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Anticipatory coordination of digit centers of pressure and forces for torque control in young and elderly adults and patients with chronic stroke

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Dissertation

Medical Graduate Center

Technical University of Munich

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1 Summary

There is growing evidence that manual dexterity declines with age and can be impaired at both hands following stroke. However, the underlying mechanisms remain poorly understood. Precisely coordinating fingertip positions and forces to compensate for external torques resulting from an object's mass distribution relative to the handle is crucial for dexterously grasping and lifting objects, preventing object tilt without exerting excessive grip force (GF). In our research, we conducted two separate studies to investigate the mechanisms of anticipatory coordination of finger positions and forces to compensate for external torques, and we compared young and elderly adults as well as patients with chronic stroke using their ipsilesional hand and hand matched controls.

In the first study, we mathematically delineate how grip force economy depends upon the distribution of the centers of pressure (∆CoP) across opposing grip surfaces. We then conducted an experiment to explore how the control of ∆CoP, forces, and the resulting compensatory torque during grasping and lifting an object with varying center of mass (CoM) and surface properties differed between young and elderly subjects, depending on whether they were instructed to perform the task regularly or as efficiently as possible. We found that providing the instruction to strive for force efficiency led a more adequate ∆CoP modulation in both groups and consequently lower GF levels, although to a lesser extent in the elderly group. Moreover, we observed a refined torque compensation only in the young group. Increased grip forces in elderly participants could be attributed to a less precise ∆CoP control in the force-efficiency condition and decreased mechanical fingertip friction levels, whereas GF safety margins were not elevated. Our study results demonstrate that young participants possess a higher capacity to adapt their higher-level motor control of object manipulation to complex object properties and task goals than elderly participants and underscores the importance of precise task instructions when investigating GF control.

In the second study, we investigated the sensorimotor and visuomotor learning of manual torque control of patients with chronic stroke when lifting an object with an eccentric weight distribution with the ipsilesional hand. Surprisingly, we found that the torque resulting from grip force being applied at different vertical finger positions was biased depending on the location of the center of mass (CoM) of the object in patients with left-hemispheric- and, to a lesser degree, also right hemispheric stroke. This bias favored an ipsilesional CoM and disadvantaged a contralesional CoM when relying on sensorimotor memories. However, this bias was compensated by a shift of the torque generated by differential vertical load forces on both sides of the handle in the opposite direction, resulting in an overall similar compensatory torque to that of hand-matched controls. When geometric cues on object CoM were provided, no group differences were observed, suggesting an intact visuomotor transformation. The study findings are consistent with a shift of sensorimotor attention and intention away from the contralesional- and towards the ipsilesional object side, possibly representing evidence for an object-centered premotor neglect following stroke.

In summary, this thesis has expanded the understanding of the anticipatory control of finger positions, forces and torques in young and elderly adults and stroke patients and provides novel insights into the mechanism of declining dexterity associated with aging and following stroke.

2 Zusammenfassung

Es gibt zunehmend Hinweise darauf, dass die manuelle Geschicklichkeit mit dem Alter abnimmt und nach einem Schlaganfall in beiden Händen beeinträchtigt sein kann. Die zugrundeliegenden Mechanismen sind jedoch bisher unzureichend verstanden. Eine präzise Koordination von Fingerspitzenpositionen und -kräften zur Kompensation externer Drehmomente, die sich aus der Massenverteilung eines Objekts relativ zum Griff ergeben, ist entscheidend, um Objekte geschickt zu greifen und zu heben, ohne übermäßige Griffkraft (GF) auszuüben. Im Rahmen dieser Dissertation haben wir zwei separate Studien durchgeführt, um die Mechanismen der vorausschauenden Koordination von Fingerpositionen und -kräften zur Kompensation externer Drehmomente zu untersuchen. Dabei haben wir junge und ältere Erwachsene sowie Patienten mit chronischen Schlaganfällen, die ihre ipsiläsionale Hand benutzen, und handabgestimmte gesunde Teilnehmer miteinander verglichen.

In der ersten Studie haben wir zunächst mathematisch beschrieben wie die Griffkrafteffizienz von der Verteilung der Fingerdruckpunkte an gegenüberliegenden Griffflächen (ΔCoP) abhängt. Experimentell untersuchten wir in der Folge wie die Kontrolle von ΔCoP, Kräften und dem daraus resultierenden Drehmoment beim Greifen und Heben eines Objekts mit variierendem Massenschwerpunkt (CoM) und Oberflächeneigenschaften zwischen jungen und älteren Probanden variiert, je nachdem, ob sie angewiesen waren, die Aufgabe normal oder so Griffkraft effizient wie möglich durchzuführen. Wir stellten fest, dass die Anweisung Griffkraft effizient zu greifen in beiden Gruppen zu einer angemesseneren ΔCoP Modulation und folglich zu niedrigeren GF Werten führte, wenn auch in geringerem Ausmaß in der älteren Teilnehmergruppe. Darüber hinaus beobachteten wir nur in der jungen Gruppe eine verfeinerte Drehmomentkompensation. Erhöhte Griffkräfte bei älteren Teilnehmern konnten auf eine weniger präzise ΔCoP-Kontrolle bei effizienter Aufgabenausführung und abnehmende mechanische Reibungskoeffizienten an den Fingerspitzen zurückgeführt werden, während die GF-Sicherheitsmargen nicht erhöht waren. Unsere Studienergebnisse zeigen, dass junge Erwachsene besser darin sind die motorische Kontrolle der Objektmanipulation an komplexe Objekteigenschaften und Aufgabenziele anzupassen als ältere Teilnehmer und unterstreichen die Notwendigkeit einer präzisen Aufgabenanweisung bei der Untersuchung der GF-Kontrolle.

In der zweiten Studie untersuchten wir das sensomotorische und visuomotorische Lernen der manuellen Drehmomentkontrolle bei Patienten mit chronischen Schlaganfällen beim Heben eines Objekts mit exzentrischer Gewichtsverteilung mit der ipsilesionalen Hand. Überraschenderweise stellten wir fest, dass das Drehmoment, das durch die Anwendung von Griffkraft an unterschiedlichen vertikalen Fingerpositionen entsteht, in Abhängigkeit von der

Position des Massenschwerpunkts (CoM) des Objekts bei Patienten mit links- und in geringerem Maße auch rechts-hemisphärischem Schlaganfall zugunsten eines ipsiläsionalen CoM und zum Nachteil eines contraläsionalen CoM verzerrt war, wenn sie sich auf sensomotorische Erinnerungen verlassen mussten. Dieser Bias wurde jedoch durch eine Verschiebung des durch differentielle vertikale Lastkräfte auf beiden Seiten des Griffs erzeugten Drehmoments in die entgegengesetzte Richtung kompensiert, was zu einer insgesamt ähnlichen Drehmomentkompensation wie bei handangepassten Kontrollen führte. Wenn geometrische Hinweise auf das CoM des Objekts gegeben wurden, konnten keine Gruppenunterschiede beobachtet werden, was auf eine intakte visuomotorische Transformation hindeutet. Die Studienergebnisse sind konsistent mit einer Verschiebung der sensomotorischen Aufmerksamkeit und Intention weg von der kontraläsionalen und hin zur ipsiläsionalen Objektseite und können als Hinweis auf einen objektzentrierten prämotorischen Neglect nach einem Schlaganfall dienen.

Zusammenfassend hat diese Arbeit unser Verständnis für die vorausschauende Kontrolle der Koordination von Fingerpositionen – und kräften zur Drehmomentkompensation bei jungen und älteren Gesunden sowie Schlaganfallpatienten erweitert und bietet neue Einblicke in die Mechanismen der abnehmenden Geschicklichkeit im Zusammenhang mit Alterung und nach einem Schlaganfall.

3 List of publications

- **Publication I (study I):** Schneider, T. R. and J. Hermsdörfer (2021). "Intention to be force efficient improves high-level anticipatory coordination of finger positions and forces in young and elderly adults." Journal of Neurophysiology.
- **Publication II (study II):** Schneider, T. R. and J. Hermsdörfer (2022). "Object-centered sensorimotor bias of torque control in the chronic stage following stroke." Scientific Reports **12**(1): 14539.

Table of content

4 Introduction

To dexterously grasp- and lift the immense variety of items and objects we encounter every day, which differ in size, shape and material composition and thus in their weight, weight distribution relative to the selected grip as well as their surface friction properties, in a way resulting in the desired object movement, we must utilize our knowledge of object properties to plan where we position our fingertip and how we apply forces (for review see: (T. Schneider & Hermsdorfer, 2016)). In this introduction, we will first outline the concept of internal models governing anticipation in object manipulation. Subsequently, we will review behavioral studies on the anticipatory scaling of finger-tip forces when lifting an object with a balanced center of mass straight upwards as well as studies dealing with the anticipatory coordination of fingertip positions and -forces to compensate for external torques when lifting objects with an eccentric center of mass relative to the grip. Next, we will review the body of literature on grip force efficiency when lifting objects with the hand. Finally, we will summarize the literature on grip force scaling deficits found in elderly subjects and patients with chronic stroke. Moreover, the research gaps concerning changes of the digit force- to position coordination for torque compensation in aging and following a stroke which are addressed in this thesis will be highlighted.

4.1 Anticipatory object control is governed by internal models

The findings of behavioral studies on the anticipatory control of fingertip forces, positions and torques in object manipulation are consistent with and have been interpreted in the context of neural internal models (Franklin & Wolpert, 2011; Nowak, Glasauer, & Hermsdorfer, 2013; Wolpert, 1997; Wolpert & Flanagan, 2010). It has been proposed that the neural control of manual object manipulation actions with internal models functions in two complimentary ways (**see**

Figure 1 for illustration). On the one hand, internal models store information of object properties based on our object knowledge, a visual analysis of the object appearance and sensorimotor memories of prior object interactions. Internal models integrate these object related information, the current state of the body and the desired motor action goals to generate a motor plan, e.g. information on the object weight and the goal to lift it with a certain speed straight upwards are integrated to program adequate fingertip forces. This mode of action has been referred to as inverse internal model (Kawato, 1999). Besides, internal models also predict upcoming actions and their sensory consequences in a feedforward-fashion based on these representations of the effectors and the object as well as an efference copy of the motor command issued by the executive motor system (von Holst & Mittelstaedt, 1950). Predicted sensory consequences and actual tactile and visual sensory feedback are compared at crucial time points of the task execution, e.g. at the expected moment of object-lift off and shortly thereafter (Johansson & Flanagan, 2009). If prediction errors are detected, e.g. no object lift-off is detected at the predicted time point, motor corrections are triggered (e.g. further force increases) and erroneous internal representations are updated (e.g. stored object weight is updated). By combining the inverse- and feedforward action mode, well-trained internal models allow for a nimble object manipulation by anticipating object properties and according to the action goals. This anticipatory mode of object control consequently prevents errors in the task execution.

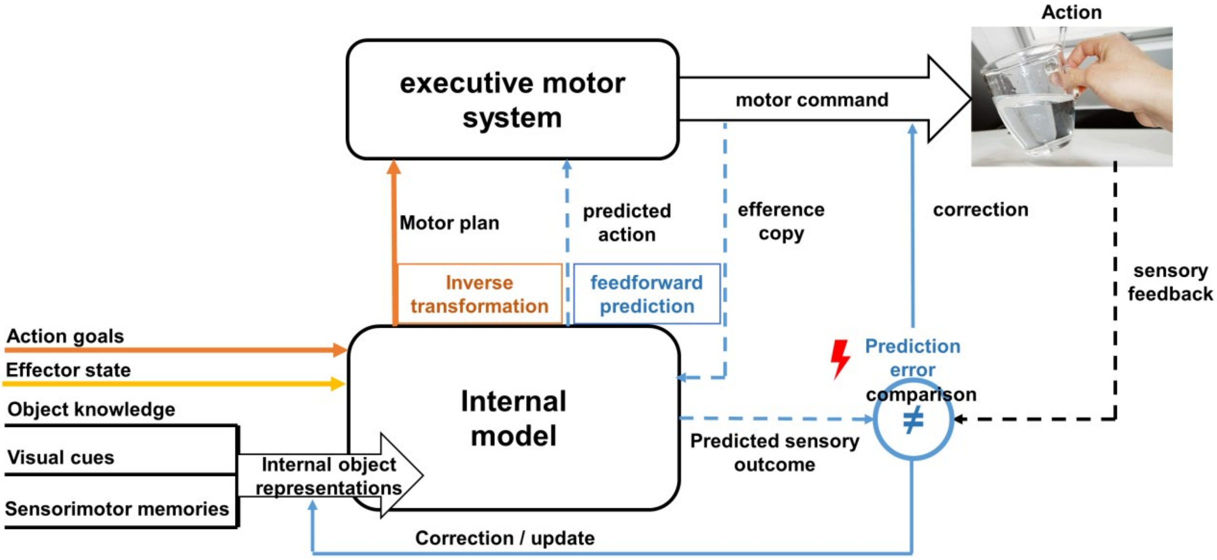


Figure 1: Schematic overview of the concept of inverse- and feed forward internal models.

4.2 Anticipatory scaling of forces

When we grasp- and lift objects with a balanced weight distribution relative to our grip in a precision grip, we apply forces directed upwards to overcome gravity, which are termed load force (LF), as well as forces directed orthogonal to the grip surfaces, coined grip force (GF) that safeguard the object from slipping out of our hand (Johansson & Westling, 1984a). The grip- and load force rise in parallel after the fingers contact the object (Johansson & Westling, 1984a) and remain tightly coupled without time lags when dynamically moving a hand-held object up- and down in cyclic movements which indicates that they are jointly programmed in an anticipatory feed-forward fashion (J. R. Flanagan & Tresilian, 1994; J. R. Flanagan & Wing, 1995; Hermsdorfer, Hagl, Nowak, & Marquardt, 2003). In well planned dexterous object lifts, the load- and grip force rise rates form a one-peaked, bell-shaped trajectory. The peaks of the grip force- and load force rate occur prior to object lift-off – i.e. before sensory feed-back of object weight is available - and reflect the anticipated object weight (J. R. Flanagan, Merritt, K., & Johansson, R. S. , 2009; Johansson & Westling, 1984a). It was shown that the first force rate peaks correlate with actual object weight when lifting well-known objects of everyday life (Gordon, Westling, Cole, & Johansson, 1993; Hermsdörfer, Li, Randerath, Goldenberg, & Eidenmuller, 2011). When lifting novel objects for the first time, visual size and material cues are utilized to predictively scale grip force rates (Buckingham, Cant, & Goodale, 2009; Cole, 2008; J. R. Flanagan & Beltzner, 2000; Gordon, Forssberg, Johansson, & Westling, 1991). Moreover, finger-tip forces are programmed according to sensorimotor memories of object properties and the sensed force effort (Quaney, Rotella, Peterson, & Cole, 2003) from prior lifts (Johansson & Westling, 1984a, 1988). Reliance on these sensorimotor memories is especially helpful when object weight cannot be inferred from object appearance. Furthermore, the sensorimotor learning of object weight can be linked to arbitrary cues, e.g. a color signal displayed prior to a lift, and later retrieved by these cues to guide force scaling (Ameli, Dafotakis, Fink, & Nowak, 2008).

4.3 **Anticipatory torque control to prevent object tilt**

To prevent object tilt when lifting an object whose center of mass lies eccentric to the grip midpoint, e.g. when lifting a cup of tea at the handle, arising torques must be counteracted already at the moment of lift-off to prevent object tilt. As full sensory feedback of the external torque only becomes available after lift-off, an anticipatory compensation of torques is essential for the initial object stability after lift-off before sensory feedback-based corrections take effect. Two torque components constitute the total applied torque: a) the torque generated by the product of the load force difference between grip sides and half the grip-width ($\Delta LF \times w/2$), and the product of the GF and the vertical distance between the centers-of-pressure (ΔCoP) on both grip sides ($\Delta CoP \times GF$) (Fu, Zhang, & Santello, 2010). ΔCoP is determined by the digit positions and also the GF sharing pattern among the fingers on the same grip side if more than one finger contacts one object side. Consequently, digit positions, grip- and load forces must be coordinated to generate the intended torques when lifting an object (for reviews see (Santello, 2018; T. Schneider & Hermsdorfer, 2016)). Healthy adults learn to coordinate digit ΔCoP and forces by placing the digit(s) higher and applying more load force on the side of the center of mass according to sensorimotor memories of previous lifts resulting in adequate compensatory torques minimizing object tils (Fu et al., 2010; Lee-Miller, Marneweck, Santello, & Gordon, 2016; Zhang, Gordon, Fu, & Santello, 2010) and even rely on prior sensorimotor memories when object dynamics change unpredictably (Lukos, Choi, & Santello, 2013; T. R. Schneider, Buckingham, & Hermsdorfer, 2019). When salient visual object geometry cues on the mass distribution are available, these are utilized to infer the weight distribution of the object and generate adequate compensatory torques already at the first object lift (Fu & Santello, 2012; Lee-Miller et al., 2016; Salimi, Frazier, Reilmann, & Gordon, 2003; T. R. Schneider, Buckingham, &

Hermsdorfer, 2020). To account for the considerable, inter trial variability of finger-positions and maintain accurate torque compensation across repeated object lifts, digit -forces are covaried as a function of digit placement. This covariation of forces according to digit placement is a general high-level-control mechanism in object manipulation (Davare, Parikh, & Santello, 2019) and was shown for two finger- (Fu et al., 2010) and tripod precision grips (Fu, Hasan, & Santello, 2011) as well as whole hand- (Marneweck, Lee-Miller, Santello, & Gordon, 2016) and bimanual grips (Lee-Miller, Santello, & Gordon, 2019).

4.4 **Force efficiency when lifting objects**

To safely hold an object between the fingertips without object slips, the ratio between the grip- and load force must exceed the inverse of the static coefficient of friction at each digit-object contact. If the GF/LF ratio drops below this minimum, tactile feedback of emerging slips will be conveyed by fast-adapting mechanoreceptors and trigger fast reactive grip force increases in an attempt to secure the object from slipping out of the hand (Johansson & Flanagan, 2009; Park et al., 2016). When lifting objects with a balanced weight distribution and uniform surface materials in a precision pinch grip, young adults scale their fingertip-grip forces (GF) according to the respective surface-fingertip friction with. The applied GF surpasses the minimal grip force necessary to secure the grip only by a small safety margin of some 20% (Cadoret & Smith, 1996; Cole & Johansson, 1993; Forssberg, Eliasson, Kinoshita, Westling, & Johansson, 1995; Johansson & Westling, 1984b, 1987; Smith, Cadoret, & St-Amour, 1997; Westling & Johansson, 1984). When the coefficient of friction differs between the involved finger tips, .e.g. when different materials cover the contact sides, force control is challenged because a higher GF/LF ratio is needed at the side with the lower surface friction while the applied GF must be equal between both sides to prevent side movements. In this situation, young adults were shown to partition their load forces in a way that the fingers contacting a more slippery surface exert lower load forces than fingers with higher surface friction in order to maintain a high grip force efficiency (Aoki, Niu, Latash, & Zatsiorsky, 2006). This load force partitioning is already established at the moment of object lift -off (Zhang, Gordon, McIsaac, & Santello, 2011) and represents a general feature of manual control as it was demonstrated for a two finger precisions grip (Edin, Westling, & Johansson, 1992; Quaney & Cole, 2004), a tripod grip (Burstedt, Flanagan, & Johansson, 1999; J. R. Flanagan, Burstedt, & Johansson, 1999) as well as for the five finger grasp (Aoki, Latash, & Zatsiorsky, 2007; Aoki et al., 2006; Niu, Latash, & Zatsiorsky, 2007; Shim, Latash, & Zatsiorsky, 2003; Zatsiorsky, Gao, & Latash, 2003; Zhang et al., 2011). However, differential load forces in response to differing finger-surface friction properties among fingers also result in torques which in turn must be prevented by modulating ΔCoP and GF. It was confirmed that participants modulate ΔCoP by redistributing the GF among their fingers in five finger object-grasps to compensate for self-induced torques caused by an asymmetric load force sharing in response to differing finger-surface properties (Aoki et al., 2006; McIsaac, Santello, Johnston, Zhang, & Gordon, 2009; Zhang et al., 2011). Although one can apply a target torque by any combination of ΔCoP, ΔLF, and GF, it seems obvious that the choice of ΔCoP will affect GF efficiency and that it is advantageous to place the fingers higher on the side of the object CoM than on the opposing side (Fu et al., 2010). However, the relationship between object weight and weight distribution relative to the grip, surface friction at the fingertip contacts, ΔCoP and GF is complex and has neither been formally nor experimentally studied in an unconstrained grasping task, yet.

4.5 **Aging and GF control**

Elderly subjects were consistently found to apply higher GF levels than young adults in studies employing a grasp-to lift tasks with constrained – i.e. predefined – finger positions and a symmetric object weight distribution (for review see: (Diermayr, McIsaac, & Gordon, 2011)). Even after accounting for the age related decrease of fingertip-surface friction which necessitate a higher minimum GF/LF ratio in the elderly, studies employing a precision grip demonstrated an increase in the GF safety margin, i.e. the GF exerted in excess of the minimum GF to secure the grip in the elderly (Cole, 1991; Cole, Rotella, & Harper, 1998, 1999; Kinoshita & Francis, 1996). In contrast, studies on multi-finger grasping also reported equal or even decreased GF safety margins in the elderly (Solnik, Zatsiorsky, & Latash, 2014; Varadhan, Zhang, Zatsiorsky, & Latash, 2012). Until now, only one study compared the control of finger-positions in the context of GF control between young and elderly adults (Parikh & Cole, 2012). In this study, elderly adults initially failed to align their fingers collinearly when lifting an object with a symmetric mass distribution in a precision grip resulting in increased unwanted torques. However, elderly participants learned to align their fingers and minimize unintended torques and the applied GF in the course of trials similarly as young adults. Moreover, in a study examining lifts of an object with an unbalanced CoM in patients with Parkinson’s disease and elderly controls, a learning curve similar to that of young adults was found for the modulation digit positions and the minimization of object roll (Lukos, Lee, Poizner, & Santello, 2010). However, the applied torques were not recorded. Apart from this, the age-related changes in the high-level control of digit positions, forces and torques in challenging situations, especially when lifting objects with a lateralized center of mass, have not been examined, yet.

4.6 **Manual dexterity is impaired at both hands following stroke**

With 135,705 (122,078 - 150,613) incident stroke cases and 1,317,688 (1,212,550 - 1,428,861) prevalent cases in in Germany in 2019 (Collaborators, 2021), stroke is still one of the leading causes of long-term functional disabilities in western countries (Benjamin et al., 2018). Some 26% of stroke survivors older than 65 years lose their functional independence following a stroke (Go et al., 2014). One of the most frequent reasons for a loss of functional independence and quality of life following stroke are impairments of dexterous upper-limb function (Jorgensen et al., 1995; Langhorne, Coupar, & Pollock, 2009; Roby-Brami, Jarrasse, & Parry, 2021). Contralesional upper limb weakness, spasticity and impaired selective finger movements consequent to lesions of the primary cortex or the corticospinal tract as well as manual dexterity impairments resulting from somatosensory deficits linked to thalamic or parietal cortical lesions are the functionally most important sequelae of stroke (for review see (Roby-Brami et al., 2021)). Consequently, stroke patients with contralesional dexterity impairments must strongly rely on their ipsilesional, non-paretic, hand in performing activities of daily living. However, concurring studies show that dexterity may be impaired at both hands following stroke (Barry et al., 2020; Kitsos, Hubbard, Kitsos, & Parsons, 2013). Dexterity impairments of the ipsilesional hand have been demonstrated in finger-tapping tasks (de Groot-Driessen, van de Sande, & van Heugten, 2006; Hermsdorfer & Goldenberg, 2002), the Nine- Hole Peg Test (Desrosiers, Bourbonnais, Bravo, Roy, & Guay, 1996; Johnson & Westlake, 2021; Maenza, Good, Winstein, Wagstaff, & Sainburg, 2020; Noskin et al., 2008; Wetter, Poole, & Haaland, 2005) and the Jebsen Hand Function Test (Barry et al., 2020; Chestnut & Haaland, 2008; Desrosiers et al., 1996; Sunderland, 2000; Sunderland, Bowers, Sluman, Wilcock, & Ardron, 1999; Wetter et al., 2005). Even subtle dexterity deficits of the ipsilesional hand may result in poorer performance in activities of daily living as was shown for the one-handed binding of shoes (Poole, Sadek, & Haaland, 2009) and meal preparation (Poole, Sadek, & Haaland, 2011). Accordingly, ipsilesional dexterity is highly relevant for the regaining of functional independence following left hemisphere stroke (Jayasinghe, Good, Wagstaff, Winstein, & Sainburg, 2020). It remains crucial to improve the understanding of the mechanisms and the detection of impaired ipsilesional dexterity to develop targeted rehabilitation regimes and to improve patient outcomes.

4.7 Impairments of digit force scaling in stroke patients

Patients suffering from middle cerebral artery (MCA) stroke applied excessive grip forces and failed to scale their force programming according to differing surface-friction- and weight-properties when lifting objects straight-upwards with their contralesional, slightly to moderately paretic, hand (Allgower & Hermsdorfer, 2017; Blennerhassett, Matyas, & Carey, 2007; Hermsdorfer et al., 2003). There is conflicting evidence whether force scaling deficits also extend to the ipsilesional hand. While some authors reported disproportionately high and variable grip forces for object lifts with the ipsilesional hand (Hsu et al., 2018; Nowak et al., 2007; Quaney, Perera, Maletsky, Luchies, & Nudo, 2005), other studies found no GF increase in lifts with the ipsilesional hand (Buckingham, Bienkiewicz, Rohrbach, & Hermsdorfer, 2015; Eidenmuller, Randerath, Goldenberg, Li, & Hermsdorfer, 2014; Li, Randerath, Goldenberg, & Hermsdorfer, 2011). Patients with MCA stroke of either hemisphere could not utilize arbitrary visual- or auditory cues signaling object weight and adapt their digit forces accordingly when using their contralesional hand, whereas only patients with left hemispheric stroke also failed with their ipsilesional hand (Bensmail, Sarfeld, Ameli, Fink, & Nowak, 2012). Similarly, patients with left hemispheric lesions could not scale their digit forces according to the weight of well-known everyday objects when lifting them with their ipsilesional hand, whereas ipsilesional force scaling was intact in patients with right-hemispheric stroke (Eidenmuller et al., 2014) suggesting a dominant role of the left hemisphere for anticipatory digit force scaling. In contrast, the visuomotor processing of size cues to program digit forces with the ipsilesional hand was found normal in patients with stroke irrespective of the affected hemisphere (Buckingham et al., 2015; Li et al., 2011). Until now, no study has investigated whether the coordination of digit positions and forces to generate compensatory torques when lifting an object with an eccentric center of mass is altered in patients following stroke.

5 Materials and Methods

5.1 Participants

- **Study I**: 15 young (9 female, 6 male, 12 right-handed, 3 left-handed, 18-28 years, mean age 22.1 ± 2.7years) and 10 elderly (4 female, 6 male, all right-handed, 62-76 years, mean age 69.3 ± 4.8 years) adults with no reported history of neurological disorders or musculoskeletal disorders of the involved hand participated in study I.
- **Study II**: Patients who suffered a single unilateral stroke more than 6 months ago with no evidence of bilateral lesions in their medical reports were recruited from the community with the help of physiotherapists, occupational therapists, speech therapists and neuropsychologists in the greater Munich area. Age- and hand matched healthy adults served as controls. Overall, 13 patients with chronic-stage left hemispheric stroke (SL group: 6 female, 7 male, mean age 63.3 ± 16.3 years, mean years since onset of stroke (YOS): 6.06 ± 4.10 years) and 9 patients with chronic-stage right hemispheric stroke (SR group: 5 female, 4 male, mean age 63.9 ± 6.7 years, mean YOS 7.5 ± 5.7 years) who performed the experimental procedures with their ipsilesional hand as well as 15 healthy controls who conducted the experiment with their left hand (CL group: 6 female, mean age 63.0 ± 13.1 years) and 9 healthy controls who conducted the experiment with their right hand (CR group: 4 female, mean age 69.8 ± 3.8 years) participated in the study. All participants were self reportedly right handed.

All subjects were naïve to the purpose of the study and gave written informed consent to participate in the respective experiments. The experimental procedures were approved by the Institutional Review Board of the School of Medicine at the Technical University of Munich and were in accordance with the Declaration of Helsinki. Study measurements took place in the offices of the Chair of Human Movement Science, TUM, or at the author's or participants homes. All participants received 20 € as reimbursement for their participation.

5.2 **Apparatus**

In both studies, participants had to repeatedly grasp and lift a custom made, grip device at the handle using a tripod-grip with the thumb opposing the index and the middle finger (see **Figure 2 A** and **Figure 3**) while preventing the object from tilting.

The grip handle element incorporated two 6-axis force/torque-sensors (ATI Nano-17 SI-50-0.5, ATI Industrial Automation; force range: 50,50, and 70 N for x-, y-, and z-axes, respectively; force resolution: 0.012 N; torque range 0.5 Nm; torque resolution: 0.063 Nmm, sampling rate 200 Hz) mounted underneath opposing aluminum grip surfaces (120x40 mm) which recorded the forces and torques applied on both grasp sides (see **Figure 2 A**). Position and orientation data of the device were measured by a lightweight magnetic position/orientation-tracker (TrakSTAR, Ascension Technology Corporation, accuracy: 1.4 mm RMS, 0.5 degrees RMS, sampling rate 200 Hz) fixed on top of the horizontal base. The handle element could be positioned on sockets on top of a horizontal base and a 250 g aluminum could be placed into one of the cavities along the horizontal axis of the base which were concealed from sight by an aluminum lid (see **Figure 3**). Consequently, the center of mass (CoM) relative to the middle of the grip surfaces could be varied by changing the position of either the handle – giving participants a salient geometric cue on the CoM - or the position of the hidden aluminum weight - offering no visual cues on the CoM. The total object weight was always 750 g.

In **study I**, the surface properties of both grip surfaces could be changed independently by attaching beige crepe (Crepe-varnish tape, Tesa, Hamburg, Germany) or white copy paper (100 g/m^2, HP, Paolo Alto, USA) covered pads to the lateral handle sides via a clipping system. Throughout the study, the handle position was in the center, whereas the hidden weight was either in the left, middle or right cavity resulting an external torque of -0.21 Nm, 0 Nm and 0.21 Nm at lift-off, respectively (see **Figure 2** B, convention: negative signs denote a counter-clockwise external torque).

In **study II**, the grip surfaces were covered with fine-grained sand paper (2000 grit). Two cue conditions were studied. In the no-cues condition, the handle was positioned in the center while the position of the hidden weight was changed between the left and right cavity (± 0.21 Nm). In the geometric cue condition, the handle position was varied between the left and right edge of the base (± 0.46 Nm, see **Figure 2** C).

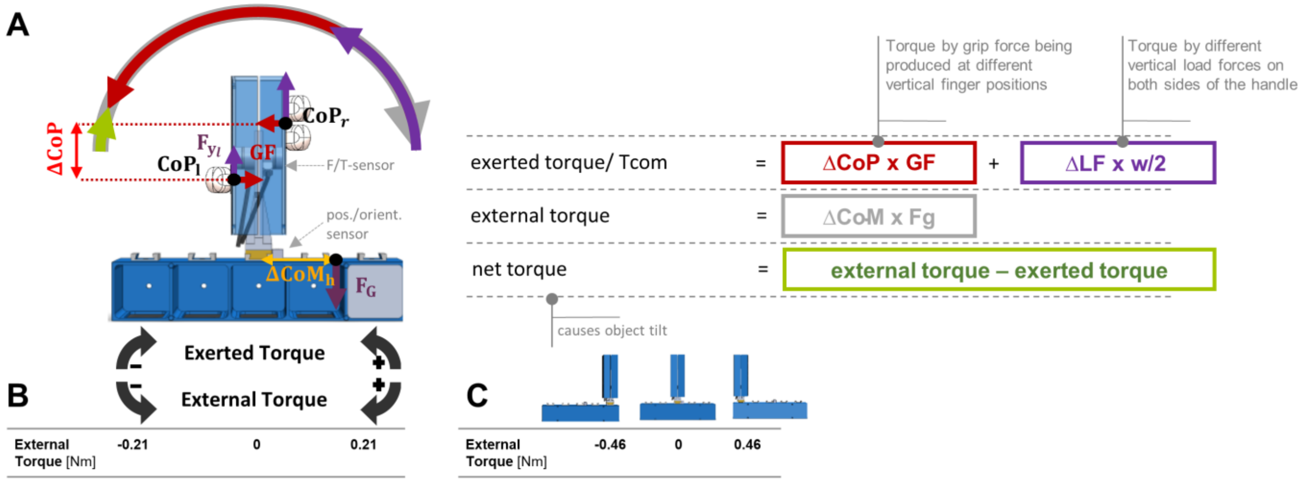


Figure 2. (A) The custom-built grip-device consists of a handle element which can be mounted on sockets along a horizontal bar (frontal view). Subjects could freely choose their digit placement along the grip surfaces (40 x 120mm). Two 6-axis-force/torque (F/T) sensors were mounted under the grip surfaces and a position/orientation sensor was mounted on top of the base. The total exerted torque equals the sum of the torque produced by grip force being applied at different vertical finger center of pressure (ΔCoP x GF) and the torque generated by different load forces on both sides of the handle (ΔLF x w/2). **(B)** Summaries of the external torques arising at lift-off for the handle being mounted onto the central socket and the hidden weight placed in the left, central and right cavity, respectively **(C)** for the handle being mounted onto the right, central and left socket with the hidden weight being placed in the central cavity. The illustration has been adapted from (T. R. Schneider & Hermsdorfer, 2022).

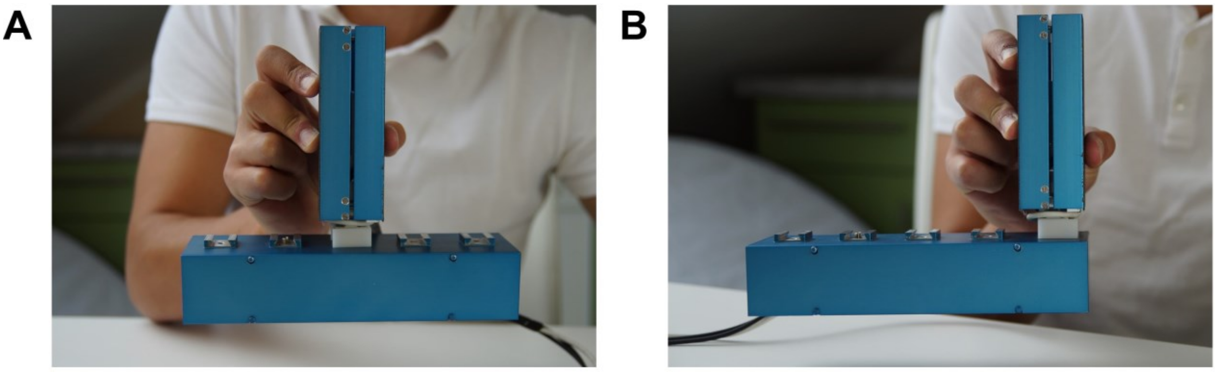


Figure 3: Pictures of the grip-device with the handle being placed onto the central **(A)** and left (**B**, perspective of subject) socket.

5.3 Experimental Task

In both studies, the main experimental task was to repeatedly grasp, lift, hold and replace the experimental object while preventing object tilts. Specifically, participants were instructed to start reaching for the grip-device after the first signal tone, contact the grip surfaces with the fingertips of the thumb-, index- and middle finger in a tripod precision grip, lift it from the table in a smooth movement to a height of ~5-10 cm while minimizing object tilts and to hold the object steady thereafter (see also **Figure 3**). Four seconds after the first, another signal tone signaled the participants to replace the object onto the table.

