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Is there a relation between Mirror Movements and Developmental Disregard in Children with unilateral Cerebral Palsy?

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Abstract

Aim: In children with unilateral Cerebral Palsy (uCP) it was proposed that mirror movements (MMs) contribute to developmental disregard (DD), a phenomenon characterized by neglect of use of the affected hand (AH) despite preserved capacity. We aimed to test whether mirror movements (MMs) are related to DD and to clarify the relation between MMs and bimanual function.

Method: A repetitive squeezing task simultaneously measuring both hands' grip-forces was developed to assess MMs by using cross-correlation (CCC_{max}) as well as strength measures ($MM_{strength}$). DD, bimanual performance, and capacity was assessed using a validated video-observation method. Twenty-one children with uCP participated (Mdn_{age}=10.58y,IQR_{age}=10.09-12.71). Outcome measures of MMs were correlated to DD, bimanual performance, and capacity scores using Spearman's correlations (significance level:$\alpha<.05$).

Results: MMs were not related to DD. However, enhanced MMs in the less-AH were related to reduced performance (CCC_{max}: rho=-.526, p=.007; $MM_{strength:}$ rho=-.750, p<.001) and capacity (CCC_{max}: rho=-.410, p=.033; $MM_{strength:}$ rho=-.679, p<.001).These relations were only moderate (performance:$MM_{strength}$:rho=-.504,p=.010), low (capacity:$MM_{strength}$:rho=-.470,p=.016) or absent for MMs in the AH. Additionally, seven children showed stronger movements in their less-AH when actually being asked to move their AH.

Interpretation: These findings show no relation between MMs and DD, but support an association between MMs and bimanual function.

Short title

Mirror movements and developmental disregard

What this paper adds

- Mirror movements are likely not related to developmental disregard
- Mirror movements in the less-affected hand correlate with poor upper-limb function
- Mirror movements in the affected hand correlate weakly with poor upper-limb function
- In some children mirror movements might assist affected-hand movements

In some children with unilateral Cerebral Palsy (uCP) bimanual performance is more restricted than what would be expected based on the capacity of the affected hand (AH)[1,2]. These children appear to disregard their AH during typical bimanual daily activities. This lack of spontaneous daily use in combination with preserved AH capacity is frequently referred to as developmental disregard (DD)[1,3]. Next to the direct negative impact of DD on spontaneous daily functioning, the lack of use of the AH might in turn also lead to reduced upper-limb function, as movements are not being automated and neural substrates serving entire classes of behaviours might not be established during development[3].

One suggested underlying cause for DD is the persistence of mirror movements (MMs) occurring in the upper-limbs[2,4]. MMs are simultaneous involuntary movements that accompany voluntary movements of homologous muscles on the opposite side of the body[4]. For example, when one hand moves voluntarily, the other hand involuntarily performs the same action. Even though MMs are considered to be a normal feature of motor behaviour in young children due to immaturity of the central nervous system, they are known to gradually disappear during the first decade of life[5]. However, in many children with uCP these MMs are more pronounced and persistent[6]. They are observed more frequently in the less-AH (LAH) when actively moving the AH and are reported to be stronger compared to MMs in the AH [4,6].

There are two proposed mechanisms which may underlie MMs in children with uCP. First, the motor cortex of the less-affected hemisphere is controlling both hands via both contralateral projections to control the LAH and preserved ipsilateral projections to control the AH-movements, causing MMs in both, but especially the AH[7,8]. Second, widespread and bilateral cortical activation occur when actively moving the AH related to the sensorimotor impairments of this AH. This lack of interhemispheric inhibition leads to motor overflow causing MMs in the LAH[7,8,9]. MMs in the AH have thus been proposed to be indicative for one motor cortex controlling both hands[8], while MMs in the LAH might be simply explained by sensorimotor impairments of the AH.

