



Review article

Two hands, one brain, and aging



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ABSTRACT

Many activities of daily living require moving both hands in an organized manner in space and time. Therefore, understanding the impact of aging on bimanual coordination is essential for prolonging functional independence and well-being in older adults. Here we investigated the behavioral and neural determinants of bimanual coordination in aging. The studies surveyed in this review reveal that aging is associated with cortical hyper-activity (but also subcortical hypo-activity) during performance of bimanual tasks. In addition to changes in activation in local areas, the interaction between distributed brain areas also exhibits age-related effects, i.e., functional connectivity is increased in the resting brain as well as during task performance. The mechanisms and triggers underlying these functional activation and connectivity changes remain to be investigated. This requires further research investment into the detailed study of interactions between brain structure, function and connectivity. This will also provide the foundation for interventional research programs towards preservation of brain health and behavioral performance by maximizing neuroplasticity potential in older adults.

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Abbreviations: BOLD, blood-oxygen-level dependent; CC, corpus callosum; CRUNCH, compensation-related utilization of neural circuits; DLPFC, dorsolateral prefrontal cortex; DMN, default mode network; dMRI, diffusion magnetic resonance imaging; DTI, diffusion tensor imaging; EEG, electroencephalography; FC, functional connectivity; fMRI, functional magnetic resonance imaging; GTNA, graph theoretical network analyses; HARDI, high angular resolution diffusion imaging; M1, primary motor cortex; OA, older adults; PET, positron emission tomography; PMd, dorsal premotor cortex; S1, primary somatosensory cortex; SII, secondary somatosensory cortex; SMA, supplementary motor area; SPL, superior parietal lobule; SUCAS, age-related subcortico-cortical activation shift; TMS, transcranial magnetic stimulation; VL Nc, ventrolateral thalamic nucleus; VPL Nc, ventral posterolateral thalamic nucleus; YA, young adults.

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1. Introduction

Many tasks of daily life have a bimanual signature, such as dressing yourself, tying shoelaces, lifting and carrying objects, eating, or typing an email. However, despite their abundance in daily life, bimanual coordination skills have been studied much less intensively than unimanual skills. Equally, in the context of motor learning paradigms, most research has been done on adaptation and sequencing tasks, primarily performed by a single limb (King et al., 2013). However, as a subfield of study in movement control and neuroplasticity, bimanual coordination is generating increasing interest from various scientific disciplines, such as movement sciences, neurosciences, clinical neurology, and neurorehabilitation (Swinnen and Gooijers, 2015). This interest stems from the unique control principles found in bimanual tasks (Kelso et al., 1979; Swinnen, 2002) that cannot necessarily be inferred from the study of unimanual movement. Examples are the preference to activate the homologous muscle groups across both limbs simultaneously or to move in the same direction in extrinsic space with both limbs (Serrien et al., 1999; Swinnen et al., 1997a,b, 1998a, 2001). Because of this underuse of bimanual tasks, our understanding of the neural basis of bimanual coordination is still fragmentary and basic knowledge about the functional contribution of brain areas constituting the bimanual motor network is incomplete at best (Swinnen, 2002; Swinnen and Wenderoth, 2004). Here, we discuss this bimanual motor network and how it is affected by aging to pave the way for future research.

1.1. A useful clinical tool

Because many bimanual skills develop spontaneously during childhood, we consider them as easy and take them for granted. However, these skills hide a considerable behavioral complexity and depend on sophisticated neural architecture. This becomes critically apparent when incurring a temporary dysfunction of one arm after an injury or when confronted with chronic consequences of

stroke, leading to hemiparesis of one side of the body. As such, restoring or improving bimanual skill is a critical target for neurorehabilitation intervention (Lewis and Byblow, 2004; Reinkensmeyer et al., 2016; Stinear and Byblow, 2004; van Delden et al., 2012). Clinical tests such as the Purdue Pegboard Test (Desrosiers et al., 1995a; Tiffin and Asher, 1948) or the TEMPA test (Desrosiers et al., 1995b) are used to assess bimanual coordination. Moreover, clinical test batteries such as the Katz Index of Independence in Activities of Daily Living (Katz et al., 1970) or the Unified Parkinson's Disease Rating Scale (UPDRS; Movement disorder society task force on rating scales for Parkinson's disease, 2003) often include bimanual tasks to measure performance capabilities. Sometimes bimanual skills can even become critical tools to characterize prominent clinical expressions of disease. For example, research on Parkinson's disease has demonstrated that freezing episodes can be triggered during performance of simple bimanual cyclical tasks (Nieuwboer et al., 2009; Vercruyse et al., 2014). This temporary disruption of movement is a kinematic and neural signature of Parkinson's disease that is very similar in the upper and lower limbs (i.e., freezing of gait). Such endeavors open up avenues for investigating the neural underpinnings of upper limb freezing episodes in these patients, using medical imaging techniques in constrained environments that are less optimal for the study of lower limb movements (Vercruyse et al., 2014). More generally, bimanual skills constitute a critical marker of functional independence across the lifespan and in patients recovering from neural insults.

1.2. A tool with potential benefits for the promotion of healthy aging

As bimanual coordination is a meaningful tool to diagnose, assess, and rehabilitate patients, a research effort towards improving our basic understanding of the neural control of bimanual coordination across the lifespan should be encouraged. Bimanual coordination is particularly critical in the older population, because moving both hands in an organized way in both space

Table 1
Behavioral studies.