In **study I**, participants were asked to consecutively follow two additional instructions for one half of the trials each. The instructions were to either execute the lifts in a regular and natural way, or with the lowest possible grip forces, i.e. force efficiently.

In **study II,** no additional instructions were given.

5.4 Determining the static coefficient of friction, μ_s, at slip onset

In both studies, the static coefficient of friction, μ_s, was determined prior to the main experiment for the used surface materials. Additionally, μ_s estimates were also obtained at the end of study I. Subjects were asked to lift and hold the grip device positioning their thumb as collinearly in opposition to the index and middle fingers as possible. Subsequently, they were instructed to slowly decrease the GF until the object began to slip out of the hand. This was repeated for at least three times. We estimated the average static friction coefficient, μ_s, at the digit - surface contacts as the ratio between the load- and grip force at the moment of the first object slip onset. The Object slip onset was visually detected by a sudden drop in the load force, followed by an object downward movement. In study I, μ_s-estimates for each experimental trial were interpolated using subject- wise linear regression models as visuals inspection suggested μ_s might have changed over the course of trials in some individuals although the main regression estimate of the measurement time (prior and after the experiment) was not found to be a significant predictor of μ_s on the group level.

5.5 Clinical evaluation of patients with stroke (study II)

5.5.1 Modified Rankin Scale (mRS)

We administered the modified Rankin Scale (mRS) using the simplified questionnaire proposed by Bruno et al. (Bruno et al., 2010) as an overall disability measure.

5.5.2 Apraxia Tests

Patients with stroke were examined for signs of Apraxia using tests of the imitation of meaningless gestures of hand- and finger postures as well as of pantomime introduced by Goldenberg (Buchmann, Randerath, Liepert, & Büsching, 2018; Goldenberg, 1999; Goldenberg & Hagmann, 1997; Goldenberg, Munsinger, & Karnath, 2009). Patient performance was video-recorded for later analysis adhering to the established scoring instructions and diagnostic cutoffs (see **Figure 4**), i.e. imitation scores below 18 of 20 points for hand- and 17 of 20 points for finger-postures as well as pantomime scores below 45 of 55 points were considered as suggestive of apraxia.

Figure 4: Video Scoring of the imitation of gestures and pantomime according to Goldenberg.

5.5.3 Tests of visual hemispatial neglect

The presence of visual hemispatial neglect was investigated with a) the line bisection-test in which a deviation of more than 6 mm from the midpoint indicates hemispatial neglect (Agrell, Dehlin, & Dahlgren, 1997), b) the letter cancellation test with performance scored using the center of calculation (CoC) metric introduced by Rorden and Karnath (Rorden & Karnath, 2010) – i.e. an absolute CoC score above 0.083 indicates a hemispatial neglect – as well as c) a Posner type spatial cueing test (Posner, Snyder, & Davidson, 1980) implemented in the free computer test battery PEBL (version 0.14, (Mueller & Piper, 2014)). In the latter, we calculated the standardized median reaction time difference between trials with stimuli to the left and to the right of fixation as a continuous measure of a shift of visual attention. However, no established cut-off exists for defining hemispatial neglect with this approach.

5.6 Experimental protocol

5.6.1 Study I:

The protocol of study I was set up to assess how young and elderly participants learn to coordinate digit-positions and forces in order to generate compensatory torques for varying mass distribution and surface properties and whether the instruction to perform the task force efficiently impacts this coordination.

In this experiment, object properties remained constant for blocks of 6 trials each. Between blocks of trials, both the surface materials on both handle sides (4 conditions: (1) uniform crepe (CC, crepe on both grip sides), (2) non-uniform crepe-paper (CP, crepe on left handle side, paper on right side), (3) non-uniform paper–crepe (PC), and (4) uniform paper (PP, paper on both grip sides), as well the position of the hidden weight and herewith the external torque (3 external torques: -0.21 Nm, 0 nm, 0.21 Nm) were changed while subjects had their eyes closed. Participants were either provided with the instruction to perform the task as normally, i.e. as naturally as possible for the first 12 blocks, and subsequently as force efficiently as possible during the latter 12 blocks, or vice versa. The order in which the surface and external torque conditions were altered and the sequence of the instructions (normal vs. force efficient) were randomly assigned to each participant. Overall, each subject performed 24 lifting blocks (2 instructions x 3 external torques x 4 surface conditions) à 6 trials summing up to 144 lifting trials. **Figure 5** shows an representative experimental protocol of one participant.

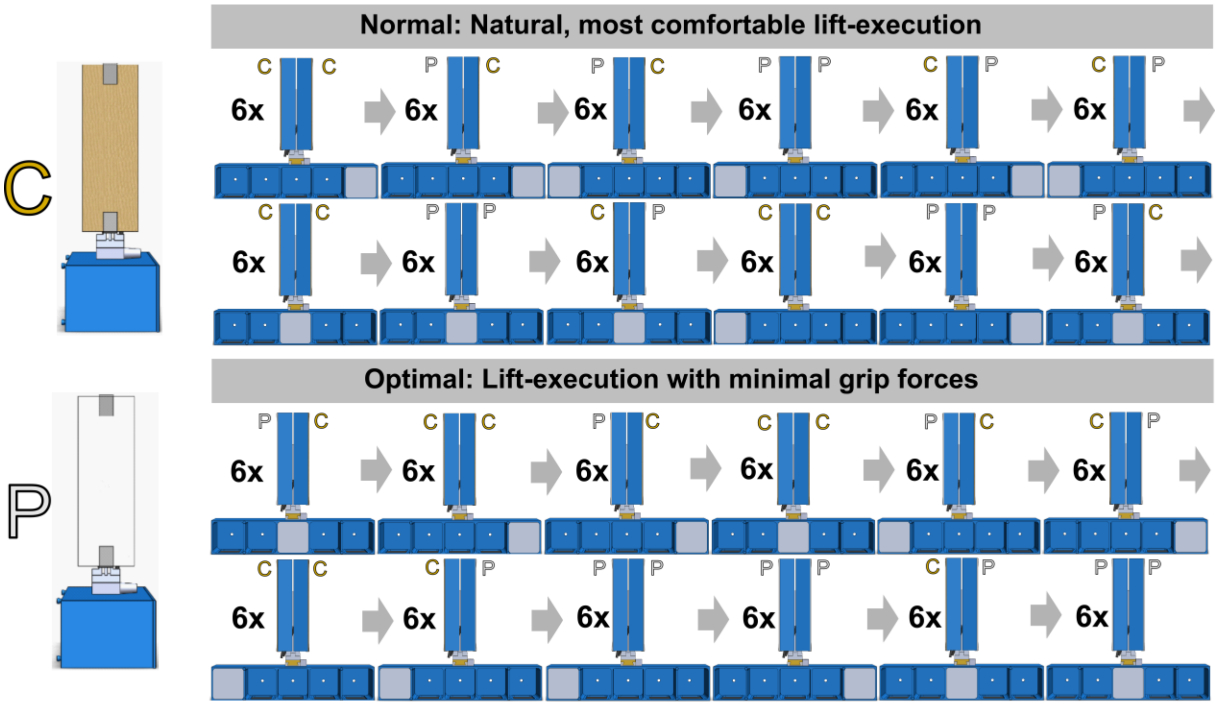


Figure 5: Representative experimental protocol of study I.

5.6.2 Study II:

The protocol of study II was designed to assess the impact of chronic stroke on the learning of compensatory torque production with the ipsilesional hand, when having to solely rely on sensorimotor experience, i.e. in the absence of visual cues, as well as when being provided with a salient geometric cue on object CoM. Two sequence and two cue conditions were studied. In the ‘no cues condition’, the hidden 250 g aluminum weight was placed into either the outer left or outer right hidden cavity of the horizontal base while the handle was attached over the center of the base (external torque ± 0.21 Nm). In the ‘geometric cues condition’, the handle was either positioned on top of the left or right base edge with the hidden weight remaining in the center gravity resulting in an asymmetric L-shape of the object and external torques of ± 0.46 Nm (**see Figure 2 C**).

In both cue-conditions, a ‘pseudorandom’ sequence-condition encompassing 37 trials in which the CoM was changed from trial-trial in a predefined pseudo random sequence which could not be predicted by the participants was followed by a ‘blocked’ sequence-condition encompassing 33 trials in which the CoM was only changed to the other side after each block of 8 trials in which the CoM remained constant. Participants were informed that the CoM would change to the opposing side between blocks but had to close their eyes during all CoM changes and also between all trials of the ‘no cues – pseudorandom’ conditions in which the hidden weight was retracted and put back either into the same or the opposite cavity position. In total, 140 lifting trials which were preceded by 6 practice trials in which the CoM was below the grip center had to be performed. The order of the two cue conditions and the initial CoM side for the first trial of the no-cues- and geometric-cues conditions was randomly assigned to the participants. **Figure 6** depicts a representative individual experimental protocol.

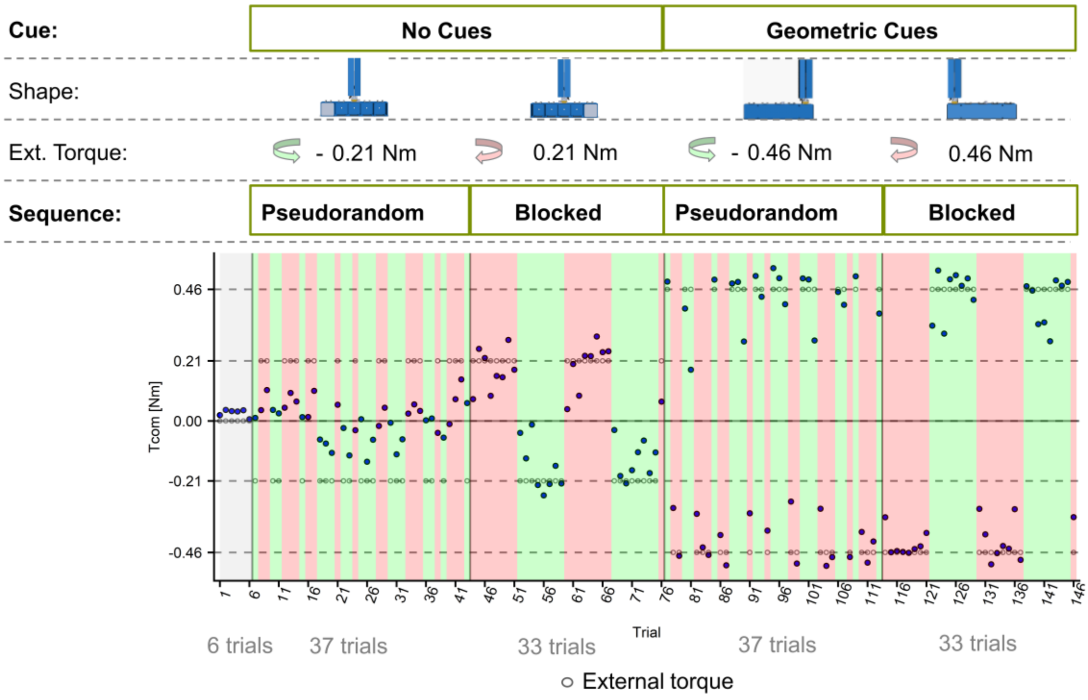


Figure 6: Representative experimental protocol of study II. Counterclockwise external torques are color coded as green, clockwise external torques as red. Empty black circles

denote the external torques, blue circles participant's Tcom. The illustration has been published in (T. R. Schneider & Hermsdorfer, 2022).

5.7 Data Processing

Sensor recordings were processed with custom software written in Matlab 2016a. The variables of interest were calculated according to the task mechanics detailed in **Figure 7**. Importantly, we could only measure the net mechanical forces and moments of the index and middle finger contacting the same grip side which must hence be considered as a virtual finger (Arbib, Iberall, & Lyons, 1985). The force/torque data was filtered with a sixth-order Butterworth low-pass filter with a cutoff frequency of 14 Hz.

5.8 Kinetic variables

In the following sections, the torque- and GF related variables of interest will be introduced (see also **Figure 8**).

5.8.1 Torque variables

1) **Tcom** denotes the exerted compensatory torque at object lift off which was defined as the moment 10ms prior to which the vertical position of the object surpassed a threshold of 0.2 mm). Tcom is an established indicator of anticipatory torque control (Fu & Santello, 2015; Fu et al., 2010; Salimi, Hollender, Frazier, & Gordon, 2000) and is highly correlated with the initial object tilt following lift-off which was confirmed in our lab (T. R. Schneider et al., 2020). **Tcom** is the sum of: a) **ΔCoP x GF**, the product of GF and the vertical distance between the digit centers of pressure on the right and left grip sides, ΔCoP, and b) **ΔLF x w/2**, the torque generated by the product of the difference between the right and left load force and half the distance between the grip-surfaces ($\frac{w}{2}$ = 20.8 mm in study I and 20.4 mm in Study II). Choosing these sign conventions, clockwise exerted torques were defined as negative and counter-clockwise torques as positive (see **Figure 7**). Therefore, Tcom matches in sign with the external torque when it is directed in the opposing direction to the external torque, i.e. compensates the external torque. To assess the relative success of torque anticipation we calculated the respective **ratios** between the torque variables and the external torque to compensate for, i.e.: $\frac{\text{Tcom}}{\text{External Torque}}$, $\frac{\Delta\text{LF x w/2}}{\text{External Torque}}$ and $\frac{\Delta\text{CoP x GF}}{\text{External Torque}}$. Positive ratios indicate that torques were directed in the correct direction with a ratio of 1 corresponding to a perfect torque compensation and negative ratios indicate that torques were directed in the wrong direction.

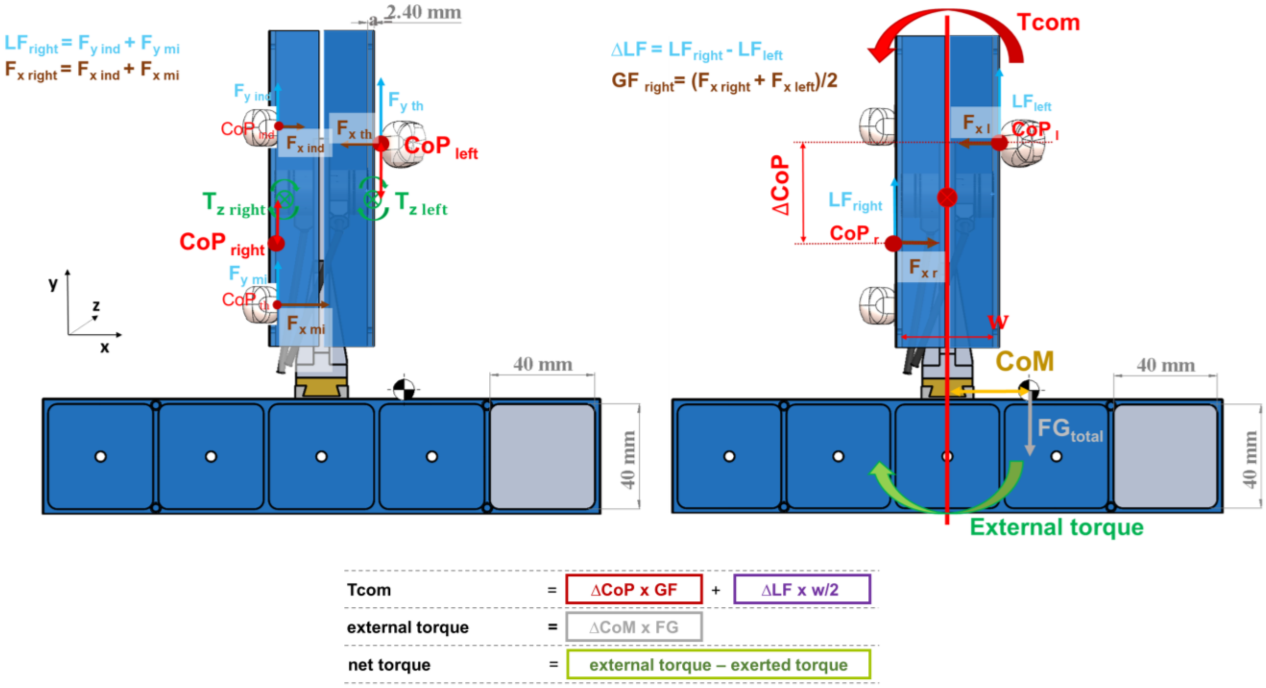


Figure 7: Task mechanics. A) Depiction of the forces 'F' acting on the object in a 3-finger tripod grip, with the left hand with the subscript 'ind' denoting the index finger, 'mi' the middle finger and 'th' the thumb. The registered torques around the z-axis of the F/T-Sensors $\mathbf{T_{z_i}}$ result from the sum of the product of the load force $\mathbf{LF_n}$ of the respective side, n, and the distance between the grasp surface and the sensor surface a (a=2.4 mm) and the product of the grip force of the respective side $\mathbf{GF_n}$ and the vertical $\mathbf{CoP_n}$ relative to the sensor reference point: $\mathbf{T_{z_n}} = \mathbf{a\ x\ LF_n} + \mathbf{CoP_i\ x\ F_{x_n}}$. Therefore, the center of pressure (CoP) relative to the sensor reference point in the center of each sensor surface can be calculated as: $\mathbf{CoP_n} = \frac{\mathbf{T_{z_n} - a\ x\ LF_n}}{\mathbf{F_{x_n}}}$. **B)** Depiction and calculation of the external and applied torques acting on the object around z-axis going through the center between the F/T-sensors. The external torque arising at lift-off is caused by the mass asymmetry of the object and is equivalent to the product of the gravitational force vector of the device Fg and the horizontal center of mass CoM_h: (external torque = ΔCoM x Fg). As a convention, we denote clockwise external torques and compensating counter clockwise exerted torques with a positive sign. The torque exerted by participants is the sum of two torque components: (1) the product of the side difference between the load force acting on the right and left handle side ΔLF and half the distance between the grasp-surfaces w/2 (w/2 = 20.8 mm in study I and 20.4 mm in Study II): **ΔLF x w/2** and (2) the product of the mean grip force (GF = 0.5 x (Fx_1 + Fx_2)) and the side of the vertical position of the CoP between the right and left grip sides, (ΔCoP = CoP_{right} – CoP_{left}): : **ΔCoP x GF**. Hence: **Tcom = ΔLF x w/2 + ΔCoP x GF**. The illustration has been adapted from the supplementary material of (T. R. Schneider et al., 2019).

5.8.2 Variables of GF control

1) Grip force (**GF**) is defined as the mean normal force directed orthogonal towards the grip surfaces and was analyzed at the moment of lift-off (both studies) and during the static phase (study I).

2) The static coefficients of friction, μ_s, of each participant (and for each surface material in study I) was calculated by averaging the ratios between the load force and grip force at the moment at which slips occurred in the slip-task.

Additionally, the following variables related to GF efficiency were calculated in study I to attribute GF excess to either errors in ΔCoP modulation or the keeping of a GF safety ratio. A detailed physical description of these variables will be given in **subsection 5.8.3** (Physical details regarding GF efficiency when lifting an object straight upwards while preventing object tilts).

3) **GF$_{\mathbf{min}}$** denotes the minimal GF needed to achieve a stable grip given the object weight and current frictions conditions and was calculated according to equation Eq. 5 as $\mathrm{GF_{min}} = \frac{\mathrm{F_G}}{\mu_{\mathrm{left}}+\mu_{\mathrm{right}}}$.
4) **ΔCoP$_{\mathbf{ideal}}$**, the ΔCoP necessary to achieve a stable grip with GF$_{\mathrm{min}}$, depends on the object and friction properties and was calculated according to equation Eg. 7 as: $\mathbf{\Delta COP_{ideal}} = \frac{\mathrm{T_{ext}}}{\mathrm{F_G}} * \left(\mu_{\mathrm{left}} + \mu_{\mathrm{right}}\right) - \frac{\mathrm{w}}{2} * \left(\mu_{\mathrm{right}} - \mu_{\mathrm{left}}\right) = \frac{\mathrm{T_{ext}}}{\mathrm{F_G}} * \left(\mu_{\mathrm{left}} + \mu_{\mathrm{right}}\right) + \frac{\mathrm{w}}{2} * \left(\mu_{\mathrm{left}} - \mu_{\mathrm{right}}\right)$
5) **GF$_{\mathbf{min\ at\ \Delta CoP}}$**, the minimal grip force to achieve a stable object grip given the actual ΔCoP, and object- and surface properties. **GF$_{\mathbf{min\ at\ \Delta CoP}}$** was determined by solving the linear system of equations and inequalities in Equation Eq. 10 using the package ‘limsolve’ in R (Van den Meersche, Soetaert, & Van Oevelen, 2009).
6) The ratio $\frac{\mathbf{\Delta CoP_{lift\ onset}}}{\mathbf{\Delta CoP}_{\mathrm{ideal}}}$ quantified the relative adequacy of anticipatory ΔCoP modulation. The ratio was only calculated for an eccentric weight distribution because ΔCoP$_{\mathrm{ideal}}$ becomes very small for a symmetric weight distribution (external torque = 0) and even becomes zero if the surface friction is additionally equal between grip sides.
7) The ratio $\frac{\mathbf{GF}}{\mathbf{GF_{min\ at\ \Delta CoP}}}$ at lift-off or during static phase corresponds to GF safety ratio with values > 1 indicating that participants applied higher GF than necessary for the object properties, friction conditions and current ΔCoP.
8) The ratio $\frac{\mathbf{GF_{min\ at\ \Delta CoP}}}{\mathbf{GF_{min}}}$ at lift-off or during static phase can be coined as the excess GF ratio due to a ΔCoP deviating from ΔCoP$_{\mathrm{ideal}}$.

Using these GF ratios, an observed GF excess can be attributed to a) suboptimal ΔCoP modulation and b) the keeping of a GF safety ratio while controlling for individual surface friction differences.

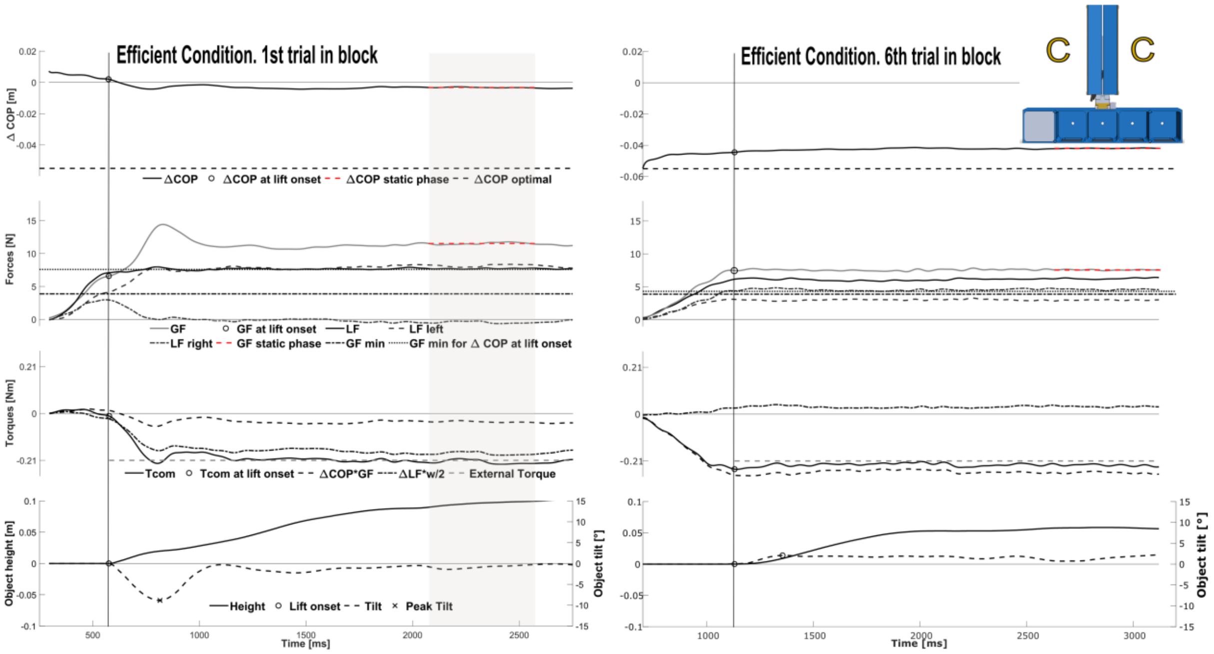


Figure 8: Representative trials of the first and last trial of a block in study I (participant #1, m, 25, right handed) depicting the task variables, derived variables and principal findings of the study. The participant was instructed to be GF efficient, the hidden aluminum weight was positioned in the left cavity (external torque = - 0.21 Nm), the surface condition was crepe on both sides. In the first trial, ΔCoP was around zero, indicating a collinear finger positioning. At object lift-off (vertical line) no torque was exerted. Consequently, an object tilt to the left occurred which was subsequently corrected by a repartitioning of load forces in a way that the required load force was exclusively exerted at the left side generating a compensatory clockwise torque (ΔLF x w/2). In the 6th trial, the digit(s) CoP was clearly higher on the left than right side resulting in ΔCoP close to ΔCoP_{ideal}, the ΔCoP which allows an object lift with the lowest possible GF (GF_{min}). Here, the torque component ΔCoP x GF almost perfectly compensates for the external torque (horizontal dashed line) already at lift off. Consequently, load forces could be partitioned uniformly between the sides and virtually no object tilt occurred. Regarding GF economy, due to the inadequate ΔCoP in the first trial of the block, the lowest necessary GF to support a safe object grip given the object properties and chosen ΔCoP ($GF_{\text{min at }\Delta CoP\text{ at lift onset}}$, dotted horizontal line 3^{rd} subplot) was increased. As a consequence, the applied GF at lift-off fell below the necessary GF threshold such that GF had to be subsequently increased following object lift-off. In contrast, in the 6^{th} trial the calculated $GF_{\text{min at }\Delta CoP\text{ at lift onset}}$ was almost as low as the minimal GF for the finger-surface coefficients of friction (GF_{min}). As a consequence, a markedly lower actual GF could be applied at lift-off which subsequently remained stable during the static holding phase (GF_{static}, horizontal red dashed line). The illustration has been published in (T. R. Schneider & Hermsdorfer, 2021).

5.8.3 Physical details regarding GF efficiency when lifting an object straight upwards while preventing object tilts

When lifting an object at two parallel surfaces straight upwards and holding it steady thereafter, the normal forces orthogonal to the grip surfaces on both sides, Fx_n, must be equal, as the object must not be accelerated horizontally.

$$\mathbf{Fx}_{\mathbf{left}} = \mathbf{Fx}_{\mathbf{right}} = \mathbf{GF}$$ **Eq. 1**

The static coefficient of friction μ_s is defined as the ratio between the force tangential to the surface, which is exclusively directed upwards when lifting an object straight upwards, $\mathrm{LF_n}$, and the orthogonal force, $\mathrm{Fx_n}$, at the moment of slip onset. Hence, the normal force at slip onset can be regarded as the lower limit to guarantee a stable finger-object contact ($\mathrm{Fx_{n\,min}}$).

$$\mu_{\mathrm{n}} = \frac{\mathbf{LF}_{\mathbf{n}}}{\mathbf{Fx}_{\mathbf{n\,min}}}$$ **Eq. 2**

GF must surpass the lowest possible orthogonal force needed to prevent object slip at both grip sides. The lowest possible grip force, $\mathrm{GF_{min}}$, is equal to the lowest possible orthogonal force on both sides which in turn must be equal($\mathbf{Fx}_{\mathbf{left\,min}} = \mathbf{Fx}_{\mathbf{right\,min}}$). Otherwise, if the lowest possible orthogonal forces were different between sides, Fx_{n} on the side with the lower $\mathrm{Fx_{n\,min}}$ must be scaled up to match the higher $\mathrm{Fx_{m\,min}}$ as orthogonal forces must be equal between sides (Eq. 1). This can be formulated as:

$$\mathbf{GF}_{\mathbf{min}} = \mathbf{Fx}_{\mathbf{left\,min}} = \mathbf{Fx}_{\mathbf{right\,min}} \xrightarrow{\text{with Eq.2}} \frac{\mathbf{LF}_{\mathbf{left}}}{\mu_{\mathrm{left}}} = \frac{\mathbf{LF}_{\mathbf{right}}}{\mu_{\mathrm{right}}}$$ **Eq. 3**

As the sum of the tangential load forces of both grip sides sum up to match the gravitational force of the object ($\mathrm{F_G} = \mathbf{LF}_{\mathrm{left}} + \mathbf{LF}_{\mathrm{right}}$), the ratio of the tangential forces must be proportional to the relation of the coefficients of static fractions μ_n on both grip sides (Aoki et al., 2006). This allows for the calculation of the optimal load forces acting on both sides and consequently $\mathrm{GF_{min}}$:

$$\mathrm{F_G} = \mathbf{LF}_{\mathbf{left}} + \mathbf{LF}_{\mathbf{right}} \text{ and (with Eq. 3) } \mathbf{LF}_{\mathbf{right}} = \mathbf{LF}_{\mathbf{left}} * \frac{\mu_{\mathrm{right}}}{\mu_{\mathrm{left}}} \xrightarrow{\text{yields}} \mathrm{F_G} = \mathbf{LF}_{\mathbf{left}} + \mathbf{LF} * \frac{\mu_{\mathrm{right}}}{\mu_{\mathrm{left}}} \xrightarrow{\text{yields}}$$

$$\mathrm{F_G} = \mathbf{LF}_{\mathbf{left}}\left(1 + \frac{\mu_{\mathrm{right}}}{\mu_{\mathrm{left}}}\right) \xrightarrow{\text{yields}}$$

$$\mathbf{LF}_{\mathbf{left}} = \frac{\mathrm{F_G}}{1 + \frac{\mu_{\mathrm{right}}}{\mu_{\mathrm{left}}}} \text{ and } \mathbf{LF}_{\mathbf{right}} = \frac{\mathrm{F_G}}{1 + \frac{\mu_{\mathrm{left}}}{\mu_{\mathrm{right}}}}$$ **Eq. 4**

Hence, combining Eq. 3 and Eq. 4:

$$\mathbf{GF_{min}} = \mathbf{Fx_{left\,min}} = \mathbf{Fx_{right\,min}} = \frac{\mathbf{LF_{left}}}{\mu_{left}} = \frac{\mathbf{LF_{right}}}{\mu_{right}} = \frac{F_G}{\left(1 + \frac{\mu_{right}}{\mu_{left}}\right) * \mu_{left}}$$

$$= \frac{F_G}{\left(1 + \frac{\mu_{left}}{\mu_{right}}\right) * \mu_{right}} \xrightarrow{\text{yields}}$$

$$\mathbf{GF_{min}} = \frac{F_G}{\mu_{left} + \mu_{right}} \qquad \textbf{Eq. 5}$$

The compensatory torque along a sagittal axis going through the midline between the grip surfaces, $\mathbf{T_{com}}$, must compensate the external torque, T_{Ext}, arising at lift-off due to a mass distribution eccentric to the grip axis to prevent object tilt. As defined in subsection 5.8.1 this can be formulated as:

$$\mathbf{T_{com}} = T_{Ext} = (\mathbf{LF_{right}} - \mathbf{LF_{left}}) * \frac{w}{2} + \mathbf{\Delta COP} * \mathbf{GF}, \text{with } \Delta COP = COP_{right} - COP_{left} \qquad \textbf{Eq. 6}$$

If the lowest possible GF, GF_{min}, was to be applied, distinct load forces must be applied on both sides (see Eq. 4). As a consequence, Tcom can only be generated with a distinct, ideal ΔCoP, $\mathbf{\Delta COP_{ideal}}$:

$$\text{with (Eq. 4, 5, 6): } T_{ext} = \left(\frac{F_G}{1+\frac{\mu_{left}}{\mu_{right}}} - \frac{F_G}{1+\frac{\mu_{right}}{\mu_{left}}}\right) * \frac{w}{2} + \mathbf{\Delta COP} * \frac{F_G}{\mu_{left}+\mu_{right}} \xrightarrow{\text{yields}} \mathbf{\Delta COP_{ideal}} =$$

$$\frac{T_{ext} - \frac{w}{2} * \left(\frac{F_G}{1+\frac{\mu_{left}}{\mu_{right}}} - \frac{F_G}{1+\frac{\mu_{right}}{\mu_{left}}}\right)}{\frac{F_G}{\mu_{left}+\mu_{right}}} =$$

$$\frac{\left(T_{ext} - \frac{w}{2} * \left(\frac{F_G}{1+\frac{\mu_{left}}{\mu_{right}}} - \frac{F_G}{1+\frac{\mu_{right}}{\mu_{left}}}\right)\right) * (\mu_{left}+\mu_{right})}{F_G} = \frac{\left(T_{ext} - \frac{w}{2} * \left(\frac{\mu_{right} * F_G - \mu_{left} * F_G}{\mu_{left}+\mu_{right}}\right)\right) * (\mu_{left}+\mu_{right})}{F_G} =$$

$$\frac{\left(T_{ext} * (\mu_{left}+\mu_{right}) - \frac{w}{2} * (\mu_{right} * F_G - \mu_{left} * F_G)\right)}{F_G} = \frac{\left(T_{ext} * (\mu_{left}+\mu_{right}) - \frac{w}{2} * F_G * (\mu_{right} - \mu_{left})\right)}{F_G} \xrightarrow{\text{yields}}$$

$$\mathbf{\Delta COP_{ideal}} = \frac{T_{ext}}{F_G} * (\mu_{left} + \mu_{right}) - \frac{w}{2} * (\mu_{right} - \mu_{left})$$

$$\mathbf{\Delta COP_{ideal}} = \frac{T_{ext}}{F_G} * (\mu_{left} + \mu_{right}) + \frac{w}{2} * (\mu_{left} - \mu_{right}) \qquad \textbf{Eq. 7}$$

In real life situations, ΔCoP never exactly matches $\Delta \mathrm{COP}_{\mathrm{ideal}}$.Therefore, the minimal possible grip force for the object- and friction properties and the current ΔCoP, $\mathbf{GF}_{\mathbf{min\ at\ \Delta CoP}}$, must be determined by solving the following linear system of equations and inequalities which account for the aforementioned relations:

Eq. 8

I) $\text{with Eq. 6:} -\frac{w}{2} * \mathbf{LF}_{\boldsymbol{left}} + \frac{w}{2} * \mathbf{LF}_{\boldsymbol{right}} + \Delta\mathrm{COP} * \mathbf{GF} = \mathrm{T}_{\mathrm{ext}}$

II) $\mathbf{LF}_{\boldsymbol{left}} + \mathbf{LF}_{\boldsymbol{right}} = \mathrm{F}_{\mathrm{G}}$

III) $\mathbf{GF} \geq \mathbf{Fx}_{\mathbf{left\ min}} \geq \frac{\mathbf{LF}_{\boldsymbol{left}}}{\mu_{left}} \xrightarrow{\text{yields}} \mathbf{GF} - \frac{1}{\mu_{left}} * \mathbf{LF}_{\boldsymbol{left}} \geq 0$

IV) $\mathbf{GF} \geq \mathbf{Fx}_{\mathbf{right\ min}} \geq \frac{\mathbf{Fy}_{\boldsymbol{right}}}{\mu_{right}} \xrightarrow{\text{yields}} \mathbf{GF} - \frac{1}{\mu_{right}} * \mathbf{LF}_{\boldsymbol{right}} \geq 0$

These can be reformulated as:

Eq. 9

I) $-\frac{w}{2} * \mathbf{LF}_{\mathbf{left}} + \frac{w}{2} * \mathbf{LF}_{\mathbf{right}} + \Delta\mathrm{COP} * \mathbf{GF} = \mathrm{T}_{\mathrm{ext}}$

II) $1 * \mathbf{LF}_{\mathbf{left}} + 1 * \mathbf{LF}_{\mathbf{right}} = \mathrm{F}_{\mathrm{G}}$

III) $-\frac{1}{\mu_1} * \mathbf{LF}_{\mathbf{left}} + 1 * \mathbf{GF} \geq 0$

IV) $-\frac{1}{\mu_2} * \mathbf{LF}_{\mathbf{right}} + 1 * \mathbf{GF} \geq 0$

With $\mathbf{LF}_{\mathbf{left}} = \mathbf{x}_1$, $\mathbf{LF}_{\mathbf{right}} = \mathbf{x}_2$, $\mathbf{GF} = \mathbf{x}_3$, the linear systems of equations and inequalities can be written and solved as Eq. 10:

Eq. 10

$$\begin{bmatrix} -w/2 & w/2 & \Delta\mathrm{COP} \\ 1 & 1 & 0 \end{bmatrix} = \begin{bmatrix} \mathrm{T}_{\mathrm{ext}} \\ \mathrm{F}_{\mathrm{G}} \end{bmatrix}$$

$$\begin{bmatrix} -1/\mu_{\mathrm{left}} & 0 & 1 \\ 0 & -1/\mu_{\mathrm{right}} & 1 \end{bmatrix} \geq \begin{bmatrix} 0 \\ 0 \end{bmatrix}$$

5.9 Statistical Analysis

All statistical analyses were performed in the R environment for statistical computing (version 4.0.3, (R Core Team, 2018), R Project for Statistical Computing, (RRID):SCR_001905). We fit separate linear mixed effects models (LMM) with random-intercepts estimating the random variance across subjects using the restricted maximum likelihood criterion as implemented in the ‘lme4’- (D. Bates, Mächler, Bolker, & Walker, 2015) package for the dependent primary and secondary outcome variables. By accounting for the random interindividual performance variation in a repeated measures study design, LMMs may safeguard against anti-conservative inference (Aarts, Verhage, Veenvliet, Dolan, & van der Sluis, 2014; J. C. P. D.

