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Grasping Social Apathy: The Role of Reach-To-Grasp Action Kinematics for the Assessment of Social Apathy in Mild Neurocognitive Disorders

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Abstract.

Background: Social apathy, a reduction in initiative in proposing or engaging in social activities or interactions, is common in mild neurocognitive disorders (MND). Current apathy assessment relies on self-reports or clinical scales, but growing attention is devoted to defining more objective, measurable and non-invasive apathy proxies.

Objective: In the present study we investigated the interest of recording action kinematics in a social reach-to-grasp task for the assessment of social apathy.

Methods: Thirty participants took part in the study: 11 healthy controls (HC; 6 females, mean age = 68.3 ± 10.5 years) and 19 subjects with MND (13 females, mean age = 75.7 ± 6.3 years). Based on the Diagnostic Criteria for Apathy, MND subjects were classified as socially apathetic (A-MND, $N = 9$) versus non-apathetic (NA-MND, $N = 10$). SensRing, a ring-shaped wearable sensor, was placed on their index finger, and subjects were asked to reach and grasp a can to place it into a cup (individual condition) and pass it to a partner (social condition).

Results: In the reach-to-grasp phase of the action, HC and NA-MND showed different acceleration and velocity profiles in the social versus individual condition. No differences were found for A-MND.

Conclusion: Previous studies showed the interest of recording patients' level of weekly motor activity for apathy assessment. Here we showed that a 10-min reach-to-grasp task may provide information to differentiate socially apathetic and non-apathetic subjects with MND, thus providing a tool easily usable in the clinical practice. Future studies with a bigger sample are needed to better characterize these findings.

Keywords: Apathy, diagnosis, intention, motivation, motor activity, neurocognitive disorders, social behavior, social isolation

INTRODUCTION

Apathy is a clinical syndrome characterized by a reduction in self-initiated, goal-directed activity, which is not driven by primary motor or sensory

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impairments, or other comorbidities such as drug intoxication or intercurrent illness [1–4]. Apathy represents the most common behavioral and psychological symptom in people with Alzheimer's disease (AD) [5] and is prevalent in other neurological and neurocognitive disorders, such as Parkinson's disease (PD), vascular dementia, mild cognitive impairment (MCI), stroke, traumatic brain injury, amyotrophic lateral sclerosis, small vessels disease, and frontotemporal dementia, as well as in psychiatric diseases such as major depression and schizophrenia [6]. The presence of apathy significantly affects the patient's quality of life and the caregiver's burden [7, 8]. In neurocognitive disorders (ND), apathy can appear at the early stages of the disease progression [9] and is more frequent in amyloid-β positive patients [10]. The presence of apathy is associated with a faster cognitive and functional decline [11], representing a risk factor for the AD conversion in patients with MCI [12–14], and for dementia conversion in patients with small vessels disease, even after controlling for the effects of depression, age, cognition, and education [15]. Critically, preliminary evidence suggests that interventions targeting apathy in people with MCI (through repetitive transcranial magnetic stimulation, rTMS) may be effective to improve the global cognitive functioning [16], thus suggesting that identifying apathy early in disease progression—and putting in place early treatment options—could offer new opportunities for dementia prevention [17].

Apathy is a multi-componential syndrome and can be manifested across different dimensions [1, 18]. These include: behavior (e.g., reduced level of activity at home or work, or difficulty to accomplish tasks spontaneously, without being prompted); cognition (e.g., reduced interests in leisure activities, news or personal health and wellbeing); emotions (e.g., reduced feelings and emotional expressions in response to self- or other-related events); and social interactions (e.g., reduced social relationships with family and friends, homebound). There is evidence that the various apathy domains can be differently impaired over the time-course of different diseases, such as PD, AD, and frontotemporal dementia [19, 20], and that they contribute differently to individual cognitive profiles [21]. While the behavioral, cognitive, and emotional dimensions of apathy had been previously identified and extensively investigated in clinical ND (see [6, 19] for reviews), social apathy—the loss of social motivation—has been only recently recognized as a separate apathy dimension [1, 18, 22]. A preliminary study [23] suggested that social apathy is present in 25% of patients with mild neurocognitive disorders (MND, characterized by cognitive/behavioral impairment that does not affect the patient's autonomy in activities of daily living), and 77% of patients with major ND (presenting cognitive/behavioral decline that impairs autonomy), suggesting a high prevalence in the ND population. Furthermore, studies on healthy participants and patients with ND suggest that social apathy is separable from the cognitive/behavioral and emotional apathy dimensions [22–25].

Today, apathy assessment is mainly performed employing clinical scales and interviews based on the clinician's, caregiver's or patient's reports [26]. A self-report scale, the Apathy Motivation Index (AMI), has been recently developed to assess social motivation and social apathy in the adult population [22, 27], thus allowing for a direct social apathy screening. However, questionnaires and interviews may suffer from subjectivity and self-report biases. Indeed, self-report may be biased in patients suffering from cognitive impairment: questions revolve around the behaviors, interests, emotions, and social interactions experienced in the last weeks, so responses heavily rely, among others, on episodic memory and self-awareness, which are commonly impaired in patients with ND [28, 29]. The diagnostic criteria for apathy and the clinical scales administered by clinicians to patients and caregivers represent today the gold standard for apathy assessment [18, 26, 30]. However, also these scales are intrinsically subjective, and depends on the quality and quantity of information available [31], thus making apathy assessment, including the assessment of social apathy, strongly clinician-dependent. For these reasons, growing attention is devoted to developing non-invasive, objective, affordable, and reliable solutions to complement the classical clinical assessment, to provide clinicians with additional information to refine apathy diagnosis [17, 18]. As apathy is a multi-componential syndrome that manifests across emotional, behavioral, social (verbal and non-verbal), and cognitive impairments, no index, in isolation, can capture apathy as a whole. Rather, the idea is to find a number of objective indexes that capture different apathy aspects and dimensions and can be used, combined together and with the classical clinical assessment, to improve objective apathy assessment [32]. In this context, new technologies are offering novel opportunities to develop customizable and easy-to-use instruments allowing to quantify not only cognitive performance but also neuropsychiatric symptoms [18, 31].