MMs presented in the upper- limbs and their relation with upper-limb function has repeatedly been studied in children with uCP[4,9-12]. Even though results vary, they generally point towards an association between pronounced manual MMs and diminished bimanual performance[4,9,10]. However, findings are inconclusive, with some studies showing associations between diminished bimanual performance and MMs in either hand[4,10], while others only report this association for MMs in the LAH[9]. Still, the reported findings led authors to conclude that the symmetric nature of MMs hinders efficient bimanual task execution[4,9,10]. As most daily activities require asymmetrical actions of both hands (typically with the AH having a holding or stabilizing function), it was repeatedly suggested that pronounced MMs might even lead to the exclusion of the AH in spontaneous bimanual activities[2,4]. On the one hand, in the typical stabilizing function of the AH, MMs in this AH will result in difficulties in stabilising objects when performing manipulative tasks with the LAH. On the other hand, when actively moving the AH during bimanual asymmetric activities, MMs in the LAH cause a reduction in independent control of this “good hand”[2]. It has therefore been suggested that MMs in either hand contribute to the phenomenon of DD in children with uCP through a process of learned non-use[2,4,9,10.]

Although some studies explored the relation between MMs and bimanual performance while controlling for the capacity of the AH[9,10], the relation between MMs and DD has never been studied directly. By using a standardised measurement to assess DD[13], the main aim of the current study was to test if enhanced manual MMs are related to a greater degree of DD in children with uCP. Second, by using a newly developed continuous scale with which distal manual MMs in both hands are registered separately (i.e. MMs in the AH when actively moving the LAH and MMs in the LAH when actively moving the AH), we aimed to clarify the relationship between MMs in either hand and the previously reported impact on bimanual performance[4,9,10].

Method

Participants

Children and adolescents with uCP, aged 7-18 were recruited from different rehabilitation centres in the Netherlands and the UK. Inclusion criteria were diagnosis of uCP with a MACS level of I–III[14]. Many children were part of larger studies exploring neurocognitive processes, brain structures, and/or functions related to upper limb movements using EEG, neuroimaging and/or transcranial magnetic stimulation. The study was approved by the National Research Ethics Service (NRES), UK, as well as by the local Ethical Committee (CMO) of the region Arnhem-Nijmegen, the Netherlands. All parents provided written informed consent for participation of their children at the study as well as for publication of the results. Children over 12 also provided written assent.

Clinical assessment of upper-limb capacity, performance, and Developmental Disregard

For the clinical assessment of DD, upper-limb capacity, and performance, the "revised Video-Observation Aarts and Aarts module: Determine Developmental Disregard" (VOAA-DDD-R) was used[13]. Here, capacity is defined as the frequency of AH-use during a task that is requiring bimanual hand-use. Performance is defined as the frequency of AH-use during a task that stimulates bimanual hand-use, but is not essential to performance of the task (i.e. it is possible to perform the task with only one hand). DD is defined as the difference between the duration of AH-use between both tasks, the 'demanding' and the 'stimulating' task[13]. Whenever this DD score was higher than a previously validated cut-off score (i.e. 17.2%)[13], children were classified as having DD.

Quantitative assessment of Mirror Movements

A custom-made repetitive squeezing task was developed to quantitatively register distal manual MMs. During this so-called "Windmill-task", MMs were assessed by placing two grip-force transducers (equipped with micro load cells: 0-5kg; weight 45g, circumference: 10cm) between thumb and index- plus middle-finger of the children's hands. When the child was not able to hold the transducer with these three fingers (e.g. due to muscle weakness or spasticity), additional fingers were allowed to stabilize the grip. The grip of the LAH was always matched to the grip of the AH: when using additional fingers with the AH the same fingers were used with the LAH.

One of the transducers was connected to a little windmill (see figure 1). The motor of the windmill was programmed in a way that the mill started rotating once the connected transducer was pressed beyond a certain threshold (approximately 1,5 kg). To speed up the rotation of the mill, the grip had to be returned to a lower threshold by loosening the grip (approximately 1 kg) and again reach the upper threshold within 1000ms, so that a repetitive squeezing pattern was induced (≥1Hz frequency). Children were instructed to hold the transducers in both hands with the hands lifted to chest level. With one hand (active hand) they were asked to repetitively squeeze the transducer in order to rotate the mill of the windmill as fast as possible. With the other hand, children were asked to simply lift and hold the second transducer (passive hand, tested for MMs). To measure the grip-force, the grip objects were equipped with strain-gauge load cells that converted the force into an electrical signal (mV/V). The time-locked grip-force signal of both hands was sampled at 50Hz, digitized, and stored on a computer.