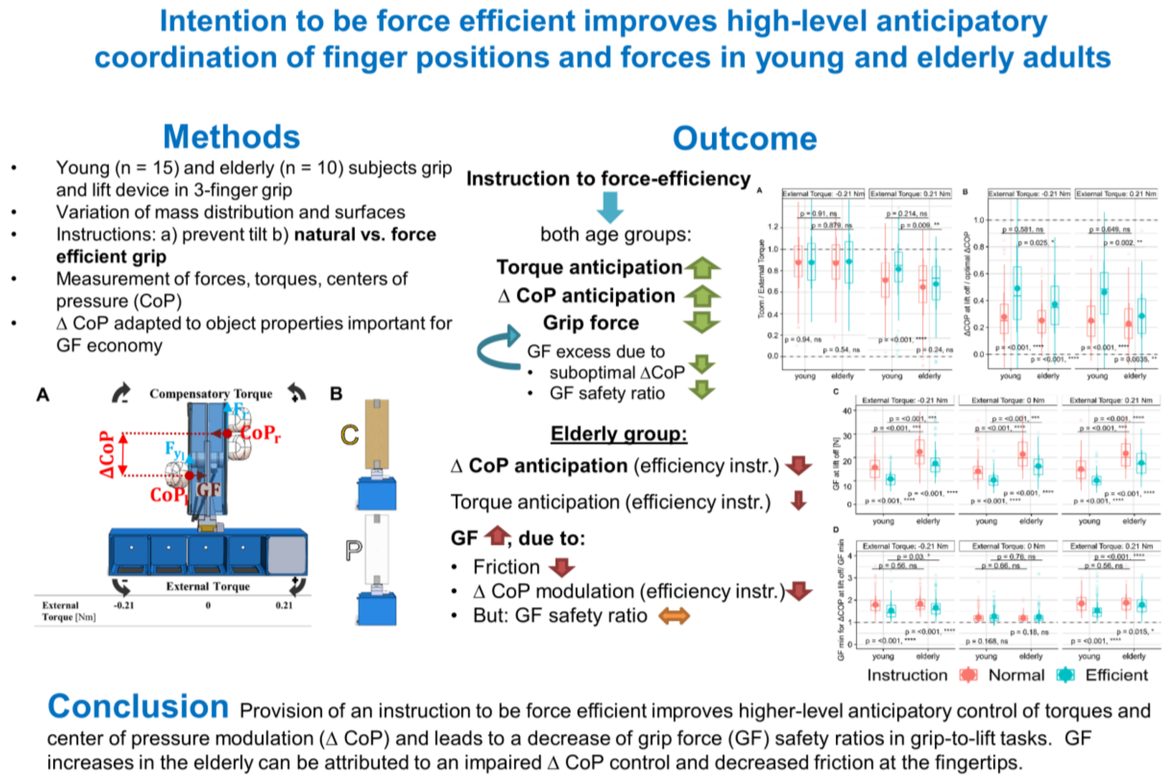
M. Bates, Pinheiro, Pinheiro, & Bates, 2000; Long, 2011). In both studies, we conducted omnibus Wald-type F-tests of the respective model predictors with type-III analyses of variance (ANOVA) using the ‘lmerTest’ package (Kuznetsova, Bruun Brockhoff, & Haubo Bojesen Christensen, 2016) as well as post-hoc t-Tests of pairwise comparisons between groups of interest (study I: young vs. elderly, study II: hand-matched control vs. stroke groups (CL-SL, CR-SR)) and also between the experimental instructions in study I (normal vs. force-efficient task execution) based on the marginal means of the LMMs with Holm-Bonferroni correction for multiple testing using the ‘emmeans’ package (Lenth, 2020). The Kenward-Roger method was used to approximate the models predictors’ degrees of freedom as implemented in the ‘pbkrtest’-package (Halekoh & Højsgaard, 2014). Besides, exploratory analyses of variance (ANOVA) tests for numerical data (respectively t-tests if data were only obtained for the stroke groups) and chi-square tests for categorical data were conducted in study II to compare the demographic and clinical characteristics of the control- and stroke groups using the ‘arsenal’ package (Ethan Heinzen, 2021).

Details on the statistical models are provided in the study publications and the model result tables are presented in the respective supplementary materials of (T. R. Schneider & Hermsdorfer, 2021, 2022).

6 Studies

6.1 Study I: Intention to be force efficient improves high-level anticipatory coordination of finger positions and forces in young and elderly adults

This study was published in the *Journal of Neurophysiology* in 03/2021 by Thomas Schneider and Joachim Hermsdörfer. In this case-control study, we compared the capacity of fifteen young and ten elderly healthy adults to coordinate their digit positions and forces with respect to the predictive compensation of external torques and grip force economy when lifting an object with varying mass distributions and surface properties both when performing the task naturally as well as when being prompted to perform the task as force-efficient as possible. We were the first in the field to mathematically outline the importance of an adequate modulation of the digit centers of pressure on opposing handle sides (∆CoP) showing that the lowest possible stable grip force level for the weight and surface-friction properties can only be achieved with a distinct, ideal ∆CoP. Consequently, the observed grip force excess could be attributed to both a deviation of ∆CoP modulation and the keeping of a GF safety ratio. In the natural task execution condition, the learned ∆CoP modulation was far from ideal in both age groups and the relative grip force excess due to both the ∆CoP deviation and the application of a safety margin were of similar magnitude in both age groups. However, when trying to perform the task as grip-force efficiently as possible young participants were more successful in optimizing ∆CoP modulation which also resulted in an improved torque compensation in the young while both groups reduced the applied safety margins to a similar degree resulting in a drop of GF levels. Higher GF levels in the elderly could be attributed to a lower finger-tip friction and a worse ∆CoP modulation when trying to be grip force efficient. Taken together, our results demonstrate that the sensorimotor integration of object- and friction properties for torque and force control is similar in young and elderly adults in a natural lifting condition, whereas a decrease in the sensorimotor integration capacity becomes evident in the elderly when force-efficiency is the task goal. **Figure 9** is a graphical abstract that summarizes the main study findings and conclusions. The publication is attached in the Appendix (12.1).



Intention to be force efficient improves high-level anticipatory coordination of finger positions and forces in young and elderly adults

Methods

- Young (n = 15) and elderly (n = 10) subjects grip and lift device in 3-finger grip
- Variation of mass distribution and surfaces
- Instructions: a) prevent tilt b) **natural vs. force efficient grip**
- Measurement of forces, torques, centers of pressure (CoP)
- Δ CoP adapted to object properties important for GF economy

Outcome

Instruction to force-efficiency

both age groups:

Torque anticipation ⬆

Δ CoP anticipation ⬆

Grip force ⬇

GF excess due to

- suboptimal ΔCoP ⬇
- GF safety ratio ⬇

Elderly group:

Δ **CoP anticipation** (efficiency instr.) ⬇

Torque anticipation (efficiency instr.) ⬇

GF ⬆**, due to:**

- Friction ⬇
- Δ CoP modulation (efficiency instr.) ⬇
- But: GF safety ratio ⬄

Conclusion Provision of an instruction to be force efficient improves higher-level anticipatory control of torques and center of pressure modulation (Δ CoP) and leads to a decrease of grip force (GF) safety ratios in grip-to-lift tasks. GF increases in the elderly can be attributed to an impaired Δ CoP control and decreased friction at the fingertips.

Figure 9: Graphical abstract of study I. The graphical abstract was published online with (T. R. Schneider & Hermsdorfer, 2021).

6.1.1 Contributions

Thomas Schneider was the primary composer and first author of the manuscript. Thomas Schneider developed the experimental design, conducted the measurements, performed the technical and statistical analyses and drafted the first version of the manuscript. Joachim Hermsdörfer contributed to the data analysis and interpretation. Thomas Schneider and Joachim Hermsdörfer both contributed to the revision of the manuscript.

6.1.2 Abstract

Successful object manipulation requires anticipatory high-level-control of finger positions and forces to prevent object slip and -tilt. Unlike young adults, who efficiently scale grip forces (GF) according to surface conditions, old adults were reported to exert excessive grip forces. Here, we theoretically show how grip force economy depends on the modulation of the centers of pressure on opposing grip surfaces (∆CoP) according to object properties. In a grasp-to-lift study with young and elderly participants we investigated how the instruction to lift the object with efficient GF influences the anticipation of torques, ∆CoP and GF control during complex variations of mass distributions and surface properties. Provision of the explicit instruction to strive for force efficiency prompted both age groups to optimize their ∆CoP modulation - although to a lesser degree in the elderly - and also led to a refinement of torque anticipation for a right-sided weight distribution in the young- but not the elderly participants. Consequently, marked drops in GF levels resulted. Furthermore, participants enhanced ∆CoP modulation and lowered GF safety ratios in challenging surface conditions. Higher GF in the elderly was due to decreased skin-surface friction but also worse ∆CoP modulation for lateralized mass distributions when trying to be force-efficient. In contrast, safety margins were not elevated in the elderly suggesting preserved GF control. Our findings demonstrate how task goals influence high-level motor control of object manipulation differentially in young and elderly participants and highlight the necessity to control for both instructions and friction when investigating GF control.

6.2 Study II: Object-centered sensorimotor bias of torque control in the chronic stage following stroke

This study was published in *Scientific Reports* in 08/2022 by Thomas Schneider and Joachim Hermsdörfer. In this case-control study, we examined how 13 patients with chronic stage, left hemispheric- (SL) and nine patients with right hemispheric stroke (SR) learned to predictively compensate torques when lifting an object with an asymmetric center of mass with the fingertips of their ipsilesional hand at a handle while having to prevent object tilt. Patients‘ performance was compared with that of age- and hand matched healthy controls. We found that the torque resulting from grip force being applied at different vertical finger positions was biased depending on the location of the center of mass (CoM) of the lifted object in patients with left-hemispheric- and, to a lesser degree, also right hemispheric stroke, favoring an ipsilesional CoM over a contralesional CoM when having to rely on sensorimotor memories. In contrast, the torque generated by different vertical load forces on both sides of the handle was biased in the opposite direction in SL-patients resulting in a similar total torque compensation between groups. No group differences were found when a geometric cue on the object CoM was provided. The study findings are consistent with a shift of sensorimotor attention and intention away from the contralesional- and towards the ipsilesional object side and could represent preliminary evidence for an object-centered reference frame of premotor neglect in basic object manipulation. **Figure 10** summarizes the main group differences in the sensorimotor learning condition. The publication is attached in the Appendix (12.2).

6.2.1 Contributions

Thomas Schneider was the primary composer and first author of this manuscript. Thomas Schneider and Joachim Hermsdörfer developed the experimental design and set up the study. Thomas Schneider collected the data from the participants, performed the technical and statistical analyses and drafted the first version of the manuscript. Joachim Hermsdörfer contributed to the data analysis and interpretation. Thomas Schneider and Joachim Hermsdörfer both contributed to the final version of the manuscript.

6.2.2 Abstract

Background

When lifting objects whose center of mass (CoM) are not centered below the handle one must compensate for arising external torques already at lift-off to avoid object tilt. Previous studies showed that finger force scaling during object lifting may be impaired at both hands following stroke. However, torque control in object manipulation has not yet been studied in patients with stroke.

In this pilot study, thirteen patients with chronic stage left hemispheric stroke (SL), nine patients with right hemispheric stroke (SR) and hand-matched controls had to grasp and lift an object with the fingertips of their ipsilesional hand at a handle while preventing object tilt. Object CoM and therewith the external torque was varied by either relocating a covert weight or the handle. The compensatory torque at lift-off (Tcom) is the sum of the torque resulting from 1) grip force being produced at different vertical finger positions (ΔCoP x GF) and 2) different vertical load forces on both sides of the handle (ΔFy x w/2).

Results

When having to rely on sensorimotor memories, ΔCoP x GF was elevated when the object CoM was on the ipsilesional-, but decreased when CoM was on the contralesional side in SL, whereas ΔFy x w/2 was biased in the opposite direction, resulting in normal Tcom. SR patients applied a smaller ΔCoP x GF when the CoM was on the contralesional side. Torques were not altered when geometric cues were available.

Conclusion

Our findings provide evidence for an object-centered spatial bias of manual sensorimotor torque control with the ipsilesional hand following stroke reminiscent of premotor neglect. Both intact finger force-to-position coordination and visuomotor control may compensate for the spatial sensorimotor bias in most stroke patients. Future studies will have to confirm the found bias and evaluate the association with premotor neglect.

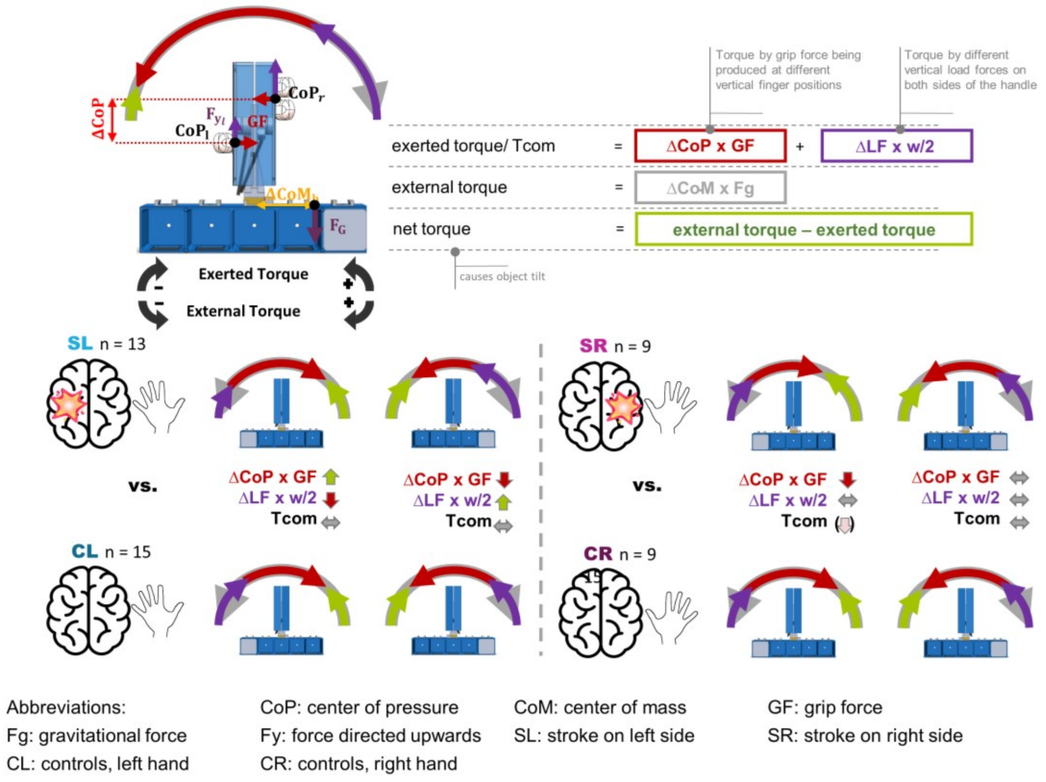


Figure 10: Graphical abstract of the main findings of the sensorimotor learning condition study II in the sensorimotor learning condition.

7 General Discussion

The following general discussion should be regarded as a summary and synthesis of discussions presented in the manuscripts of the conducted studies. It must be emphasized that the studies were conducted without any directed funding and without a clinical cooperation partner. Therefore, clear limitations, especially small sample sizes and a heterogenous and not optimally characterized stroke patient cohort, render the study findings preliminary. Nevertheless, the aims of the thesis were accomplished to the maximal degree that was possible by the given resources. We will review the most important findings of the conducted studies, summarize the tentative conclusions drawn and outline how the study findings will guide future research on the higher-level control of object manipulation in neurologic patient populations.

7.1 Basic sensorimotor and visuomotor learning processes are preserved in the elderly and following stroke (both studies)

To begin with, both young and elderly healthy participants in study I as well as the predominantly elderly healthy controls and patients with chronic stroke quickly learned to predictively compensate arising torques by relying on sensorimotor memories of previous object lifts when no cues on object CoM were present. The overall learning curves were qualitatively similar across all groups and the extent to which the torque compensation was learned in a block of trials was similar across all groups. Our findings stand in line with previous studies examining young adults (e.g. (Fu & Santello, 2015; Zhang et al., 2010)). In both studies, sensorimotor learning took about two- to three trials after which torque compensation remained stable. Participant did not only rely on sensorimotor memories of previous trials when they knew that object properties would remain constant but also continued to plan torques according to the most recent lifting trial even when the object center of mass changed unpredictably between trials in study II. This stands in line with previous investigations of young and elderly adults (Lukos et al., 2013; T. R. Schneider et al., 2019). Moreover, participants failed to transfer the learned sensorimotor torque planning to a new situation when they were explicitly told that the CoM would change to the other side for a new block of trials resulting in torques applied in the wrong direction (Zhang et al., 2010). When the mass distribution could be inferred from the geometric shape of the object (L-Shape), both stroke and elderly participants successfully predictively compensated for arising torques already in the first object lift, even when the object geometry changed from trial to trial (study II). As in previous studies (Fu & Santello, 2012, 2015; T. R. Schneider et al., 2020), torques were mainly applied by modulating the centers of pressure on both grip sides (ΔCoP x GF) when a geometric cue was provided, whereas the torque resulting from the load force distribution across opposing handle sides (∆LF x w/2) was negligible in the geometric cue condition. We had already previously shown that the visuomotor planning of fingertip positions and forces to compensate torques according to object geometry does not differ between young and elderly healthy adults (T. R. Schneider et al., 2020). While fundamental sensorimotor- and visuomotor torque control was preserved in the elderly and chronic stroke patients, we found evidence for a deterioration of higher-level sensorimotor control with aging when the sensorimotor system was challenged and demonstrated an object-centered spatial bias of the sensorimotor control of finger positions and forces in chronic stroke patients.

7.2 Anticipatory high-level coordination of finger positions and forces for torque control and force efficiency (Study I)

High-level control denotes the concept that the sensorimotor system learns how to achieve task goals, in this case the compensation of arising torques at lift-off, without necessarily storing the exact lower-level, effector variables like the exact positions and forces of each specific finger, i.e. effector, of prior task executions. Studies on torque control have supported that torques are indeed controlled on task- and not effector level. While digit positions and forces vary considerably across subsequent lifting trials, the torque variance remains low as digit forces are kept in close correlation with the current digit positions. This coordination of finger-forces according to finger positions is a general high-level-control mechanism in object manipulation which was demonstrated for different one- and two hand grip types (Davare et al., 2019; Fu et al., 2011; Fu et al., 2010; Lee-Miller et al., 2019; Marneweck et al., 2016). Furthermore, learned torques are reproduced after changes of the number of involved fingers (Fu et al., 2011), a phenomenon coined motor equivalence (Lashley, 1930). This clearly contradicts the storing of effector level variables and supports the concept of higher-level control. In study I, we outlined that an adequate ∆CoP modulation strongly impacts how grip force efficiently an object lift can be performed. The choice of the ideal ∆CoP is complicated as the weight and weight distribution – and herewith the arising external torque - of the object, the grip width as well the surface friction on both handle sides must all be considered. Unsurprisingly, although both young and elderly participants positioned their fingers higher on the side of the object CoM, ∆CoP was far from ideal in both group when participants were endorsed to perform the task as naturally as possible. This demonstrates that finding an adequate fingertip ∆CoP for varying object properties is a sensorimotor challenge. However, when explicitly proclaiming grip force efficiency as an additional task goal both groups improved their ∆CoP modulation although the extent of improvement was clearly and significantly higher in young adults. Still, ∆CoP at lift off was still only about half as high in young adults as would have been ideal stressing how demanding the sensorimotor integration task is. Apart from improving ∆CoP and therewith

GF economy, we also observed an improvement of torque compensation in young adults when striving for force efficiency. As humans increase grip forces when torque perturbations threaten the grip-stability (Naceri et al., 2017), a more precise torque compensation may indeed help to minimize grip forces during object lift. This might also explain our side finding, that torque control was more precise when the grip surfaces were covered with paper on both sides as stronger grip force correction might be necessary if torque errors occur under slippery surface conditions. Taken together, the improved ΔCoP and torque compensation at lift-off when trying to perform the task grip force efficiently constitute further evidence for a higher-level, i.e. task-level, control of object manipulation integrating object- and effector properties as well as task goals. Our findings are consequently also consistent with and can be interpreted as evidence for inverse internal models as introduced in section 4.1.

7.3 Subtle deterioration of higher-level motor control with aging explains reduced GF efficiency in the elderly (Study I)

As in previous studies, absolute grip force levels both at lift off and during the static holding of the object were markedly higher in elderly participants which could partly be attributed to the decreased friction at the fingertips presumably due to reduced skin hydration (Cole et al., 1999; Diermayr et al., 2011; Kinoshita & Francis, 1996). A principal merit of this thesis is that we could further differentiate the GF excess caused by a suboptimal ∆CoP from the GF excess due to keeping a GF safety margin/ratio. Moreover, and surprisingly, this is to the best of our knowledge the first study on grip force efficiency in which an explicit instruction to perform the task as grip force efficiently as possible was given. Previous studies assumed that grip force efficiency was a strong implicit natural task goal. The presented findings clearly challenge this assumption as GF levels dropped in both groups when participants tried to be force efficient since participants improved their ∆CoP modulation, and lowered their GF safety ratios. GF safety ratios were not elevated in the elderly and were reduced to a similar relative extent as in young adults when grip force efficiency was a priority while the absolute grip forces were decreased by an even higher extent in the elderly- than in the young group. This stands in line with a study in which old adults were shown to grip fragile objects with lower GF levels than young participants (Gorniak, Zatsiorsky, & Latash, 2011). Therefore, we found no evidence for a deterioration of basic GF control with age. However, as our elderly group was rather young with a mean age of 69 years, we cannot preclude that GF control deteriorates later in life.

While the relative GF excess due to a suboptimal ∆CoP given an eccentric object weight distribution was similar in both age groups in the natural lifting condition, elderly participants failed to improve their ∆CoP to a similar extent as young participants when trying to be force efficient which resulted in a significantly higher GF excess attributed to a ∆CoP deviation in the elderly in that condition. As summarized above, the modulation of ∆CoP to improve GF efficiency is a sensorimotor challenge because effector- and object properties as well as task goals must be integrated. Furthermore, improving ∆CoP may also be cognitively demanding. Unfortunately, we did not perform a cognitive examination of the participants. In agreement with our study results, force-field studies also found a reduced motor adaptation in elderly adults which was tightly coupled with a reduction in explicit learning capacities and associated with volume loss in the striatum, prefrontal and sensorimotor cortical regions, as well as the medial temporal lobe, including the hippocampus (Vandevoorde & Orban de Xivry, 2019; Wolpe et al., 2020). A more pronounced decline with age, especially in the seventh decade, was demonstrated for the anticipatory planning of hand postures according to situational constraints and upcoming actions in a bar transport tasks (Scharoun, Gonzalez, Roy, & Bryden, 2016; Stockel, Wunsch, & Hughes, 2017; Wunsch, Weigelt, & Stockel, 2017), which is an established indicator of the anticipatory motor control of kinematics (Rosenbaum et al., 1990). Again, anticipatory posture planning and manual dexterity were highly correlated with cognitive performance, especially processing speed and cognitive flexibility (Stockel et al., 2017).

Taken together, our results suggest that while the higher-level control of fingertip positions and forces does not significantly differ in elderly participants, their sensorimotor capacity to adapt their higher-level planning according to task goals and complex variations of object properties may be reduced. This could represent an important factor underlying the age-related decline of dexterity. Future studies, will have to further investigate the relationship between sensorimotor integration in simple object lifting tasks and cognitive performance, respectively decline in elderly participants.

7.4 Object centered spatial bias of anticipatory torque control as evidence for an allocentric premotor neglect? (study II)

The principal finding of study II was that the torque resulting from grip force being produced at different vertical centers of pressure, ∆CoP x GF, was smaller in patients with both left-hemispheric as well as right-hemispheric stroke than in the respective hand-matched controls when the object CoM was located on the contralesional side, i.e. on the right side for left-hemispheric stroke patients and on the left-side for right hemispheric stroke patients. In contrast, left hemispheric stroke patients applied a higher, i.e. more adequate, ∆CoP x GF, than controls when the CoM was on their ipsilesional left side. The torque resulting from load force differences between opposing handle sides (∆LF x w/2), on the contrary, was spatially biased in the opposite direction than ∆CoP x GF in patients with left hemispheric stroke, i.e. ∆LF x w/2 was higher than in controls for a CoM on the right- and lower for a CoM on the left side. As a consequence, the torque component ∆LF x w/2 largely compensated for the shift of ∆CoP x GF resulting in overall torques at lift-off which were not significantly different between stroke patients and controls on the group level.

We argue that the sensorimotor bias of the torque component ∆CoP x GF represents a shift of the explicit context-dependent motor anticipation away from the contralesional side towards the ipsilesional side. We presume that motor anticipation is primarily affected because the difference of the centers of pressure on opposing grip sides (∆CoP) in a three-finger precision grip predominately depends upon the finger positioning (Fu & Santello, 2015) and is already established when the fingers contact the handle surface and hardly changed thereafter (see also **Figure 8**). In contrast, the diametric shift of the torque due to the load force distribution (∆Fy x w/2) shows that the coordination of forces as a function of finger-positions for torque control is intact following stroke (Davare et al., 2019; Fu & Santello, 2014; Fu et al., 2010; Mojtahedi, Fu, & Santello, 2015; Shibata & Santello, 2017). The load force distribution across sides is highly flexible during the whole task execution and torque errors at lift-off are mostly corrected by quickly adapting ∆LF x w/2 according to sensory feedback (see also **Figure 8** for illustration). However, all studies on torque control conducted in our lab (T. R. Schneider et al., 2019, 2020; T. R. Schneider & Hermsdorfer, 2021, 2022) provide evidence that torque corrections already take place prior to object-lift off despite full sensory feedback about the external torque only being available thereafter. Therefore, our results suggest that the sensorimotor attention and intention is shifted from the contralesional to the ipsilesional object side following stroke which can largely be compensated by an intact sensory-feedback driven force-to position modulation. As noted earlier, torques were successfully planned and mainly applied by ∆CoP x GF when participants could infer the CoM from object geometry. We found no evidence for a spatial bias of ∆CoP x GF in this visuomotor condition, pointing towards a purely sensorimotor bias of attention and/or intention which can be compensated for by visuomotor control. The found object centered sensorimotor bias may be taken as evidence for an allocentric premotor neglect. Premotor neglect (PMN, also known as directional hypokinesia) is a motor manifestation of neglect which is defined as an intentional, voluntary, and directional (e.g. eye, hand, and head) motor disorder of movements in or to the contralesional space which equally affects the limbs on both sides (Saevarsson, 2013; Saevarsson, Eger, & Gutierrez-Herrera, 2014). Patients show an abnormal movement initiation (hypo- or akinesia) as well as slowed (bradykinesia) and hypometric reaching movements towards goals in their contralesional hemispace even when tested with their ipsilesional hand (Heilman, Bowers, Coslett, Whelan, & Watson, 1985; Husain, Mattingley, Rorden, Kennard, & Driver, 2000; Mattingley, Bradshaw, Bradshaw, & Nettleton, 1994; Mattingley, Bradshaw, & Phillips, 1992). Moreover, they deviate towards the ipsilateral side when pointing straight ahead when being blindfolded which is suggestive of a shift in the egocentric reference frame (Bartolomeo &

Chokron, 1999; Farne, Ponti, & Ladavas, 1998). In our study, participants could adjust the position and orientation of the object on the table in a way allowing for a comfortable wrist position and usually positioned the object in the ipsilesional hemispace. Therefore, the reference frame of the sensorimotor torque bias is object, i.e. allocentric, rather than egocentric as in previous studies. Intriguingly, no stroke patient showed clear signs of a perceptual hemispatial neglect in the conducted pen-and-paper based tests. To the best of our knowledge, this is the first study to report signs of an allocentric premotor-neglect in an everyday object manipulation task. However, the relevance of the sensorimotor torque anticipation bias in daily object manipulation might be small as can be compensated for by both intact force-to position modulation as well as visuomotor control.

7.5 Lesion symptom studies are needed to find the neural correlates of torque control in object manipulation

Only recently, TMS and neuroimaging studies have begun to explore the neural mechanism of the coordination of finger-positions and forces for torque control when finger positioning is not constrained. A recent TMS study revealed that virtual lesions of the contralateral primary motor cortex (M1) inhibit the planning of digit positions as well as the covariation of the load force distribution, whereas virtual lesions of the primary sensory cortex (S1) only reduced the asymmetric load force sharing but not the retrieval of learned finger positions (Parikh, Fine, & Santello, 2020). Consequently, contralateral M1 is probably directly involved in using trial-by trial sensory feedback of digit positions to adapt forces in unconstrained, i.e. natural, grasping, whereas the role of S1 could be the sensing and comparison of expected and actual finger placement to allow for control of load forces in collaboration with M1 (Parikh et al., 2020). In an fMRI study a widespread network comprising the cerebellum, BA44 and PMv was found to be differently activated when participants were allowed to freely choose their finger positioning instead of having to place them on predefined positions (Marneweck, Barany, Santello, & Grafton, 2018). The same research group (Marneweck & Grafton, 2020c) also reported that a set of regions (PMv AIPn SPL7, somatosensory PSC, ventral LOC and cerebellum) are involved in finger-positioning and force control when lifting an object with an off-centered center of mass, although at different time points. Recent studies using Bayesian variational representational similarity analyses of deconvolution-modeled fMRI data showed that planning the lift of objects with an asymmetric weight distribution in the absence of congruent visual cues led to an early emergence of CoM-specific pattern distances, most distinctly in ventral visual stream regions as well as in cerebellar and selected dorsal stream regions (Marneweck & Grafton, 2020a). A follow up study suggested that there might be only minor differences in the way that the brain encodes anticipatory control of load force sharing between the presence and absence of salient visual shape cues with early ventral stream input being of particular importance for lift force planning in more uncertain situations in the absence of congruent visual cues (Marneweck & Grafton, 2020b). Despite these first efforts to uncover the neural correlates of the coordination of finger-positions and forces, it remains to be shown which brain regions are really necessary to accomplish a successful anticipatory torque control. Unfortunately, we could no contribute to this endeavor because we were not able to retrieve CT- or MRI scans of a sufficient number of the participating stroke patients. Future larger scaled studies on torque control following stroke should conduct a voxel-based symptom lesion analysis to detect the brain regions necessary for the anticipatory coordination of finger-positions and forces in manual torque control.

7.6 **Implications for the study of object manipulation in patients with stroke**

Lastly, our studies bear implications for future studies of manual kinetic control in neurologic patients. First, we confirmed the importance of controlling for peripheral friction properties when investigating the neural control of GF. Secondly, to study the capacity for optimal force efficiency participants must be given the explicit instructions to perform the task force efficiently as this has a profound impact on the high-level control of object manipulation.

Future studies must confirm and further investigate the claimed presence of an object-centered sensorimotor premotor neglect in object manipulation following stroke. We argue that the methodologic approach of studying digit kinetics when having to compensate external torques in object lifts is ideal to study premotor neglect as well as motor neglect, i.e. the underuse of the contralesional side of the body in the absence of - or out of proportion to - weakness or sensory impairments (Laplane & Degos, 1983; Punt & Riddoch, 2006; Saevarsson, 2013). As the prevalence of motor neglect is estimated to range between 12% and 33% of patients with acute stroke and some 8 % of patients with chronic stroke while the prevalence of premotor neglect is not known (Buxbaum et al., 2004; Siekierka-Kleiser, Kleiser, Wohlschlager, Freund, & Seitz, 2006) larger cohorts of acute stage stroke patients with unilateral cortical lesions seen on MRI-imaging are needed to further study the motor manifestations of neglect in object manipulation. Future studies should include a detailed assessment of primary motor- and sensory impairments, egocentric- and allocentric visual- as well as personal neglect, as well as current tests of motor- and premotor neglect. To differentially examine for signs of motor and premotor neglect, both hands (motor neglect?), object positions in both hemispaces (egocentric premotor neglect?) and object weight distributions on both sides (allocentric premotor neglect?) as well as both a sensorimotor and geometric-visual cue condition should be investigated in a crossed 2x2x2x2 design while controlling for the impact of primary sensorimotor impairments.

8 Conclusion

In conclusion, the two studies constituting this thesis expanded the understanding of the higher-level control of finger-positions, -forces and torques significantly and yielded novel insights into the mechanisms underlying dexterity detriments with age and following a stroke. Moreover, the study findings guide the design of future studies of object manipulation in neurologic patients which will have to confirm and further investigate the preliminary conclusions drawn in this thesis. Future larger scale studies of patients with stroke will also help to uncover the neural correlates of the higher-level control of finger-positions, -forces and torques.