Specifically, there is evidence that new technologies and sensors such as eye-tracking [33], tablet applications [34], automated speech analysis [35], and automated video analysis [36, 37] can provide relevant information to improve apathy assessment in ND. One of the most studied apathy proxies in ND is the global level of activity, assessed during long timeframes (e.g., one week) using actigraphy [38–40]. Indeed, results suggest that apathetic patients show a decreased daytime motor activity [38, 39] and more sleep disturbances [39] compared to patients without apathy. Despite alterations of the global level of activity are not specific of apathy (they are present in other disorders, such as major depression [41] and catatonic schizophrenia [42]), they are considered a reliable index to complement apathy assessment in patients with ND [39]. However, measuring the level of activity during a long timeframe to assess apathy is not always feasible in clinical practice.

In the present study, we investigated if assessing motor parameters during a short reach to grasp protocol using a non-invasive wearable device can provide relevant information to distinguish socially apathetic versus non-apathetic subjects with MND, thus providing additional elements for the assessment of the non-verbal aspects of social apathy in this population. The idea to employ this research protocol for social apathy assessment derived from three considerations. First, in healthy controls, action kinematics are sensitive to the social versus individual context in which the actions take place. Several previous studies showed that social intentions can influence action planning and execution: if we grasp an object to hand it to someone (social intention), the kinematics of the reach to grasp action is different from what observed when grasping the object to put it on a base (individual action), even if the object and its initial and final positions are exactly the same [43–47]. Specifically, both the kinematics of the reach-to-grasp phase (amplitude of maximum grip aperture and the speed at which the hands open, and movement smoothness) and the place phase (point of maximum trajectory height, peak velocity and time to peak velocity, movement smoothness) indicate a more careful approach in the social condition compared to the individual condition, thus suggesting a modulation of action kinematics based on the prior intentions. Second, this modulation of action kinematics based on the social versus individual context seems disrupted in patients with impairments, among others, in social motivation, such people with PD. Straulino and colleagues [48, 49] employed the very same paradigm of reach-to-grasp actions in individual versus social action context in patients with PD, well known to have both motor and motivational problems related to apathy, with a very high prevalence of social apathy [24]. They found that, while healthy controls and the PD patients in an 'on' l-Dopa medication state adopted different kinematic patterning for the social and the individual conditions, the PD patients in the 'off' medication state were unable to kinematically differentiate between the two conditions. Even though social apathy was not directly assessed in these studies, these results suggest that l-Dopa treatment, which is known to improve both motor symptoms and apathy [6], had positive effects on translating social intentions into specific motor patterns in PD patients, thus suggesting that apathy-related circuits may impact modulation of social action kinematics. Third, action planning and control mechanisms implied in goal-directed reach-to-grasp motor sequences are largely overlapping with those of motivated behavior [6, 50–54]. Indeed, both the modulation of reach-to-grasp planning and execution based on prior intentions and motivated behavior relies on a complex neural network of interconnected structures in the parietal and frontal lobes and is modulated by the activity of the dopaminergic system [50–55]. Dysfunctions in these networks can lead to deficits in motor planning and execution, and apathy in several different pathological conditions [6, 55].

In order to verify whether modulation of action kinematics in a social versus individual context may be used to implicitly assess basic, non-verbal aspects of social apathy in ND, here we investigated whether older healthy adults and patients with MND with and without social apathy modulated action kinematics based on the social versus individual intentions. Employing the previously described paradigm, subjects were asked to reach and grasp an object in two conditions: an individual condition, in which the object was grasped and then placed in a cup; and a social condition, in which the object was grasped and then passed to the experimenter. Instead of using the classical optoelectronic motion-capture systems, here we asked subjects to wear on the index finger of their dominant hand the SensRing, a newly developed wearable device [46, 47] which is non-invasive and easy to use, and thus more usable in clinical, non-laboratory settings. Given the action planning and control required in simple, natural gestures such as object grasping is usually preserved in people with MND [56], we expected only minor differences between healthy controls and subjects with MND in baseline action kinematics, except for reaction times, which are known to be longer in apathetic subjects [2]. Based on previous studies comparing individual versus social action kinematics, we hypothesized that significant difference between the individual and the social condition could be found in movement velocity [43, 45] and acceleration/smoothness profiles [46, 47] in both the reach-to-grasp and the place phases in healthy elderly controls, confirming the presence of action modulation based on the type of intention. We expected to find a similar action modulation also for non-apathetic MND subjects, as basic action planning is usually preserved [56]. Critically, we hypothesized that, similarly to people with PD [48, 49], kinematic action modulation may be impaired in apathetic MND subjects, resulting in fewer differences in action kinematics (movement velocity and acceleration/smoothness) between the individual and the social condition, especially in the reach-to-grasp phase, which is identical between the individual and the social conditions.