Study	n YA/OA/OO	Age YA/OA/OO mean(range)	MMSE/MoCA score(mean)	Handedness	Task	Joints	Conditions	Dependent Variables	Training
Weller and Latimer-Sayer (1985)	119	16–87	na	R	Pegboard test	Shoulders + elbows + wrists	Right/Left/Both hands Block/alternating trials	Time Number of pegs moved	no
Stelmach et al. (1988)	10/10	22(21–25) /70(67–75)	na	All Rbut 1 YA	Choice reaction time	Shoulders + elbows + wrists	Symmetric/ Asymmetric	Mvt initiation time Mvt time	no
Ferron (1992)	16/16/16	24(20–42) /70(65–74) /79(75–86)	na	R	Finger tapping	Index fingers	Right hand/Left hand/Right-leads/Left-leads	Tapping rate Accuracy ratio	no
Spirduso and Choi (1993)	13/18	21 ± 2(18–23) /70 ± 6(61–81)	na	na	Force coordination	fingers	Index fin- gers/Thums/Left index-Right thumb Day 1/2/3 Press right and left/press right + release left/release right + press left	Time Error	yes
Moes et al. (1995)	21/32	22(19–29) /70(60–85)	na	R	Multi-frequency tracking	fingers	Left hand (0°)/Right hand (180°)/clockwise 1:1-1:2-2:1 ratios (45–22.5–67.5°)/inward 1:1-1:2-2:1 ratios (135–112.5–157.5°) Visual/no visual feedback	Time Error Reversals	no
Greene and Williams (1996)	10/10/10	(23–32) /(60–68)/(70–78)	na	R	Cyclical movements	Wrists	Unimanual/Bimanual In-phase/Anti-phase Preferred/Max freq 80/100/120% of max freq Switching AP to IP/IP to AP 80/100/120% of critical freq	Frequency Amplitude Relative phase Critical freq Switching response time	no
Krampe and Ericsson (1996) – Study 1	12/12	25 ± 3(20–31) /60 ± 4(52–68)	na	na	Speeded coordination	Fingers	Mirror/Different movements	Intetap interval Error rate	no
					Finger tapping	Index fingers	Right hand/Left hand/Anti-phase	Intertap interval	no
Krampe and Ericsson (1996) – Study 2	14/14	24 ± 3(19–30) /71 ± 7(60–81)	na	All Rbut 1 OA	Finger tapping	Index fingers	Right hand/Left hand/Anti-phase	Interrtap interval	no

Table 1 (Continued)

Study	n YA/OA/OO	Age YA/OA/OO mean(range)	MMSE/MoCA score(mean)	Handedness	Task	Joints	Conditions	Dependent Variables	Training
Serrien et al. (1996)	7/7	(21–30) /(66–77)	na	na	Cyclical movements	Wrists	In-phase/Anti- phase (1 Hz) Vision/No vision Vibration/No vibration	Relative phase Cycle duration Peak to peak amplitude Velocity	no
Shammi et al. (1998)	18/18	(20–35) /(60–75)	na	R	Finger tapping	Index fingers	Externally (0.5 Hz)/self- paced Right hand/anti- phase	Intertap interval	no
Swinnen et al. (1998a)	9/9	19 ± 1/73 ± 5	29	na	Cyclical movements	Wrists	In-phase/Anti- phase/90° phase offset Vision/No vision/augmented concurrent feedback	Relative phase Cycle duration Peak to peak amplitude	yes
Serrien et al. (2000)	8/8	24/75	na	R	Cyclical movements	Elbows	In-phase/Anti- phase	Relative phase Cycle duration Peak to peak amplitude	no
Wishart et al. (2000) – exp1	10/20	23(16–25) /72(65–83)	≥23	na	Cyclical movements	Shoulders	In-phase/Anti- phase Preferred speed/0.5/1/1.5/2 Hz	Relative phase Mvt frequency	no
Wishart et al. (2000) – exp2	16/16	19(19–23) /71(66–75)	≥23	na	Cyclical movements	Shoulders	In-phase/Anti- phase 1/1.5/2/2.5 Hz Stay/do-not- intervene	Relative phase Mvt frequency	no
Lee et al. (2002)	12/12	22(20–22) /70(65–74)	≥27 (29)	na	Cyclical movements	Shoulders	In-phase/anti- phase 1/2 Hz Single/Dual task (additions)	Relative phase Mvt frequency	no
Wishart et al. (2002) – pilote	12/11	22(20–24) /73(64–81)	na	na	Cyclical movements	Shoulders	90° phase offset Terminal augmented visual feedback	Mean error	yes

Table 1 (Continued)

Study	n YA/OA/OO	Age YA/OA/OO mean(range)	MMSE/MoCA score(mean)	Handedness	Task	Joints	Conditions	Dependent Variables	Training
Wishart et al. (2002) – exp.	18/18	21(19–23)/66(65–70)	≥26 (29)	na	Cyclical movements	Shoulders	90° phase offset Day 1/2/3 Concurrent + terminal/ terminal augmented visual feedback	Relative phase Mvt frequency	yes
Sparrow et al. (2005)	8/8	23 ± 6/73 ± 4	na	na	Cyclical movements	Shoulders + elbows + wrists	Anti-phase/90° phase offset Dual task (reaction time) Scarfs/Balls	Relative phase Heart rate O2 consumption	yes
Voelcker-Rehage and Willimczik (2006)	9/7	5–89	na	na	Juggling	Upper limbs		Number of thrown and caught scarfs and balls	yes
Perrot and Bertsch (2007)	31/33	24 ± 3/67 ± 4	na	na	Juggling	Upper limbs	Balls	Number of thrown and caught balls	yes
Bangert et al. (2010)	17/17	20 ± 1/72 ± 4	≥27(29 ± 1)	R	Continuous circle drawing	Wrists + fingers	Symmetric/ Asymmetric Self-determined/ maximum freq Right hand/Left hand/In-phase/Right-leads-left/Left-leads-right Intertap interval: 800/1000/1200 ms	Between-hand lag	no
					Finger tapping			Tapping rate	no
Summers et al. (2010)	12/12	21(18–30)/64(60–75)	na	R	Continuous and Intermittent circle drawing	Shoulders + elbows + wrists	Symmetric/ Asymmetric Self-determined freq /50% faster In-phase/Anti-phase 0.5/1/1.5/2/2.5 Hz Do-not-intervene	Relative tangent angle Duration variation Self-determined freq Pause duration	no
Temprado et al. (2010)	13/15	26 ± 3/71 ± 5	na	na	Cyclical movements	elbow		Frequency Amplitude Relative phase Number of phase transitions Time to transition SD of relative phase in pre-transition period	no
Ringenbach et al. (2011)	15/15	26 ± 5 /69 ± 8	>24	R	Continuous drawing	Shoulders + elbows + wrists	Right/Left/In-phase/Anti-phase (Left vs. Right hand moving to cues) Visual/Auditory/Verbal cues	Cycle time Amplitude Relative phase	no

Table 1 (Continued)