9 List of abbreviations in order of occurrence

GF	grip force
LF	load force
∆LF	difference of load force between opposing handle sides
w	width of the handle
∆CoP	vertical distance between the centers of pressure on opposing handle sides
CoM	center of mass of an object
MCA	medial cerebral artery
SL	patients with chronic left hemispheric stroke
SR	patients with chronic right hemispheric stroke
CL	controls who conducted experiment with left hand
CR	controls who conducted experiment with right hand
YOS	years since stroke onset)
SD	standard deviation
n	number
f	female
m	male
ANOVA	analysis of variance
i	ischemic stroke
h	hemorrhagic stroke
mRS	modified Rankin Scale
NA	not available
ID	participant identifier
CoC	center of cancellation
LMM	linear mixed-effects model
fMRI	functional magnetic resonance imaging

TMS	transcranial magnetic stimulation
M1	primary motor cortex
S1	primary sensory cortex
BA44	Brodmann area 44
PMv	ventral premotor cortex
AIP	anterior intraparietal area
SPL7	superior parietal area 7
PSC	primary central sulcus
LOC	lateral occipital cortex

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12 Appendix

12.1 Publication I: Intention to be force efficient improves high-level anticipatory coordination of finger positions and forces in young and elderly adults

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RESEARCH ARTICLE

Control of Movement

Intention to be force efficient improves high-level anticipatory coordination of finger positions and forces in young and elderly adults

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Abstract

Successful object manipulation requires anticipatory high-level control of finger positions and forces to prevent object slip and tilt. Unlike young adults, who efficiently scale grip forces (GFs) according to surface conditions, old adults were reported to exert excessive grip forces. In this study, we theoretically show how grip force economy depends on the modulation of the centers of pressure on opposing grip surfaces (ΔCoP) according to object properties. In a grasp-to-lift study with young and elderly participants, we investigated how the instruction to lift the object with efficient GF influences the anticipation of torques, ΔCoP and GF control during complex variations of mass distributions and surface properties. Provision of the explicit instruction to strive for force efficiency prompted both age groups to optimize their ΔCoP modulation, although to a lesser degree in the elderly, and also led to a refinement of torque anticipation for a right-sided weight distribution in the young, but not the elderly participants. Consequently, marked drops in GF levels resulted. Furthermore, participants enhanced ΔCoP modulation and lowered GF safety ratios in challenging surface conditions. Higher GF in the elderly was due to decreased skin-surface friction but also worse ΔCoP modulation for lateralized mass distributions when trying to be force efficient. In contrast, safety margins were not elevated in the elderly, suggesting preserved GF control. Our findings demonstrate how task goals influence high-level motor control of object manipulation differentially in young and elderly participants and highlight the necessity to control for both instructions and friction when investigating GF control.

NEW & NOTEWORTHY Previous studies have shown that forces are covaried as a function of centers of pressure (CoPs) to exert adequate torques. Here, we demonstrate that force-efficient object manipulation requires the modulation of CoPs and show that providing the instruction to be force efficient and challenging surface conditions elicits a GF safety ratio reduction as well as an optimization of anticipatory CoP modulation and torques in the young and, to a lesser degree, in the elderly.

finger positioning; grasping; grip force control; sensorimotor memories; torque compensation

INTRODUCTION

In dexterous object manipulation, we use our knowledge of object properties based on previous experience and the visual processing of object features to plan where we position our fingers and how we apply load and grip forces with our fingertips when we grasp and lift an object. Sensory feedback of finger-surface friction, object weight, and arising torques may trigger reactive responses and update these object based information, which are also called internal representations (1–9). To safely hold an object without the fingertips slipping, the ratio between the grip forces (GFs) acting perpendicular to the grip surface and the load forces (LFs) directed upward must exceed the inverse of the static coefficient of friction at each fingertip. Fast-adapting mechanoreceptors convey tactile feedback of emerging slips which triggers fast reactive grip force increase to secure object grip (5, 10). A plethora of studies reported that young participants scale fingertip-grip forces (GFs) according to the respective surface-fingertip friction and add only a small safety margin to the lowest possible grip force necessary to achieve grip stability when holding objects with an uniform surface material in a precision pinch grip (6, 11–15). When the frictional conditions differ among the involved fingers, force controlled is challenged,

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as unaltered load forces would result in very different safety margins for the two surfaces. However, during holding an object with an off-centered center of mass (CoM) young adults partitioned load forces in a way that the fingers contacting a more slippery surface exerted lower load forces improving grip force efficiency (16). This behavior was shown for grasps with a two finger precisions grip (17, 18), tripod grip (19, 20), and in five finger grips (16, 21–25) and is already established at the moment of object lift off (25).

Another essential goal in successful object manipulation besides grip force economy is the prevention of unintended object tilts, for example, when lifting a cup of hot coffee at the handle. Therefore, torques must be exerted to counteract external torques arising from mass asymmetries of the lifted object already at the moment of object lift-off to avoid object tilt. The overall exerted torque comprises two components: the torque generated by asymmetric load force distributions between grip sides by the lever arm of the grip width, and the product of the GF and the lever arm of the vertical distance between the center-of-pressure (ΔCoP) on both grip sides (26). ΔCoP is determined by the digit positions and when more than one finger per side contacts the object also by the GF sharing pattern among the fingers on that grip side. In five finger object-grasps with constrained, that is, predefined, digit positions, participants were shown capable of modulating ΔCoP by redistributing the GF among digits II–V to account for external torques due to asymmetric mass distributions (16, 23). In addition, the modulation of ΔCoP by GF redistribution also compensates for self-induced torques caused by asymmetric load force sharing in response to differing finger-surface friction among fingers (16, 25, 27).

When participants are allowed to freely position their fingers at the grip surfaces, they modulate both digit positions and load force sharing patterns in an anticipatory fashion to predictively compensate for torques according to sensorimotor memories of previous lifts (26, 28, 29) and according to the geometric object shape indicating the mass distribution (30–32). To account for intertrial digit position variability during repeated lifting, subjects maintain an accurate torque control across trials by adjusting force distributions as a function of the actual finger positions (26, 33). The covariation of forces according to digit placement is a general high-level-control mechanism of the sensorimotor system which relies on both the predicted finger position and sensory feedback of the actual positions (34) and has been demonstrated in grasps with a precision grip (26), tripod grip (35), whole hand grasps (36), and in bimanual grasps (37). Although, torques can be exerted by an infinite number of combinations of digit positions and force sharing patterns, it seems obvious that force efficiency is higher when the fingers on the side to which the center of mass of an unbalanced object is shifted are placed higher than on the opposing side (26). However, the relationship between ΔCoP adaptation and force economy has not been formally and experimentally studied in unconstrained grasping, yet. Moreover, it is not known whether the experimental instruction on force efficiency influence the anticipatory coordination of digit positions and forces, as well as the success of torque compensation.

In this study, we deduced that one distinct, ideal, ΔCoP exists which allows to hold an object with the lowest possible GF. This ideal ΔCoP depends on the combination of the object properties, weight, weight distribution, handle width, and the coefficients of finger-surface friction. This allowed us to evaluate anticipatory ΔCoP modulation in terms of force efficiency. Although previous studies on GF control in constrained grasping have focused on the measure of GF safety margins, defined as the grip force excess in relation to the grip force at which object slip occurs, we also quantified the GF excess ratio due to ΔCoP deviations.

Previous studies on the effect of aging on sensorimotor GF control in constrained grasping have consistently found that elderly participants exert higher absolute GF levels than young adults [for review, see Diermayr et al. (38)]. However, although some studies reported elevated GF safety margins after accounting for age-related fingertip-surface friction decreases (39–42), other studies of multifinger grasping also reported equal or even decreased safety margins (43, 44). Concerning the control of finger positions, Parikh and Cole (45) found that older adults initially misalign finger positions when lifting an object with a balanced weight distribution with a precision grip which resulted in increased unwanted net object torques but eventually learned to reduce this misalignment and minimized the application of unwanted torques to match the young group and also reduced the GF magnitude. To best of our knowledge, age-differences in high-level control of digit positions and forces in challenging situations, especially when lifting objects with a lateralized center of mass have not been studies, yet.

In the present study, we investigated how the explicit instruction to be grip force efficient and the variation of surface properties of the grip sides influences integrative high-level control of finger positions and forces in an unconstrained grasp to lift task in which the mass distribution varied between blocks of trials. Moreover, we compared whether the influence of these factors changes with age by comparing behavior of young and old adults.

We hypothesized that participants of both age groups would quickly learn to anticipate external torques and to modulate ΔCoP according to object properties (26, 46). However, we expected that ΔCoP modulation especially for lateral weight distributions, which require the largest CoP displacement, would stay below the ideal ΔCoP and thus contribute to GF excess. Moreover, we presumed that GF safety ratios would be higher for asymmetric than symmetric weight distributions in line with Naceri et al. (47) who demonstrated general GF increases following object perturbations. We expected subjects to consciously lower GF safety margins when trying to be force efficient, especially when the weight distribution was symmetric as shown for fragile objects (48). In contrast, we did not expect that the explicit instruction to be force efficient would influence the anticipatory control of torques and finger positions as a number of studies had shown that even explicit knowledge of object CoM was not sufficient to guide finger positioning and torque anticipation in two-finger precision grip (29, 49–53). However, it must be noted that Lukos et al. (54) demonstrated that knowledge of object CoM enabled participants to modulate finger positioning in a five-finger grip but did not examine whether this extended to ΔCoP modulation or torque compensation. Due to the reported deficits of force and digit control in the elderly, the proposed association of impaired manual dexterity and deficits in tactile processing (55–57), and the sensorimotor challenge posed by alterations of both the mass distribution and surface properties, we hypothesized that elderly participants would present deficits in the modulation of ΔCoP and GF efficiency for both force efficiency instructions. However, as both healthy elderly adults and patients with Parkinson's disease were capable to learn to prevent object tilts (46), we did not expect to find differences in the learning of torque anticipation.

MATERIALS AND METHODS

Calculations: Efficient Force Control in the Grasp to Lift Task

When subjects grasp an object at two parallel surfaces and lift it straight upward, horizontal accelerations are negligible. Hence, the normal forces orthogonal to the grip surfaces, $\mathrm{Fx_n}$ (with n as index of left or right side) are equal for a vertical object orientation, that is, they are equal to the GF (mean $\mathrm{Fx_n}$):

$$\mathbf{Fx_{left}} = \mathbf{Fx_{right}} = \mathbf{GF}. \tag{1}$$

The coefficient of static friction μ_s is defined as the quotient of the force tangential to the surface divided by the normal force, $\mathrm{Fx_n}$, at the moment of slip onset. Hence, the normal force at slip onset must be surpassed to guarantee a stable finger-object contact ($\mathrm{Fx_{n\ min}}$). As the upward-facing load forces, $\mathrm{Fy_n}$, mainly constitute the tangential force when lifting an object upward, the following simplification is appropriate:

$$\mu_n = \frac{\mathbf{Fy_n}}{\mathbf{Fx_{n\,min}}}. \tag{2}$$

As a consequence, the lowest possible grip force, $\mathrm{GF_{min}}$, is reached if the grip force equals $\mathrm{Fx_{n\ min}}$, the lowest possible orthogonal force to prevent object slip on each grip surface. $\mathrm{Fx_{n\ min}}$ equals the quotient of the respective load force divided by the coefficient of friction of the respective side μ_n. When the quotients are inequal, the lowest possible grip force equals the higher minimal normal force, $\mathrm{Fx_{n\ min}}$, that is, the higher quotient. Only if $\mathrm{Fx_{left\ min}} = \mathrm{Fx_{right\ min}}$, GF can exactly equal the absolute minimal normal force to prevent object slip on both sides, that is, $\mathrm{GF_{min}}$.

$$\mathbf{GF_{min}} = \mathbf{Fx_{left\,min}} = \mathbf{Fx_{right\,min}} \xrightarrow{\text{with } (2)} \frac{\mathbf{Fy_{left}}}{\mu_{\text{left}}} = \frac{\mathbf{Fy_{right}}}{\mu_{\text{right}}}. \tag{3}$$

Therefore, in order to obtain the minimal sufficient grip force, $\mathrm{GF_{min}}$, the tangential load forces of both grip sides which add up to the gravitational force of the object ($\mathrm{F_G} = \mathrm{Fy_{left}} + \mathrm{Fy_{right}}$) must be proportional to the relation of the coefficients of static fractions μ_n of both sides (16). This allows for the calculation of the optimal load forces per side and $\mathrm{GF_{min}}$:

$$\begin{aligned}
&\mathrm{F_G} = \mathbf{Fy_{left}} + \mathbf{Fy_{right}} \text{ and } \mathbf{Fy_{right}} = \mathbf{Fy_{left}} \times \frac{\mu_{\text{right}}}{\mu_{\text{left}}} \xrightarrow{\text{yields}}\\
&\mathrm{F_G} = \mathbf{Fy_{left}} + \mathbf{Fy_{right}} \times \frac{\mu_{\text{right}}}{\mu_{\text{left}}} \xrightarrow{\text{yields}}\\
&\mathrm{F_G} = \mathbf{Fy_{left}}\left(1 + \frac{\mu_{\text{right}}}{\mu_{\text{left}}}\right) \xrightarrow{\text{yields}}\\
&\mathbf{Fy_{left}} = \frac{\mathrm{F_G}}{1 + \frac{\mu_{\text{right}}}{\mu_{\text{left}}}} \text{ and } \mathbf{Fy_{right}} = \frac{\mathrm{F_G}}{1 + \frac{\mu_{\text{left}}}{\mu_{\text{right}}}}.
\end{aligned} \tag{4}$$

Hence,

$$\begin{aligned}
\mathbf{GF_{min}} &= \mathbf{Fx_{left\,min}} = \mathbf{Fx_{right\,min}} = \frac{\mathbf{Fy_{left}}}{\mu_{\text{left}}} = \frac{\mathbf{Fy_{right}}}{\mu_{\text{right}}}\\
&= \frac{\mathrm{F_G}}{\left(1 + \frac{\mu_{\text{right}}}{\mu_{\text{left}}}\right) \times \mu_{\text{left}}} = \frac{\mathrm{F_G}}{\left(1 + \frac{\mu_{\text{left}}}{\mu_{\text{right}}}\right) \times \mu_{\text{right}}} \xrightarrow{\text{yields}}\\
\mathbf{GF_{min}} &= \frac{\mathrm{F_G}}{\mu_{\text{left}} + \mu_{\text{right}}}.
\end{aligned} \tag{5}$$

The torque along a sagittal axis going through the midline between the grip surfaces consists of two torque components: *1*) the product of the difference between the right and left load force, $(\mathrm{Fy_{right}} - \mathrm{Fy_{left}})$, (directions of the differences according to proprietary convention) and the lever arm of half the distance between the grip-surfaces (here: $\frac{w}{2} = 20.8$ mm) and *2*) the product of the grip force and the lever arm of the difference between the center of pressure on the right and left side of the grip surfaces (ΔCoP). The exerted torque must compensate for the external torque around the same axis, $\mathrm{T_{Ext}}$, to prevent object tilt:

$$\mathbf{T_{com}} = \mathrm{T_{Ext}} = (\mathbf{Fy_{right}} - \mathbf{Fy_{left}}) \times \frac{w}{2} + \mathbf{\Delta CoP{*}GF}, \text{ with } \Delta\mathrm{CoP} = \mathrm{CoP_{right}} - \mathrm{CoP_{left}}. \tag{6}$$

As a consequence, $\mathrm{T_{com}}$ can only be exerted with distinct load forces which allow for a grip with the lowest possible grip force, $\mathrm{GF_{min}}$ (*Eqs. 4* and *5*), in a grip with a distinct, ideal ΔCoP. Hence, ideal modulation of relative finger positioning and forces on both grip sides is required to allow for a grip with $\mathrm{GF_{min}}$:

$$\begin{aligned}
&\text{with } (5,6)\text{: } \mathrm{T_{ext}} = \frac{\mathrm{F_G}}{1 + \frac{\mu_{\text{left}}}{\mu_{\text{right}}}} - \frac{\mathrm{F_G}}{1 + \frac{\mu_{\text{right}}}{\mu_{\text{left}}}}) \times + \mathbf{\Delta CoP} \times \frac{\mathrm{F_G}}{\mu_{\text{left}} + \mu_{\text{right}}} \xrightarrow{\text{yields}}\\
&\mathbf{\Delta CoP_{ideal}} = \frac{\mathrm{T_{ext}} - \frac{w}{2} \times \left(\frac{\mathrm{F_G}}{1+\frac{\mu_{\text{left}}}{\mu_{\text{right}}}} - \frac{\mathrm{F_G}}{1+\frac{\mu_{\text{right}}}{\mu_{\text{left}}}}\right)}{\frac{\mathrm{F_G}}{\mu_{\text{left}} + \mu_{\text{right}}}} = \frac{\mathrm{F_G}}{1 + \frac{\mu_{\text{left}}}{\mu_{\text{right}}}} - \frac{\mathrm{F_G}}{1 + \frac{\mu_{\text{right}}}{\mu_{\text{left}}}}) \times \frac{w}{2}\\
&\qquad + \mathbf{\Delta CoP} \times \frac{\mathrm{F_G}}{\mu_{\text{left}} + \mu_{\text{right}}} \text{ yields} \, \mathbf{\Delta CoP_{ideal}}\\
&= \frac{\mathrm{T_{ext}} - \frac{w}{2} \times \left(\frac{\mathrm{F_G}}{1+\frac{\mu_{\text{left}}}{\mu_{\text{right}}}} - \frac{\mathrm{F_G}}{1+\frac{\mu_{\text{right}}}{\mu_{\text{left}}}}\right)}{\frac{\mathrm{F_G}}{\mu_{\text{left}} + \mu_{\text{right}}}} = \mathbf{\Delta CoP_{ideal}} = \frac{\mathrm{T_{ext}}}{\mathrm{F_G}} \times (\mu_{\text{left}} + \mu_{\text{right}})\\
&- \frac{w}{2} \times (\mu_{\text{right}} - \mu_{\text{left}}) = \frac{\mathrm{T_{ext}}}{\mathrm{F_G}} \times (\mu_{\text{left}} + \mu_{\text{right}}) + \frac{w}{2} \times (\mu_{\text{left}} - \mu_{\text{right}}).
\end{aligned} \tag{7}$$

In a grip with $\mathrm{COP_{ideal}}$ and $\mathrm{GF_{min}}$, torques are exerted with an ideal torque compensation strategy.

In practice, ΔCoP never exactly matches $\mathrm{CoP}_{\mathrm{ideal}}$. In this situation, the minimal possible grip force for the current ΔCoP, $\mathrm{GF}_{\mathrm{min\ at\ \Delta CoP}}$, can be determined by solving the following linear system of equations and inequalities:

$$\begin{aligned}
&\text{I)} \quad \text{with (6)}: -\frac{\mathrm{w}}{2} \times \mathbf{Fy}_{\boldsymbol{left}} + \frac{\mathrm{w}}{2} \times \mathbf{Fy}_{\boldsymbol{right}} + \Delta\mathrm{CoP} \\
&\qquad \times \mathbf{GF} = \mathrm{T}_{\mathrm{ext}} \\
&\text{II)} \quad \mathbf{Fy}_{\boldsymbol{left}} + \mathbf{Fy}_{\boldsymbol{right}} = \mathrm{F}_{\mathrm{G}} \\
&\text{III)} \quad \mathbf{GF} \geq \mathbf{Fx}_{\mathbf{left\ \ min}} \geq \frac{\mathbf{Fy}_{\boldsymbol{left}}}{\mu_{left}} \overset{\text{yields}}{\rightarrow} \mathbf{GF} - \frac{1}{\mu_{left}} * \mathbf{Fy}_{\boldsymbol{left}} \geq 0 \\
&\text{IV)} \quad \mathbf{GF} \geq \mathbf{Fx}_{\mathbf{right\ \ min}} \geq \frac{\mathbf{Fy}_{\boldsymbol{right}}}{\mu_{right}} \overset{\text{yields}}{\rightarrow} \mathbf{GF} - \frac{1}{\mu_{right}} \times \mathbf{Fy}_{\boldsymbol{right}} \geq 0.
\end{aligned} \tag{8}$$

These can be reformulated as:

$$\begin{aligned}
&\text{I)} \quad -\frac{\mathrm{w}}{2} \times \mathbf{Fy}_{\mathbf{left}} + \frac{\mathrm{w}}{2} \times \mathbf{Fy}_{\mathbf{right}} + \Delta\mathrm{CoP} \times \mathbf{GF} = \mathrm{T}_{\mathrm{ext}} \\
&\text{II)} \quad 1 \times \mathbf{Fy}_{\mathbf{left}} + 1 \times \mathbf{Fy}_{\mathbf{right}} = \mathrm{F}_{\mathrm{G}} \\
&\text{III)} \quad -\frac{1}{\mu_1} \times \mathbf{Fy}_{\mathbf{left}} + 1 \times \mathbf{GF} \geq 0 \\
&\text{IV)} \quad -\frac{1}{\mu_2} \times \mathbf{Fy}_{\mathbf{right}} + 1 * \mathbf{GF} \geq 0.
\end{aligned} \tag{8}$$

With $\mathbf{Fy}_{\mathbf{left}} = \mathbf{x}_1$, $\mathbf{Fy}_{\mathbf{right}} = \mathbf{x}_2$, $\mathbf{GF} = \mathbf{x}_3$, the linear systems of equations and inequalities can be written and solved as *Eq. 8*:

$$\begin{aligned}
&\begin{bmatrix} -\mathrm{w}/2 & \mathrm{w}/2 & \mathrm{CoP} \\ 1 & 1 & 0 \end{bmatrix} = \begin{bmatrix} \mathrm{T}_{\mathrm{ext}} \\ \mathrm{F}_{\mathrm{G}} \end{bmatrix} \\
&\begin{bmatrix} -1/\mu_{\mathrm{left}} & 0 & 1 \\ 0 & -1/\mu_{\mathrm{right}} & 1 \end{bmatrix} \geq \begin{bmatrix} 0 \\ 0 \end{bmatrix}.
\end{aligned} \tag{8}$$

Participants

Twenty-five participants, consisting of 15 young (9 female, 6 male, 12 right-handed, 3 left-handed, 18–28 yr, mean age: 22.1 yr, SD: 2.7 yr) and 10 elderly (4 female, 6 male, all right-handed, 62–76 yr, mean age: 69.3 yr, SD: 4.8 yr) individuals with normal or corrected to normal vision took part in the experiment. Handedness was assessed by self-report. All subjects were naïve to the purpose of the study and gave written informed consent to participate in the experiment. The experimental procedures were approved by the Institutional Review Board of the School of Medicine at the Technical University of Munich and were in accordance with the Declaration of Helsinki. Upon questioning, none of the subjects reported a history of neurological disorders or musculoskeletal disorders of the involved upper limb, nor did they report the intake of drugs which were classified as centrally acting by the experimenter. The participants received 20 € for their participation in the experiment which lasted ~2 h.

Experimental Design and Statistical Analyses

Apparatus.

Subjects were instructed to reach, grasp, lift, and replace a custom made, inverted T-shaped grip device (28), originally introduced by the groups of Gordon (53) and later with unconstrained grip handle by the group of Santello (26) (see Fig. 1*A*). Beige crepe (Crepe-varnish tape, Tesa, Hamburg, Germany) or white copy paper (100 g/m^2, HP, Paolo Alto) covered pads could be attached to the lateral handle sides used for grasping (40 × 120 mm) via a clipping system. A 250 g aluminum weight was inserted into either the outer left, middle, or outer right cavity of the horizontal base with the view of the weight cavities being blocked by a detachable aluminum lid during lifting trials. The static external torques for the vertical object orientation amounted to −0.210 Nm, 0 Nm, and 0.210 Nm, respectively (see Fig. 1*A*). As convention, negative signs denoted a counter-clockwise external torque. Total object weight summed up to 750 g.

Two 6-axis force/torque-sensors mounted underneath the aluminum grip sides (see Fig. 1*A*), concealed from sight, recorded the forces and torques exerted on both sides (ATI Nano-17 SI-50-0.5, ATI Industrial Automation; force range: 50, 50, and 70 N for *x*-, *y*-, and *z*-axes, respectively; force resolution: 0.012 N; torque range 0.5 Nm; torque resolution: 0.063 Nmm, sampling rate: 200 Hz). The data were digitally converted and transferred to a laptop by a Net-F/T-Transducer-box (ATI Industrial Automation). A lightweight magnetic position/orientation-tracker (TrakSTAR, Ascension Technology Corporation, accuracy: 1.4 mm RMS, 0.5° RMS,

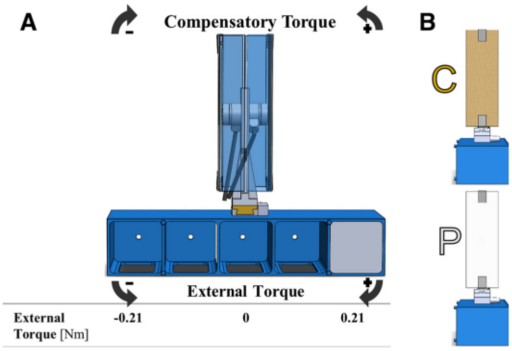

Figure 1. Apparatus and experimental procedures. *A*: the custom-built grip device consists of a handle element mounted centrally on a horizontal bar (frontal view). The handle element allowed subjects to freely choose digit placement on the grip surfaces (40 × 120 mm) consisting of either beige crepe or white paper (side view, *B*). The aluminum panels underneath the surfaces were mounted on 6-axis-force/torque sensors and blocked the sensors from view (the panels are rendered transparent for illustrative purposes). A magnetic position/orientation tracker was mounted on the horizontal bar (*A*). C, crepe; P, paper.

sampling rate 200 Hz) was fixed on top of the horizontal base to record and digitize the position and orientation of the device. Data collection was synchronized using custom software written in MATLAB (MATLAB, RRID:SCR_001622).

Experimental procedure.

Following a signal tone, subjects were asked to reach for the grasp device with their dominant hand, grasp it at the grip surfaces with the fingertips of the thumb , index, and middle finger in a precision grip, lift it in a smooth movement to a height of ~5–10 cm and hold it steady thereafter. A second tone 4 s after the first signaled them to replace the device.

In this experiment, subjects had to lift the object in blocks of six trials in which the object properties remained constant. Before each block, subjects were asked to close their eyes while the experimenter relocated the aluminum weight and exchanged the surface pads. Care was taken to ensure that participants could neither visually nor acoustically infer the position of the weight. Here, we used four surface conditions: *1*) uniform crepe (CC, crepe on both grip sides), *2*) nonuniform crepe-paper (CP, crepe on left handle side, paper on right side), *3*) nonuniform paper crepe (PC), and *4*) uniform paper (PP). The surface materials clearly differed in texture (plain paper texture vs. crepe with horizontally orientated elevations) and in color (white paper, beige crepe; see Fig. 1*B*).

Although the main task throughout the experiment was to prevent the object from tilting, subjects were asked to simultaneously follow one of two additional instructions. When we provided the "normal" instruction subjects should execute the lifts in a comfortable and natural way, whereas we instructed the participants to exert the lowest possible grip forces during lift execution in the "efficient" instruction. Each instruction was valid for 12 consecutive lifting blocks, that is, one half of the experiment, in which subjects performed trial blocks with each combination of weight placements/external torques (−0.21 Nm, 0 Nm, 0.21 Nm) and surface conditions ("CC," "CP," "PC," "PP"). The sequence of the instructions as well as the combinations of external torque and surface condition for each instruction were randomly determined for each participant a priori. We did not tell subjects what the second instruction would be when we gave the first instruction. Overall, each subject performed 24 lifting blocks (2 instructions × 3 external torques × 4 surface conditions) each comprising 6 trials, for a total of 144 trials.

To determine the static friction coefficients, μ_s, at the digit-surface contacts, an object slip task was repeatedly performed both before and after the experiment. In brief, subjects were asked to lift and hold the grip device in a three-finger precision grip with the thumb, index, and middle finger of their dominant hand and slowly release it until the object slipped. We asked the subjects to position their fingers as collinearly as possible. The handle sides were equipped with either paper or crepe on both sides and the aluminum weight was located in the middle cavity resulting in a centered weight distribution. Slips were detected by the first sudden decrease in the upward-directed load forces sum, which was followed by a drop in object height. The ratio between the load force and grip force at slip onset was used as an estimate of the static coefficients of friction, μ_s. With this procedure, we were not able to determine the μ_s of the individual involved fingers, which we assumed to be similar in the individual hands. We refrained from having subjects wash their hands with soap throughout the experiment as we intended to study object control under natural conditions and with natural skin properties.

Data processing.

Data were processed and analyzed with custom software written in MATLAB 2016a. The collected force/torque data were filtered through a sixth-order Butterworth low-pass filter with a cutoff frequency of 14 Hz. The index and middle finger contacting the same grip side produced net mechanical forces and moments equivalent to the sum of their individual actions and were hence considered as a virtual finger (58).

Our analysis of the variables outlined below were focused on the time point of "lift off," defined as the moment 10 ms before which the vertical position of the object raised above a threshold of 0.2 mm, as well as the variables averaged over the "static phase," defined as the 500 ms time period 1.5–2 s after lift-off.

We examined the following experimental variables (see also Fig. 2):

1) The average static coefficients of friction, μ_s, obtained in the slip experiment prior and after the main experiment were averaged for each participant, measurement time point, and surface. Although we found no main effect of the measurement time [prior and after the experiment, see *Static Friction Coefficients* μs and Supplemental Table S1 (all Supplemental Material is available at https://doi.org/10.6084/m9.figshare.12782420)], we fit subject-wise linear regression models with the predictor trial (1 and 144) to interpolate μ_s-estimates for the intermediate trials as visuals inspection suggested μ_s might have changed over the course of trials for some individuals. We assigned these interpolated μ_{left} and μ_{right} values according to the current handle surface on the left and right side.

2) Grip force (GF) was defined as the mean normal force directed orthogonal towards the grip surfaces.

3) ΔCoP was defined as the vertical difference between the center of pressure (CoP) on the right and the left grip sides. The center of pressure on the side of the virtual finger is determined by both the actual positions of the fingers and the distribution of applied normal forces between them. Thus, participants could still influence ΔCoP by redistributing the normal forces between the index and middle finger.

4) Exerted torques: We calculated the compensatory torque which subjects exerted at the moment of object lift off, $\mathbf{T_{com}}$, as an established indicator of motor prediction before full-sensory feedback about the object weight and weight distribution becomes available (26, 31, 53). T_{com} is the sum of: *a*) $\mathbf{T_{\Delta Fy \times w/2}}$: the torque generated by the product of the difference between the right and left load force and half the distance between the grip-surfaces ($\frac{w}{2} = 20.8$ mm) and *b*) $\mathbf{T_{\Delta CoP \times GF}}$: the product of GF and ΔCoP. With our chosen sign conventions, T_{com} matches in sign with the external torque when it

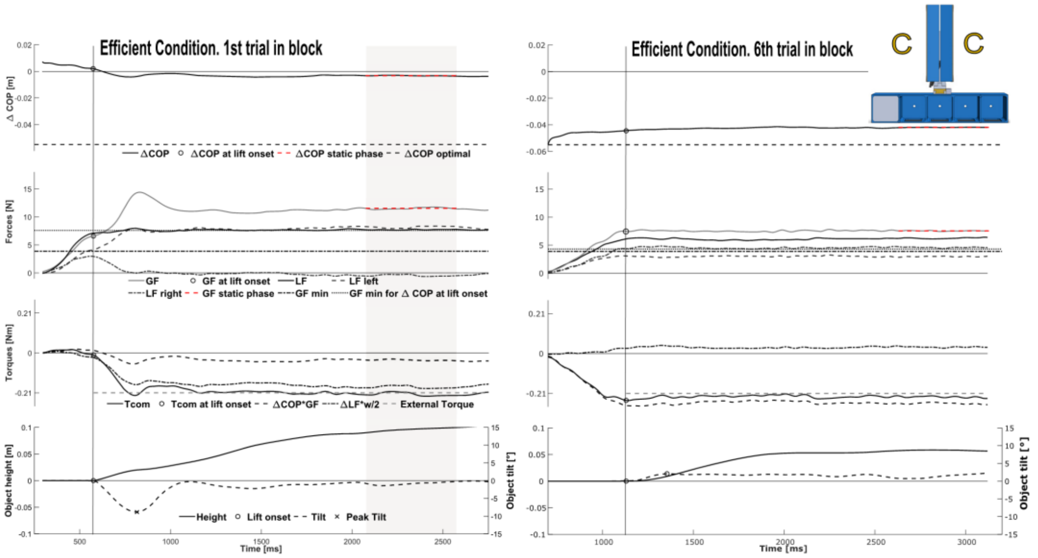

Figure 2. Two representative trials of the first and last trial of a block of representative subject no 1 (m, 25, right handed) in which the hidden aluminum weight was positioned on the left (external torque = −0.21 Nm), the surface condition was crepe on both sides and the participant had to be grip force (GF) efficient, to illustrate the task variables, derived variables and principal findings of the study. On the first trial, ΔCoP, the difference between the centers of pressure (CoP) on the right and left side, is around zero, indicating a collinear finger positioning. The upward-directed load force sum (LF) exceeds the gravitational force at object lift-off (vertical line). In the first trial, the lift forces are partitioned equally between the sides until lift off. At lift off subject no. 1 exerted virtually no torque to compensate the arising external torque (gray dashed line) and the net torque caused an object tilt (dashed line, 4th subplot). Reactively, forces are repartitioned such that the required load force is exclusively exerted at the right side to exert a compensatory torque (ΔLF × w/2) after lift-off load. In the sixth trial, ΔCoP approaches ΔCoP_{ideal}, the ΔCoP which allows a grasp with the lowest possible grip forces, GF_{min}, at lift-off. Especially the torque component ΔCoP × GF almost perfectly compensates for the external torque (horizontal dashed line) already at lift off. Consequently, almost no object tilt occurs. This torque strategy allows for almost uniform load force sharing. In the first trial, GF (the mean force acting orthogonal toward the grasp surfaces) is below the necessary GF to support a safe grip at lift off for the current ΔCoP and finger-surface coefficients of friction ($GF_{min\ at\ \Delta CoP\ at\ lift\ onset}$, dotted horizontal line 3rd subplot) and is subsequently increased in the further course of the trial. In the sixth trial the calculated $GF_{min\ at\ \Delta CoP\ at\ lift\ onset}$ is almost as low as the minimal GF for the finger-surface coefficients of friction (GF_{min}). The GF remains stable after lift onset and is markedly lower than in the first trial during the static phase (GF_{static}, horizontal red dashed line). C, crepe; GF_{min}, lowest possible grip force.

counterbalances the exerted torque, for example, is directed in opposing direction to the external torque. Hence, clockwise exerted torques were defined as negative and counter-clockwise torques as positive (see Fig. 1*A*). Details on the task mechanics and the calculations are presented in the Supplemental material of Schneider et al. (28) (https://doi.org/10.6084/m9.figshare.7683707).

5) Calculated variables:
   a) $\mathbf{GF_{min}}$, the lowest sufficient GF for the current surface condition was calculated according to *Eq. 5* as $\frac{F_G}{\mu_{left} + \mu_{right}}$.
   b) $\mathbf{\Delta CoP_{ideal}}$, the ΔCoP necessary to achieve GF_{min}, was calculated according to *Eq. 7* as: $\frac{T_{ext}}{7.3575} * (\mu_{left} + \mu_{right}) + 0.0208 \times (\mu_{left} - \mu_{right})$ [m].
   c) $\mathbf{GF_{min\ at\ \Delta CoP}}$, the lowest sufficient grip force for the actual ΔCoP (at lift off or during static phase) was determined by solving the linear system of equations and inequalities in *Eq. 8* with the package "limSolve" in R (59).
6) Derived response variables:
   a) To compare torque and ΔCoP anticipation success between blocks with a lateralized object CoM, we calculated the relative success ratios $\frac{T_{com}}{\text{External Torque}}$ as measure of relative torque anticipation and
   b) the ratio $\frac{\Delta CoP_{lift\ onset}}{\Delta CoP_{ideal}}$, quantifying relative success of predictive ΔCoP modulation. For the middle position (external torque = 0) no normalization was performed.
   c) The ratio $\frac{GF}{GF_{min\ at\ \Delta CoP}}$ at lift-off or during static phase is the safety GF ratio, with values > 1 indicating that participants applied higher GF than necessary for the current ΔCoP.
   d) The ratio $\frac{GF_{min\ at\ \Delta CoP}}{GF_{min}}$ at lift-off or during static phase is the excess force ratio due to a ΔCoP modulation deviating from the ideal ΔCoP, with values > 1 indicating that a ΔCoP deviation has resulted in an increase of the lowest possible GF.