MATERIALS AND METHODS

Participants

Thirty participants took part in the study. These included 11 older healthy controls (HC; 6 females and 5 males, mean age = 68.3 ± 10.5 years) and 19 subjects diagnosed with MND based on the DSM-5 [57] (13 females and 6 males, mean age = 75.7 ± 6.3 years; see Table 1). All participants reported to be right-handed. Participants were recruited at the Memory Center (CMRR) of Nice University Hospitals (CHU of Nice, France) and at the CoBTeK research lab of the Université Cote d'Azur in the context of Marco-Sens multi-centric research protocol. Participants with MND were recruited in a 2-month timeframe among the patients followed at the Nice Memory Center. The study was proposed to all the patients meeting the study inclusion/exclusion criteria. All the patients that accepted to take part in the study were enrolled. Participants were not included if they had sensory or motor impairments interfering with the protocol completion, a score at the Mini-Mental State Examination (MMSE) < 22 [58], a Frontal Assessment Battery (FAB) score lower than 11 [59], and if they were diagnosed with major depression (and/or they were under antidepressant medication), PD, or other conditions associated to motor impairments. Healthy controls were recruited at the CMRR among the patients' caregivers, subjects that came for a consultation but had no sign of cognitive impairment, and CMRR personnel. A brief screening (including the MMSE) was performed to ascertain the absence of any cognitive decline. The study was performed in compliance with the Declaration of Helsinki and was approved by the National Ethical Committee - Comité de Protection des Personnes - on 15/04/2019 (N° ID RCB: 2019–A00342-55). All participants received detailed written explanations on the study aims and procedures and provided their informed written consent before taking part in the study.

Clinical assessment

Based on the Diagnostic Criteria for Apathy [18], participants in the MND group were classified as 'socially apathetic' (A-MND; criterion "B3 - Social Interaction" present, N = 9) and 'socially non-apathetic' (NA-MND; criterion "B3 – Social Interaction"

Table 1
Socio-demographic and cognitive variables in healthy controls (HC), participants with minor neurocognitive disorders without social apathy (NA-MND), and participants with minor neurocognitive disorders with social apathy (A-MND). The presence of apathy was assessed based on the Diagnostic Criteria for Apathy, social dimension (B3; [18])

	HC ($n = 11$)	NA-MND ($n = 10$)	A-MND ($n = 9$)	p
Female, n (%)	6 (54.5%)	7 (70.0%)	6 (66.7%)	0.741^b
Age (y), mean ± SD	68.3 ± 10.5	74.2 ± 7.2	77.4 ± 4.9	0.120^a
Level of education, n (%)				0.628^b
Primary	1 (9.1%)	1 (10.0%)	0 (0.0%)	
Secondary education	3 (27.3%)	5 (50.0%)	5 (55.6%)	
Higher education	7 (63.6%)	4 (40.0%)	4 (44.4%)	
MMSE, mean ± SD	29.3 ± 0.9	26.4 ± 2.9	25.6 ± 3.0	**0.007^a**
AMI – Total score	1.2 ± 0.4	1.0 ± 0.4	1.6 ± 0.4	**0.012^a**
AMI – Social Motivation	1.4 ± 0.7	1.1 ± 0.5	2.2 ± 0.6	**0.001^a**
AMI – Behavioral Activation	1.1 ± 0.6	0.7 ± 0.4	1.6 ± 0.9	0.059^a
AMI – Emotional Sensitivity	1.4 ± 0.6	1.2 ± 0.5	1.1 ± 0.5	0.349^a

MMSE, Mini-Mental State Examination; AMI, Apathy Motivation Index. ^{a}Kruskal-Wallis test. $^b\chi^2$ test.

absent, N = 10). For all participants, the level of apathy was assessed through the AMI, an 18-item self-report scale developed to quantify apathy in the healthy population [22].

Instrument

SensRing is a ring-shaped wearable device, worn on the proximal phalanx of the index finger, able to fully track the orientation and movement of the finger (Fig. 1). It is characterized by a 9-axes inertial measurement unit (IMU) LSM9DS1 (STMicroelectronics, Italy), which includes a 3D digital linear acceleration sensor (full scale: ±2/±4/±8/± 16 g), a 3D digital angular rate sensor (full scale: ±245/ ±500/±2000 dps) and a 3D digital magnetic sensor (full scale:±4/±8/±12/±16 gauss). It is based on an ARM®Cortex™-M3 32-bit STM32-F103 microcontroller (STMicroelectronics, Italy) which acquires, filters and stores data at a frequency of 50 Hz. Further details about the instrument can be found in [46, 47].

The reach-to-grasp task and procedures

The subjects were asked to wear SensRing on the proximal phalanx of the index finger of the right (dominant) hand. Participants were sitting in a quiet room, in front of a rectangular table with the hand in the starting position marked with a blue rectangle, 3 cm away from the edge of the table in a midsagittal position, 15 cm away from the midsection. A closed 150 ml drink can (diameter = 5 cm, height = 8.5 cm) was positioned on the table in front of the participant at 21 cm from the hand starting position along the midsagittal plane (object position marked with a yellow square). After 5 s of acquiring the baseline static position (with the wrist and little finger touching the table, hand palm facing the participant's chest, fingers slightly bent and touching the thumb), a tone signaled to the participant to start the task. Participants were asked to reach and grasp an object in two conditions, adapted from [43]. In the Individual condition (IND), subjects had to reach the can, grasp it, and put inside a cup (diameter = 7 cm), placed on the table and located 28 cm at the right side with respect to the initial position of the can (position marked with a green rectangle). The experimenter (a 25-year-old female) seated to the right side of the table with her hands hidden below the table (see Fig. 1a). In the Social condition (SOC), subjects had to reach the can, grasp it, and pass it to a partner. The experimenter, who was also the action partner, seated to the right side of the table with the hand resting on the same target position as in the IND condition (wrist on the table, with fingers simulating a concave shape similar to the cup) ready to close the fingers to grasp the can when it reached the hand (see Fig. 1b). The experimenter's hand was completely still until the object reached it. When the subject put the object in the hand, the experimenter closed their fingers to grasp it. The experimenter's hand never moved from the target position, and her fingers closed to grasp the object only at the very end of the action, to simulate a natural 'receiving the object' action. In both conditions, each action sequence was repeated 10 times. So, overall, each subject performed 20 trials, for a total duration of approximately 5 to 10 min. After each trial, the experimenter repositioned the can on its initial position. The order of administration of the IND and SOC conditions was randomized across participants.