Procedure

After administering the VOAA-DDD-R[13], participants were seated on a chair in front of a table upon which the windmill was placed. A standardized protocol of 5 seconds of squeezing and 5 seconds of rest with a total of 20 repetitions was conducted for each hand (100 seconds of squeezing data for each hand). A pre-recorded voice indicated the start and stop for rotating the mill. Both hands were tested separately, always with the LAH first (LAH-squeezing condition) to prevent early frustration. Thus, distal manual MMs in both hands were tested separately: 1.MMs in the AH during LAH-squeezing and 2.MMs in the LAH during AH-squeezing. A short practice session for each condition was conducted prior to the task (2 trials of 5seconds of squeezing).

Data pre-processing

First, to quantify MMs, the force pattern of both hands during each squeezing session (20 x 5 seconds) was compared by cross-correlating both signals[15]. Both grip-force signals were correlated by iteratively shifting one signal forwards in time against the other signal. A correlation-coefficient (Pearson's *r*) was calculated for each phase shift (steps of 20ms at a 50Hz sampling rate), resulting in a time series of Pearson's *r* values. This time series was representing a correlation function at each increment of the phase shift between the two input signals[15]. In a second step, an average cross-correlation function was obtained from all squeezing sessions. The maximum correlation-coefficient of this averaged function (CCC_{max}) was used as an index of the similarity between the two squeezing signals. Hence, CCC_{max} is indicative of the intensity of MMs, with r=0 reflecting no mirroring of the passive hand during active hand movement and r=1 reflecting that the passive hand is performing the exact same movement as the active hand. Whenever CCC_{max} was ≥.30, children were classified as having MMs, as a correlation-coefficient <.30 is considered negligible[16].

To further operationalize the intensity of the MMs, the mean grip-force of the passive hand during each squeezing session was calculated as the difference between the peaks and the troughs of the force signal. These values were averaged across all trials and normalized by dividing them by the mean force values of the same hand when actively squeezing ($MM_{strength}$). A higher $MM_{strength}$ indicated increased strength in the passive hand during the squeezing period, hence pronounced MMs.

CCC_{max} and $MM_{strength}$ calculations were performed separately for both conditions (AH-squeezing vs. LAH-squeezing). The active squeezing period started 500 ms after the “start” signal and lasted 5 seconds to control for the slight delay following the auditory “start” signal. All trials were individually inspected and excluded from the analyses if the active hand did not show a repetitive squeezing pattern (at least 5 repetitions ≥1Hz) within this period (3.1% data exclusion in the AH-squeezing condition; 1.2% in the LAH-squeezing condition).

Statistical analysis

Shapiro-Wilk tests indicated that most variables were not normally distributed (only the CCC_{max} variables for both conditions were normally distributed). Furthermore, only small numbers of participants (N< 30) were included for the current study. Therefore, for statistical analysis non-parametric tests were applied.

Aim 1: To test the relation between enhanced distal hand MMs and higher DD scores, CCC_{max} and $MM_{strength}$ values were related to the individuals' DD scores for both conditions separately (AH-squeezing vs. LAH-squeezing) using one-tailed Spearman rank (rho) correlations.

Aim 2: To clarify the relation between MMs in either hand and upper-limb function, we first verified if MMs were stronger in the LAH when the AH was actively moving. Two Wilcoxon Signed-Rank tests were used to compare CCC_{max} and $MM_{strength}$ scores between both hands.

Subsequently, one-tailed Spearman rank (rho) correlations were applied between VOAA-DDD-R[13] outcomes of upper-limb performance and CCC_{max} and $MM_{strength}$ scores for both conditions separately (AH-squeezing vs. LAH-squeezing). The same was done for the VOAA-DDD-R[13] upper-limb capacity scores.