Study	n YA/OA/OO	Age YA/OA/OO mean(range)	MMSE/MoCA score(mean)	Handedness	Task	Joints	Conditions	Dependent Variables	Training
Sommervoll et al. (2011)	30/31	23 ± 2(20–26) /72 ± 4(67–80)	>27(29)	R and L	Finger tapping	Fingers	Bimanual 1/2/3/4 Hz Anti-phase Single/dual task (color naming)/(word reading)	Intertap interval	no
Bernard and Seidler (2012)	33/23	21 ± 2/70 ± 4	≥26 (29 ± 2)	R and L	Pegboard test	Shoulders + elbows + wrists	Right/Left/ Bilateral/Assembly	Number of pegs /pairs /pieces assembled	no
Gorniak and Alberts (2013)	10/10	28 ± 5 /66 ± 8	na	R	Pinch grip	Shoulders + elbows + wrists + fingers	Connect/Disconnect /Rotation/Non- Rotation /Dynamic right hand/dynamic left hand	Task time, grip delay, load delay, grip force	no
Metzler et al. (2013)	12/18	23(19–28) /75(59–95)	na	R and L	Finger coordination	Fingers	Left hand/ Right hand/ Symmet- ric/Asymmetric	Speed errors	no
Boisgontier et al. (2014a)	35/31	22 ± 2/70 ± 6	≥26	R	Cyclical movements	Wrists	In-phase/Anti-phase No vision /Vision of Active Limb/Vision of Passive Limb Central vision /Peripheral Vision	Relative Phase Amplitude	no
Piedimonte et al. (2014)	20/20	25(20–30) /76(60–80)	na	R	Continuous drawing	Wrists + fingers	vertical line with both hands /right: vertical lines-left: circles	Ovalization index	no
Salimpour and Shadmehr (2014)	10/10	22 ± 3 /59 ± 8	na	R	Force production	Shoulders + elbows + wrists	Right arm/Left arm /Bimanual 16 targets	Force measures	no
Bhakuni and Mutha (2015)	15/12	23/64(>60)	ns	R	Serial reaction time task	Middle + index fingers	Sequence/ Random	Response time Switch cost	yes
Hoff et al. (2015)	26/26	26 ± 1 /61 ± 1	ns	R	Serial reaction time task	Middle + index fingers	Between hand switches /within hand switches	Response time Number of errors Switch cost Track deviation	yes
Pauwels et al. (2015)	48/48	20 ± 2 /67 ± 5	≥26	R	Multi- frequency tracking	Wrists + thumbs + index fingers	Clockwise/ Counterclockwise 1:1–2:3–1:2 frequency ratios		yes
Ren et al. (2015)	24/48	(20–29) /(61–79)	ns	ns	Cyclical movements	Wrists	In-phase/ Anti-phase/90° phase offset haptic/haptic + visual feedback	Proportion of the trial duration within an error bandwidth of the target phase	yes
Leinen et al. (2016)	14/14	(18–28) /(65–77)	Na	R	Cyclical movements	Wrists	Left hand moving 2× faster Load 0/0.5/1 kg	Frequency ratio Relative phase	no

freq = frequency, L = left, MMSE = Mini Mental State Examination, MoCA = Montreal Cognitive Assessment, mvt = movement, na = not available, OA = older adults, OO = older old adults, R = right, YA = young adults.

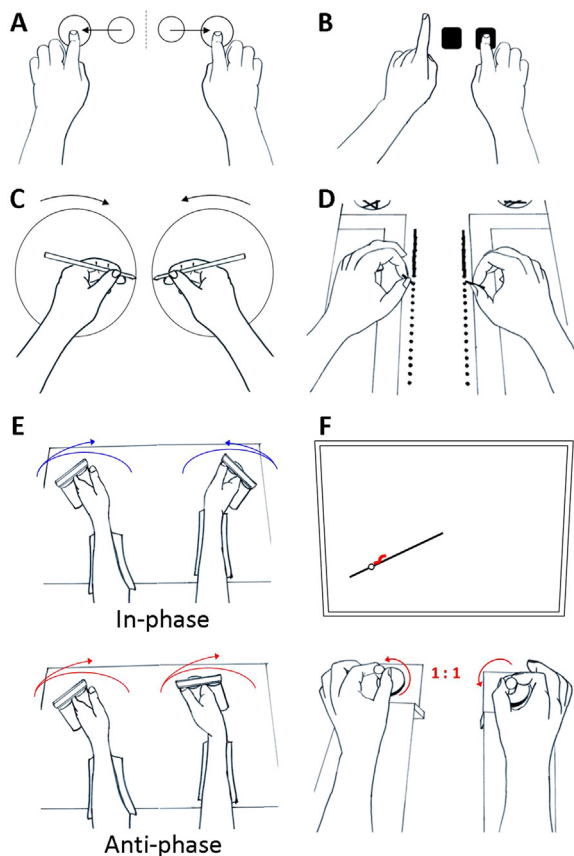


Fig. 1. Bimanual coordination tasks. **A. Fast reaching movements.** Participants begin the task with the index finger of each hand in a home position and are instructed to respond to the presence of a single stimulus and by reaching lateral targets as fast as possible. **B. Finger tapping task.** Participants are instructed to tap on the keys with their index fingers as fast as possible within a certain time window, and to maintain a constant interval between successive taps. **C. Intermittent and continuous circle drawing tasks.** Participants are instructed to trace the contour of template circles with both hands in either a symmetrical or asymmetrical pattern. In intermittent circle drawing tasks, a pause is inserted at each end of a cycle which makes the task more attention-demanding and assesses higher-level cognitive processes relative to the continuous version. **D. Purdue Pegboard Test.** This test consists of a board with two parallel rows of 25 holes. Participants are instructed to place cylindrical metal pegs in the holes as quickly as possible with both hands, within a certain time window. **E. Cyclical 1-degree-of-freedom movement task.** Participants are instructed to track an active or passive (e.g., motor-driven) movement of one hand with the other hand as accurately as possible in space and time. Typical movement modes are in-phase (upper panel), anti-phase (lower panel), and 90° phase offset. The in-phase coordination pattern is midline symmetric and involves simultaneous contraction of homologous muscles, whereas the anti-phase coordination pattern is midline asymmetric and involves alternate contractions of homologous muscles. Blue and red arrows illustrate movement trajectories in the in-phase and anti-phase mode, respectively. **F. Multi-frequency tracking task.** Participants are instructed to track a white target dot moving along a line on a screen by rotating two dials simultaneously, using their thumb and index finger. The left and right hand control movements on the vertical and horizontal axis, respectively. Rotating the dials moves a red cursor on the screen. The goal of the task is to match the white target dot moving along a target line as accurately as possible in both space and time. Multiple task variants can be used by alternating the coordination pattern and/or frequency ratio. The required coordination pattern depends on the direction of the proposed line and can impose a rotation of both hands inwards, outwards, clockwise, or counterclockwise. Each of these coordination patterns can be performed according to different frequency ratios such as 1:1, 1:2, 1:3, 2:1, and 3:1 (left hand:right hand) resulting in target lines with a different slope. Here, the counterclockwise 1:1 ratio is illustrated in red. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

and time is required in many activities of daily living which will co-determine their functional independence. Prolonging functional independence is a critical challenge for the health and well-being of older adults (OA). Here, we survey behavioral and neural literature pertaining to bimanual coordination in healthy aging. Our purpose is threefold: (1) to identify the signature of motor and coordination deficits in OA and whether and how this is mediated by the nature of the task, (2) to investigate the impact of age on learning capabilities in the context of bimanual coordination, and (3) to provide an overview of age-related changes in brain activation, brain connectivity and brain structure that may covary with coordination deficits. Altogether, this effort is intended to provide a body of knowledge about coordination in the healthy aging system in relation to alterations in the brain and to provide a benchmark to compare it with performance in patients suffering from various disorders that exhibit increased prevalence at higher age.