The aforementioned variables 1–5 are illustrated in the representative trials depicted in Fig. 2.

Data management.

Due to technical errors, 0.58% (21/3600) of the measurements were faulty and the respective observations were discarded. We obtained 381 μ_s estimates employing the slip method.

Statistical analysis.

All statistical analyses were conducted in the R environment for statistical computing [v. 4.0.3, (60), R Project for Statistical Computing, (RRID):SCR_001905]. We fit linear mixed effects regression models (LMM) for all dependent variables with the restricted maximum likelihood criterion using the "lme4" (61) package. *P* values of the predictor estimates of all LMMs were calculated based on Wald-type *t* tests and additionally on type III-F tests of the predictor estimates for using the Kenward–Roger approximation of the degrees of freedom as implemented in the "pbkrtest" package (62). Post hoc *t* tests of pairwise comparisons of estimated marginal model means were conducted with Bonferroni correction for multiple testing as specified below. Bonferroni adjusted post hoc *t* test of pairwise comparisons between the age groups and instructions were performed with the "emmeans" package (63).

Linear mixed effects model of the static coefficient of friction μ_s. We built a random intercept linear mixed effects model of the dependent variable μ_s with the predictors surface condition (crepe as reference), trial (categorical: 0 and 144), age group, and the interaction between surface and age group. Post hoc *t* tests examined pairwise differences between the age groups for both surface materials and between the surface materials for both age groups.

Linear mixed effects models and post hoc t tests of variables of torque anticipation, ΔCoP, and gf variables. We fit linear mixed effects models of the respective dependent variables $\frac{T_{com}}{\text{Externall Torque}}$, $\frac{\Delta CoP_{\text{liftl onset}}}{\Delta CoP_{\text{ideal}}}$ (blocks with external torque = ± 0.21 Nm), **Tcom**, **ΔCoP** (blocks with external torque = 0 Nm), $\mathbf{GF_{lift\ off}}$, $\mathbf{GF_{static\ phase}}$, as well as the safety GF ratio, $\frac{GF}{GF_{\text{minl atl }\Delta CoP}}$, and the force excess ratio due to ΔCoP deviations from ideal ΔCoP, $\frac{GF_{\text{minl atl }\Delta CoP}}{GF_{\text{min}}}$, the latter two ratios at lift-off and during the static phase. We only used data of the "third to sixth trials of a block." We focused on these trials to study the extent to which the control of the dependent variables is learned as performance was observed to mainly improve over the first 1–2 trials (See Fig. 4 and Supplemental Figs. S1 and S2). The fixed-effects predictors of all models were *1*) the external torque (categorical), the instruction ("normal" instruction as reference vs. force efficiency instruction), the age group (young group as reference vs. elderly group), and all two- and three-way interactions between these variables and *2*) the surface combination [crepe on both sides ("CC") as reference vs. crepe on the left and paper on the right ("CP"), paper on the left and crepe on the right ("PC"), and paper on both sides ("PP")] as well as the interaction between the surface condition and the age group. It must be noted that the analyses of derived grip force variables should be considered as explorative as the derived ratios might be prone to measurement errors of the included parameters (e.g., μ_s). Subsequently, we performed post hoc *t* tests based on the LMMs of *1*) differences between the age groups for both instructions grouped by external torque level, *2*) differences between the instructions per age group grouped by external torque levels, and *3*) differences between the age groups per surface combination.

RESULTS

Static Friction Coefficients μ_s

Overall, we determined 381 static coefficients of friction μ_s, corresponding to an average of 3.81 μ_s per subject, surface condition, and measurement time point (SD 0.84, median 4, range 2–8). We found significant main effects showing that μ_s estimates were lower for the paper surface ($t_{353.2}$= −24.00, $P < 0.001$) and in the elderly ($t_{25.3}$= −4.632, $P < 0.001$). In addition, we found a positive interaction effect between surface and age group ($t_{353.2}$ = 3.308, P = 0.001). There was no significant main effect of trial ($t_{353.3}$= −0.008, P = 0.429). Post hoc *t* tests confirmed that μ_s in the young (crepe: Ø 0.84, SD 0.125, paper: Ø 0.543, SD 0.155) were higher than in the elderly group (crepe: Ø 0.638, SD 0.140, paper: Ø 0.400, SD 0.143) in both surface conditions (crepe: $t_{25.3}$ = 4.632, P = 0.0001, paper: $t_{25.3}$ = 3.196, P = 0.0037, see Fig. 3, *top*). Moreover, μ_s was higher for crepe than paper in both age groups (young: $t_{353.2}$ = 24.00, $P < 0.0001$, elderly: $t_{353.2}$ = 15.60, $P < 0.0001$, see Fig. 3, *bottom*). Supplemental Table S1 details the results of the LMM.

Learning of Anticipatory Torque Compensation

Relative T_{com} (external torque: ± 0.21 Nm).

LMM results indicated that relative torque anticipation success was lower for lifts when the weight was on the right side than for a weight placement on the left (t_{1550} = −8.21, $P <$ 0.001) and that this was less pronounced when the efficiency

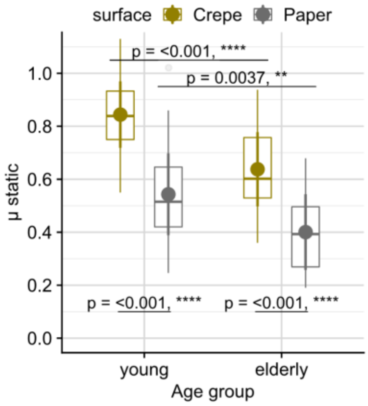

Figure 3. Static coefficients of friction. Mean static coefficient of friction, μ_s, ± 1 SD with box and whiskers plots in the style of Tukey (central horizontal line: median, lower, and upper hinges: 25th and 75th percentiles, upper and lower whiskers extend up to 1.5 × interquartile ranges) of both age groups for the paper and crepe. Post hoc *t* test of the estimated marginal means of the LMM show that μ_s were significantly higher in the young compared with the elderly age group for both surface materials and that μ_s was lower for paper than crepe in both age groups. LMM, linear mixed effects regression model. $^{**}P \leq 0.01$, $^{****}P \leq 0.0001$.

instruction was provided (t_{1550} = 3.60, $P < 0.001$). Moreover, a negative three-way interaction between external torque, age group, and instruction reached significance (t_{1550}= −1.98, P = 0.048). Post hoc t tests showed a more successful torque anticipation of the young than elderly group for an external torque of 0.21 when participants strived for force efficiency (P = 0.009, Fig. 5*A*, *top*). Young participants improved anticipatory torque compensation for this weight distribution when provided with the instruction to be force efficient as compared with the normal instruction ($P < 0.001$, Fig. 5*A*, *bottom*), whereas no difference between instructions was found in the elderly subjects (P = 0.24). Neither of the age groups improved T_{com} when trying to be force efficient when the weight was placed on the left. Besides, we found a higher T_{com} in the most slippery surface condition with paper on both grip sides (LMM, t_{1550}= 2.02, P = 0.044). However, performance did not differ between age groups for any surface condition in post hoc testing (see Supplemental Fig. S3*A*). Supplemental Table S2 summarizes the LMM results. Figure 4*A* depicts the trajectories of T_{com} across the trials of a block for all weight distributions and both instructions and age groups.

T_{com} (external torque: 0 Nm).

A negative interaction between age group and the surface combination paper on the left and crepe on the right side was the only significant effect of the LMM for the dependent variable T_{com} for blocks in which the external torque was zero (t_{762}= −2.823, P = 0.005). Indeed, post hoc testing showed that the elderly exerted a more negative T_{com} than the young group given this surface combination (P = 0.22, Supplemental Fig. S3*B*). There were no differences between the combinations of instructions and age groups (Fig. 5*B*). Full model details are provided in Supplemental Table S3.

Learning of Anticipatory ΔCoP Modulation

Relative ΔCoP at lift off (external torque: ± 0.21 Nm).

Model results suggested that relative ΔCoP modulation was more successful when the instruction to be efficient was provided (t_{1550} = 13.21, $P < 0.001$) and for all surface conditions when compared with the crepe on both sides condition ($P \leq 0.001$, see Supplemental Table S4 for full model results). Furthermore, we found a significant negative two-way interaction between age group and instruction (t_{1550} = −3.539, $P < 0.001$). Post hoc testing corroborated the model findings. Although both groups' relative ΔCoP modulation was more

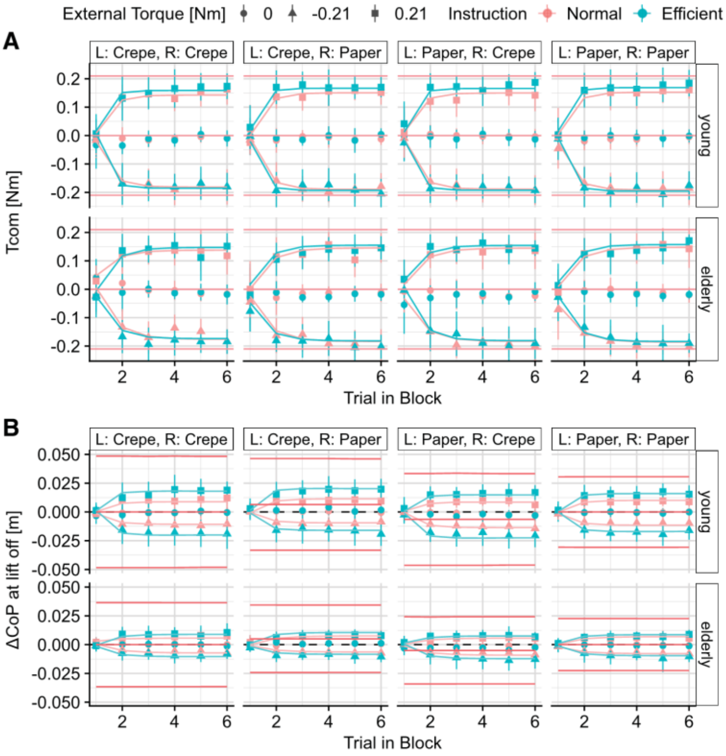

Figure 4. T_{com} and $\Delta CoP_{lift\ off}$ across trials of a block. Mean T_{com} (*A*) and $\Delta CoP_{lift\ off}$ (*B*) ± 1 SD across trials in a block for the two instructions "normal" (magenta) and "efficient" (green) plotted separately for the four surface conditions and the age groups. Data traces for the three levels of the external torque are plotted with different shapes. The solid red horizonal lines show the static external torques (*A*), respectively, ΔCoP_{ideal}. The plotted lines depict predictions of nonlinear asymptotic models. ΔCoP, vertical distance between the center-of-pressure; GF_{min}, lowest possible grip force.

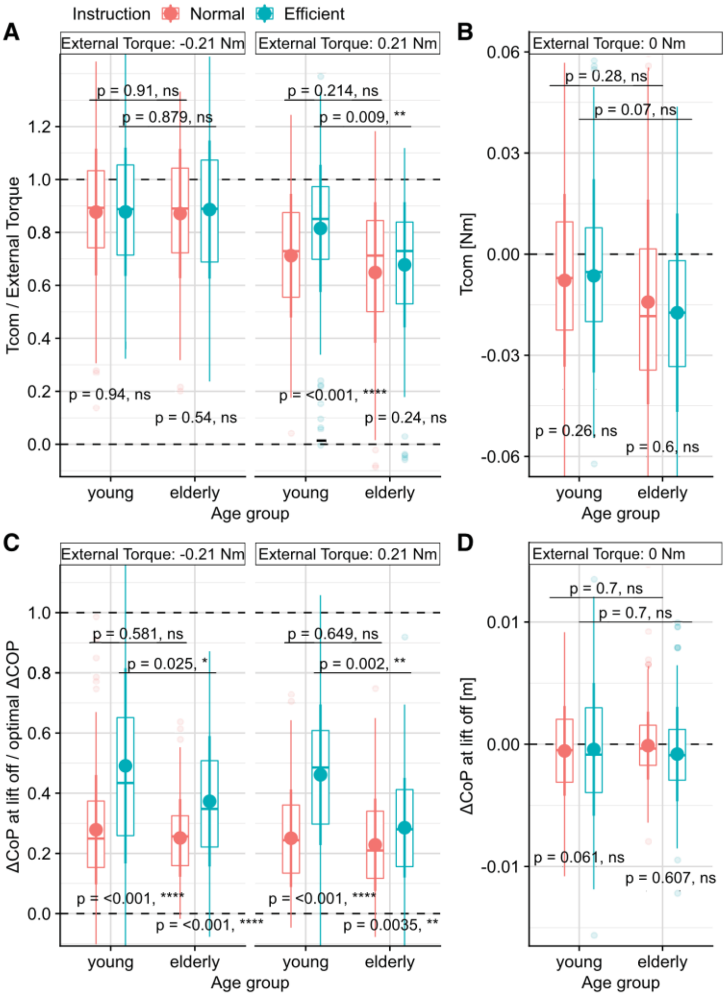

Figure 5. T_{com} and ΔCoP anticipation for trials 3–6 per external torque. $\frac{T_{com}}{\text{External Torque}}$ (*A*), T_{com} (external torque = 0) (*B*), $\frac{\Delta CoP_{lift\ off}}{\Delta CoP_{ideal}}$ (*C*), and $\Delta CoP_{lift\ off}$ (external torque = 0) (*D*) plotted for both age groups, both instructions and grouped by the external torque (weight distribution) together with Bonferroni adjusted *P* values of post hoc *t* tests of pairwise differences between age groups per instructions (*top*) and between instruction per age group (*bottom*). ΔCoP, vertical distance between the center-of-pressure; GF_{min}, lowest possible grip force. ns, $P > 0.05$, $*P \leq 0.05$, $**P \leq 0.01$, $****P \leq 0.0001$.

successful when being asked to be force efficient in both eccentric weight distributions (see Fig. 5*C*, *bottom*), ΔCoP modulation was better in the young than in the elderly group when participants tried to be force efficient in both eccentric mass distributions (Fig. 5*C*, *top*). No differences between age groups were found when participants were instructed to grip comfortably. Post hoc testing revealed no age group differences for any surface combination (Supplemental Fig. S3*C*). Figure 4*B* depicts the trajectories of $\Delta CoP_{lift\text{-}off}$ across the trials of a block for all weight distributions and both instructions and age groups.

ΔCoP lift off (external torque: 0 Nm).

In the blocks with a centered mass distribution, participants' center of pressure was higher on the left side when the left side was covered with paper and the right with crepe and higher on the right side for the reversed surface combination (main effect of surface CP: 0.001 m, t_{762} = 3.266, P = 0.001, main effect of surface CP: −0.002 m, t_{762} = −4.664, $P <$ 0.001). No further significant results were found in the LMM or post hoc testing (Supplemental Table S5, Fig. 5*D*, and Supplemental Fig. S3*D*).

Grip Force Economy

GF $_{\text{lift off}}$.

Concerning the within-subject predictors in the LMM, we found a significant increase of GF $_{\text{lift off}}$ for a weight placement in both lateral slots when compared with a central weight placement (main effect of external torque −0.21 Nm: 1.66 N, t_{2341} = 5.25, $P < 0.001$; external torque 0.21 Nm: 0.894 N, t_{2341} = 2.82, $P = 0.005$) and for all three more challenging surface combinations when compared with the crepe on both sides reference ($P \leq 0.001$, Supplemental Table S6). On the contrary, participants exerted markedly lower GF $_{\text{lift off}}$ when being provided with the force efficiency instruction (−3.66 N, t_{2341} = −11.50, $P < 0.001$). The GF saving was higher for blocks with a lateral CoM as evidenced by negative two-way interactions ($P \leq 0.023$). The elderly group applied considerably higher GF $_{\text{lift off}}$ than the young group (+6.34 N, $t_{26.48}$ = 4.04, $P < 0.001$), which was further increased for the surface combinations "PC" and "PP" as evidenced by two-way interactions ($P < 0.001$). In contrast, a negative interaction between the elderly and the "efficiency" instruction (t_{2341} = −2.61, $P = 0.009$) implies that elderly participants were capable to reduce GF $_{\text{lift off}}$ to a greater extent than the young group when this was the goal. Moreover, we found a significant three-way interaction between age group, instruction, and weight placement on the right (t_{2341} = 2.764, $P = 0.006$).

Post hoc testing confirmed that GF $_{\text{lift off}}$ was lower when provided with the force efficiency instruction than when provided with the natural instruction in both age groups and all three weight distributions (Fig. 6*A*, *bottom*, all $P < 0.001$). GF$_{\text{lift off}}$ was lower in the young group than in the elderly group in all combinations of weight distribution and instruction (Fig. 6*A*, *top*, all < 0.001) as well for all surface conditions (Fig. 7*A*, P values < 0.001). Supplemental Fig. S1 depicts the course of GF $_{\text{lift off}}$ and the derived GF variables at lift off across trials of a block.

GF $_{\text{static phase}}$.

The results of the LMM of GF $_{\text{static phase}}$ resembled the ones of the GF $_{\text{lift off}}$ model outlined for GF $_{\text{lift off}}$. In summary GF $_{\text{static phase}}$ was higher for both eccentric weight distributions as well as all three more challenging surface combinations and lower when participants tried to be force efficient (all: $P < 0.001$). Trying to be force efficient led to higher GF savings in the eccentric weight distributions ($P < 0.001$). Again, GF $_{\text{static phase}}$ were higher in the elderly group ($P < 0.001$) and this was accentuated in the more challenging surface conditions (two-way interaction between elderly group and surface conditions: all P values ≤ 0.005). Supplemental Table S9 outlines the detailed model results. Post hoc test results were very similar to the ones of GF $_{\text{lift off}}$ and confirmed significantly lower GF $_{\text{static phase}}$ for all weight distributions and for both age groups when force efficiency was required than when participants were allowed to perform the lift normally (Supplemental Fig. S4*A*, *bottom*, all $P < 0.001$) and lower GF $_{\text{static phase}}$ in the young than in the elderly participants in all combinations of weight distribution and instruction (Supplemental Fig. S4*A*, *top*, all $P < 0.001$) as well for all surface conditions (Supplemental Fig. S5*A*, P values < 0.001). Supplemental Fig. S2 depicts the course of GF $_{\text{static phase}}$ and the derived GF variables.

Factors contributing to excessive grip forces.

We will present only significant results of the statistical random-intercept models of *1*) the safety force ratio $\frac{GF}{GF_{min\ \ at\ \ \Delta CoP}}$ and *2*) $\frac{GF_{min\ \ at\ \ \Delta CoP}}{GF_{min}}$, the force ratio attributing force excess to deviations from ideal ΔCoP modulation. Results are presented first for the moment of lift off and subsequently for the static phase. Detailed results of the LMMs are provided in Supplemental Tables S8–S11.

Force ratios at lift-off. GF safety ratios at lift off: We studied the ratio $\frac{GF_{lift\ \ off}}{GF_{min\ \ at\ \ \Delta CoP\ \ lift\ \ off}}$ as an indicator of the GF safety ratio at lift off. Interestingly, the LMM implied that this safety ratio was lower for asymmetric than symmetric weight distributions ($P < 0.001$ for both external torques: ± 0.21 Nm, see Supplemental Table S8) which stands in contrast with the absolutely increased GF $_{\text{lift off}}$ for these weight distributions. Asking subjects to hold the object as force efficiently as possible led to a significant reduction of the force ratio (main effect of "efficiency" instruction: −0.628, t_{2341}= −15.67, $P < 0.001$): This decrease was smaller for the eccentric weight distribution as evidenced by a positive two-way interaction ($P < 0.001$). Furthermore, the safety ratio was lower in all three challenging surface conditions when compared with the crepe on both sides (all $P < 0.001$). Importantly, the main effect of the elderly age group was not significant and the model suggested that the safety ratio was lower in the elderly when the weight was placed on the right as evidenced by a negative two-way interaction ($P = 0.002$). Post hoc testing revealed that both age groups significantly lowered $\frac{GF_{lift\ \ off}}{GF_{min\ \ at\ \ \Delta CoP\ \ lift\ \ off}}$ in all weight distributions (Fig. 6*B*, *bottom*, all < 0.001) when being asked to be force efficient. However, we found no significant differences between age groups (Fig. 6*B*, *top*; Fig. 7*B*).

Force excess due to suboptimal ΔCoP modulation at lift off: The LMM of the ratio $\frac{GF_{min\ \ at\ \ \Delta CoP\ \ lift\ \ off}}{GF_{min}}$, which was introduced as indicator of the force excess due to suboptimal ΔCoP modulation, suggested an increase of the ratio for both lateral weight placements as compared with the central weight placement (both P values < 0.001, see Supplemental Table S9). Although the main effect of the efficiency instruction, which pertains to the reference of a weight placement in the middle cavity did not reach significance, we found significant negative interactions between the instruction to be force efficient and the lateral weight placement ($P < 0.001$). Taken together these findings imply that in "natural" grasp to lift behavior a failure to sufficiently adapt ΔCoP modulation according to an asymmetric weight distribution contributes to a GF increase. However, participants can reduce this force excess due to an erroneous ΔCoP modulation when they try to be force efficient. A significant positive three-way interaction between a weight placement on the right, the "efficiency" instruction, and the elderly group ($P = 0.002$) in the absence of a significant main effect of age group or two-way interactions with age group suggests that this optimization might be smaller in the elderly for a weight placement on the right. Post hoc testing confirmed that both age groups reduce their force excess ratio attributed to erroneous ΔCoP

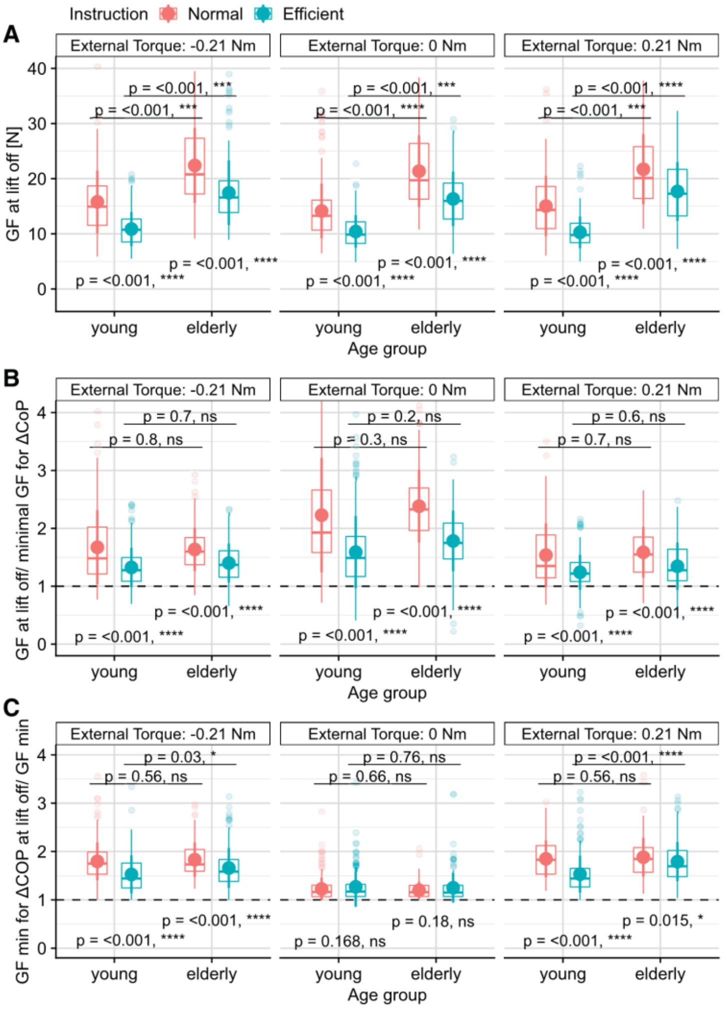

Figure 6. Mean grip force (GF) and force rates $\frac{GF}{GF_{min\,at\,\Delta CoP}}$ (~safety ratio) and $\frac{GF_{min\,at\,\Delta CoP}}{GF_{min}}$ (~force excess ratio due to ΔCoP deviations) at lift off for trials 3–6 per external torque. GF $_{lift\ off}$ (*A*), $\frac{GF_{lift\ off}}{GF_{min\ at\ \Delta CoP\ lift\ off}}$ (*B*), and $\frac{GF_{min\ at\ \Delta CoP\ lift\ off}}{GF_{min}}$ (C) plotted for both age groups, both instructions, and grouped by the external torque (weight distribution) together with Bonferroni adjusted *P* values of post hoc *t* tests of pairwise differences between age groups per instruction (*top*) and between instructions per age group (*bottom*). ΔCoP, vertical distance between the center-of-pressure; GF_{min}, lowest possible grip force. ns, $P > 0.05$, $*P \leq 0.05$, $***P \leq 0.001$, $****P \leq 0.0001$.

modulation for lateral weight placements when trying to be force efficient (Fig. 6*C*, *bottom*) and that the ratio was significantly lower in the young group than in the elderly for both asymmetric weight distributions when the "efficiency" instruction was given (Fig. 6*C*, *top*, $P \leq 0.026$).

Force ratios during the static phase. GF safety ratios during the static phase: The results of the within-subject predictors of the safety-force ratio, $\frac{GF_{static\ phase}}{GF_{min\ at\ \Delta CoP\ static\ phase}}$, were similar to the ones for the ratio at lift off. Again, we found a decrease for the lateral weight placements, the more challenging surface conditions and when participants tried to be force efficient, although the latter effect was smaller for the lateral weight placements (all $P < 0.001$, see Supplemental Table S10). We found a negative two-way interaction between the lateral weight placements and the "efficiency" instruction ($P \leq 0.001$) in the absence of a significant main effect of the age groups suggesting that the safety ratio during the static phase in the elderly might be lower in the elderly in natural lifting. However, a positive three-way interaction between a weight placement on the right, the elderly group, and the "efficiency" instruction ($P = 0.002$) suggests that this might not be the case for the efficiency instruction. Post hoc testing verified that safety force ratios were reduced in both age groups for all weight placements when participants tried to be force efficient (Supplemental

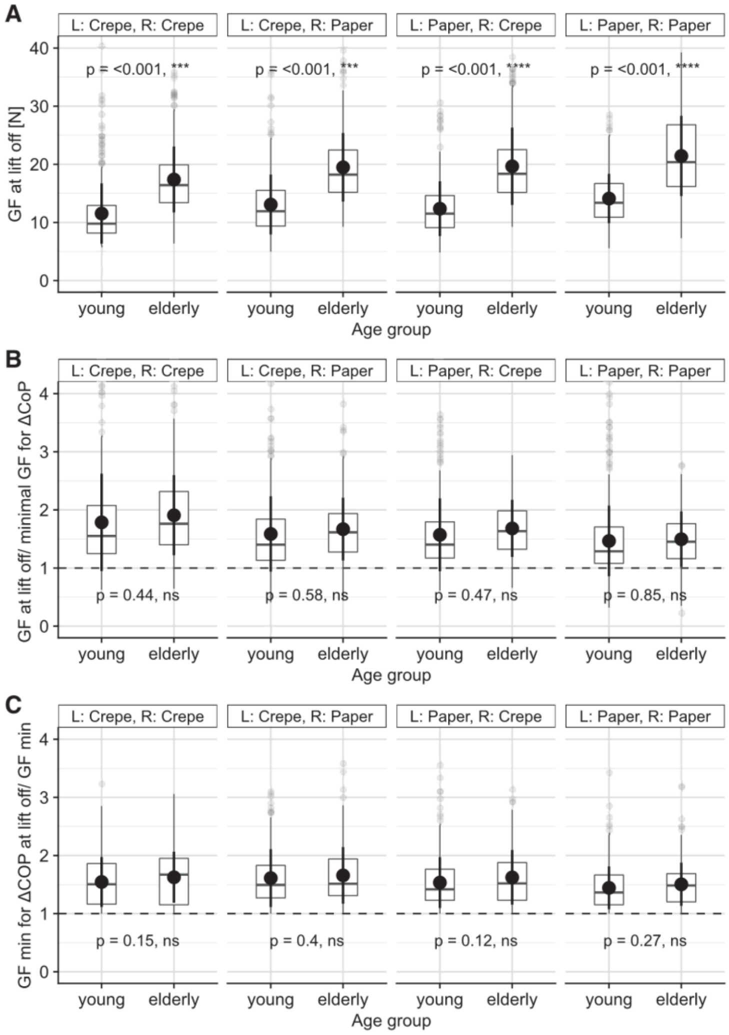

Figure 7. Mean grip force (GF) and force rates $\frac{GF}{GF_{min\ at\ \Delta CoP}}$ (~safety ratio) and $\frac{GF_{min\ at\ \Delta CoP}}{GF_{min}}$ (~force excess ratio due to ΔCoP deviations) at lift off for trials 3–6 per surface condition. GF $_{lift\ off}$ (*A*), $\frac{GF_{lift\ off}}{GF_{min\ at\ \Delta CoP\ lift\ off}}$ (*B*), and $\frac{GF_{min\ at\ \Delta CoP\ lift\ off}}{GF_{min}}$ (*C*) plotted against age groups for the four surface conditions together with Bonferroni adjusted *P* values of post hoc *t* tests of pairwise differences between age groups. ΔCoP, vertical distance between the center-of-pressure; GF_{min}, lowest possible grip force. ns, $P > 0.05$, ****$P \leq 0.0001$.

Fig. S4*B*, *bottom*). No age group differences were found for the combinations of weight placement and instruction (Supplemental Fig. S4*B*, *top*) and surface combinations (Supplemental Fig. S5*B*).

Force excess due to suboptimal ΔCoP modulation during the static phase: The results of the within-subject predictors of the excess force ratio which can be attributed to suboptimal ΔCoP modulation in the static phase, $\frac{GF_{min\ at\ \Delta CoP\ static\ phase}}{GF_{min}}$, were basically identical to the findings for the moment at lift off with a ratio increase for the lateral weight placement and a negative interaction between both eccentric weight placements and the "efficiency" goal (all $P < 0.001$, see Supplemental Table S11). In addition, we found evidence for a higher ratio for the "CP" and a lower ratio for the "PP" surface combination. Post hoc testing confirmed that both age groups reduce this force excess ratio for lateral weight placements when trying to be force efficient (Supplemental Fig. S4*C*, *bottom*). The only significant age group difference in favor of the young group was found for a weight placement on the right when trying to be force efficient (Supplemental Fig. S4*C*, top, $P \leq 0.026$). Again, we found no age group differences for the surface conditions (Supplemental Fig. S5*C*).

DISCUSSION

This study was set out to investigate *1*) whether the provision of explicit force efficiency instructions and of distinct surface conditions influence the integratory high-level control of digit positions and forces in terms of both torque control and GF economy and *2*) whether young and elderly subjects' behavior differs when aiming for force efficiency instruction and under challenging surface conditions. In this study, young and elderly adults employed a tripod grip to repeatedly grasp, lift, and hold an object whose mass distribution and surface materials varied across blocks. Besides having to prevent object tilts, we instructed participants to either perform the task in the most comfortable, that is, natural, or in the most GF efficient way. By first delineating the relationship between ΔCoP modulation according to object and friction properties and GF demands, we attempted to attribute the observed GF excess to ΔCoP deviations from $\Delta\text{CoP}_{\text{ideal}}$ and the GF safety ratio. We found that both the provision of the instruction to be force efficient as well as provision of challenging surface conditions had a strong impact not only on GF safety margins but also on anticipatory ΔCoP and torque control in both age groups, but, regarding the latter aspects, to a lesser degree in the elderly. We summarize and discuss our findings in the following sections.

Learning of Anticipatory Torque Compensation

Both age groups learned predictive torque compensation to a similar extent when they were instructed to behave normally. This corroborates recent findings of a study examining implicit adaptation in a visuomotor rotation learning task which suggested that internal model recalibration was intact or even increased in older, compared with young adults (64). Curiously, participants learned to anticipate torques to a lesser degree when the mass distribution was shifted to the right. Similarly, Zhang et al. (29) reported higher torques due to asymmetric load-force partitioning (here: $T_{\Delta Fy \times w/2}$) for a weight placement on the left, although the authors did not state whether the side difference pertained to the overall T_{com}. Remarkably, young participants learned to more precisely match the external torque at lift off when the weight was placed on the right when they tried to act as force-efficiently as possible (Fig. 5*A*). A study by Naceri et al. (47) demonstrated that humans react to torque perturbations with a synchronous, synergistic grip force increase to maintain stable grasp. To this end, the demonstration that young participants minimize object perturbations to improve GF efficiency provides evidence for a task level, that is, high level, coupling of anticipatory torque and force control. This improvement with the force efficiency instruction was not present in elderly subjects who exerted significantly less precise compensatory torques in this condition. Viewed differently, however, our results also imply that participants did not try to minimize torque errors to their full capability when the object CoM was on the right side in the natural condition although the prevention of object tilts was proclaimed as the primary task goal. However, provision of the force efficiency instruction did not influence torque anticipation when the weight was placed on the left, which might be due to the already very successful torque compensation in the natural condition.

Unexpectedly, participants learned to counteract torques more accurately in the most slippery surface condition with paper on both sides. Possibly, participants' error tolerance was lower in this surface condition as the occurrence of net torques necessitates load force and in turn grip force adjustments, which are higher for more slippery surfaces. In blocks with a symmetric weight distribution, the extent of unwanted torques did not differ between age groups for neither force instruction corroborating the findings of Parikh and Cole (45). In contrast, elderly participants exerted more negative unwanted torques at lift-off when paper was on the left and crepe on the right grip side (Fig. 6*B*) pointing toward reduced torque accuracy for challenging, side-different surface conditions.

High-Level Control of Anticipatory ΔCoP Modulation

The success of learned $\Delta\text{CoP}_{\text{lift off}}$ modulation for blocks with an eccentric weight distribution was far away from the ideal ΔCoP and similar in both age group groups when participants were instructed to behave naturally. Importantly, asking participants to be force efficient markedly improved $\Delta\text{CoP}_{\text{lift off}}$ modulation in both age groups but to lesser degree in the elderly resulting in significantly more successful relative $\Delta\text{CoP}_{\text{lift off}}$ modulation in the young (Fig. 5*C*). Similarly, eventual $\Delta\text{CoP}_{\text{lift off}}$ modulation was more accurate for all three more challenging surface conditions when force efficiency was the goal with no significant differences between age groups. When no external torque had to be compensated and the surface materials differed between the grip sides, CoP was higher on the side of the more slippery paper surface confirming previous reports (16–18, 25). This allows for portioning a greater share of the load force to the side covered by the rougher crepe material as resulting unwanted torques may be compensated by counter-directed torques generated by the product of ΔCoP and the GF. Consequently, smaller normal forces must be applied on the side fitted with paper and GF can be reduced. In line with Parikh and Cole (45), no age group differences were found in the symmetric center of mass condition.