For all analyses, the significance level was set at α <.05. Correlation coefficients >.70 were considered as high, .50-.70 as moderate, .50-.30 as low and <.30 as negligible[16].

Results

Participants

Twenty-three children and adolescents with uCP participated. Two were excluded as they were not able to perform the task with their AH (MACS III). For the remaining participants (12 males; 5 MACS I, 14 MACS II, 2 MACS III) the median of age was 10.58 years (IQR= 10.09-12.71; 12 AH right). Nine participants were classified as having DD (DD score≥17.2%; 6 male; 6 AH right; $\bar{x}_{age}$=10.7years). Seven children did not show any MMs (CCC_{max}<.30; 4 male; 4 AH right; $\bar{x}_{age}$=11.1years), six children showed MMs only in the LAH when the AH was actively moving (4 male; 4 AH right; $\bar{x}_{age}$=10.5years), seven children showed MMs in both hands (4 male; 4 AH right; $\bar{x}_{age}$=12.8years), and one child showed only MMs in the AH when the LAH was actively moving (male; AH right; age=7.1years).

Aim 1:DD scores were not related to MMs in the AH (CCC_{max}: rho=.091, *p*=.348; $MM_{strength}$: rho=.201, *p*=.191) or LAH (CCC_{max}: rho=-.113, *p*=.313; $MM_{strength}$: rho=.129, *p*=.289).

Aim 2: More MMs were observed in the LAH, evidenced by significantly higher CCC_{max} and $MM_{strength}$ values when the AH was actively moving (CCC_{max}:Mdn=.39;IQR=.20-.67; $MM_{strength}$:Mdn =.077;IQR=.009-.792) compared to when the LAH was actively moving (CCC_{max}:Mdn=.22;IQR=.13-.49, *p*=.046; $MM_{strength}$:Mdn=.065;IQR=.019-.144; *p*=.035; see figure 2).

For MMs in the LAH, correlation analyses showed moderate to high associations between low scores on upper-limb performance and enhanced MMs. This was evidenced by a significant negative correlation between performance and CCC_{max} scores (rho=-.526, *p*=.007) as well as between performance and $MM_{strength}$ values (rho=-.750, *p*<.001). For upper-limb capacity, low to moderate significant negative correlations were observed (CCC_{max}: rho=-.410, *p*=.033; $MM_{strength}$: rho=-.679, *p*<.001; see figure 3: AH-squeezing).

MMs in the AH also showed significant, low to moderate negative correlations with bimanual performance ($MM_{strength}$: rho=-.504, *p*=.010) and capacity scores ($MM_{strength}$: rho=-.470, *p*=.016; see figure 3: LAH-squeezing). Correlations between CCC_{max} scores and bimanual performance (rho=-.352,*p*=.059) as well as capacity (rho=-.191,*p*=.204) did not reach significance.

Additional findings

During the "AH-squeezing" condition seven children (5 male, 3 AH right, Mdn_{age}: 11.83years) displayed a stronger force pattern in the passive, LAH (Mdn=2831.35, IQR=2275.01-2924.79) compared to the active, AH (Mdn=1655.80, IQR=1065.66-1949.10). In all of these seven children, the time-lag information of the CCC_{max} values were negative, indicating that the LAH was moving slightly before the AH. This pattern was only observed in children with greater impairments in manual ability (MACS≥2).

Discussion

The main finding of the current study is that distal manual MMs during a unimanual squeezing task in uCP are not related to the phenomenon DD. Earlier studies have suggested a direct relation between manual MMs and non-use or disregard of the AH[2,9,10]. This suggestion was based on the observed association between pronounced MMs and diminished bimanual performance[4,9,10]. It has been argued that when MMs occur in the AH, which mostly has a holding or stabilizing function, MMs cause less stability. Furthermore, MMs cause a reduction in independent control of the LAH when occurring while actively moving the AH during bimanual asymmetric activities. Our findings concur with these hypotheses, showing a relation between pronounced MMs in either hand and diminished bimanual performance. Previous hypotheses have posited that MMs may therefore lead to a non-use of the AH in spontaneous bimanual activities, i.e. DD [9,10]. The present study is the first to directly test this suggested relation between manual MMs and DD and results show a lack of this association.