1.3. A unique asset for understanding interhemispheric interactions

The study of bimanual coordination is a unique vehicle for understanding the neural interactions between both hemispheres. In this respect, the corpus callosum (CC) is the principal structure that enables these interactions (Gooijers and Swinnen, 2014). Decades ago, seminal work has been conducted on bimanual deficits in split brain human and non-human primates (Preilowski, 1972). More recently, analysis of white matter microstructural organization using noninvasive imaging techniques has focused on associations between brain structure and behavior, revealing correlations between subregions of the CC and behavioral performance in normally functioning individuals (Fling et al., 2013; Gooijers et al., 2013, 2014) as well as patients (Bonzano et al., 2008; Caeyenberghs et al., 2011; Wahl et al., 2016). Beyond the study of brain-behavior associations, interhemispheric interactions have been studied in detail using noninvasive brain stimulation techniques, such as Transcranial Magnetic Stimulation (TMS). Such techniques can reveal more specific information about interhemispheric facilitatory or inhibitory interactions between homologous and non-homologous brain areas (Bäumer et al., 2006; Fujiyama et al., 2016a,b; Mochizuki et al., 2004). Along the same lines, multi-limb reaction time tasks (requiring responses of from one up to four limb segments) have also been used to investigate the hemispheric interactions at play across limbs, both in terms of facilitation and inhibition (Boisgontier et al., 2014b, 2016; Serbruyns et al., 2015a).

1.4. A large scope for experimental manipulations

There is a rich variety of bimanual movements we perform in daily life, ranging from tasks requiring symmetrical to asymmetrical contributions from each arm, hand, or finger(s). Symmetrical coordination, characterized by equal kinematics of each limb such that one limb produces the mirror movement of the other, is often used to lift and carry heavy objects and to secure propulsion in the water during breaststroke or while canoeing. This is also known as in-phase coordination that is associated with simultaneous activation of homologous muscle groups in both limbs. During crawl swimming, however, each body side also makes a similar contribution but this time one limb moves with a time lag relative to the other, called anti-phase (or 180° phase offset) coordination requiring the alternated activation of homologous muscle groups. These coordination patterns have been studied extensively because they are part of the intrinsic motor repertoire of human systems (Beek et al., 2002; Byblow et al., 1994; Carson et al., 2000; Kelso, 1984, 1995; Post et al., 2000; Swinnen et al., 1997a,b; Temprado et al., 1999). Research on characterizing different modes of coordination while registering movement kinematics online for several hours

Table 2
Brain studies.

Study	n YA/OA	Age YA / OA mean(range)	MMSE /MoCA score(mean)	Handedness	Task	Segments Joints	Conditions	Dependent variables	Training	Brain metrics (technique)
Boyke et al. (2008)	24/50	22 ± 2/67 ± 4	na	na	Juggling	Upper limbs	Balls	Juggling time	yes	Grey matter (VBM)
Coxon et al. (2010)	15/15	25(21–30) /68(60–74)	≥27	R	Continuous circle drawing	Wrists Index fingers	50% max freq Inward /outward/clockwise /counterclockwise Right-hand switch /continue Sym to asym /Asym to sym In-phase /Anti-phase /Rest 45 /60/75 /90% of critical frequency Right hand /Left hand /In-phase /Right-leads-left /Left-leads-right 1Hz	Circle size Mvt freq Switch response time Switch cost Contralateral disruption	no	Brain activity (Event-related fMRI)
Goble et al. (2010)	16/16	26(21–31) /68(61–79)	≥27	R	Cyclical movements	Wrists	Right Hand /bimanual simultaneous /bimanual independent task	Relative phase Cycling frequency Mvt amplitude	no	Brain activity (Event-related fMRI)
Fling et al. (2011)	14/16	23 ± 3/72 ± 5	(29 ± 1)	R	Finger tapping	Index fingers	Right Hand /bimanual simultaneous /bimanual independent task	Intertap interval Between-hand lag	no	White matter (DTI)
Fling and Seidler (2012)	21/18	22 ± 3(18–28) /67 ± 5(65–76)	(29 ± 1)	R	Force coordination	Index fingers	In-phase/anti-phase /rest 45/60/ 75/90% of critical frequency	Mean force Error	no	White Matter (Tractography) Brain function (TMS)
Heitger et al. (2013)	16/16	68 ± na /26/68 ± na	>27	R	Cyclical movements	Wrists	In-phase /Anti-phase /Intermediate Visual /auditory /visual+auditory stimulus	Relative phase Cycling frequency Mvt amplitude	no	Functional connectivity (Graph- theoretical analysis)
Blais et al. (2014)	10/10	23 ± 2 /68 ± 7	>24 (28 ± 2)	R	Finger tapping	Index fingers		Task-related power (EEG)	no	

Table 2 (Continued)

