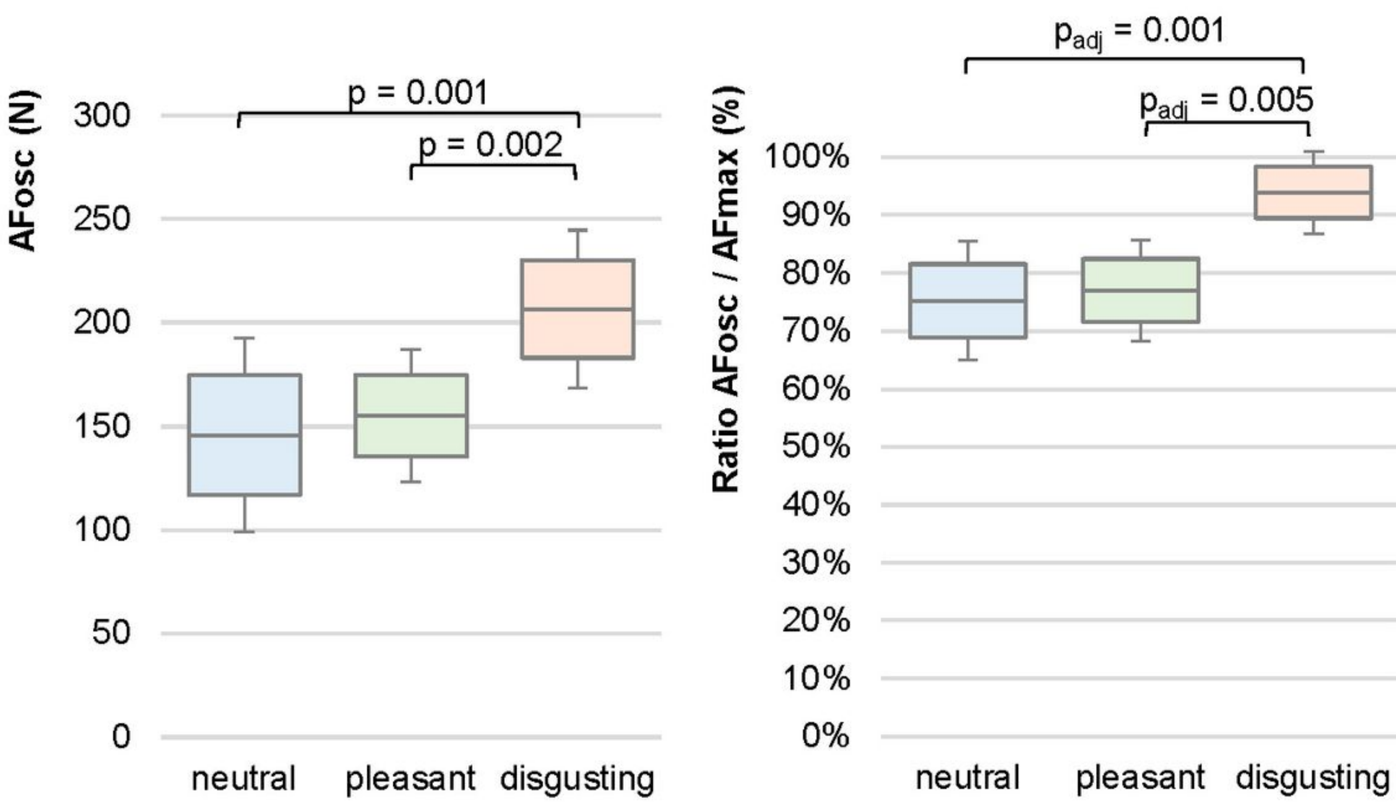

Figure 7

Adaptive Force at onset of oscillations. Displayed are the arithmetic means, standard deviations (error bars) and 95%-CIs of (A) the Adaptive Force at the moment of onset of oscillations (AFosc) and (B) the ratio of AFosc to AFmax comparing the different odors neutral (blue), pleasant (green) and disgusting (orange). The p-values of significant comparisons are given.

Supplementary Files

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- SupplementaryAFolf.pdf