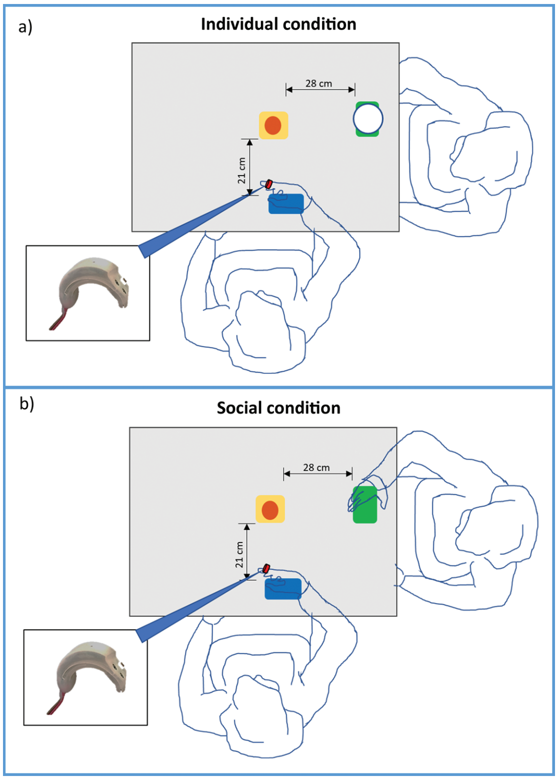

Fig. 1. Schematic representation of the experimental setup. The subject wore the SensRing on the proximal phalanx of the index finger of the dominant hand. The subject sat in front of a rectangular table with the hand in the starting position. Prompted by an auditory cue, he/she reached and grasped a drink can in two conditions. In the Individual condition (a), he/she grasped the can and put inside a cup. In the Social condition (b), he/she grasped the can and passed it to a partner. The position of the hand of the experimenter and the cup was identical.

Data analysis

Clinical and demographic data

Descriptive statistics were used to present demographic and clinical characteristics. Sex and level of education (qualitative variables) were presented using frequency and percentage, and age, MMSE, and scores at the AMI (quantitative variables) were presented using mean and standard deviation (SD). Qualitative variables were compared using Chi² test. Quantitative variables were compared using the Kruskal-Wallis test, with LSD corrected *post-hoc* paired comparisons.

Motion data

Inertial data acquired with SensRing were stored and offline processed by using MATLAB R2018a (The MathWorks, Inc., Natick, MA, USA). Triaxial accelerations and triaxial angular velocities, provided by the accelerometer and gyroscope, were pre-processed with a fourth-order low-pass digital Butterworth filter using a 5 Hz cut-off frequency to erase high-frequency noise. Custom made algorithms were applied to extract characteristic times aimed to distinguish between the reaching phase (RG), from the beginning of the action to the grasping of the object, and a placing phase (PL) from the grasping of the object to reaching the final position. Precisely, angular rates around the dominant axis were used to divide the signal. For each trial, a set of kinematic parameters was obtained from acceleration and angular velocities of the SensRing (see). All the kinematic parameters were calculated both in the RG and the PL phases, except for the reaction time, and the amplitude and the time of maximum hand excursion that were measured during RG phase only. In total, 15 features were extracted for each trial (9 for the RG, 6 for the PL phase) (see). Some kinematic parameters were chosen because they may be relevant to investigate differences in the baseline motor performance between healthy controls and MND subjects, such as reaction time, execution times and movement duration [48, 60, 61]. Other parameters were selected because, as previously demonstrated, they are sensitive to variations in the action context (social versus individual), such as the amplitude of peak velocity during both the RG and the PL phases, with the corresponding time instant, the amplitude of maximum aperture of the hand during the reaching phase with its associated time instant [43, 45], and the movement smoothness and variability [46, 47] in the RG and PL phases.

Data were expressed as mean ± SD for all the conditions. As the data were not normally distributed (according to Kolmogorov–Smirnov tests), and due to the small sample size, non-parametric analyses were employed. As it was not possible to analyze simultaneously within- and between-subject effects using non-parametric analyses, data were submitted to two separate analyses: a) inter-group analysis to study the effect of the group using Kruskal-Wallis one way ANOVA, followed by LSD corrected *post-hoc* paired comparisons; b) intra-group analyses, to investigate significant differences between the two experimental conditions (IND, SOC) in each group (HC, A-MND and NA-MND) using paired-sample Wilcoxon test.

For all the analyses, a p-value ≤ 0.05 was considered as statistically significant. Statistical analyses were performed using IBM SPSS Statistics 20.0.0 version and MATLAB R2018a (The MathWorks, Inc., Natick, MA, USA) to compute non-parametric *post-hoc* corrected tests and non-parametric partial correlations.

RESULTS

Clinical and demographic characteristics

Clinical and demographic characteristics of apathetic MND (A-MND), non-apathetic MND (NA-MND), and HC are presented in Table 1. Participants in the three groups did not differ in terms of age ($\chi^2_{(2)} = 4.24$, $p = 0.120$), gender ($\chi^2_{(2)} = 0.60$, $p = 0.741$), and education ($\chi^2_{(4)} = 2.60$, $p = 0.628$). Significant differences were found on the global level of cognitive functioning, as revealed by the MMSE score (Kruskal-Wallis $\chi^2_{(2)} = 10.02$, $p = 0.007$). Specifically, significant differences between HC and subjects with MND (NA-MND, $p = 0.003$; A-MND, $p = 0.020$) were found, but not between subjects with NA-MND and A-MND ($p = 0.592$). Similarly, NA-MND and A-MND groups did not differ concerning the global level of impairment in executive functions, as revealed by the FAB scores (Mann-Whitney $U_{(2)} = 40.5$, $p = 0.731$). Significant differences across groups were found on the AMI total score ($\chi^2_{(2)} = 8.85$, $p = 0.012$) and AMI-Social Motivation subscale score ($\chi^2_{(2)} = 13.15$, $p = 0.001$). Specifically, as expected, A-MND showed higher apathy scores compared to NA-MND (AMI – Total score, $p < 0.001$; AMI – Social Motivation, $p = 0.003$) and HC (AMI – Total score, $p = 0.011$; AMI – Social Motivation, $p = 0.042$). No differences in apathy scores were found between NA-MND and HC