Study	n YA/OA	Age YA / OA mean(range)	MMSE /MoCA score(mean)	Handedness	Task	Segments Joints	Conditions	Dependent variables	Training	Brain metrics (technique)
Kiyama et al. (2014)	20/20	25 ± 5(19–39) /68 ± 4(61–74)	>26 (29 ± 2)	R	Finger coordination	Index and middle fingers	In-phase /anti-phase 1/1,5/2 Hz	Correct responses	no	Functional connectivity (Structural equation modeling)
Serbruyns et al. (2015a)	33/33	25 ± 5 /69 ± 6	≥26	R	Pegboard test	Shoulders Elbows Wrists	In-phase	Number of pegs	no	White matter (DTI)
					Finger Tapping	Index fingers	In-phase/Anti- phase	Number of taps	no	
					Multilimb reaction time	Wrists Ankles	10 limb combinations	Bimanual reaction time	no	
					Multi- frequency tracking	Wrists Thumbs Index fingers	Inward/ Outward Clockwise /Counterclock- wise 1:1-1:2-2:1- 1:3-3:1 ratios	Number of pegs	no	
Sallard et al. (2014)	29/27	24 ± 2/69 ± 5	na	R	Finger tapping	Index fingers	Switch from unimanual to bimanual In-phase	Intertap interval	no	EEG
Serbruyns et al. (2015b)	91	20–79	≥26	R	Pegboard test	Shoulders Elbows Wrists	In-phase			Grey matter (Shape)
Fujiyama et al. (2016b)	15/15	23 ± 3/66 ± 3	≥26	R	Multi- frequency tracking	Index fingers	1:1, 3:1, 1:3 ratios	Target deviation	no	White matter (DTI)
Van Ruitenbeek et al., 2017	94	(20–80)	na	R	Multi- frequency tracking	Wrists Thumbs Index fingers	Inwards /Outwards Clockwise /Counterclock- wise 1:1, 1:2, 2:1, 1:3, 3:1 ratios	Target deviation	no	Brain function (TMS)
Loehrer et al. (2016)	23/28	25 ± 2/61 ± 7	≥25	R	Finger coordination	Fingers	Spatially cou- pled/uncoupled	Error rate Time	No	Connectivity analysis (EEG)
Boisgontier et al. (2016)	35/30	23 ± 3/70 ± 6	≥26	R	Multilimb reaction time	Wrists Ankles	10 limb combinations	Bimanual reaction time	no	Grey matter (Shape)

asym = asymmetric, DTI = Diffusion Tensor Imaging, EEG = Electroencephalography, fMRI = functional Magnetic Resonance Imaging, freq = frequency, MMSE = Mini Mental State Examination, MoCA = Montreal Cognitive Assessment, mvt = movement, na = not available, OA = older adults, R = right, sym = symmetric, TMS = Transcranial Magnetic Stimulation, VBM = Voxel-Based Morphometry, YA = young adults.

during typical daily tasks has revealed that these basic in-phase and anti-phase coordination modes are observed more frequently than other (out-of-phase) coordination modes (Howard et al., 2009). Accordingly, they can be considered basic synergies or movement primitives. These coordination modes constitute the scaffold for the development of new and/or less preferred coordination modes. Such non-intrinsic coordination modes are appropriate for use in learning experiments because practice is required to perform this new spatiotemporal organization between the limbs (Debaere et al., 2004a,b; Fontaine et al., 1997; Kovacs et al., 2010; Lee et al., 1995; Puttemans et al., 2005; Ronsse et al., 2011; Smethurst and Carson, 2001; Summers et al., 1993; Swinnen et al., 1997a,b; Zanone and Kelso, 1992; Zanone et al., 2010). Moreover, such tasks can be mathematically specified according to their frequency, amplitude, and phasing characteristics. Finally, dependent measures can be inferred from the basic features of sine wave-like kinematics to determine learning progress.

Nevertheless, not all tasks have a cyclical or continuous nature. Many discrete tasks that we perform every day require a distinct yet unique contribution of each limb for goal achievement, such as opening a bottle or peeling a banana. Such asymmetrical tasks have a unique signature in terms of division of labor whereby one hand is assigned the focal action and the other hand serves to stabilize the object on which an operation is being performed, e.g., turning the jar lid with the right hand while holding the bottle with the left hand. Particularly the latter tasks are vastly under-represented in bimanual coordination research even though some attempts have been made to develop task setups under strict experimental control in which such manipulative hand actions have been studied in detail (Dietz et al., 2015; Johansson et al., 2006).

2. Methods

A computer based search was carried out on August 2016 in PubMed. The search included papers from 1980 until 2016 using the following key words: bimanual and coordination and aging/aged. Moreover; the search was extended to references of the retrieved articles. As the goal of this review was to determine the effects of the healthy aging process on bimanual coordination; we only selected studies assessing both young adults (YA) and OA.

Database search identified 190 articles for consideration. After a reference search and applying the selection criteria, 51 studies were considered for this review. Thirty-six studies were behavioral reports (Table 1) and 15 studies also investigated brain metrics (Table 2). As required by the selection criteria, all these studies compared YA and OA and two of them also tested a subgroup of older OA (Ferron, 1992; Green and Williams, 1996). In 23 studies, the Montreal Cognitive Assessment (MoCA) or Mini Mental State Examination (MMSE) was used to ensure absence of cognitive impairment. In 36 studies, hand preference was documented. Finally, in 12 studies the effect of training/practice on bimanual coordination was studied.

3. Bimanual coordination tasks

In the 51 studies that have been included here, a large variety of bimanual coordination tests or tasks was reported. Some of them are illustrated in Fig. 1. However, the ambition here was not to provide a complete overview of the existing bimanual tasks, but to describe the ones that have been used to study aging-related questions. The tasks are classified into three main categories, namely discrete, serial and continuous bimanual movements, which can be further subdivided based on the complexity and difficulty of the task (Fig. 2). In this section, we describe the tasks used in the selected studies, report the goal of each study, and define how