The factors contributing to the phenomenon of DD are not yet fully understood. Originally, it was argued that DD is a behavioural phenomenon, resulting from the negative experience each time the AH is used[17]. However, recent experimental findings aiming at unravelling DD[18,19], as well as related theoretical frameworks[2,3,20,21] suggest that this phenomenon may also be the result of compromised visuo-spatial attention as well as a developmental delay related to higher order motor executive functions, thereby challenging the earlier accounts of DD[16]. Our current finding that MMs are not related to DD, adds to this body of knowledge, by showing that reduced bimanual efficiency does not necessarily lead to DD in children with uCP.

Another important facet of our study was the clarification of the nature of the relationship between distal manual MMs and bimanual performance. This was done by using an objective quantitative assessment tool to assess distal hand MMs in both hands separately and relating this data to a bimanual performance measure. Previously reported results have been inconclusive, with some study results showing associations between diminished bimanual performance and MMs in both hands[4,10], while other findings only report this association for MMs appearing in the LAH[9]. These earlier studies did however either only use a subjective, ordinal rating scale for assessing MMs[9,10] or lacked standardized testing when assessing bimanual performance[4]. We were able to show significant moderate to high correlations between bimanual performance and MMs appearing in the LAH when the AH was actively moving. Additionally, low to moderate correlations were also observed between bimanual performance and MMs appearing in the AH when the LAH was actively moving. By confirming these relations, we showed that MMs in either hand might be related to reduced performance during bimanual asymmetric activities. At the same time, our finding of a lack of the relation between these MMs and DD indicates that this does not necessarily lead to a non-use or disregard of the AH during spontaneous daily activities.

Next to the explanation that MMs are directly related to a reduced performance during bimanual asymmetric activities, the negative correlation between bimanual performance and MMs might also be simply explained by the type and/or severity of the children's lesion. The neuropathology would than in turn explain both, the reduced bimanual performance as well as the enhanced MMs (due to widespread bilateral activation during unimanual movements or even ipsilateral cortico-spinal connections from the less-affected hemisphere to the AH[7,8,9]). This interpretation is supported by the current finding that MMs were also correlated to hand capacity, as it has also been reported earlier[9]. However, without details of the extent and location of the individual lesions or direct unimanual capacity measures, it is not possible to elaborate the discussion on the cause of the observed reduced bimanual performance.

Our results furthermore replicated earlier findings that many children with uCP display significantly more MMs in the LAH compared to the AH[4,6,9]. There are three potential explanations for this finding. First, the more dextrous use of the LAH compared to the AH might contribute to a more discrete and lateralized pattern of neural control of the LAH compared to the AH, leading to reduced MMs in the

AH when the LAH is actively moving[4,9]. Second, the enhanced MMs in the LAH might be related to the sensorimotor impairments of the AH and evolve due to inefficient interhemispheric inhibition from the affected hemisphere resulting in bilateral excitatory activity[19]. Third, MMs appearing in the LAH might represent a non-specific motor overflow phenomenon which indirectly assists AH movements[9]. This latter explanation is based on the notion that children with reduced manual ability of the AH may move both hands simultaneously when asked to only move their AH, in order to overcome the lack of selectivity and strength of their AH. This is, because symmetrical movements are performed more easily[22]. This possible assisting strategy might be especially useful during predominantly symmetric bimanual activities and potentially also during the less frequently observed phenomenon of unimanual AH movements (e.g. letting go of an object by actively opening the LAH). Thus, MMs in the LAH may in some cases be considered to assist controlled movements of the AH.