Table 2

Kinematic parameters extracted from SensRing

Variable	Parameter	Phase
RmseJ	Root mean square of the rate of change of the acceleration: its value represents the smoothness of the movement (m/s^3).	RG, PL
Skew	Skewness of the acceleration: it measures the asymmetry of the distribution.	RG, PL
Kurt	Kurtosis of the acceleration: it measures the shape of the tail of the distribution.	RG, PL
T	Execution time spent to perform the movement (s).	RG, PL
V_{peak}	Amplitude of peak velocity (m/s).	RG, PL
T_{Vpeak}	Time of peak velocity: it is the time instant corresponding to the peak velocity (s).	RG, PL
RT	Reaction time: it is the elapsed time from the beep to starting the movement (s).	RG
Exc	Hand excursion: it is the amplitude of the maximum angular excursion of the hand during the grasping of the object (deg).	RG
T_{exc}	Time of maximum excursion: it is the time instant corresponding to the maximum hand excursion (s).	RG

(AMI – Total score, $p = 0.266$; AMI – Social Motivation, $p = 0.233$). For participants in the A-MND group, impairment in social interaction dimension (B3 in the Diagnostic Criteria for Apathy) was associated to impairment in the B1 dimension (Behavior/Cognition) in 4 participants, and with impairments in B2 dimension (Emotion) in 1 participant, for a total of 5 out of 9 participants that meet the full set of Diagnostic Criteria for Apathy [18].

Movement-related parameters

Intergroup analyses

In subjects with MND, motor impairments are much less common than in PD, and we excluded from the study participants with motor problems (see Participants section). However, there is evidence that advanced motor parameters reflecting motor planning and control may vary between healthy subjects and people with cognitive impairment, for instance in the context of dual tasks [56]. In order to investigate the existence of baseline differences in the motion-related parameters across groups in a reach-to-grasp task, we submitted each extracted parameter in the two experimental conditions to separate between-subject analyses.

For the *individual condition,* the comparison between the three groups revealed a significant effect of the group on the skewness of the reach-to-grasp phase (*Skew*, $\chi^2_{(2)} = 7.44$, $p = 0.024$; see Fig. 2). Specifically, skewness was significantly higher in the HC compared to A-MND participants ($p = 0.007$), that get a negative value of skewness, indicating a wider variability for the acceleration vector in performing the movement with respect to the more symmetrical distribution shown by HC subjects. Comparisons between NA-MND and HC, and between NA-MND and A-MND were not statistically significant. A significant difference across groups was also found in reaction times (*RT*, $\chi^2_{(2)} = 6.49$, $p = 0.039$), with A-MND participants being significantly slower than HC ($p = 0.041$). This is in line with the apathy literature suggesting that apathetic patients have often deficits in action initiation [2].

For the *social condition,* the only significant difference across groups was the time of peak velocity

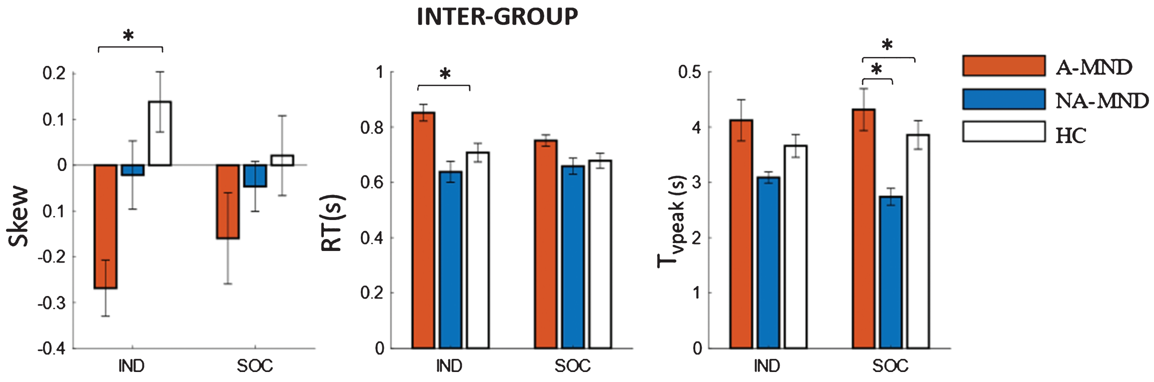

Fig. 2. Graphical representation of significant parameters (*$p < 0.05$) at the inter-group analysis (A-MND, NA-MND, HC) for two conditions (IND, SOC). Error bars represent the standard error of the means.

in the place phase (*Tvpeak*, $\chi^2_{(2)} = 7.14$, $p = 0.028$), which was significantly higher for A-MND, indicating a sharper movement with respect to both HC and NA-MND, that seems to better modulate the action.

Intra-individual analyses

Previous studies on healthy subjects showed that the action kinematics in a social condition (passing an object to someone) are different from those in an individual condition (putting the object on a base), in both the reach-to-grasp and place action phases [43, 44]. This is the case also in PD subjects in an 'on l-Dopa' medication state. However, when PD subjects are 'off l-Dopa' medication state, no differences in action kinematics can be found between the individual and the social conditions [48, 49]. To explore the existence of differences in the kinematic parameterization depending on whether the action was performed with the intent of acting individually or socially, we compared the 15 kinematic parameters (listed in) in the individual versus social condition in each group in both the reach-to-grasp phase (which is identical in the two conditions) and the place phase (in which the experimenter's hand and the cup pose slightly different action constraints). Correlations among the different kinematic variables are reported in the Supplementary Material (Supplementary Tables 1–4).