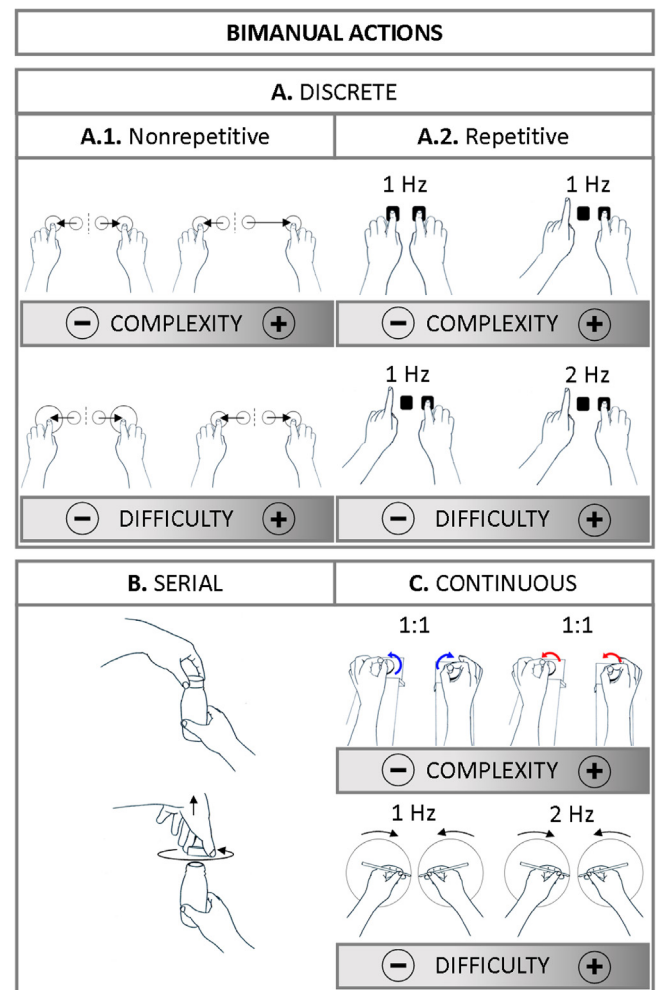


Fig. 2. Categorization of bimanual actions. In actions requiring the coordination of the hands, a distinction can be made between discrete, serial, and continuous actions (Schmidt and Lee, 2005). Within these categories, we can distinguish between actions with lower and higher levels of complexity and/or difficulty. **A. Discrete bimanual actions.** Discrete bimanual actions involve tasks with an explicit pause inserted between each movement, i.e., with a clear beginning and end. Such tasks can be performed in a repetitive or nonrepetitive mode. **A1.** Symmetrical nonrepetitive discrete actions such as fast reaching movements towards a visual stimulus are less complex than asymmetric ones. Moreover, decreasing the size of the targets in these fast reaching movements increases difficulty. **A2.** Simultaneous discrete repetitive tasks such as finger tapping tasks are less complex than alternated ones. Moreover, performing this type of task at 1 Hz is less difficult than at 2 Hz. **B. Serial bimanual actions.** Serial bimanual actions involve are made up of multiple actions performed in series, with the order of the actions being important. **C. Continuous bimanual actions.** Continuous bimanual actions involve simultaneous movements or force applications which are repeated over time without a pause in between repetitions. In-phase or body midline symmetric movements are known to be the default mode of the motor system and are less complex than anti-phase movements (upper panel). Continuous circle drawing is less difficult at 1 Hz than 2 Hz (Lower panel).

performance is usually assessed. Admittedly, the proposed classification bears limitations because some tasks possibly fit under more than one category, depending on how exactly the task is being performed.

3.1. Discrete bimanual actions

Discrete bimanual actions involve tasks with an explicit pause inserted between each movement, i.e. with a clear beginning and end (Bangert et al., 2010; Kennerley et al., 2002; Schmidt and Lee, 2005). Examples of such bimanual discrete tasks in aging include finger tapping and finger coordination tests, reaction time tests,

intermittent circle drawing, discrete force tasks, and the Purdue Pegboard Test. Within this category we make a distinction between nonrepetitive and repetitive discrete bimanual movements.

3.1.1. Nonrepetitive discrete bimanual actions

Discrete bimanual actions are considered nonrepetitive if the movement (with a clear beginning and end) is performed in isolation. **Simple and choice reaction time tasks** form one type of such nonrepetitive discrete tasks. Reaction time refers to the time elapsing between a presented stimulus and a detectable movement occasioned by the occurrence of the stimulus. Reaction time tasks are simple means to assess speed and efficiency of central processing afforded by the brain and its potential deficits. Simple reaction time tests require the participant to respond to the presence of a single stimulus, whereas choice reaction time tests require distinct responses for each type of stimulus. In both task variants, a longer reaction time is assumed to be indicative of lower processing efficiency of the brain network. Bimanual variants of reaction time tests are, for example, bimanual serial (see also below) reaction time tests during which the participant is required to press a button in response to visually presented stimuli using index and middle fingers of both hands (Bhakuni and Mutha, 2015; Hoff et al., 2015). Symmetrical or asymmetrical fast reaching movements towards a visual stimulus (Fig. 1A; Stelmach et al., 1988), or lifting both hands as fast as possible in response to a visual cue also belong to this category of bimanual reaction time movements (Boisgontier et al., 2014b, 2016).

3.1.2. Repetitive discrete bimanual actions

Discrete bimanual actions are considered repetitive if multiple movements (with a clear beginning and end) are performed one after another until this is arbitrarily stopped. The most widely used repetitive discrete task to explore bimanual coordination is finger tapping. The **finger tapping test** (Fig. 1B) is a simple task involving low inertial forces. Typically, participants are instructed to tap on keys with their index fingers as fast as possible within a certain time window or/and to maintain a constant interval between successive taps. This task is used to assess neurologically-driven motor control with an emphasis on basic movement speed while trajectory control is rather trivial. Performance on this task is usually assessed using the tapping rate and/or intertap interval. More complex finger tapping tasks, known as **finger coordination tests**, have also been used in aging. In these tasks, at least two fingers of each hand are involved and move according to more complex coordination modes such as symmetric versus asymmetric relative to body midline. Finger coordination tests require higher level (cognitive) resources relative to the basic finger tapping tests. Performance is assessed using the number of correct responses and between-hand latency. A third example of repetitive discrete bimanual movements is **drawing intermittent circles** (Fig. 1C) with both hands simultaneously. At each end of a cycle a pause is inserted which makes the task more attention-demanding and assesses higher-level cognitive processes relative to the continuous version (see Section 3.3). Lastly, standardized bimanual tests are used for clinical assessment. The **Purdue Pegboard Test** is one example (Fig. 1D; Desrosiers et al., 1995a; Tiffin and Asher, 1948). This test is used to assess fingertip dexterity combined with movement of the hands and fingers. It consists of a board with two parallel rows of 25 holes. In the bimanual condition, participants are instructed to place cylindrical metal pegs in the holes as quickly as possible with both hands. The indicator of performance is the number of pins placed within 30 s across different trials.

3.2. Serial bimanual actions

Serial bimanual actions involve movements or force applications which are made up of “multiple actions performed in series, with the order of the actions being important” (Schmidt and Lee, 2005), such as the tennis serve or playing a melody on the piano. Other examples are **bimanual force tasks**, in which there is focus on serial force production rather than movement. One task adopted in the aging literature involves placing one object on top of another using the thumb and index fingers of both hands, and rotating the top object while stabilizing the lower object (i.e., a realistic action like opening and closing a jar). During this task, average and maximum grip, load forces, and the time needed to perform the task are recorded (Gorniak and Alberts, 2013).

3.3. Continuous bimanual actions

Continuous bimanual actions involve simultaneous movements or force applications which are repeated over time without a pause in between repetitions (Bangert et al., 2010; Kennerley et al., 2002). Examples of such continuous tasks that have been used in aging include bimanual cyclical 1-degree-of-freedom movements (e.g., flexion vs. extension of the arm/hand), circle drawing, isometric tasks, multi-frequency tracking tasks, and juggling.