In line with the suggestion that MMs appearing in the LAH might occur to assist AH movement, we found that seven children displayed a stronger force pattern in the LAH when these children were actually asked to actively move their AH. These children also started moving their LAH slightly earlier. This additional finding may imply that these children facilitate the movement of their AH by moving their LAH. That is, they appear to 'use' their MMs as a strategy to facilitate movements of the AH. This pattern was only observed in children with reduced manual ability (MACS≥2). Therefore, the slight delay of the AH movement might also be explained by biomechanical processes related to this reduced manual ability. Further research is warranted to unravel the possible strategic use. In particular, to answer the question whether this possible strategic use of MMs leads to a better unimanual or bimanual control of the AH during some daily activities.

The current study was limited by the small group size, especially of the more severely impaired children (i.e. MACS III). Additionally, two children had to be excluded as they were not able to complete the task with their AH. For future studies, the task needs to be adapted in a way that the thresholds for moving the windmill are scaled to the individuals' maximal force capacities. Another limitation affecting performance is our block design, where the LAH always started. This may have led to possible carry-over effects that would have been avoided with a randomized design. Finally, and inherent to the studied population, is the heteroginity of the studied groep (e.g. aetiology, underlying differences in brain injury).

To conclude, no relation between MMs and DD in children with uCP was observed. Furthermore, using a newly developed quantitative tool to assess MMs, earlier findings on MMs were supported: MMs were related to reduced manual performance. Furthermore, MMs were shown to be stronger in the LAH during AH movement. Finally, in a subset of the children, our new quantitive measurement uncovered a possible strategy to use MMs to control movements of the AH.

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Figure 1 A: The “Windmill-task” as positioned for a right hand active squeezing. The two objects next to the windmill represent the grip-force transducers with the right transducer being connected to the windmill. Both transducers are connected to a computer, digitizing and storing the data recorded of both hands’ time-locked grip-force (in mV/V). This figure represents a squeezing pattern with the passive hand showing no mirror movements. B: Participant performing the “Windmill-task”.

Figure 2 CCC_{max} (A) and $MM_{strength}$ (B) values representing the intensity of MMs per condition (left: AH actively squeezing; right: LAH actively squeezing) represented by the medians and inter-quartile ranges. CCC_{max} values indicate the averaged maximum cross-correlation between both hands’ force signals, with higher values reflecting more similarity between both force patterns, hence more MMs. $MM_{strength}$ values indicate the strength of the passive hand during the active squeezing period, with higher values indicating stronger MMs.

Figure 3 Depicted are correlations between upper-limb function (performance and capacity) and MMs, with * representing significance ($p<.05$) and # representing a statistical trend ($p<.1$ & $>.05$). A) Correlations between upper-limb function (upper graphs: performance; lower graphs: capacity) and the cross-correlation between both hands’ force signals, (CCC_{max}). B) Correlation between upper-limb function (upper graphs: performance; lower graphs: capacity) and the strength of the passive hand during the active squeezing condition($MM_{strength}$).

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Figure 1 The "Windmill-task" as positioned for a right hand active squeezing