Reach-to-grasp phase

In the HC group, paired-sample Wilcoxon test showed significant differences between the individual and the social condition concerning the root mean square of the jerk, which is the rate of change of the acceleration vector (*RmseJ*, Wilcoxon $Z = -2.22$, $p = 0.026$), and the amplitude of peak velocity (*Vpeak*, $Z = -2.22$, $p = 0.026$, see Fig. 3). Specifically, converging with previous findings, both acceleration and velocities were higher in the individual versus the social condition, suggesting a more careful approach when grasping the object to handle it to another person. No other significant differences were found. In the NA-MND group, a significant difference between conditions was found for the time of peak velocity (*Tvpeak*, $Z = -2.30$, $p = 0.022$), which was anticipated in the social versus the individual condition. This implies a longer deceleration phase for the social condition, thus a more careful action when passing the object into the partner's hand. The only significant difference between the individual and the social condition for A-MND was reaction time (*RT*, $Z = -2.38$, $p = 0.017$), which was longer in the individual versus social condition.

Place phase

In the HC group, significant differences were found on the rate of change of the acceleration vector (*RmseJ*, $Z = -2.76$, $p = 0.006$), and the kurtosis (*Kurt*, $Z = -2.85$, $p = 0.004$), as well as on peak velocity (*Vpeak*, $Z = -2.93$, $p = 0.003$; see Fig. 4). Thus, similarly to the reach-to-grasp phase, both acceleration and velocity were higher in the individual condition compared to the social condition, again

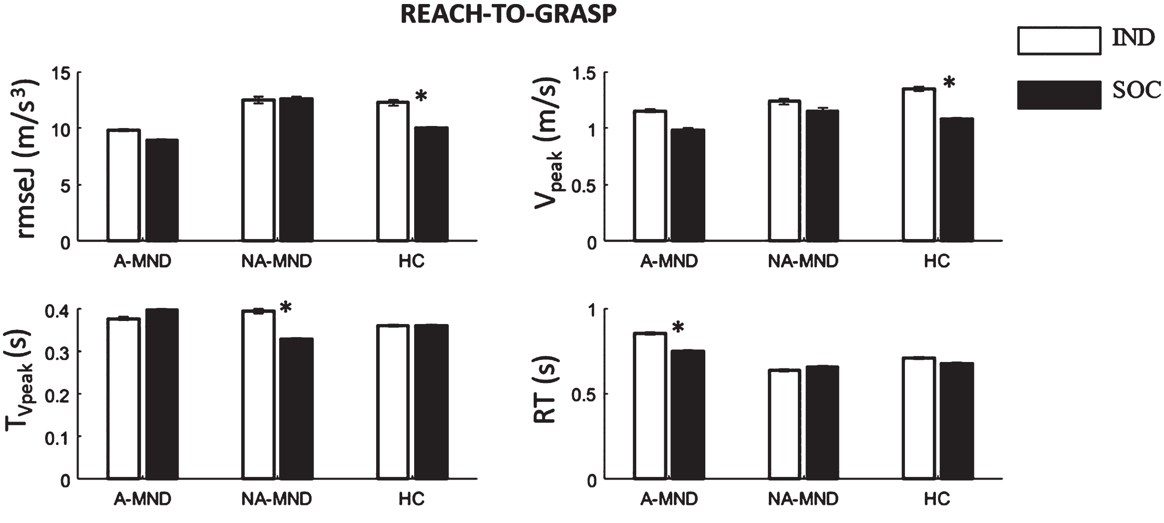

Fig. 3. Graphical representation of significant parameters ($*p < 0.05$) at the intra-group analysis (IND, SOC) for the three groups (A-MND, NA-MND, HC). The reported parameters refer to the reach-to-grasp phase. Error bars represent the standard error of the means.

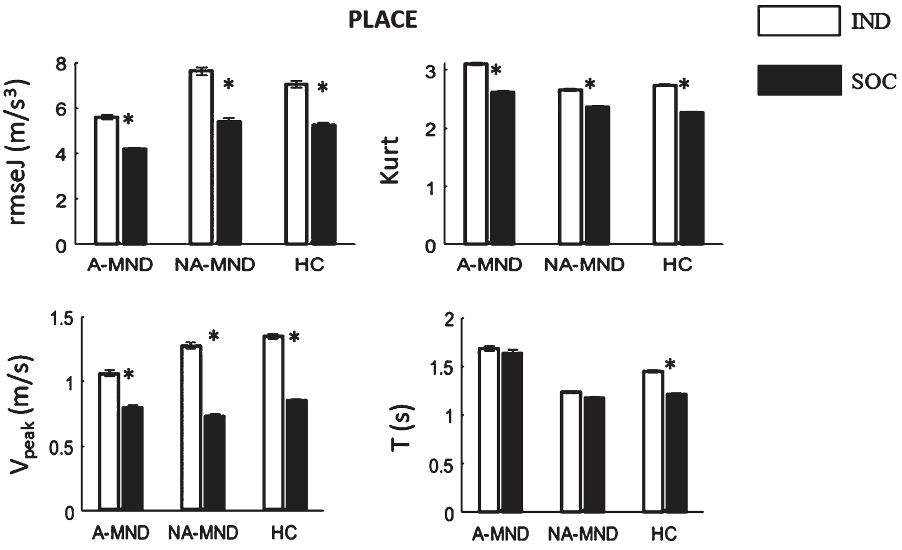

Fig. 4. Graphical representation of significant parameters ($^*p < 0.05$) at the intra-group analysis (IND,SOC) for the three groups (A-MND, NA-MND, HC). The reported parameters refer to the place phase. Error bars represent the standard error of the means.