The most commonly used set of continuous bimanual tasks is **cyclical 1-degree-of-freedom tasks**. Cyclical movement tasks (Fig. 1E) included here assess bimanual coordination with a focus on phase-accuracy and usually involve a single upper limb joint (finger, wrist, elbow) on each side of the body. Participants are instructed to move both limb segments actively together or to track a passive (e.g., motor-driven) movement of one hand with the other hand as accurately as possible in space and time. As mentioned in the introduction section, typical coordination modes are in-phase, anti-phase, and 90° (or other) phase offsets. The in-phase coordination pattern is midline symmetric and involves simultaneous contraction of homologous muscles (Fig. 1E, upper panel), whereas the anti-phase coordination pattern is midline asymmetric and involves alternate contractions of homologous muscles (Fig. 1E, lower panel). Although these patterns are both stable, the in-phase pattern is the most preferred whereas the anti-phase pattern is more vulnerable to experimental manipulation. This is demonstrated by an automatic switch from the anti-phase to the in-phase pattern when cycling frequency is progressively increased (Greene and Williams, 1996; Wishart et al., 2000). These patterns are used to assess the intrinsic accuracy of the motor system as they do not require much training. Conversely, in the 90° phase offset movement, one limb follows the movement of the other limb while lagging a quarter of a cycle. This task is used to assess the ability to learn a pattern outside of the preferred coordination repertoire or movement primitives (i.e., in-phase and anti-phase). The level of difficulty of this type of task can be modulated by movement frequency (i.e., driving up the cycling frequency is equivalent to increasing the difficulty). Another way to increase task difficulty is to combine phase offsets by moving both limbs at different frequency ratios (i.e., non-1:1 ratio). In these tasks, timing is usually assessed by the relative phase error. The relative phasing between joint angle pairs is obtained from the instantaneous phase of each signal. Relative phase is defined as the subtraction of the phase angle of a joint from that of the other joint. This can be done according to a discrete (one data point in the cycle, such as at the displacement peak) or continuous estimate of relative phase (each single data point). Spatial performance is assessed by the amplitude error, which is the difference between the continuous (or peak) displacement series for each joint. **Circle drawing tasks** (Fig. 1C) are a specific type of continuous movements requiring inter-joint coordination (e.g., fingers, wrists, and elbows) and the repetition of

a circular movement. Such tasks require more advanced levels of trajectory control. Participants are generally instructed to trace the contour of template circles with both hands in either a symmetrical or asymmetrical pattern. The indicators of performance are usually based on the duration of each cycle, between-hands asynchrony, and circularity of the trajectory (Carson et al., 1997; Byblow et al., 1999).

Another type of continuous bimanual tasks focuses on force production rather than movement, namely **bimanual continuous force tasks**. For example, the task can require the application of a constant force with one limb and a force intensity varying according to a sine wave with the other limb (Fling and Seidler, 2012). The task can also require controlling the displacements of a cursor on a screen through the variation of forces applied by the upper limbs controlling movements on the vertical and horizontal axis. In bimanual force coordination tasks, variability in force output and pattern of force production serve as the typical indicators of performance (Spirduso and Choi, 1993).

The two final categories of continuous bimanual actions are complex tasks requiring some training. In the **multi-frequency tracking task** (Fig. 1F), participants are instructed to track a white target dot moving along a target line on a screen by rotating two dials simultaneously, using their thumb and index finger. The left and right hand control movements on the vertical and horizontal axis, respectively. Rotating the dials moves a red cursor on the screen serving as an online visual (augmented) feedback signal. The goal of the task is to match the white target dot movement with the red dot as accurately as possible in both space and time. Multiple task variants can be used by varying the coordination pattern and/or frequency ratio. The required coordination pattern depends on the direction of the projected line on the screen and can imply a rotation of both hands inwards, outwards, clockwise, or counter-clockwise. Each of these coordination patterns can be performed according to different frequency ratios such as 1:1, 1:2, 1:3, 2:1, and 3:1 (left hand:right hand) resulting in target lines with a different slope. Performance is calculated by the target deviation score of the time series. At last, **juggling** is a skilled continuous movement characterized by tossing and catching multiple objects/balls, and is usually assessed by the juggling time and/or the number of thrown and caught objects/balls.

4. Aging and bimanual coordination

In this section, we provide an overview of the effect of aging on bimanual coordination and its interaction with task-related experimental manipulations (i.e., complexity, difficulty, visual feedback, and dual tasking) and training in both discrete and continuous bimanual movements. In this respect, there were no studies available using serial bimanual actions. Importantly, we only focus on studies that report a direct comparison of bimanual coordination performance between young and older adults.

4.1. Discrete bimanual actions and aging

A large variety of both nonrepetitive and repetitive discrete bimanual coordination tasks have demonstrated a consistent age-related decline in performance accuracy and/or speed, as well as performance variability (Bangert et al., 2010; Bernard and Seidler, 2012; Boisgontier et al., 2016; Ferron, 1992; Fling and Seidler, 2012; Fling et al., 2011; Kiyama et al., 2014; Krampe and Ericsson, 1996; Metzler et al., 2013; Sallard et al., 2014; Serbruyns et al., 2015a,b; Sommervoll et al., 2011; Weller and Latimer-Sayer, 1985). Furthermore, OA generally demonstrated longer reaction times than YA in choice reaction times tasks (Boisgontier et al., 2016; Shammi et al., 1998; Serbruyns et al., 2015a).

4.1.1. Task complexity

In this review, we make a distinction between making a task **more complex** by manipulating its spatiotemporal organization (e.g., in-phase versus anti-phase or 90° phase offset) and making a task **more difficult** (e.g., performance of the same task but at different speeds/cycling frequencies) (Fig. 2). In the dynamic pattern theory (Kelso, 1995), the former is considered an order parameter (describing macroscopic behavior of the system) and the latter a control parameter (inducing changes within a given macroscopic behavior).