Taken together, these results suggest that ΔCoP modulation is controlled on a high level considering both the friction properties and mass distribution of the object and that this high level control can be adjusted to the explicit intention to save forces. Our findings provide evidence that this high-level control is already less accurate at the age of seventy. However, one must keep in mind that in the studied three-finger grip ΔCoP is not only determined by the actual finger positions but also by the normal force distribution between the index and middle finger. The precise control of this force distribution may be subjected to finger-enslaving, i.e., the involuntary force production of finger when another finger applies a force (65). Whether finger enslaving increases with age (66, 67) or not (68–70) seems to depend on the specifics of task dynamics and wrist support (66) and remains controversial. Moreover, whether finger enslaving hampers ΔCoP modulation in healthy aging remains elusive. Lastly, the poor relative anticipation of $\Delta\text{CoP}_{\text{ideal}}$ observed in the natural performance condition also implies that force efficiency might not be a priority for ΔCoP modulation in natural object manipulation.

GF Control

Revisiting the safety margin/ratio concept.

Traditionally, the safety force margin ($\frac{GF}{GF_{min}} - 1$), was introduced to quantify the excess GF participants exerted on top of the lowest possible GF required to securely hold an object (6, 7, 12). In this study, we derived from basic physics that the lowest possible GF to securely hold an object while counteracting external torques, GF_{min}, only equals $\frac{F_G}{\mu_{left} + \mu_{right}}$ for a distinct, ideal ΔCoP. ΔCoP_{ideal} depends on the mass and mass distribution of the object, the grip-width and the fingertip-surface friction coefficients on both sides (see *Eq. 7* in *Calculations: Efficient Force Control in the Grasp to Lift Task*). For every deviating ΔCoP, the lowest possible grip force, $GF_{min\ at\ \Delta CoP}$, must be separately determined by a system of equalities and inequalities (see *Eq. 8* in *Calculations: Efficient Force Control in the Grasp to Lift Task*). Employing this concept allows to evaluate the two sources of force excess: *1*) the force excess ratio attributable to deviations from ideal ΔCoP modulation and *2*) the safety force ratio $\frac{GF}{GF_{min\ at\ \Delta CoP}}$. Separate analyses of these force ratios hold the promise to help foster the understanding of the mechanisms underlying excessive GF. However, our present analyses of these ratios must be treated with caution and regarded as exploratory as all derived variables might be highly susceptible to measurement errors of the static coefficient of friction (see also limitations) and this might also pertain to the statistical analyses.

GF scaling when lifting objects with off centered weight distributions.

The generation of compensatory torques to balance an object does not necessarily require a higher GF to control the grip (as $GF_{min} = \frac{F_G}{\mu_{left} + \mu_{right}}$). However, ΔCoP_{ideal} is largest for asymmetric weight distributions. As a result of deviations from ΔCoP_{ideal} asymmetric load forces must be applied to compensate for the external torque and the GF required to stabilize the grip rises, especially if large load forces have to be exerted at a grip side with low friction. In agreement with these considerations, grip forces at lift off and during the static phase were significantly higher for the asymmetric weight distributions. Indeed, this increase can be attributed to an inadequate ΔCoP modulation as the force excess ratio due to deviations from ideal ΔCoP modulation were elevated for off-centered weight distributions, whereas the safety ratios were lower.

The influence of surface materials on GF control.

Already at lift off participants scaled GF according to surface conditions and exerted higher grip forces for the more slippery and/or asymmetric surface conditions. Immediate feedback may have supported these adjustments (5, 6, 12, 18, 25, 71). In our experimental design, participants could also view the differently colored and structured grip surfaces which might have further aided anticipatory GF control. In addition, experience from the preceding trials of the block has probably also influenced GF production. Absolute GF in the more slippery and asymmetric surface material conditions remained elevated during the static phase. In contrast to absolute GF increases, safety force ratios dropped for all three more challenging surface conditions corroborating previous findings (16, 19). Moreover, in line with improvements of ΔCoP modulation in the more challenging surface conditions, the force excess ratios due to an inadequate ΔCoP were lower for the "CP" and "PP" condition. All in all, we propose that the motor system minimizes GF increases due to more slippery grip interfaces by both lowering safety ratios as well as optimizing ΔCoP modulation.

GF control when trying to be GF efficient.

Here, we show that explicitly instructing participants to aim for GF efficiency resulted in a marked reduction of GF both at lift off and during the static phase and that this could be attributed to both a reduction of the employed safety ratios and an improvement of ΔCoP modulation, especially when the object weight was asymmetrically distributed. This supports the concept that GF control represents a high-level cognitive process (72). Moreover, our results challenge the assumption that healthy adults naturally strive for GF efficiency in object manipulation at least in complex task condition as in present here.

The effect of aging on GF control.

Absolute grip forces both at lift off and during the static phase were markedly increased in the elderly (Figs. 6 and 7). Because friction at the fingertip-surface interface deteriorates with age (Fig. 3) due to reduced skin hydration (38, 41, 42), old adults require higher GF levels to prevent object slips. Hence, inference on changes of neural GF control should be based on force ratios/margins which control for finger-surface friction. Our analyses of GF safety ratios provided no evidence for an age-related deterioration of proportionate GF scaling. Moreover, we only found evidence for an increase of the force excess ratio due to impaired ΔCoP modulation when aiming for force efficiency but not when performing the grasp-to-lift task in a natural fashion (Fig. 6).

On the opposite, the elderly group reduced absolute grip forces to an even higher extent than the young group when trying to be GF efficient. This stands in line with a study by Gorniak et al. (48) who demonstrated that old adults grip fragile objects with lower GF levels than young participants. The outlined deficit to improve ΔCoP modulation when trying to be force efficient translated to an increase of GF excess due to ΔCoP deviations for weight placement on the left and right in the elderly group (Fig. 6*C*). All remaining comparisons between the age groups did not reveal significant differences between age groups. Taken together, our results do not support the notion that neural GF control deteriorates with age, despite deficits in the improvement of anticipatory ΔCoP modulation when the task goal is GF efficiency. Instead, elevated GF in the elderly can be attributed to decrements of friction at the finger-tip contacts with aging and possibly less accurate higher-level control of ΔCoP in complex grasp situations.

The Impact of Aging on Higher-Level Cognitive Processing

We compared age-related differences of the extent by which the provision of the instructions to be force efficient and of challenging surface condition influence GF safety margins as well as anticipatory torque and ΔCoP modulation. As outlined above, these aspects of motor performance are interlinked and must be jointly optimized according to the object properties, in order to achieve the task goals of both tilt control and GF efficiency. Therefore, we consider task performance as indicative of high-level cognitive motor control. Key results showed worse performance on the anticipatory compensation of clockwise external torques when being asked to be force efficient as well as smaller improvements of anticipatory ΔCoP for this instruction. In contrast, GF safety margins were reduced to a similar extent in both age groups. Moreover, challenging surface conditions did not disrupt performance in the elderly with the notable exception that elderly participants applied higher unwanted torques for the "PC" surface condition when the weight distribution was balanced. The found deficits are reminiscent of the reduced motor adaptation in old adults reported in a force-field study which was tightly coupled with an reduction in explicit learning capacities (64). Recently, Wolpe et al. (73) confirmed this correlation of reduced motor adaptation in aging with memory and reported associations with volume loss in striatum, prefrontal, sensorimotor cortical regions, and medial temporal lobe, including the hippocampus. However, deficits in ΔCoP and T_{com} anticipation found in the present study were restricted to performance when the force efficiency instruction was provided. This stands in contrast to studies showing that the anticipatory planning of hand postures according to situational constraints and future actions in a bar transport tasks (74), which is a well-known indicator of anticipatory motor planning of kinematics, was shown to sharply decline in healthy aging, especially in the seventh decade (75–77). Moreover, Stöckel et. al. (76) could demonstrate that anticipatory posture planning but also manual dexterity were highly correlated with cognitive factors, especially processing speed and cognitive flexibility. The stronger impact of aging on the planning of postures than on ΔCoP modulation might be explained in the higher difficulty of predicting consequences of hand postures in the bar transport task than to predict the consequences of ΔCoP modulation for upcoming object manipulation. Furthermore, participants in the elderly groups in the cited studies were older than in the present study.

High-Level Neural Control and Neural Correlates

The free choice of finger positions and the necessary covariation of finger-tip forces as a function of digit positions are fundamental aspects of natural object manipulation which are especially important for the control of torques (26, 33). This requires a task level, that is, high-level, neural control, orchestrating the positions and forces of the low-level effectors, for example, fingertips. The principle of covariation of forces to positions for torque control was demonstrated for different numbers of involved fingertips (26, 35, 36) and also for bimanual grasps (37). Neural control shifts from predominantly anticipatory sensorimotor memory-based anticipatory mechanism to sensory feedback-based mechanisms when the certainty of predictions of finger-tip positions decreases (34, 78).

Until recently, research of the neural correlates of grasp control employed experimental paradigms in which the finger contact points were predefined such that participants could not meaningfully modulate their choice of digit positions. In these constrained grasping tasks, inhibitory transcranial magnetic stimulation (TMS) applied over M1 but not S1 disrupted the retrieval of forces adapted to object weight used in previous lifts (79–81), whereas TMS applied over the dorsal premotor cortex (PMd) disrupted the scaling of forces based on arbitrary color cues (79). Moreover, virtual TMS lesions of PMd slowed the learning of compensatory torques when arbitrary cues were given presumably by impairing the processing of multisensory feedback integration and the updating of internal models (82). Moreover, load force distribution patterns to counteract an external torque could not be retrieved after virtual TMS lesion of M1 (33). Concerning GF fine control, the supplementary and cingulate motor areas as well as the left primary sensorimotor cortex, the ventral premotor cortex and the left posterior parietal cortex were found to be significantly more active in an fMRI study when participant were instructed to hold an object as gently as possible as compared with natural object holding with higher GF (83).

A recent TMS study allowing participants to freely choose their digit positions while having to compensate external torques suggested complementary roles of M1 and S1 in mediating finger force-to-position modulation: Virtual lesions of M1 disrupted the planning of digit positions as well as the covariation of the load force distribution, whereas virtual lesions of S1 only reduced the magnitude of asymmetric load force sharing but did not affect the retrieval of learned finger positions (33). These findings imply that the role of M1 is not limited to memory-based grip force control (79, 80, 84). Instead, M1 seems to be also directly involved in using trial-by trial sensory feedback of digit position to adapt forces in unconstrained, natural, grasping. S1 seems to be essentially involved in the sensing and comparison of expected and actual finger placement to allow for control of load forces in collaboration with M1 (33). An fMRI study evaluating differences in activated brain networks between constrained and unconstrained grasping (85) found differential activation patterns for a widespread network comprising the cerebellum, BA44 and PMv. In a follow-up study Marneweck and Grafton (86) highlighted that the same set of regions (PMv AIPn SPL7, somatosensory PSC, ventral LOC, and cerebellum) are involved in finger positioning and force control when lifting an object with an off centered center of mass, although at different time points.

Implications for the Study of Object Manipulation in Neurologic Patients

Lastly, our results bear implications for future studies of manual force control in neurologic patients. For one, we confirmed the importance of controlling for peripheral friction properties when investigating the neural control of GF. Second, we demonstrated that subjects do not necessarily aspire to manipulate objects with low grip forces. Instead, explicit instructions can have a profound impact on the high-level control of object manipulation and ultimately GF. Therefore, studies must ensure to provide all participants clear instructions. Moreover, our results suggest that analyzing performance when providing the instruction to grip objects with the lowest possible forces may be especially informative of the capabilities of patients to optimize motor control.

Conclusions

To sum up, this study adds to our understanding of high-level neural control of the sensorimotor control of object manipulation and age-related changes in the following ways: we delineated that ΔCoP modulation according to mechanical object properties and the friction coefficients determines the lowest possible grip to safely hold an object. As a consequence, both inadequate ΔCoP modulation and the incorporation of safety margins contribute to GF excess and should be assessed independently. Both the instruction to be GF efficient and challenging surface conditions at the grip handle were associated with an improved high-level anticipatory neural control of finger positions, forces, and torques resulting in improved ΔCoP modulation and lower GF safety ratios. Elderly participants improved ΔCoP and torque anticipation less when trying to be GF efficient which contributed to GF excess in the elderly. In contrast, GF safety rations were not increased suggesting intact neural control of GF.

Limitations

Finally, a number of potential limitations need to be considered. First, the present study had a complex experimental design varying the external torque, surface materials, and instructions but was probably underpowered to detect small differences between age groups as the elderly group only comprised 10 participants. As no consensus on the size of relevant effect sizes of the studied measures exists, we refrained from conducting power analyses. Moreover, the elderly age group was not very old. Future studies will have to enroll larger cohorts with a better neuropsychological and clinical characterization to confirm our findings and find the underlying neural correlates. In the young participants group, both left- and right-handed subjects participated in the study such that the effects of the hand used or handedness cannot be assessed. Lastly, the employed object-slip procedure did not allow a separate determination of μ_s for the thumb and the virtual finger comprising the index and middle finger. Moreover, the method requires that assumptions like a collinear digit positioning and symmetric load force sharing are met, such that violations of these assumptions might have increased measurement errors of μ_s and consequently of calculated measures depending upon μ_s.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

T.S. and J.H. conceived and designed research; T.S. performed experiments; T.S. and J.H. analyzed data; T.S. and J.H. interpreted results of experiments; T.S. prepared figures; T.S. drafted manuscript; T.S. and J.H. edited and revised manuscript; T.S. and J.H. approved final version of manuscript.

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12.2 Publication II: Object-centered sensorimotor bias of torque control in the chronic stage following stroke

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Object-centered sensorimotor bias of torque control in the chronic stage following stroke

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When lifting objects whose center of mass (CoM) are not centered below the handle one must compensate for arising external torques already at lift-off to avoid object tilt. Previous studies showed that finger force scaling during object lifting may be impaired at both hands following stroke. However, torque control in object manipulation has not yet been studied in patients with stroke. In this pilot study, thirteen patients with chronic stage left hemispheric stroke (SL), nine patients with right hemispheric stroke (SR) and hand-matched controls had to grasp and lift an object with the fingertips of their ipsilesional hand at a handle while preventing object tilt. Object CoM and therewith the external torque was varied by either relocating a covert weight or the handle. The compensatory torque at lift-off (Tcom) is the sum of the torque resulting from (1) grip force being produced at different vertical finger positions (ΔCoP × GF) and (2) different vertical load forces on both sides of the handle (ΔFy × w/2). When having to rely on sensorimotor memories, ΔCoP × GF was elevated when the object CoM was on the ipsilesional-, but decreased when CoM was on the contralesional side in SL, whereas ΔFy × w/2 was biased in the opposite direction, resulting in normal Tcom. SR patients applied a smaller ΔCoP × GF when the CoM was on the contralesional side. Torques were not altered when geometric cues were available. Our findings provide evidence for an object-centered spatial bias of manual sensorimotor torque control with the ipsilesional hand following stroke reminiscent of premotor neglect. Both intact finger force-to-position coordination and visuomotor control may compensate for the spatial sensorimotor bias in most stroke patients. Future studies will have to confirm the found bias and evaluate the association with premotor neglect.

Many stroke survivors suffer from impairments of dexterous upper-limb function affecting their functional independence as well as quality of life[1–3]. Weakness, spasticity and a loss of selective finger movements of the contralesional upper extremity consequent to lesions of the primary cortex or the corticospinal tract as well as impaired manual dexterity due to somatosensory deficits linked to thalamic or parietal cortical lesions are clinically well recognized consequences of stroke and have been the focus of physical rehabilitation research as they contribute most to functional impairments [for review see[2]]. Consequently, stroke survivors with contralateral hemiparesis must rely on their ipsilesional, i.e. non-paretic, hand to a great extent to perform activities of daily living. However, a growing number of studies demonstrates that fine motor performance of the ipsilesional upper limb is also substantially deprived following stroke[4,5]. Impaired fine motor control of the ipsilesional hand is evident in clinical motor function tests like the Jebsen Hand Function Test[5–10], in finger-tapping[11,12], and tests of fine motor dexterity, e.g. the 9-hole-peg test[8,9,13–15]. Subtle losses in dexterity of the ipsilesional hand are relevant for performance in activities of daily living and thus threaten the regaining of functional independence following stroke. Accordingly, poorer performance with the ipsilesional hand was confirmed in activities of daily living like the one-handed binding of shoes[16] and the preparation of meals[17]. Recent research highlights that ipsilesional hand performance is highly relevant for the functional independence following left hemisphere stroke[18]. Therefore, identifying the factors underlying impaired, ipsilesional upper limb control and developing targeted rehabilitation regimes is of paramount importance.

Kinematic analyses of reaching tasks revealed that ipsilesional motor deficits are hemisphere dependent and reflect lateralization of motor function. Movements of the ipsilesional arm are slower and more variable following left hemisphere damage while final position accuracy is decreased after right hemisphere damage[18–24]. These observations led to the proposal of a "dynamic dominance" hypothesis of motor lateralization stating that the

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dominant hemisphere is specialized for the coordination of limb and task dynamics, i.e. movement trajectories, while the nondominant hemisphere is responsible for achieving the final, i.e. steady-state, end-effector positions and stabilizing external loads[22,25–27]. Ipsilesional motor deficits in reaching tasks scale with the severity of contralesional arm impairment, i.e. the more severe the contralesional arm paresis, the larger the ipsilesional motor deficits[14], and correlate with apraxia scores in patients with left-hemispheric stroke[7,8] although the relationship may be complex[21].

One elegant way to study complementary pathophysiologic aspects of manual dexterity following stroke is to examine kinetics, i.e. forces and torques, when patients execute elementary grasp-to-lift tasks. In healthy adults grip forces (GF), i.e. the force acting orthogonal to the grip surface, and load forces (LF), i.e. the forces directed tangentially upwards, rise in parallel and are precisely scaled to the anticipated characteristics of both the object (weight, frictional characteristics) according to previous experience, i.e. sensorimotor memories[28,29], and visual object characteristics, e.g. size, material, arbitrary cues, object identity[30–35], and the dynamics of the task [for review see:[36]].

Hemiparetic patients with stroke typically exert increased grip forces when lifting objects with their more affected, contralesional, hand which can be partially attributed to disturbed sensorimotor integration[37–43]. Moreover, studies investigating the ipsilesional, non-paretic, hand of stroke survivors also found elevated grip force levels[44–46] as well as an increased grip force variability[45] and disturbed anticipatory grip-to-load force coupling[46]. In contrast, gross grip strength is not reduced in the ipsilesional hand following stroke[5,9,10]. Adding to these problems in the task execution, the anticipatory planning of forces is also impaired following stroke. While the anticipatory scaling of grip forces according to object size is intact in stroke patients (Li et al.[63]), patients with left hemisphere damage failed to scale grip forces to the actual weight of objects of daily life when grasping and lifting them with their ipsilesional hand[47]. This GF scaling deficit was associated with scores of apraxia. Similarly, patients with left-sided middle-cerebral artery (MCA) stroke could not use color-cues associated with object weight to scale grip forces with either hand, whereas patients with right MCA stroke only showed impaired force scaling with their contralesional hand[48].

The control of torques when lifting an object with an eccentric center of mass (CoM) relative to the hand is another essential aspect of dexterous object handling in daily life which has been extensively studied in healthy adults over the last two decades. To prevent object tilt, e.g. when lifting a cup of tea at the handle, arising torques must be already compensated at the moment of object lift-off, i.e. before full sensory feedback of object toque is available. Two torque components add up to the total torque applied by the fingers in the direction of interest. These are a) the product of the load force difference between grasp-sides (ΔFy) and half the grasp-width (w/2) and b) the product of the distance between the finger centers of pressure on the grasp surfaces (ΔCoP) and the grip force (GF). Therefore, the digit placements and grip- and load forces must be coordinated to apply adequate counteracting torques at lift-off [for review see[49]]. Healthy adults learn to modulate both their digit centers of pressure and digit forces by placing the digit(s) on the side of the center of mass higher and applying more load force at the digit on that side according to previous experience[50–52], even when object dynamics change unpredictably[53,54]. Furthermore, subjects can visually process salient object shape/geometry cues to infer the weight distribution of the object and plan torques accordingly[51,55–57]. To generate adequate compensatory torques, digit -forces and -placements are covaried by a high-, respectively task-level control. This principle of force-to position covariation is grasp-type independent[58] and was shown for grasps with a precision grip[50], tripod grip[59], whole hand grasps[60] as well as for bimanual grasps[61]. Although torques can be applied by any combination of digit center of pressure differences between the grasp sides (ΔCoP) and load force partitioning between sides (ΔFy) as long as the resulting torque components add up to the required total torques, we recently demonstrated that an adequate finger-tip positioning and a predominant torque exertion by the product of ΔCoP and GF is essential for a force efficient task execution[62]. Whether these aspects of high-level torque control are impaired at the ipsilesional hand of patients with unilateral stroke has not been investigated, yet.

In the present study, we examined whether the anticipatory torque control with the ipsilesional hand when lifting an object with a varying asymmetric weight distribution is impaired in the chronic stage following unilateral stroke. We tested two cue conditions. The first was a 'no-cues' condition in which the position of a covert weight was changed while object shape (inverted T) was not informative of the CoM. In this condition, subjects had to rely on sensorimotor memories from the last lift or lifts. In the second condition the visually salient object geometry was congruent with weight distribution (L-shape) allowing visual inference of CoM. Moreover, two sequence conditions, one in which the mass distribution was constant over a block of trials and one in which it could change from trial to trial were employed for both cue conditions.

Since the right-hemisphere is proposed to be responsible for end-effector positions according to the "dynamic dominance" model[25] we expected that patients with right hemisphere damage would fail to learn to position their fingers for an adequate torque component $\Delta\text{CoP} \times \text{GF}$, but would correct for this by compensatory ΔFy ($\times$ w/2) resulting in successful total torque compensation.

Based on the hypothesized role of the left hemisphere in the dynamic phase of an action, we hypothesized a less accurate coordination of fingertip load forces (ΔFy) to the present ΔCoP and consequently less successful predictive torque compensation in patients with left-hemispheric-, but not right hemispheric stroke, irrespective of the side of the object center of mass (CoM). Moreover, we presumed that patients with signs of apraxia would present an accentuated impairment of force-to position coordination and consequently torque compensation.

However, as stroke patients previously exhibited mostly intact visuomotor processing of size and weight cues to scale finger-tip forces[63,64] we expected that most stroke patient can improve torque anticipation when salient-geometric cues are provided. As an exception, we presumed that patients with hemispatial neglect might fail to utilize a lateralized geometric cue indicating a CoM on the contralesional side.

Concerning grip force levels, we expected to observe elevated and more variable GF levels in both stroke groups based on previous studies[44,45].

Materials and Methods

Participants. Overall, 13 patients with chronic-stage left hemispheric stroke (SL group: 6 female, mean age 63.3 ± 16.3 years, mean years since onset of stroke (YOS): 6.06 ± 4.10 years) and 9 patients with chronic-stage right hemispheric stroke (SR group: 5 female, mean age 63.9 ± 6.7 years, mean YOS 7.5 ± 5.7 years) were tested with their ipsilesional hand. 15 healthy adults who conducted the experiment with their left hand (CL group: 6 female, mean age 63.0 ± 13.1 years) and 9 healthy adults who conducted the experiment with their right hand (CR group: 4 female, mean age 69.8 ± 3.8 years) served as control groups. Patients with a single unilateral cerebrovascular event older than 6 months and no evidence of bilateral lesions in their medical reports were recruited from the community with the help of physiotherapists, occupational therapists, speech therapists and neuropsychologist in the greater Munich area (see Acknowledgements). All participants reported to be right handed.

Table 1 provides group summaries of the demographic and clinical characteristics as well as the results of the performed neglect and apraxia tests together with the statistical results of between group tests (ANOVA, respectively t- tests for numerical data, chi-square tests for categorical data). Individual patient's data are outlined in Supplementary Table S1.

The experimental procedures were approved by the Institutional Review Board of the School of Medicine at the Technical University of Munich and were in accordance with the Declaration of Helsinki. All subjects were naïve to the purpose of the study and gave informed consent to participate in the study and have us collect relevant medical reports from their family doctor. Measurements took place at our lab as well as in patients' homes between September 2016 and April 2017. All participants received 20 € for their participation in the study which lasted ~ 2 h.

Modified rankin scale (mRS). The modified Rankin Scale (mRS) was assessed as measure of the degree of disability or dependence in the daily activities using the simplified questionnaire proposed by Bruno et al.[65].

Apraxia tests. We administered two established tests of apraxia and video-recorded them for later analysis. Firstly, we examined the imitation of meaningless gestures of hand- and finger postures with the ipsilesional hand. Imitation scores below 18 of 20 for hand- and 17 of 20 for finger-postures were considered as suggestive of apraxia[66–69]. In addition to imitation, we examined pantomime of tool-use. Here, we showed patients pictures of one of 20 tools or objects of the daily life and asked them to mime specific action as if they were holding the object in their ipsilesional hand. We scored whether hand positions and movements were correct. Scores below 45/55 were considered as suggestive of apraxia[68,70,71].

Tests of visual hemispatial neglect. The presence of hemispatial neglect was assessed by the (a) line bisection-test in which a deviation of more than 6 mm from the midpoint indicates hemispatial neglect[72], (b) the letter cancellation test with performance quantified by the center of calculation (CoC) score introduced by Rorden and Karnath[73]—i.e. an absolute CoC score above 0.083 indicates presence of hemispatial neglect—and (c) a Posner type spatial cueing test[74] implemented in the free computer test battery PEBL [version 0.14,[75]]. In the latter, patients sat in front of a 15.6-inch Lenovo laptop. After a cue to the left, right or both sides (neutral) was provided, indicating where the response is likely to be, patients had to press a key when they detected a stimulus either to the left or right of fixation. As measure of a hemispatial visual bias we calculated the standardized median reaction time difference between trials with stimuli to the left and to the right of fixation (overall 200 trials, 100 trials per stimulus side, cues were valid in 120 trials, neutral in 40 trials, and invalid in 40 trials). Reaction time differences between stimuli on the left and right side in Posner-type reaction time tests were shown to be more sensitive than paper and pencil based tests in detecting hemispatial neglect[76]. However, there is no established cut-off defining hemispatial neglect.

Experimental design and statistical analyses. *Apparatus.* Subjects were instructed to reach, grasp, lift and replace a custom made, grip device with the thumb opposing the index and the middle finger[53] (see Fig. 1A). The grasp surfaces (120 × 40 mm) were covered with fine-grained sand paper (2000 grit). Two 6-axis force/torque-sensors (ATI Nano-17 SI-50–0.5, ATI Industrial Automation; force range: 50,50, and 70 N for x-, y-, and z-axes, respectively; force resolution: 0.012 N; torque range 0.5 Nm; torque resolution: 0.063 Nmm, sampling rate 200 Hz) recorded the forces and torques applied on both grasp sides. Position and orientation data of the device were measured by a lightweight magnetic position/orientation-tracker (TrakSTAR, Ascension Technology Corporation, accuracy: 1.4 mm RMS, 0.5 degrees RMS, sampling rate 200 Hz) fixed on top of the horizontal base. Data collection was synchronized using custom software written in Matlab 2016a (MATLAB, RRID:SCR_001622). Both the position of the handle device on top of the base as well as the location of a 250 g aluminum weight which was put into cavities of the base hidden by a lid could be altered to vary the object's center of mass (CoM) relative to the hand (see Experimental Protocol).

Determining the static coefficient of friction, μ_s, at slip onset. Prior to the main experiment, subjects were asked to lift and hold the grip device in a three-finger precision grip with the thumb, index and middle fingers of the hand used for the upcoming lifting task and slowly release it until the object slipped. We estimated the average static friction coefficient, μ_s, at the digit—surface contacts, by calculating the ratio between the load- and grip force at slip onset which was visually detected by a sudden drop in the load force and height. Overall, μ_s could be successfully calculated in 121 slip-trials. The averaged μ_s estimates are based on an average of 2.63 slip-trials per subject (SD 0.77, median 3, range 1–4).

	CL ($N=15$)	CR ($N=9$)	SL ($N=13$)	SR ($N=9$)	*p* value
Age					0.564[1]
Mean (SD)	63.0 (13.1)	69.8 (3.8)	63.3 (16.7)	63.8 (6.7)	
Range	24.9–80.5	65.3–76.3	24.5–79.8	50.4–72.2	
Gender					0.907[2]
m	9 (60.0%)	5 (55.6%)	7 (53.8%)	4 (44.4%)	
f	6 (40.0%)	4 (44.4%)	6 (46.2%)	5 (55.6%)	
Stroke Type					0.042[2]
i	0	0	10 (76.9%)	5 (55.6%)	
h	0	0	0 (0.0%)	4 (44.4%)	
i, h	0	0	1 (7.7%)	0 (0.0%)	
h, i	0	0	2 (15.4%)	0 (0.0%)	
Subcort./cort. lesion					0.290[2]
sc	0	0	3 (23.1%)	4 (44.4%)	
sc, c	0	0	10 (76.9%)	5 (55.6%)	
mRS					0.702[1]
Mean (SD)	NA	NA	2.4 (0.8)	2.2 (1.2)	
Range	NA	NA	1.0–4.0	1.0–4.0	
Years since stroke onset					0.505[1]
Mean (SD)	NA	NA	6.1 (4.1)	7.5 (5.7)	
Range	NA	NA	1.1–15.0	2.2–19.9	
Coefficient of static friction					0.292[1]
Mean (SD)	0.9 (0.2)	1.0 (0.2)	0.9 (0.1)	0.9 (0.1)	
Range	0.6–1.2	0.7–1.2	0.7–1.1	0.7–1.0	
Peak voluntary GF [N]					0.609[1]
Mean (SD)	68.7 (24.1)	57.5 (17.7)	67.6 (20.7)	66.0 (16.0)	
Range	34.1–111.1	35.4–93.1	34.7–98.5	37.8–93.3	
Imitation Hand					0.070[1]
N	0	0	13	8	
Mean (SD)	NA	NA	18.7 (1.7)	19.9 (0.4)	
Range	NA	NA	15.0–20.0	19.0–20.0	
Imitation Finger					0.616[1]
Mean (SD)	NA	NA	18.6 (2.7)	19.1 (1.0)	
Range	NA	NA	11.0–20.0	17.0–20.0	
Pantomime correct items [/20]					0.224[1]
N	0	0	13	9	
Mean (SD)	NA	NA	17.2 (4.9)	19.3 (1.0)	
Range	NA	NA	3.0–20.0	18.0–20.0	
Pantomime Score [/55]					0.241[1]
Mean (SD)	NA	NA	50.2 (10.1)	54.3 (1.0)	
Range	NA	NA	19.0–55.0	53.0–55.0	
Bisection Test: mean horizontal deviation [mm]					0.432[1]
N	0	0	10	6	
Mean (SD)	NA	NA	− 0.3 (2.7)	1.0 (3.8)	
Range	NA	NA	− 4.9–4.5	− 3.8–6.6	
Letter cancellation test: center of cancellation					0.143[1]
N	0	0	11	5	
Mean (SD)	NA	NA	0.0 (0.0)	0.0 (0.0)	
Range	NA	NA	0.0–0.0	0.0–0.1	
Letter cancellation test: overall letters found [/60]					0.051[1]
Mean (SD)	NA	NA	59.1 (1.4)	57.2 (2.2)	
Range	NA	NA	57.0–60.0	54.0–60.0	
Posner test: median reaction time [ms]					0.346[1]
N	0	0	12	5	
Mean (SD)	NA	NA	557.3 (179.4)	474.4 (87.1)	
Range	NA	NA	324.0–960.5	403.5–617.0	
Posner test: relative L-R reaction time difference [%]					0.001[1]
Continued					

	CL ($N=15$)	CR ($N=9$)	SL ($N=13$)	SR ($N=9$)	*p* value
Mean (SD)	NA	NA	− 9.1 (8.3)	14.6 (16.5)	
Range	NA	NA	− 20.4–9.6	0.3–39.7	

Table 1. Group summary of the demographics, clinical data, the coefficients of fraction, maximum voluntary GF, the results of the pantomime and imitation tests of G. Goldenberg (see also[66,71,91] as well as the results of the line bisection test, letter cancellation test[73], and a Posner type reaction time test[76]. [1]Linear Model ANOVA, [2] Pearson's Chi-squared test. The *p*-values of between groups differences were based on ANOVA tests for numerical data (respectively t-tests if data were only obtained for the stroke groups) and on chi-square tests for categorical data. Abbreviations: Stroke type: i = ischemic; h = hemorrhagic; i, h = ischemic stroke followed by hemorrhage; h, i: hemorrhage with subsequent ischemic infarction. Subcort./cort. Lesion: purely subcortical (sc) or subcortical and cortical lesions (sc, c).

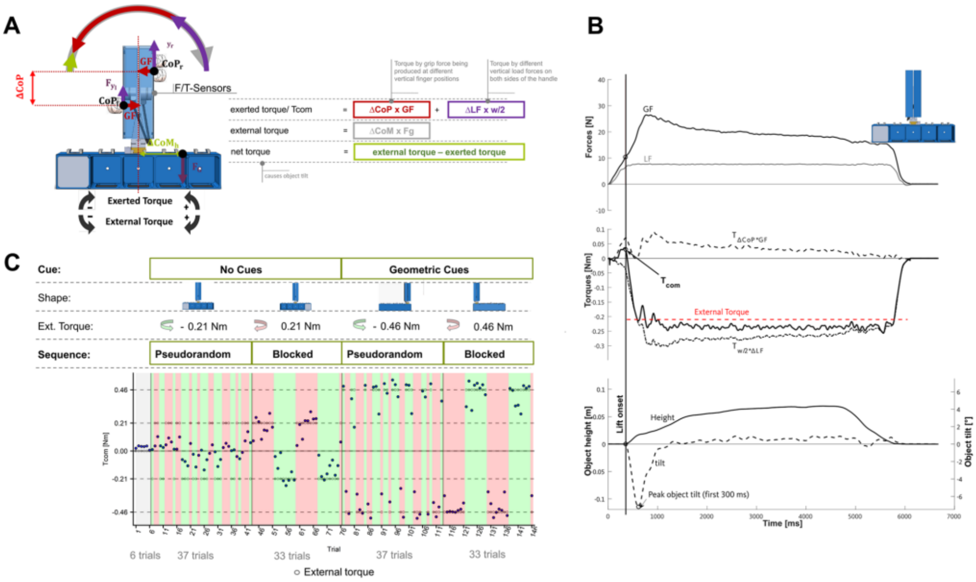

Figure 1. Experimental apparatus, variables and design. (**A**) The custom-built grip-device consists of a handle element mounted centrally on a horizontal bar (frontal view). The handle element allowed subjects to freely choose digit placement on the grip surfaces (40 × 120 mm) covered with sandpaper. Two 6-axis-force/torque sensors were mounted under the grasp surfaces. In the 'no cues' condition a hidden weight was either placed in the left or right cavity resulting in an external torque after lift-off. The exerted total torque is the sum of the torque components ΔCoP × GF and ΔFy × w/2 and must compensate for the external torque to prevent object tilt. (**B**) The recorded experimental variables are illustrated for an exemplary trial, the torque variables at lift off were considered to be indicators of anticipatory torque control. (**C**) The experimental protocol comprised the two cue- conditions 'no cues' in which the center of mass (CoM) was changed by placing a hidden weight either on the left or the right (with the handle being positioned above the middle cavity), resulting in external torque of ± 0.21 Nm after liftoff, and the 'geometric cues' condition in which the handle was either mounted above the left or right cavity (with the hidden weight inserted in the central cavity) , resulting in external torque of ± 0.46 Nm after liftoff. The order of the conditions and first CoM side was randomly assigned to participants (see Supplementary Table 1). For each cue-conditions participants first completed a pseudorandom sequence of 37 trials in which the CoM could change from trial to trial and 33 trials in which the CoM stayed constant for 8 trials before it was inverted.