suggesting a more careful approach when handing the object to another person. However, the total execution time was longer in the individual compared to the social condition (*T*, $Z = -2.31$, $p = 0.021$). This is most probably due to the fact that the object final position (the cup) required a more precise gesture for object positioning compared to passing the object to the partner, who closed the hand to grasp the object when it touched her hand. Similar results for acceleration and velocity where found for NA-MND participants, showing higher rate of change of the acceleration vector (*RmseJ*, $Z = -2.70$, $p = 0.007$), kurtosis (*Kurt*, $Z = -2.60$, $p = 0.009$) and peak velocity (*Vpeak*, $Z = -2.80$, $p = 0.005$) in the individual compared to the social condition. In the place phase, significant differences on the same parameters were also found for A-MND participants, who showed a higher rate of change of the acceleration vector (*RmseJ*, $Z = -2.07$, $p = 0.038$), kurtosis (*Kurt*, $Z = -2.31$, $p = 0.021$) and peak velocity (*Vpeak*, $Z = -2.55$, $p = 0.011$) in the individual compared to the social condition. Intergroup analyses suggested that the mean differences between individual and social condition regarding the amplitude of peak velocity were significantly different across groups ($\chi^2_{(2)} = 10.56, p = 0.005$). Specifically, differences in peak velocity between conditions were significantly bigger for HC ($p = 0.003$) and NA-MND ($p = 0.008$) compared to A-MND. No significant difference in the magnitude of any acceleration parameter across groups was found (all ps > 0.05).

DISCUSSION

Social apathy, a reduction in initiative in proposing or engaging in social activities or interactions, is very common in people with ND [23], and few clinical scales exist so far to assess this component [22, 62]. It is thus important to develop a number of rapid, objective assessment tools easily usable in the clinical practice to complement the classical evaluation. In the present study, we showed the interest of measuring action kinematics during a 10-min reach-to-grasp social task to provide information on basic non-verbal aspects of social apathy in subjects with MND. Participants were asked to grasp a drink can to put it in a cup (individual condition) or pass it to a partner (social condition) [43, 48], and action kinematics were measured during both the reach-to-grasp and the place phases with a wearable device [46, 47]. Prior social intentions can shape the way we perform actions: when grasping an object to pass it to another person, the action kinematics of both the reach-to-grasp and the pass phases are different from those observed when grasping the same object to put it in a container [43]. Converging with these previous findings [48] and our hypotheses, the results of intra-group analyses suggested that (HC) and NA-MND subjects differentiated, at the kinematic level, individual from social reach-to-grasp actions both in the 'reach-to-grasp phase', and in the 'place phase'. Specifically, in the reach-to-grasp phase, HC and people with NA-MND showed a more careful approach in the social versus the individual condition, characterized by lower acceleration and peak velocity in HC, and by a delayed time of peak velocity in NA-MND. Similar results were found for HC and NA-MND in the 'place' phase, with acceleration and peak velocity higher in the individual condition compared to the social condition, again suggesting a more careful approach when handing the object to another person. And this was observed even though putting the object into the cup may be more demanding, in terms of action control, than putting the same object into the partner's hand (as also testified by longer total movement time, in the 'place' phase, in the individual versus the social condition in HC). Indeed, as the experimenter closed her fingers to grasp the object after the subject put it in her hand, the placing action could be slightly less precise in the social condition compared to the individual condition, in which the subject was the only responsible for placing the object in the final position. Critically, A-MND subjects did not show any difference in the acceleration and movement profiles in the reach-to-grasp phase, suggesting that movements were unaffected by social intentions. The only significant difference between the individual and the social condition for A-MND was reaction time, which was longer in the individual versus social condition. This suggests that people with social apathy took longer to initiate the action in the individual condition, which could be possibly due to higher demands in action control in the object positioning, requiring a more careful action planning before action initiation. Significant differences between the individual and the social conditions were observed for A-MND in the 'place' phase, with lower velocity and acceleration profiles in the social compared to the individual condition. These differences were also found in HC and NA-MND; however, differences in peak velocity between the individual and the social condition were significantly bigger in HC compared to A-MND, suggesting that action modulation based on social intentions in the place phase, even if present in A-MND, was smaller than in HC. The reduced modulation of action kinematics in A-MND subjects converges with results collected using the same experimental paradigm in PD patients. Indeed, PD patients in the 'off' l-Dopa medication state were found to be unable to kinematically differentiate between individual and social conditions [48, 49]. Given that PD patients show motor impairments and apathy, and that both symptoms are sensitive to l-Dopa medication, in PD patients it is hard to disentangle the roles of apathy and basic motor impairment on kinematics modulation. People with MND show apathy symptoms in a similar degree compared to PD patients, but motor impairments are less common [23], thus representing an interesting condition to assess the role of apathy on action kinematics.

In terms of basic motor performance, inter-group analyses showed very few differences between HC and subjects with ND in terms of action velocity, smoothness, and duration. Specifically, similarly to previous studies [2] socially apathetic subjects (A-MND, based on the Diagnostic Criteria for Apathy – Social Interaction dimension [18]) were slower compared to HC and NA-MND to initiate the action in the individual condition. Furthermore, A-MND showed more variability in acceleration than HC when reaching the object in the individual condition, suggesting less smooth movements. Finally, in the social condition, peak velocity was reached later for A-MND, indicating sharper movements with respect to both HC and NA-MND. No main differences between groups were found for action duration, indicating that HC and subjects with MND had a quite similar motor performance in basic reach-to-grasp action sequences. It is likely that more differences in basic kinematic parameters would have been observed using more complex and/or unusual action sequences (e.g., speeded finger tapping), or using task requiring higher cognitive load, as those employed in dual-task paradigms [56].