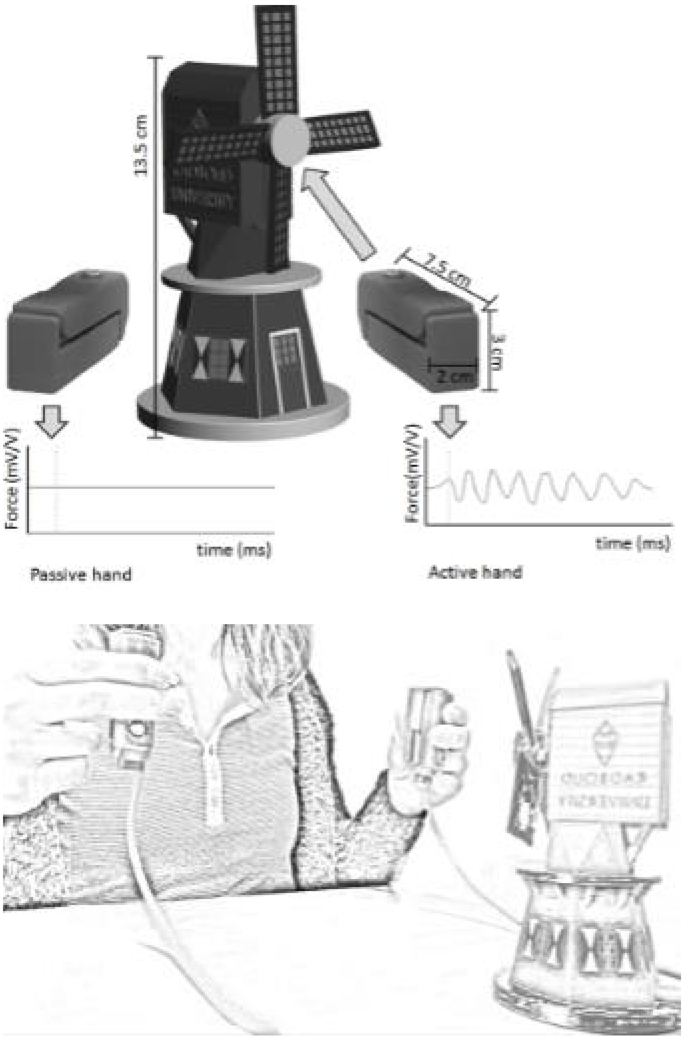

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Figure 2 CCC_{max} (A) and $MM_{strength}$ (B) values representing the intensity of MMs per condition

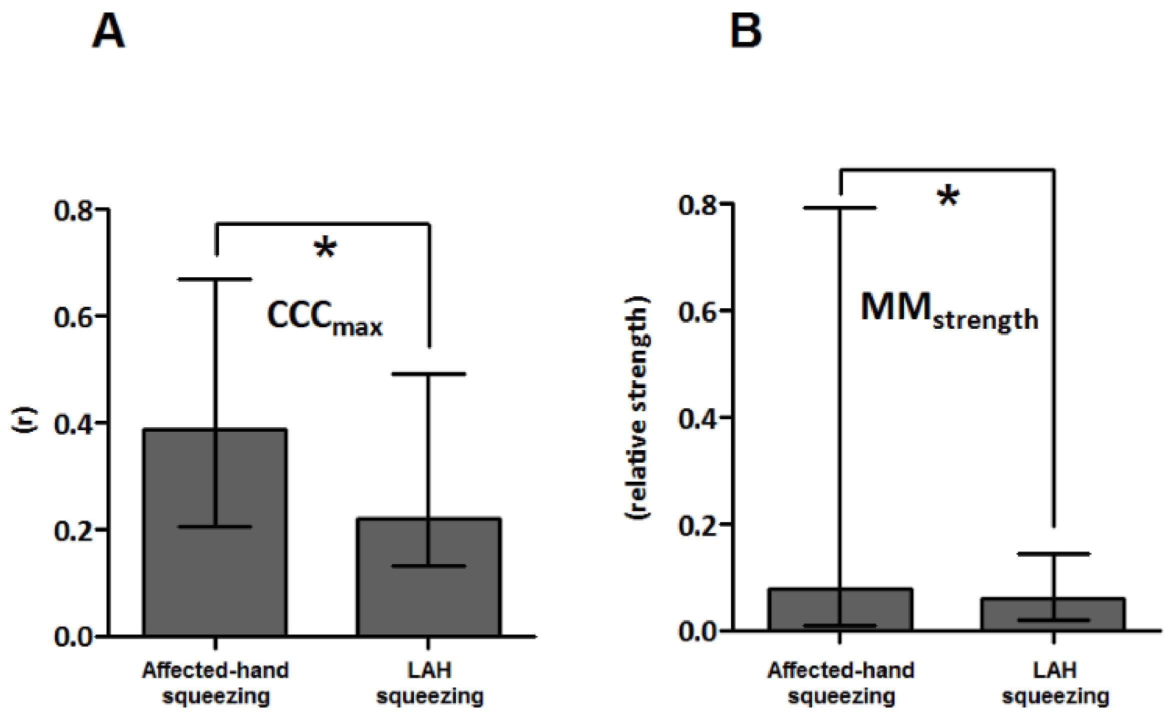

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Figure 3 Correlations between upper-limb function (performance and capacity) and MMs