Maximum GF. Prior to the main experiment we had participants pinch the grasp surfaces as hard as they could in the specified three-finger precision grip twice for five seconds and determined the highest applied GF as maximum GF.

Experimental task. For the main experiment, we instructed participants to start reaching for the grasp-device after a signal tone, grasp the grasp surfaces with the fingertips of the thumb-, index- and middle finger in a precision grip, lift it in a smooth movement to a height of ~ 5–10 cm while minimizing object tilts and hold the object steady thereafter. A second tone 4 s after the first signaled subjects to replace the device. Patients were allowed to position and orient the object on the table in a way that allowed for a comfortable wrist position for grasping.

Experimental protocol. First, participants conducted six practice grasp-to-lift trials in which the object's CoM was below the middle of the handle (zero external torque).

Subsequently, the main experimental protocol contained two sequence conditions and two cue conditions (see Fig. 1C). In the 'no cues condition', the object handle was attached over the center of the base (symmetric, inverted T-shape) and the center of mass was varied by placing a covert 250 g aluminum weight into either the outer left or outer right hidden cavity of the horizontal base, resulting in external torques of ± 0.21 Nm (see Fig. 1C). In the 'geometric cues condition', in contrast, the aluminum weight was constantly placed in the center cavity, but the handle was either positioned on top of the left or right object edge creating an asymmetric L-shape and resulting in an external torques of ± 0.46 Nm (see Fig. 1C). As convention, negative signs denote a counter-clockwise external torque. The total object weight was 750 g.

In both cue-conditions, participants first conducted 37 trials in the 'pseudorandom' sequence-condition in which the CoM was changed in a pseudo random fashion which could not be predicted by the participants (see Fig. 1C). Participants had to close their eyes while the hidden weight was removed and placed back either into the same or the opposite position after each trial.

This was followed by the blocked sequence-condition in which the CoM remained constant for 8 trials per block before the CoM changed side for the next blocks. Participants were informed about the CoM change between blocks but were restricted of watching the configuration change. The blocked-sequence encompassed 4 complete blocks and the first trial of the 5th block, i.e. 33 trials. The succession of the pseudorandom and blocked sequence-condition trials was performed for both the no-cues and geometric-cues conditions, amounting to a total of 140 main trials per participant. We randomly assigned the order of the two cue conditions and the initial CoM side for the first trial for the no-cues- and geometric-cues conditions to the participants.

Data processing. Data were processed and analyzed with custom software written in Matlab 2016a. The collected force/torque data was filtered through a sixth-order Butterworth low-pass filter with a cutoff frequency of 14 Hz. The index and middle finger contacting the same grip side produced net mechanical forces and moments equivalent to the sum of their individual actions and were hence considered as a virtual finger[77]. We analyzed the exerted total torque (Tcom) as well as the torque components ΔFy*w/2 and ΔCoP *GF outlined below as well as the grip force (GF) at the moment of object lift off, defined as the moment 10 ms prior to which the vertical position of the object raised above a threshold of 0.2 mm.

We examined the following experimental variables (see Fig. 1B):

1. Grip force (GF) was defined as the mean normal force directed orthogonal towards the grip surfaces.
2. ΔCoP at lift-off was defined as the vertical difference between the center of pressure (CoP) on the right and the left grip sides at the moment of lift-off.
3. Tcom, the compensatory torque exerted at object lift off, is an established indicator of torque anticipation[50,78,79]. Tcom is the sum of: (a) ΔCoP *GF, the product of GF and ΔCoP and b) ΔFy*w/2, the torque generated by the product of the difference between the right and left load force and half the distance between the grip-surfaces $\left(\frac{\mathrm{w}}{2} = 20.4\mathrm{mm}\right)$. With the chosen sign conventions, Tcom matches in sign with the external torque when it counterbalances the exerted torque, e.g. is directed in opposing direction to the external torque. Hence, clockwise exerted torques were defined as negative and counter-clockwise torques as positive (see Fig. 1A and the supplementary material of[53]: https://doi.org/10.6084/m9.figshare.7683707). As outcome measures in the statistical analyses, we calculated the respective ratios between the torque variables and the external torque to compensate for, i.e.: $\frac{\mathrm{Tcom}}{\mathrm{External\ Torque}}$, $\frac{\Delta\mathrm{Fy}*\mathrm{w}/2}{\mathrm{External\ Torque}}$ and $\frac{\Delta\mathrm{CoP}*\mathrm{GF}}{\mathrm{External\ Torque}}$. This allows for direct evaluation of the success of torque anticipation as a ratio of 1 indicates perfect torque compensation and negative ratios indicate torques directed in the wrong direction. $\frac{\mathrm{Tcom}}{\mathrm{External\ Torque}}$ is the primary outcome variable, $\frac{\Delta\mathrm{Fy}*\mathrm{w}/2}{\mathrm{External\ Torque}}$, $\frac{\Delta\mathrm{CoP}*\mathrm{GF}}{\mathrm{External\ Torque}}$ are the secondary outcome variables, and ΔCoP and GF represent exploratory tertiary outcome variables.
4. Additionally, we estimated the average static coefficients of friction, $\mu_{\mathbf{s}}$, of each participant by averaging the ratios between the load force and grip force at the moment at which slips occurred in the slip-task to control for possible friction differences between groups.

Data management. Due to technical errors 1.58% (106/6716) of the measurements had to be discarded. We obtained 121 $\mu_{\mathbf{s}}$ estimates employing the slip-method.

Statistical analysis. Statistical analyses were performed in the R environment for statistical computing (version 4.0.3,[80], R Project for Statistical Computing, (RRID):SCR_001905). To compare the demographic and clinical characteristic of the control- and stroke groups exploratory analyses of variance (ANOVA) tests for numerical data (respectively t-tests if data were only obtained for the stroke groups) and chi-square tests for categorical data were conducted as implemented in the 'arsenal' package[81] (see Table 1).

We fitted separate linear mixed effects models (LMM) with random-intercepts estimating the random variance across subjects using the restricted maximum likelihood criterion as implemented in the 'lme4'-[82] package for the dependent primary and secondary outcome variables and every experimental condition.

The fixed effect predictors of the models for the blocked sequence condition were: the participant 'group', the 'external torque' and the two-way 'group × external' torque interaction. We separately analyzed the trials 4–8 of each block to assess the extent of motor learning as well as of the respective first trials of blocks 2–4 to investigate the transfer of motor learning after a CoM change.

The fixed effects predictors of the models for the pseudorandom sequence condition were: the 'external torque', the 'group', the 'CoM action' (CoM-retained/inverted) and the resulting two- and three-way interactions ('external torque × CoM action', 'external torque × group', 'group × CoM action', 'external torque × CoM action × group').

We performed omnibus Wald-type F-tests of the model predictors with type-III analyses of variance (ANOVA) using the 'lmerTest' package[83] as well as post-hoc t-Tests of pairwise comparisons between the hand-matched control and stroke groups (CL-SL, CR-SR) patient- and hand-matched control groups based on the marginal means of the LMMs with Holm-Bonferroni correction for multiple testing using the 'emmeans' package[84]. The predictor degrees of freedom of the LMMs were approximated with the Kenward-Roger method. It must be noted that the used hand used influences the ANOVA omnibus main effects of 'group' and the main interaction 'external torque × group'. Therefore, statistical inferences on the impact of stroke on the torque planning were based on the results of the post-hoc pairwise comparisons controlling for the hand used. Initially planned analyses on the effect of apraxia and neglect on torque control could not be performed as too few patients showed signs of apraxia or neglect (see "Apraxia and neglect" section).

We performed a post-hoc power analyses for the torque variables in the no-cues-, blocked condition by calculating the power to detect group differences between 0.05 and 0.5 (steps of 0.05) with the alpha-level set to 0.25 using the 'Superpower' package in R[85] (for details see Supplementary Figure S5).

Ethics approval and consent to participate. The experimental procedures were approved by the Institutional Review Board of the School of Medicine at the Technical University of Munich and were in accordance with the Declaration of Helsinki. All subjects gave informed consent to participate in the study.

Results

Demographic characteristics, clinical measures and static coefficients of friction.

We found no statistically significant differences between groups regarding age ($p = 0.56$), years since stroke onset ($p = 0.51$), gender distribution ($p = 0.91$), mRS ($p = 0.70$), mean coefficient of friction ($p = 0.29$, see also Supplementary Fig. S2), nor the voluntary maximum GF in the tripod grip ($p = 0.609$) (see Table 1).

Apraxia and neglect.

The vast majority of patients scored within the normal range in the administered apraxia and neglect tests: Only three patients with left MCA strokes scored below the cutoff in the hand imitation test (< 18), two of these patients (ID24, ID27) also failed the finger imitation (< 17)—and pantomime tests (< 45, Supplementary Fig. S1). Regarding the paper-based tests of hemispatial-neglect, only one patient with right MCA stroke (ID9) showed a line bisection deviation suggestive of hemispatial neglect to the left. However, results of the letter cancellation test were within the normal range in all patients. The results of the hand- ($p = 0.070$), and finger imitation tests ($p = 0.616$), the pantomime score ($p = 0.241$) as well as the line bisection ($p = 0.43$) and the CoC on the letter cancellation test ($p = 0.201$) did not differ between patient groups. The only significant difference between the SL and SR group was found for the percentual left–right reaction time difference in the Posner test ($p = 0.001$). Whereas SL patients were about 9.1% (SD 8.3%) slower in reacting to a stimulus on the right side, SR patients were 14.6% (SD 16.5%) slower when the stimulus was on the left side. In contrast, the mean reaction time in the Posner test ($p = 0.35$) was similar between patient groups. Table 1 summarizes the demographic, clinical and grip related measures of the participant groups.

Torque compensation at lift off.

No cues, blocked condition trials 4–8: Sensorimotor learning of the anticipatory coordination of centers of pressure and grip force is spatially biased following stroke. Participants of all groups only needed some 2–3 lift trials to learn to compensate for torques at the moment of lift-off. After that, Tcom remained stable for the rest of the block (see Supplementary Fig. S3 for the individual and group-averaged Tcom trajectories across trials in the 'no cues' condition).

All groups generated similar compensatory torques at lift-off in trials 4–8 with no significant differences between stroke and control groups (main effect of 'group' n.s., significant 'ext. torque × group' interaction' F (3, 858) = 33.2, $p < 0.001$, see Supplementary Table S2, no significant post-hoc comparison of interest). However, there was a trend towards a decreased Tcom for the SR-group when the weight was on the left side which was not significant after Holm-correction (t (55.3) = − 2.15, $p = 0.071$, see Fig. 2A and Supplementary Table S3).

In contrast, the torque components at lift-off were spatially biased following a specific directional pattern in both stroke groups depending on the external torque (main effect 'group' n.s., significant 'ext. torque × group' interaction' F (10.1, 858) = 53.7, $p < 0.001$, see Supplementary Table S4). The torque generated by grip force being produced at different vertical finger positions $\left(\frac{\Delta \mathrm{CoP} * \mathrm{GF}}{\text{External Torque}}\right)$ was lower in the SL group than the CL group when the CoM was on the right, i.e. contralesional, side (post-hoc comparison SL-CL: estimate = − 0.37, ηp2 = 0.24, t (65.5) = − 4.59, $p < 0.001$, see Fig. 2B and Supplementary Table S5) but higher than in the CL group when the weight was on the left, i.e. ipsilesional, side (post-hoc comparison SL-CL: estimate = 0.33, ηp2 = 0.20, t (65.5) = 4.10, $p < 0.001$). The torque produced by different load forces at the handle sides was biased in the opposite direction (main effect 'group' n.s., significant 'ext. torque × group' interaction' F (3, 858) = 29.3, $p < 0.001$, see

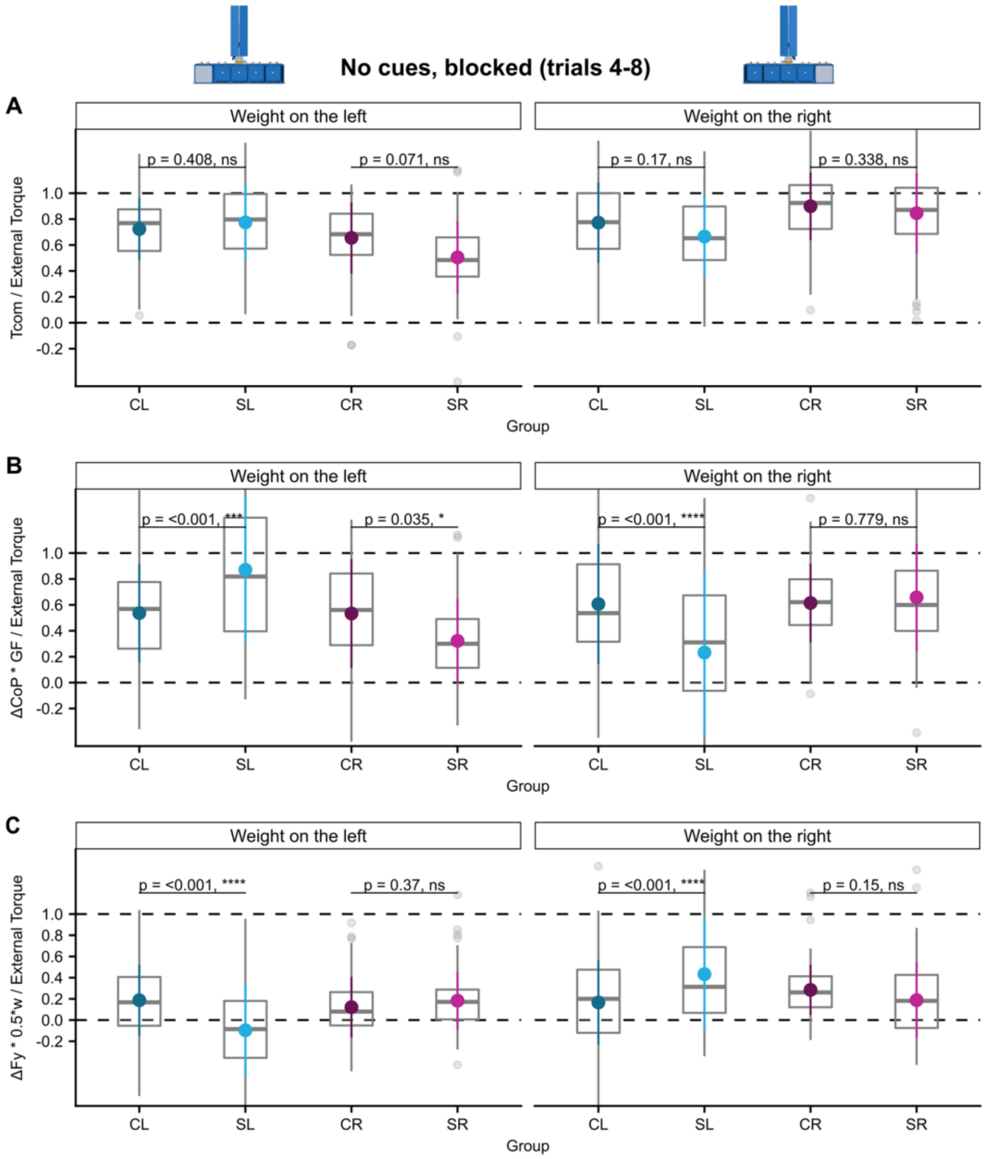

Figure 2. Sensorimotor learning of anticipatory torque compensation. Box and whiskers plots in the style of Tukey (central horizontal line: median, lower, and upper hinges: 25th and 75th percentiles, upper and lower whiskers extend up to 1.5 interquartile ranges) as well as the mean and standard deviation of the ratios of anticipatory torque anticipation success Tcom/external torque (**A**), ΔCoP * GF/External Torque (**B**), and ΔFy * 0.5*w/External Torque (**C**) for trials 4–8 of blocks in the 'no cues' condition are depicted for each group together with Holm-adjusted *p*-values of post-hoc t-tests of pairwise differences between controls and left- respectively right-hemispheric stroke patients.

Supplementary Table S6), i.e. $\frac{\Delta Fy*w/2}{\text{External Torque}}$ was higher in the SL- than the CL group for a CoM on the contralesional, right side (post-hoc comparison SL-CL: estimate = 0.27, ηp2 = 0.20, t (98.2) = 5.03, $p < 0.001$, see Fig. 2C and Supplementary Table S7) and lower for a CoM on the ipsilesional, left side (post-hoc comparison SL-CL: estimate = − 0.28, ηp2 = 0.22, t (98.2) = − 5.33, $p < 0.001$). As the patterns of the object-centered spatial bias are diametrically opposed for $\frac{\Delta CoP*GF}{\text{External Torque}}$ and $\frac{\Delta Fy*w/2}{\text{External Torque}}$ the effects seem to cancel each other out resulting in normal total torques (Tcom) as outlined above.

SR patients equally exerted less torque by grip force being produced at different vertical finger positions $\left(\frac{\Delta CoP*GF}{\text{External Torque}}\right)$ than CR controls when the CoM was on the contralesional, left side (post-hoc comparison SR-CR: estimate = − 0.22, ηp2 = 0.06, t (67.4) = − 2.16, $p = 0.035$ see Fig. 2B and Supplementary Table 5), however $\frac{\Delta CoP*GF}{\text{External Torque}}$ was not increased for the ipsilesional CoM side and we found no differences of the torque produced by differential load forces $\left(\frac{\Delta Fy*w/2}{\text{External Torque}}\right)$ at lift off in the SR group.

No cues, blocked condition, trials after CoM change: Failed transfer of sensorimotor memories to explicit CoM changes.. Despite being explicitly told that the CoM would be changed to the opposing side at the end of each block of eight trials, subjects of all groups subsequently failed to adapt to the new CoM situation and could not inverse the direction of the previously learned Tcom, i.e. transfer sensorimotor memories. This stands in line with previous studies [e.g.[52,78]]. Tcom was mostly near zero but clearly generated in the wrong, i.e. the previously learned, direction as indicated by a negative ratio of $\frac{\text{Tcom}}{\text{External Torque}}$. We observed no significant Tcom differences between stroke and control groups (main effect 'group' n.s., significant 'ext. torque × group' interaction' F (3, 858) = 33.2, $p < 0.001$, no significant post-hoc comparisons, see Fig. 3A and Supplementary Tables 8 and 9). Concerning the torque components (main effect 'group' n.s., significant 'ext. torque × group' interaction' F (3, 858) = 53.7, $p < 0.001$, see Supplementary Table S10), the SL group applied a higher torque by grip force being exerted at different vertical finger positions $\left(\frac{\Delta CoP*GF}{\text{External Torque}}\right)$ than controls when the hidden weight was transferred to the ipsilesional, left side (post-hoc comparison SL-CL: estimate = 0.33, ηp2 = 0.06, t (126.2) = 2.81, $p = 0.012$, see Fig. 3B and Supplementary Table S11). Apart from this, there were no further differences between stroke- and control groups (see also Fig. 3C and Supplementary Table S13).

No cues, pseudorandom condition: Torque planning according to sensorimotor memories despite uncertainty. In this condition the position of the hidden weight was either retained or inverted between trials in a pseudorandom fashion. After each trial the hidden weight was removed and placed back either into the same or the opposite position. Although a rational torque planning was not possible in this condition, we observed that all groups planned according to the previous lifts resulting in clearly positive Tcom ratios when the CoM was not inverted (main effect 'CoM action': F (3, 1569) = 1151.0, $p < 0.001$, see Supplementary Table S14 and Fig. 4A). Remarkably, we did not observe the generation of Tcom of similar magnitudes directed in the wrong direction following a CoM inverse. Rather, Tcom was close to zero in trials after a CoM inversion suggesting that participants must have partially corrected the exerted torque already until lift-off. We found two just significant post-hoc group differences reflecting significant 'ext. torque × group' (F (3, 1569) = 18.1, $p < 0.001$) and 'CoM-action × group' [F (3, 1569) = 3.8, $p = 0.01$] interactions. First, the SL group exerted a Tcom closer to zero when the CoM was switched to the left (post-hoc comparison SL-CL: estimate = 0.1, ηp2 = 0.01, t (236.9) = 2.28, $p = 0.046$, see Fig. 4A and Supplementary Table S15). Secondly, the SR group produced a smaller Tcom when the CoM remained on the right (post-hoc comparison SL-CL: estimate = − 0.13, ηp2 = 0.02, t (246.7) = 2.33, $p = 0.041$).

Concerning the torque components, we again found contrasting object-centered spatial biases of the torque anticipation strategies in the SL group when compared with the CL group and this was irrespective of whether the weight position was changed or not (main effect 'group' n.s., significant 'external torque × group' interaction' F (3, 1569) = 30.2, $p < 0.001$, interaction 'CoM-action × group' n.s., see Supplementary Table S16): While the torque generated by grip force being exerted at different vertical positions $\left(\frac{\Delta CoP*GF}{\text{External Torque}}\right)$ was less adequate (smaller ratio) when the weight was on the right, i.e. contralesional, side (post-hoc comparison SL-CL, CoM inverted: estimate = − 0.27, ηp2 = 0.03, t (536.5) = − 4.79, $p < 0.001$, CoM retained: estimate = − 0.21, ηp2 = 0.03, t (531) = − 3.72, $p < 0.001$, see Fig. 4B and Supplementary Table S17) but more adequate (higher ratio) than in the CL group when the weight was on the left, i.e. ipsilesional side (post-hoc comparison SL-CL, CoM inverted: estimate = 0.23, ηp2 = 0.03, t (529) = 4.22, $p < 0.001$, CoM retained: estimate = 0.24, ηp2 = 0.03,t (529) = 4.28, $p < 0.001$). Again, the torque generated by differential load forces between sides was biased in the opposite direction (main effect 'group' n.s., significant 'external torque × group' interaction' F (3, 1569) = 16.9, $p < 0.001$, interaction 'CoM-action × group' n.s., see Supplementary Table S18), i.e. $\frac{\Delta Fy*w/2}{\text{External Torque}}$ was higher in the SL than in the CL group for a CoM on the contralesional, right side (post-hoc comparison SL-CL, CoM inverted: estimate = 0.22, ηp2 = 0.02, t (537) = 4.47, $p < 0.001$, CoM retained: estimate = 0.16, ηp2 = 0.02, t (531) = 3.25, $p = 0.0025$, see Fig. 4C and Supplementary Table S19) and lower for a CoM on the ipsilesional, left side (post-hoc comparison SL-CL, CoM inverted: estimate = − 0.13, ηp2 = 0.02, t (529) = − 2.72, $p = 0.014$, CoM retained: estimate = − 0.16, ηp2 = 0.02, t (529) = 3.35, $p = 0.002$). No significant differences were detected between the right-hand groups SR and CR.

Geometric cues: successful torque anticipation in all experimental conditions. In the geometric cue condition in which the CoM was altered by attaching the handle either on the left or right edge of the base participants of all groups successfully compensated for the arising external torque at lift off both in the blocked as well as in the pseudorandom condition and even in trials following a change of the handle position in the blocked condition.

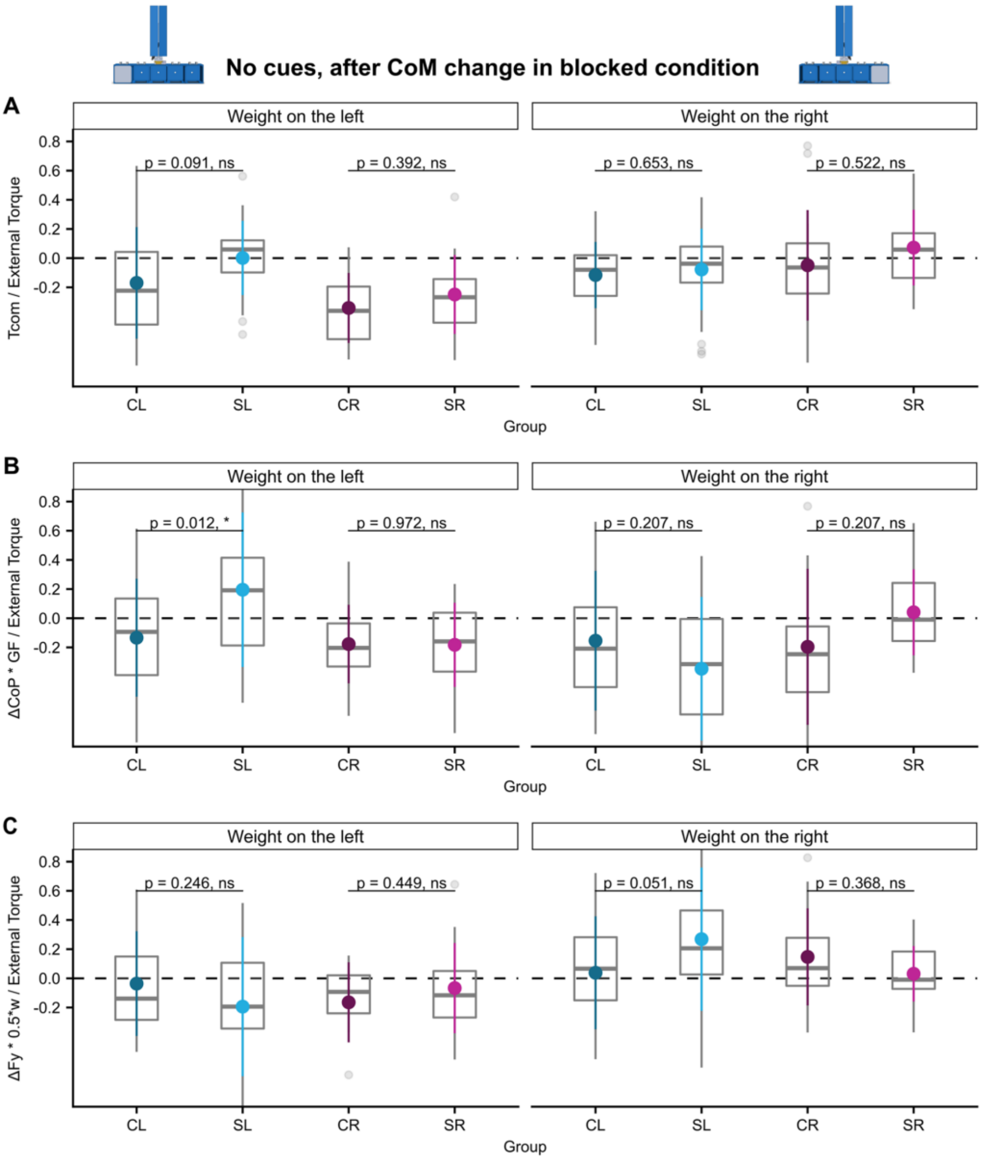

Figure 3. Transfer of sensorimotor learning of anticipatory torque compensation to explicit CoM changes. (**A**) Tcom/external torque, (**B**) ΔCoP * GF/External Torque, and (**C**) ΔFy * 0.5*w/External Torque of the first trial of a block after the CoM has changed in the 'no cues, blocked' condition (first trial of first block excluded) of all groups.

Supplementary Fig. S4 depicts the Tcom trajectories of all participants in the geometric-cue conditions. Tcom was mostly generated by GF being produced at different vertical centers of pressure and only to a lesser degree by differential load force sharing. We found no differences of Tcom success in post-hoc comparisons between

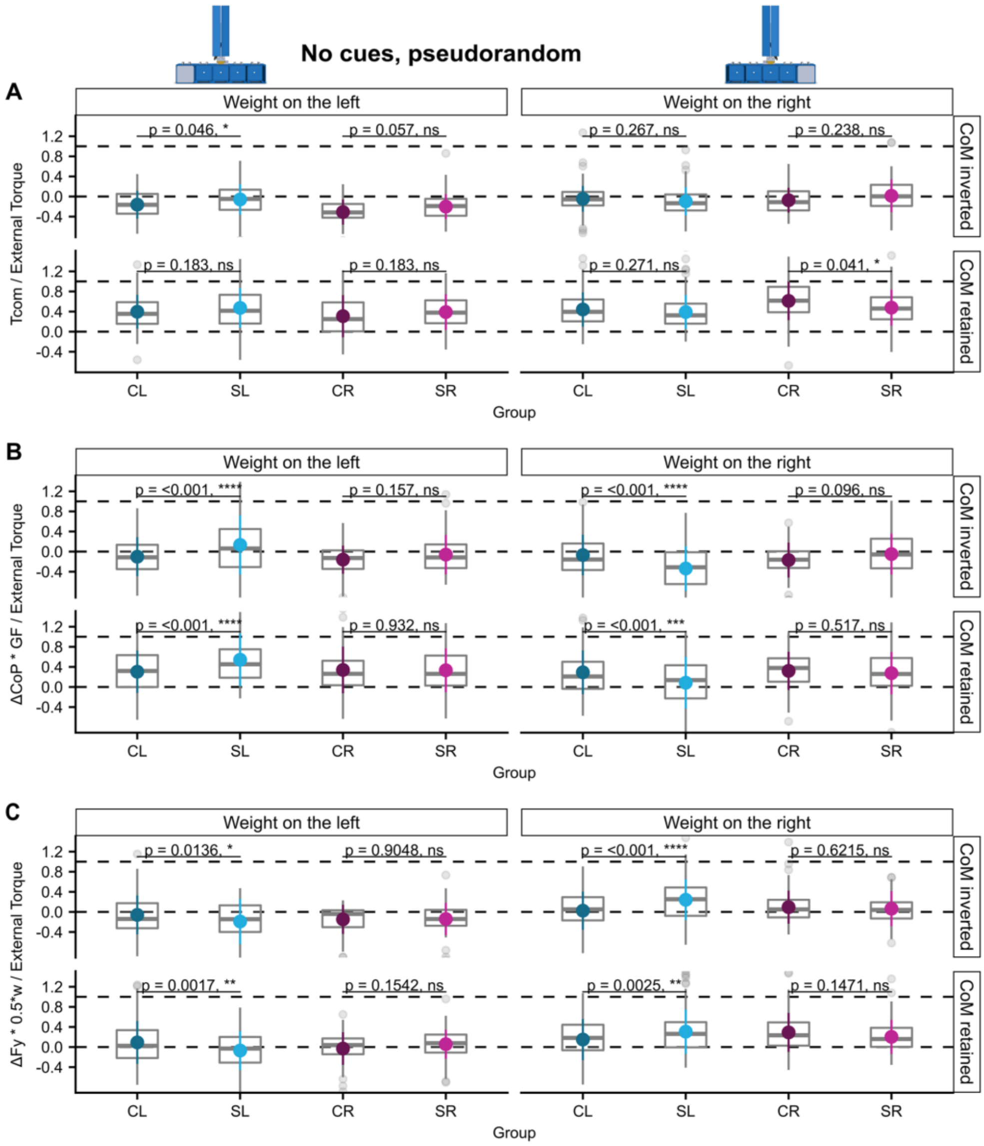

Figure 4. Sensorimotor torque control in uncertainty. (**A**) Tcom/external torque, (**B**) ΔCoP * GF/External Torque, and (**C**) ΔFy * 0.5*w/External Torque of all groups averaged for trials in which the CoM has changed and trials in which it remained constant for both possible CoMs in the 'no cues, pseudorandom' condition.

the stroke and control groups in neither the blocked- nor the pseudorandom condition despite significant 'ext. torque × group' interactions (see Figs. 5, 6, 7 and Supplementary Tables S20–36). This lack of group differences was also observed when analyzing the torque components, with the exception of the finding of less successful torque generation by $\frac{\Delta CoP * GF}{\text{External Torque}}$ in the SL group than the CL group in the first trials in the blocked condition following a change of the handle to the left, i.e. the CoM to the right side (post-hoc comparison SL-CL: estimate = −0.23, ηp2 = 0.07, t (96) = −2.60, *p* = 0.021, see Fig. 6B and Supplementary Table S29).

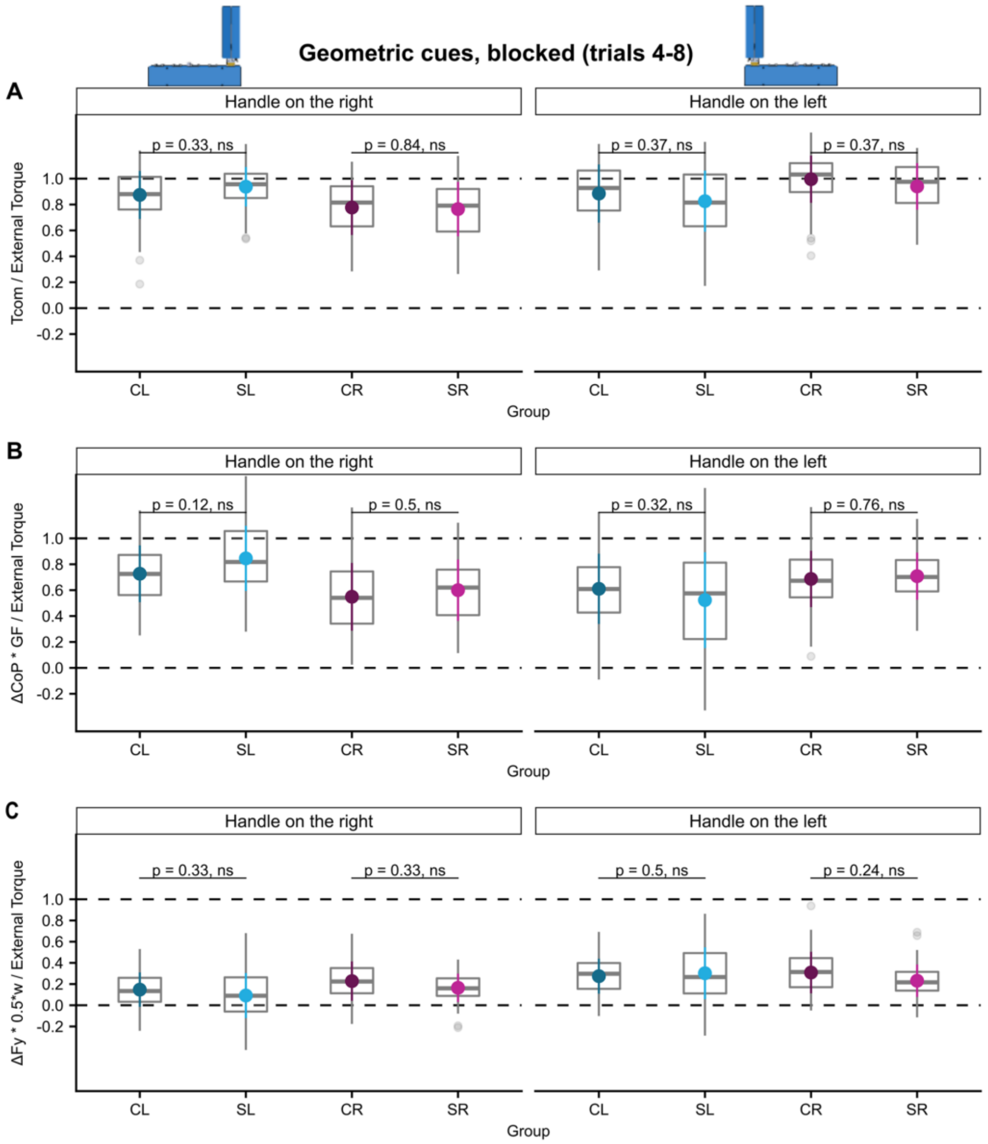

Figure 5. Learning of anticipatory torque compensation according to both geometric cues and sensorimotor memories. (**A**) Tcom/external torque, (**B**) ΔCoP * GF/External Torque, and (**C**) ΔFy * 0.5*w/External Torque for trials 4–8 of blocks in the 'geometric cues' condition of all groups.