Taken together, these results suggest that a 10-min reach to grasp protocol employing a wearable, easy to use, and minimally invasive sensor could be informative for apathy assessment in people with MND. Specifically, employing the SensRing sensor, parameters linked to the amplitude of the peak velocity and the smoothness of the movement may be particularly relevant to detect the presence or absence of kinematic modulation in the individual versus social conditions in the reach-to-grasp phase. Coupled with the assessment of other symptoms, such as reduced verbalizations, reduced social initiatives, and homebound, the reduction in kinematics modulation may thus contribute to refining social apathy assessment.

There is evidence that age-related changes in reach-to-grasp action kinematics can occur [46, 63]. However, as participants in the HC, NA-MND, and A-MND groups were balanced in terms of demographic characteristics (age, sex, and education), our findings cannot be completely explained by age-related changes in motor planning and control. Similarly, as NA-MND and A-MND participants had a similar impairment in global cognitive functioning (as indexed by the MMSE [58]) and in executive functions (as indexed by the FAB [59]), the reduced modulation in action kinematics in A-MND participants is not completely due to cognitive deterioration. As apathy was the main feature differentiating participants in the three groups, we believe that differences in kinematic parameters between the individual and the social condition may reflect differences in social apathy profiles.

Limitations and future research directions

Despite these promising results, several limitations of the present study should be noted. The first and more important is the small sample. It is possible that, for instance, including a bigger number of apathetic participants, more differences between the individual and the social conditions would have been found. Furthermore, a bigger sample would have allowed analyzing correlations between apathy scales and kinematic parameters, and to analyze simultaneously intra-group and inter-group effects, as well as their interactions, thus allowing to significantly reduce Type I errors. Future studies could use the present results to estimate the expected effect size and compute a power analysis to estimate the optimal sample size. Second, the wearable sensor we employed (SensRing), positioned on the index finger, allowed us to collect only data concerning angular acceleration and velocity of the hand. However, it did not allow to collect precise data on the finger movements (such as the amplitude of the maximum grip aperture), and spatial trajectories (such as the maximum height of the wrist trajectory from the working surface, or the length of the wrist pathway), that were found to be sensitive to social intentions in previous studies [43, 48, 64]. Future studies should investigate the interest of combining SensRing with other non-invasive sensors, such as RGBD cameras, to integrate position related data in the analyses. Third, despite trying to make the individual and the social conditions as similar as possible, they slightly differed concerning the precision required for the object positioning (in the cup versus the hand). In the next studies, it would be important to make the two conditions even more comparable, for instance by employing a larger concave base (replacing cup) and a lighter object that can be put on the hand palm without falling. Finally, precisely assessing participants' baseline motor ability may help to disentangle the effects of apathy from basic motor skills, and to explore their relationships. Indeed, even if participants with motor impairments were not included in the study, motor abilities may show remarkable individual differences in people with MND [65]. Our between-subject analysis showed very few differences in motor performance between apathetic and non-apathetic subjects. However, in future studies with bigger samples, it would be interesting to use baseline motor ability as a covariate in the analyses, to verify whether the relationship between apathy and action kinematic modulation can be found after controlling for motor dysfunctions.

In the present study, we focused only on the social dimension of apathy. In ND, social apathy is often associated with cognitive/behavioral apathy [23]. In future studies with bigger sample size, it would be interesting to analyze simultaneously the effect of the three apathy dimensions, to understand the specific role of the social, cognitive/behavioral, and emotion dimensions in action kinematics modulation. Furthermore, in ND, apathy can be associated with other neuropsychiatric symptoms such as depression, anhedonia, and fatigue [6]. In future studies, it would be interesting to investigate correlations between all these symptoms and modulation of action kinematics in a reach-to-grasp protocol. In addition, previous findings suggest that social and emotional apathy relates to the probability to engage in prosocial behavior, with individuals less socially apathetic being more prone to make efforts to benefit the others [27, 66]. It would be interesting to investigate whether reduced social apathy and reduced modulation of social action kinematics are linked to reduced prosocial behaviors in people with MND, for instance employing effort-based tasks [27, 67]. Finally, it would be interesting to create more naturalistic action contexts in which action kinematics is combined with other non-invasive objective measures—such as automated voice analysis during verbal exchanges—to capture different, complementary aspects of social apathy.

CONCLUSIONS

When reaching an object to prepare a subsequent social action (passing) versus individual action (placing), healthy subjects, including elderly people, modulate action kinematics depending on the goal of the action sequence: despite the object to be grasped is exactly the same and in the same position, social versus individual goals translate into different movement patterns already in the reach to grasp action phase [46, 68]. The main result of the present study is that socially apathetic people with MND, contrary to healthy controls and non-apathetic people with MND, did not kinematically differentiate, when reaching and object, between individual and social actions. Whether this inability to kinematically differentiate social from individual action context is a mere consequence of social apathy or may contribute to generating it (or both), is an intriguing research question, that should be explored in future studies. In the domain of autism spectrum disorders, the literature suggests that motor anomalies may impact social functioning and prosocial behavior [69–71]. Based on motor simulation accounts [72, 73], difficulties in motor planning and control, resulting in impairments in action chains (observable, for instance, in reach-to-grasp sequences [74]) may contribute to explain deficits in interpersonal synchrony and intention understanding [75, 76], thus playing a role in explaining autism abnormalities in social interactions. Whether the link between social action modulation and social apathy is bidirectional or not, if the results of the present study are confirmed in a bigger sample, action kinematic modulation may be a non-invasive, simple and fast way to complement the classical clinical assessment with quantifiable and objective data.

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SUPPLEMENTARY MATERIAL

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