ΔCoP and GF at lift-off. The total compensatory torque and its components at lift-off were the task-level variables participants had to control to prevent object tilt. While the load force sharing between grasp-sides, ΔFy, is directly proportional to the resulting torque component as the grip width is constant, both the center of pressures and the GF must be actively controlled to achieve the desired torque product ΔCoP*GF. Therefore, we were interested to evaluate whether the found spatial biases of the torque produced by vertical center of pressure modulation, ΔCoP*GF, can be traced back to distinct alterations in the control of either ΔCoP, GF or both at

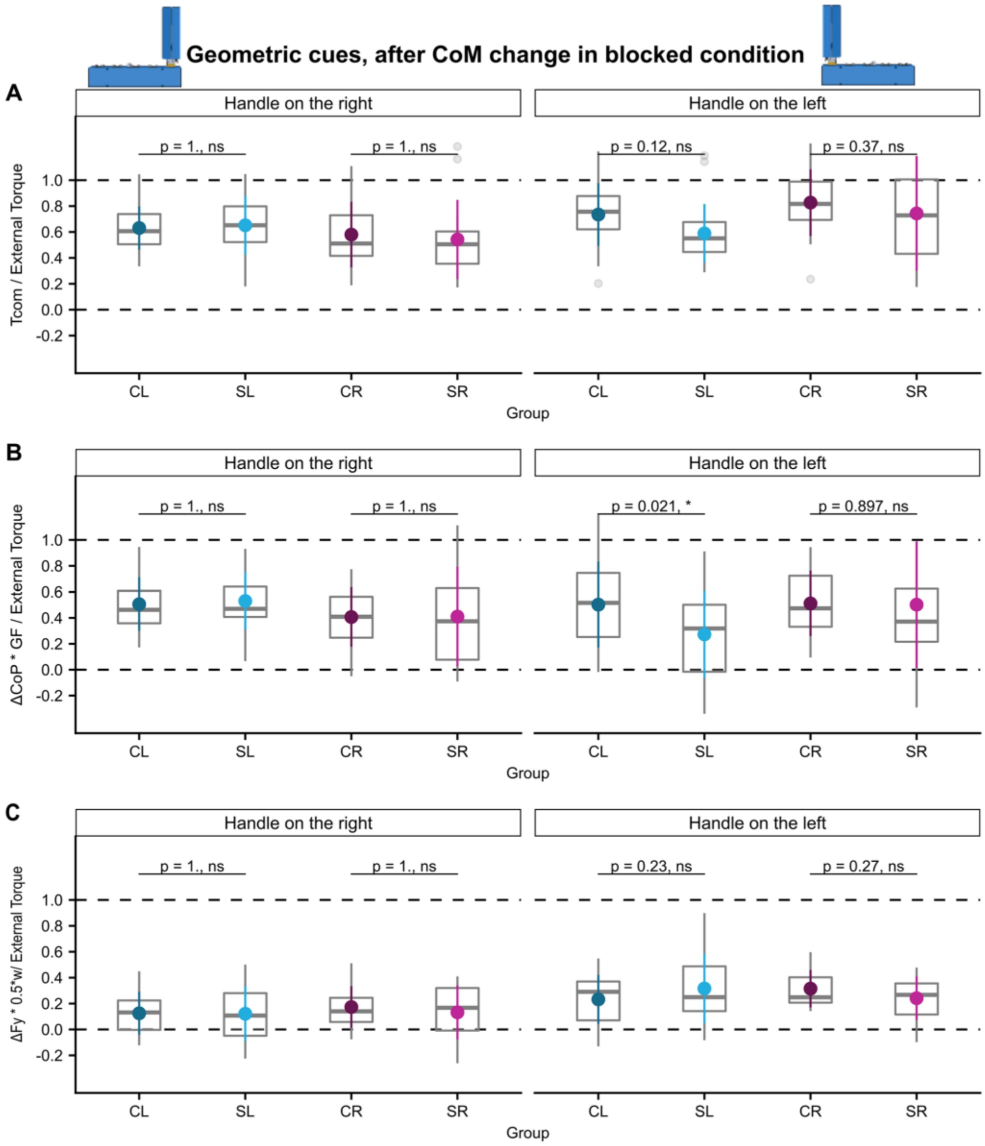

Figure 6. Interaction of visuomotor transformations and the transfer of sensorimotor learning of anticipatory torque compensation after CoM change in the blocked condition. (**A**) Tcom/external torque, (**B**) ΔCoP * GF/External Torque, and (**C**) ΔFy * 0.5*w/External Torque of the first trial of a block after the CoM has changed in the 'geometric cues' condition (first trial of first block excluded) of all groups.

lift-off. Regarding ΔCoP, we found a non-significant trend toward a better modulation in the SL than the CL group when the weight CoM was on the left side (post-hoc comparison SL-CL: t (46.0) = −2.1, $p = 0.083$, see Supplementary Tables 39) and a significantly worse modulation when the CoM was on the right side (post-hoc comparison SL-CL: estimate = −0.004 m, ηp2 = 0.11, t (46) = −2.38, $p = 0.043$, see Fig. 8A). These findings are

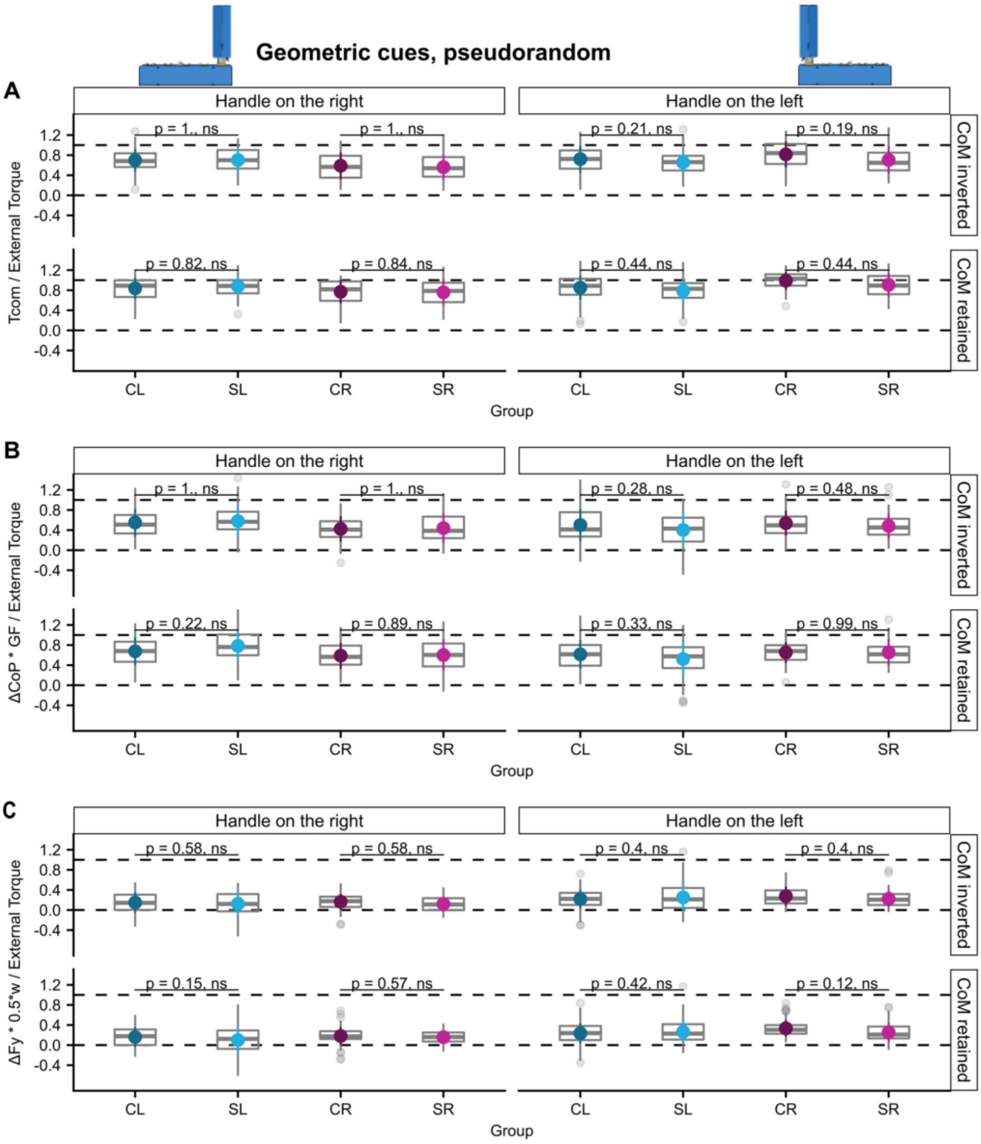

Figure 7. Interaction of visuomotor transformations and the transfer of sensorimotor learning of anticipatory torque compensation after CoM change in the pseudorandom condition. (**A**) Tcom/external torque, (**B**) ΔCoP * GF/External Torque, and (**C**) ΔFy * 0.5*w/External Torque of all groups averaged for trials in which the CoM has changed and trials in which it remained constant for both possible CoMs in the 'geometric cues, pseudorandom' condition.

consistent with the reported results for ΔCoP*GF, although less robust. Apart from that, there were no other significant differences between groups in post-hoc testing (see Fig. 8 and Supplementary Tables 37–44). Concerning GF, we did not detect any significant differences between stroke and control groups in post-hoc testing (see Fig. 9 and Supplementary Tables 45–52).

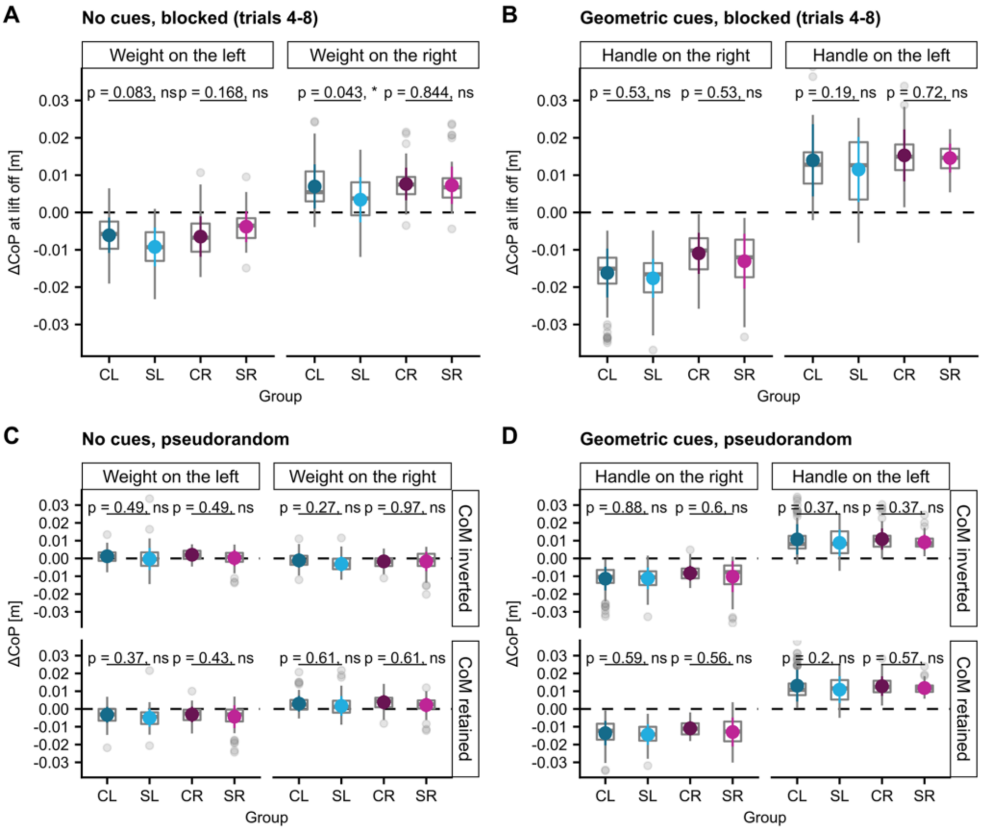

Figure 8. ΔCoP at lift-off. (**A**) the blocked, no-cues condition (trials 4–8), (**B**) the blocked, visual-cues condition (trials 4–8), (**C**) the pseudorandom, no-cues condition and (**D**) the pseudorandom, visual-cues condition.

Post-hoc power analysis. We decided on our sample size pragmatically. The final sample size was determined by the maximum number of patients with stroke we could feasibly recruit and test given financial and time constraints. We performed a post-hoc sensitivity power analysis for the main outcome measures $\frac{\text{Tcom}}{\text{External Torque}}$,$\frac{\Delta\text{Fy}*\text{w}/2}{\text{External Torque}}$ and $\frac{\Delta\text{CoP}*\text{GF}}{\text{External Torque}}$ in the no cues, blocked condition. The outcome variables were repeatedly centered for each group (separately for both external torques) to yield group differences between the stroke and control groups between 0.05 and 0.5 in steps of 0.05. The final sample size meant that the study was able to reliably detect a post-hoc estimated marginal means group difference in $\frac{\text{Tcom}}{\text{External Torque}}$ and $\frac{\Delta\text{Fy}*\text{w}/2}{\text{External Torque}}$ of 0.2 and a difference of 0.3 in $\frac{\Delta\text{CoP}*\text{GF}}{\text{External Torque}}$ between the 'CL' and 'SL' groups as well as differences of 0.25 $\left(\frac{\text{Tcom}}{\text{External Torque}}\text{and }\frac{\Delta\text{Fy}*\text{w}/2}{\text{External Torque}}\right)$ and 0.35 $\left(\frac{\Delta\text{CoP}*\text{GF}}{\text{External Torque}}\right)$ between the 'CR' and 'SR' groups with an alpha of 0.025, and > 80% power (see Supplementary Fig. S5 for details).

Discussion

This study was set out to investigate whether manual torque control with the ipsilesional hand is impaired in patients in the chronic stage following unilateral stroke when lifting objects. Using a cross-over design with two cue- and two-sequence conditions, we studied both a cue-condition in which learning had to rely on previous sensorimotor memories of recent lifts as well as a visual cue condition in which the object CoM could be inferred from object geometry. Moreover, participants performed trials both in blocked, i.e. predictable, sequence-condition as well as a pseudorandom sequence condition in which the CoM could change after each trial in an unforeseeable manner. Both our main hypotheses that (a) ΔCoP modulation was impaired in the SR group and (b) deficient load force sharing (ΔFy) in the SL group would lead to impaired torque compensation

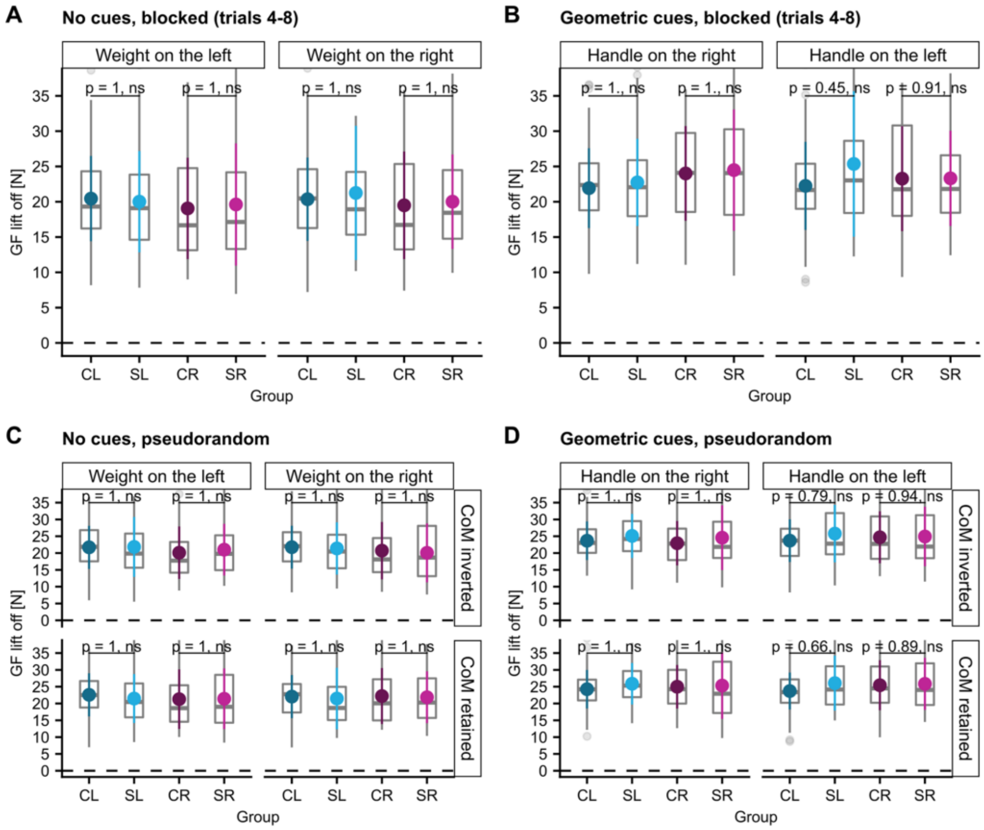

Figure 9. GF at lift-off was similar between stroke and control groups in all experimental conditions. (**A**) the blocked, no-cues condition (trials 4–8), (**B**) the blocked, visual-cues condition (trials 4–8), (**C**) the pseudorandom, no-cues condition and (**D**) the pseudorandom, visual-cues condition.

at lift-off, were not confirmed. Instead, both stroke groups learned to compensate torques at lift-off to overall similar degrees as controls in both cue conditions and patients presented neither general deficits of force-to finger position coordination, nor elevated GF levels, on a group level.

Instead, we observed a specific pattern of an object-centered spatial bias of torque components in patients with stroke when having to rely on sensorimotor memories. While torques resulting from force being produced at different vertical finger positions, $\Delta CoP \times GF$, were lower when the object CoM was on the contralesional side and higher when the CoM was on the ipsilesional side in patients with left hemispheric stroke, torques generated by differential load forces between sides ($\Delta Fy \times w/2$) were biased in the opposite direction. These biases largely cancelled each other out. SR patients also applied a distinctly smaller $\Delta CoP \times GF$ for a CoM on the contralesional, left side but showed neither a clear compensation by $\Delta Fy \times w/2$ nor an increase in $\Delta CoP \times GF$ for a CoM on the ipsilesional side. Torque control was intact in both stroke groups when a geometric cue on the weight distribution was available.

We summarize and discuss our findings in the following sections.

Preserved sensorimotor force-to position coordination despite a spatial bias of $\Delta CoP \times GF$ following stroke. In line with studies of young and elderly healthy adults[52,62,78], participants in all groups quickly learned to exert an adequate Tcom when the CoM was constant across the trials of a block. At the beginning of a new block they failed to transfer the learned torque planning to the new situation even when they were explicitly told that the CoM would be inverted. They also continued to rely on sensorimotor memories of previous lifts when the CoM could change from trial to trial[53,54]. Intriguingly, the magnitude of torques directed in the wrong direction when the CoM had unexpectedly changed from one side to the other was smaller than the torque exerted in the right direction when the CoM had stayed the same. This suggests that participants in all groups applied corrective feedback-mechanism to partially correct for erroneous torque anticipation within the short time interval prior to lift-off, although full feedback about object torque only becomes available after lift-off. This finding is consistent with our previous studies in healthy subjects[53,57] and the time course and underlying mechanism of these corrections need to be further explored in future analyses. There were no noteworthy differences of Tcom between the stroke and the control groups, despite the emergence of a distinct pattern of differences between the torque components.

The most remarkable finding of this study is that the torque resulting from grip force being produced at different vertical centers of pressure, $\Delta CoP \times GF$, and from differential load force sharing between sides, $\Delta Fy \times w/2$, were spatially biased in diametrical directions in patients with left hemispheric-stroke when participants had to exclusively rely on sensorimotor memories to guide torque control: Patients with left hemispheric stroke applied a smaller $\Delta CoP \times GF$ at lift off than controls when the CoM was on the contralesional side but a higher $\Delta CoP \times GF$ when the CoM was on the ipsilesional, i.e. left, side. In contrast, the torque resulting from differential load forces at the handle sides ($\Delta Fy \times w/2$) was spatially biased in the opposite direction in SL-patients, i.e. $\Delta Fy \times w/2$ was higher for a CoM on the right- and lower for a CoM on the left side. As a consequence, the overall Tcom did not significantly differ between left hemispheric stroke patients and controls on the group level.

Patients with right hemispheric stroke also exhibited a markedly smaller torque resulting from grip force being produced at different vertical finger positions, $\Delta CoP \times GF$, but showed no signs of a compensatory load force distribution ($\Delta Fy \times w/2$). However, this only translated to a not significant trend towards a lower Tcom. This was not significant after Holm correction as the variability was high and the sample size low. No significant differences or even visually discernible trends were found for Tcom or the torque components when the covert weight was on the ipsilesional right side.

As the center of pressure in the employed three-finger precision grip mostly depended upon the finger positioning when grasping the handle and to a lesser degree on the normal force distribution between the index and middle finger[79], the torque component $\Delta CoP \times GF$ arguably better represents explicit context-dependent motor planning in unconstrained grasping; whereas the load force distribution contributing to the total torque ($\Delta Fy \times w/2$) is modulated as a function of finger-positioning after the formation of the grasp to achieve a targeted total torque[50,58,86–88]. Consequently, the observed spatial bias of load force sharing in left hemispheric stroke patients might represent a compensatory mechanism to counteract the spatial bias of grip force exerted at different vertical positions. This supports the concept of a task-level, i.e. high-level, neural representation of the task goal, namely the compensatory total torque, which is used to orchestrate both the feedforward as well as feedback control of the positions and forces of the low-level effectors, e.g. fingertips[49,54,89].

However, the same pattern of spatial bias was evident in patients with left hemispheric stroke in the pseudorandom, no cues-condition with more successful $\Delta CoP \times GF$ for a CoM on the left and a less successful $\Delta CoP \times GF$ for a CoM on the right as well as opposing findings for the torque component $\Delta Fy \times w/2$, both for trials in which the CoM was inverted and trials in which the CoM was retained. This might suggest that the object-centered spatial torque bias depended upon the current side of the CoM but not the CoM of the previous trial on which sensorimotor memories for torque planning are based on. This could cast doubt on whether the torque component $\Delta CoP \times GF$ can really be regarded as measure of exclusively anticipatory planning. Instead, it might also be possible that the bias observed in the pseudorandom condition affected the corrections of the torque components $\Delta CoP \times GF$ and $\Delta Fy \times w/2$ just prior to lift-off according to sensory feedback. However, the results of the models fit to analyze the pseudorandom condition were complex, the standard errors high and the standardized effect sizes of significant group comparisons low. Consequently, one must be cautious in interpreting theses significant findings. In any case, it might be advisable to speak of a bias of torque control instead of torque anticipation, which implies exclusive feedforward control.

Irrespective of the relative contribution of feedforward- and feedback-mechanisms on torque generation at lift off, the opposingly directed object-centered spatial bias for $\Delta CoP \times GF$ and $\Delta Fy \times w/2$ in left hemispheric stroke patients and the isolated bias for $\Delta CoP \times GF$ in right hemispheric stroke patients corroborates the notion that different neural networks control these task level variables. This notion has previously been based on behavioral studies which could show that finger positioning represents context dependent, explicit, learning, whereas load force distribution is more influenced by effector- and use-dependent, implicit, learning processes[52,90].

Visuomotor processing of geometric cues for torque control is intact in chronic stroke patients. When the mass distribution could be inferred from the geometric shape of the object (L-Shape) all participant groups successfully compensated for torques arising at lift off mainly by adequately modulating the centers of pressure on both grip sides ($\Delta CoP \times GF$) both when learning successful manipulation over a course trials with constant object properties but also when object geometry and weight distribution changed randomly. Given a geometric cue, torques by load force partitioning ($\Delta Fy \times w/2$) only contributed a small part of the total Tcom. Changing the object geometry after a sequence of 8 trials led to an interference of sensorimotor memories of previous lifts on lift planning resulting in a slightly smaller Tcom. The found successful processing of geometric cues to guide torques and the sensorimotor inference on geometric processing confirm previous studies examining young- and elderly healthy subjects[56,57,79].

The compensatory torque and torque components did not differ in the stroke groups suggesting intact visuomotor processing of object shape to infer mass distribution. This stands in line with previous studies which showed that grip force scaling according to object size was not affected by unilateral MCI stroke on a group level[63,64,91]. Most notably, we found no evidence of a spatial bias of the torque components $\Delta CoP \times GF$ or $\Delta Fy \times w/2$ in the stroke groups suggesting that these biases following stroke are specific to sensorimotor control and can be corrected by visual control.

Evidence for an allocentric premotor neglect? The finding of an object-centric spatial bias of the sensorimotor torque control with a higher than normal $\Delta CoP \times GF$ for a CoM on the ipsilesional side (only SL group) and a lower $\Delta CoP \times GF$ for a CoM on the contralesional side (both stroke groups) could be taken as evidence for a shift of spatial attention towards eccentric loads on the ipsilesional side and away from loads on the contralesional side following unilateral stroke. This may represent a novel subtype of allocentric premotor attention bias, i.e. neglect. Concerning the association between neglect and motor control, the phenomenon of premotor neglect (PMN), i.e. an intentional, voluntary, and directional motor disorder of movements in or to the contralesional space which equally affects the limbs on both sides following stroke[92]. Patients show an abnormal movement initiation (hypo- or akinesia) as well as slowed (bradykinesia) and hypometric reaching movements towards goals in their contralesional hemispace even when tested with their ipsilesional hand[93–96]. Moreover, they deviate towards the ipsilateral side when pointing straight ahead when blindfolded which is suggestive of a shift in the egocentric reference frame[97,98]. It is important to note, however, that participants in our study were allowed to adjust the exact position and orientation of the object on the table in a way that allowed for comfortable grasping. Usually, the object was positioned in the hemispace of the involved, ipsilesional hand. Therefore, in contrast to previous studies on premotor neglect the reference frame of torque control in the current study was rather object- or hand specific, i.e. allocentric, than egocentric. To the best of our knowledge, a signs of premotor-allocentric neglect have not yet been reported for an everyday object manipulation task.

As the found bias concerns the control of object tilts due to a directed allocentric eccentric load, studies investigating the perception of the subjective vertical and -horizontal might also be relevant to the interpretation of our findings. These studies revealed that patients with left-sided as well as right-sided neglect systematically tilted the spatial orientation of the subjective vertical- and horizontal in the direction of the neglected, contraversive, side both in a visual and tactile modality- suggesting multisensory spatial orientation deficits in neglect patients[99–102]. Applied to our studied task, a shift of the targeted subjective vertical of the object handle towards the contralesional side might have led to the tendency of an under compensation of torques towards the contraversive side and to an over compensation of torques towards the ipsiversive side, as a small tilt to the contralesional side might have been perceived as ideal. However, we found this only to be true for the anticipatory torque component $\Delta CoP \times GF$, but not for the torque resulting from asymmetric load force sharing ($\Delta Fy \times w/2$). Moreover, we only found evidence for a bidirectional spatial bias in patients with left hemispheric stroke while patients with right hemispheric stroke only showed a decreased $\Delta CoP \times GF$ for a CoM on the contralesional side but no $\Delta CoP \times GF$ elevation when the CoM was on the ipsilesional side.

None of the chronic stroke patients exhibited clear signs of perceptual hemispatial neglect in the conducted pen-and-paper based tests. As we did not expect to find an object centered bias of torque control we unfortunately did not test for the presence of an allocentric neglect. Nevertheless, our finding could be viewed a subtle form of an object centered premotor attention bias regarding torques. However, this inattention might not be of relevance in daily living in the majority of stroke patients as both intact load-force coordination and visuomotor processing of object geometry can compensate for the bias.

Future research directions. Future clinical-experimental studies should aim to further investigate the association between perceptual and motor manifestations of neglect and torque control in object manipulation following stroke. The motor manifestations of neglect comprise both premotor- and motor neglect, the latter being defined as an underuse of the contralesional side of the body in the absence of—or out of proportion to—weakness or sensory impairments[92,103,104]. To this end, larger cohorts of stroke patients with unilateral cortical lesions seen on MRI-imaging in the acute stage of stroke should be included as the prevalence of motor neglect is estimated to range between 12 and 33% of patients with acute stroke and some 8% of patients with chronic stroke[105,106]. The prevalence of premotor neglect remains unclear as clinical tests of premotor neglect [e.g. Milner- or Bisiach- landmark tests[107]] might not be reliable[108]. Patients should be assessed for sensorimotor impairments, both egocentric- and allocentric visual neglect, personal neglect, the subjective vertical as motor- and premotor neglect. An ideal protocol to improve the understanding of torque control impairments in object manipulation following stroke should use a crossed-design investigating both hands (influence of sensorimotor impairments and/or motor neglect), object positions in both hemispaces (egocentric premotor neglect), object weight distributions on both sides (allocentric premotor neglect) as well as both a sensorimotor and geometric-visual cue condition ($2 \times 2 \times 2 \times 2$ design). Voxel-based lesions symptom mapping analyses will help to uncover the neural correlates of the studied aspects of torque control.

Study limitations. Finally, a number of limitations of this study must be considered. The main limitation is that the studied stroke groups were small and heterogenous regarding stroke type, localization, the time from stroke onset and the stroke related functional impairments. As only chronic stroke patients referred by outpatient therapists participated in this study we could only obtain the medical reports but failed to collect the CT or MRI imaging studies. Therefore, we cannot make claims on the role of specific neuroanatomical regions or networks in the studied tasks. Since our study is confined to highly chronic stroke patients, we cannot exclude that the pattern of torque control deficits differs in earlier phases of stroke. Moreover, we did not perform a comprehensive neurological exam. Since only few of the chronic stroke patients of the sample revealed clear signs of apraxia or neglect we could not analyze the impact of these syndromes on torque control. As we did not expect to find the object centered spatial bias of torque control a priori, we did not perform tests of allocentric neglect. Finally, it must be noted that we conducted numerous statistical tests of the primary and secondary variables of interest and experimental conditions rendering the analyses exploratory.

The current study is a pilot study which received no targeted funding and was conducted without a clinical partner. Therefore, the tested sample of patients with stroke was small and heterogenous. A post-hoc power analysis revealed that although the study seems to be appropriately powered to detect large group differences with sufficient power (in the no cues, blocked condition), it must be assumed that the study is underpowered to detect small and moderate effects.

However, despite the small samples size, patient heterogeneity and an exploratory statistical analysis plan a clear pattern of highly significant results emerged which reveal a novel aspect of impaired motor control of the ipsilesional hand following stroke and will guide the design of future studies on object manipulation following stroke.

Conclusions

In summary, we found that patients with left-hemispheric stroke show a spatial bias of the torque resulting from grip force being applied at different vertical finger position depending on the object mass distribution when relying on sensorimotor memories with the torque component being increased for a CoM on the ipsilesional but decreased for a CoM on the contralesional side. This bias was compensated for by a load-force sharing biased in the opposite direction as evidence of intact force-to-position coordination. While patients with right hemispheric stroke also exhibited lower torques due to grip force being applied at different vertical finger position for a CoM on the contralesional side, we found no evidence for an increase of this torque component for a CoM on the ipsilesional side or a compensatory bias of load force distributions. When salient, congruent geometric cues were present, patient performance was not different from controls, suggesting that visuomotor processing ameliorates the noted sensorimotor bias. The sensorimotor object-centered spatial bias of torque strategies could be a subtle sign of a premotor attention bias, respectively a premotor attention bias as a subtype of neglect, which might be even present in the absence of a an evident hemispatial neglect. The found object centered spatial bias of torque controls should be further investigated in larger and more homogenous cohorts of stroke patients in the acute stage with a refined protocol designed to evaluate the association between premotor- and perceptual (allo- and egocentric) neglect and torque control.

Data availability

The data that support the findings of this study are openly available in "figshare" at https://doi.org/10.6084/m9.figshare.17057675 .

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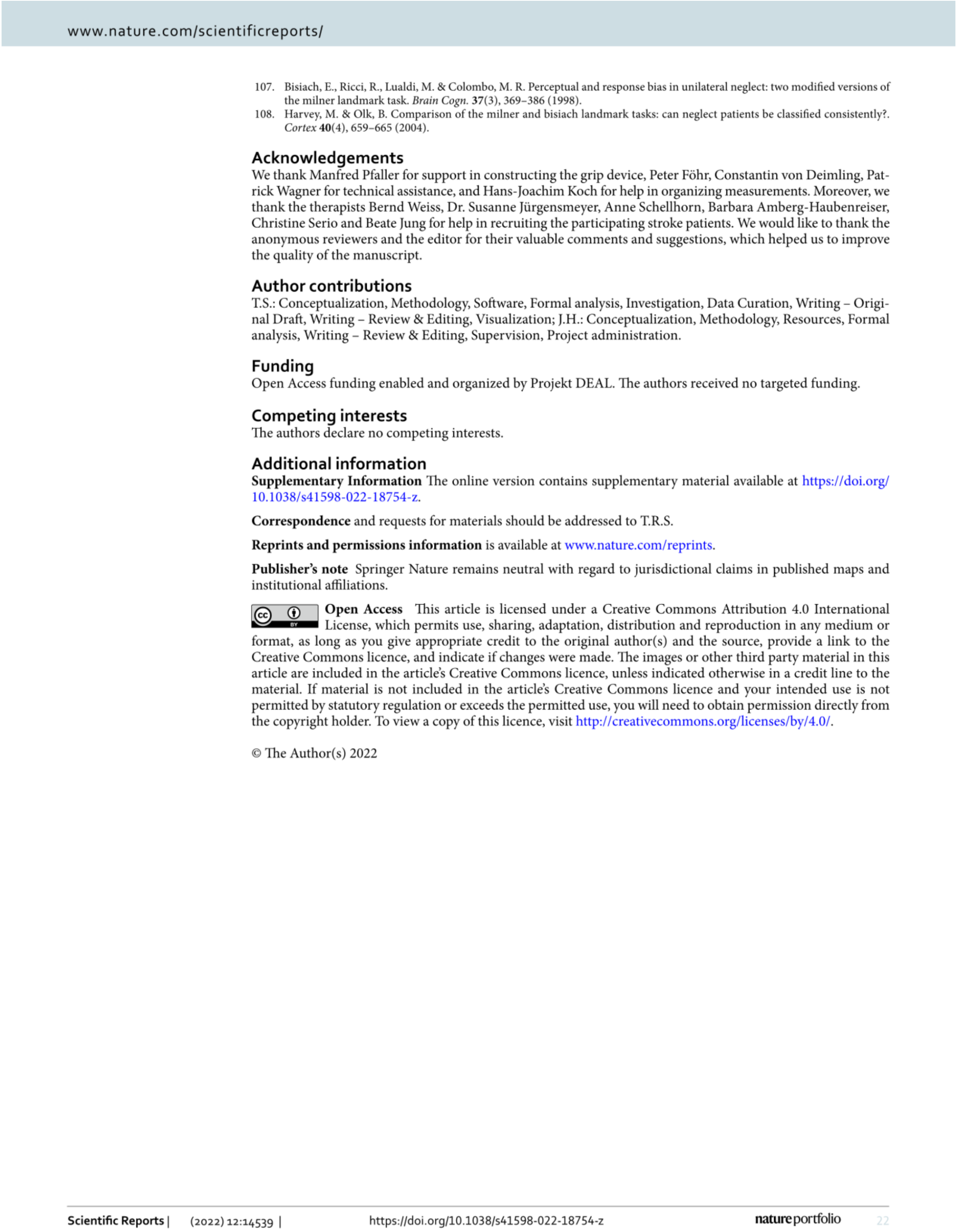

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