Many studies have revealed an age-related decrease in motor speed in **repetitive finger tapping** and **finger coordination tests**, as reflected by a lower number of taps within a given timeframe. Particularly, in the alternating tapping condition indicative of a higher complexity level relative to simultaneous tapping, clear age-related differences are reported in overall performance (Bangert et al., 2010; Ferron, 1992; Fling et al., 2011; Krampe and Ericsson, 1996; Sallard et al., 2014; Serbruyns et al., 2015a) or within-subject variability (Bangert et al., 2010; Blais et al., 2014; Shammi et al., 1998). Furthermore, the more complex variant of finger tapping (i.e., finger coordination tests) has revealed more and/or larger errors in OA than in YA (Kiyama et al., 2014; Krampe and Ericsson, 1996; Loehrer et al., 2016; Metzler et al., 2013). In the study by Krampe and Ericsson (1996), YA and OA were tested on a bimanual finger coordination test that required pressing piano keys as fast as possible in response to visual stimuli (9-element sequence). Key presses of both hands were either mirrored (simultaneous – mirror) or different (simultaneous – different) relative to each other. Results revealed that performance was poorer for OA than YA in the “mirror” condition and to a higher extent in the “different” condition. Performance decrements were reflected by impaired speed and higher error scores (Krampe and Ericsson, 1996). These findings were replicated using very similar bimanual finger coordination tasks (Kiyama et al., 2014; Metzler et al., 2013). Findings from Loehrer et al. (2016) on a comparable spatially coupled/uncoupled finger coordination task are only partly consistent with above findings. Although they revealed increased error scores as well as decreased motor speed in OA relative to YA, these effects were not amplified in the more complex coordination mode (i.e., spatially uncoupled).

Focusing on **repetitive intermittent circle drawing**, the cognitively more demanding variant of continuous circle drawing, age-related performance impairments were reflected by an increased variability in OA relative to YA in total cycle duration and pause duration. In addition, particularly during the asymmetric condition (non-mirrored) OA produced trajectories that were less circular than the ones of YA. This aging effect was not reported in the mirrored condition (Summers et al., 2010). Finally, the effect of complexity has also been studied by means of a **nonrepetitive** discrete bimanual task, namely a **choice reaction time test** that required to leave a home key and reach towards two visual stimuli (with same (symmetric) or different lengths (asymmetric)) as fast as possible. Longer reaction times and movement times were reported in OA as compared to YA across both conditions. With respect to movement initiation and termination, OA showed more asynchrony between the hands than YA, irrespective of movement condition (Stelmach et al., 1988).

4.1.2. Task difficulty

In a study by Bangert et al. (2010) YA and OA were required to tap alternately with the left and right index finger at different intertap intervals (800 ms, 1000 ms, and 1200 ms). Results revealed an interaction effect between age and intertap interval, indicating that OA were significantly slower (decreased tapping rate) than YA at longer intertap intervals (Bangert et al., 2010). In contrast, Sommervoll et al. (2011) showed no significant effect of age on

mean tapping performance during an alternating tapping task with increasing frequencies (1, 2, 3, and 4 Hz).

Moreover, in the study by [Summers et al. \(2010\)](#) in which participants were required to perform a **bimanual intermittent circling task**, performance levels were comparable for both frequency levels (i.e., self-determined frequency and 50% faster) for both YA and OA.

4.1.3. Visual feedback

We did not find any study reporting on the effect of visual feedback on discrete bimanual movements in aging.

4.1.4. Motor learning

Studies using a bimanual serial **reaction time task** (B-SRTT), requiring to respond to one of 4 stimuli appearing on the screen (corresponding to the middle (L/R) or index finger (L/R)), revealed that both YA and OA demonstrated intact learning, i.e., evidenced by reductions in response time. Although response times were always significantly longer in OA than in YA, OA showed a comparable learning rate throughout practice ([Bhakuni and Mutha, 2015](#)). Similarly, [Hoff et al. \(2015\)](#) demonstrated that both YA and OA performed significantly faster on the B-SSRT on the second training day, a week from the first day. There was no difference in the learning rate between groups ([Hoff et al., 2015](#)).

To sum-up, for discrete bimanual tasks, age-related effects seem to interact with task-related factors. With respect to task complexity, studies reported larger or gradually emerging age effects in more complex (i.e., simultaneous asymmetric) relative to less complex (i.e., simultaneous symmetric) tasks. Comparable to the work on continuous bimanual movements, the findings on the effects of difficulty level are equivocal, and perhaps, understudied. The limited number of studies available in the context of aging revealed that changing the intertap interval influenced age effects, whereas increasing the tapping/cycling frequency did not. Future studies are needed to draw firm conclusions in this respect. Finally, studies on the effect of learning all revealed that although both OA and YA improved their performance, the learning rate was comparable. These findings revealed preserved learning capabilities in discrete bimanual tasks in elderly, and therefore have implications for interventional purposes.

4.2. Continuous bimanual actions and aging

A large variety of continuous bimanual coordination tasks have demonstrated a consistent age-related decline in performance accuracy and/or speed, as well as performance stability ([Bangert et al., 2010](#); [Boyke et al., 2008](#); [Leinen et al., 2016](#); [Moes et al., 1995](#); [Pauwels et al., 2015](#); [Serbruyns et al., 2015a](#); [Solesio-Jofre et al., 2014](#); [Spirduso and Choi, 1993](#); [Stelmach et al., 1988](#); [Voelcker-Rehage and Willimczik, 2006](#)). However, the effect of aging on bimanual coordination performance can be influenced by manipulating the level of task complexity, task difficulty, the absence/presence of feedback, and the amount of training. Therefore, the effects of age on continuous bimanual movements are discussed in light of their interaction with complexity, difficulty, feedback, and practice/training.

4.2.1. Task complexity

In a **continuous circling** or **drawing task**, OA and YA showed similar scores in in-phase and/or anti-phase modes ([Bangert et al., 2010](#); [Piedimonte et al., 2014](#); [Ringenbach et al., 2011](#); [Summers et al., 2010](#)). However, switching from the symmetric to asymmetric mode was more difficult for OA. Specifically, OA showed greater variability, longer partial disruptions of the contralateral movement, and more total contralateral disruptions than YA ([Coxon et al., 2010](#)). Conversely, there was no age-related difference when

switching from the asymmetric (more complex) to symmetric (less complex) mode. When considering **cyclical 1-degree-of-freedom movements**, OA showed similar relative phase accuracy and variability as YA in the less complex in-phase mode ([Greene and Williams, 1996](#); [Ren et al., 2015](#); [Swinnen et al., 1998b](#)). In anti-phase mode, however, OA exhibited lower relative phase accuracy ([Sparrow et al., 2005](#)) and higher relative phase variability ([Greene and William, 1996](#); [Lee et al., 2002](#)) than YA. Nonetheless, other studies showed no age-related difference in the anti-phase mode ([Serrien et al., 1996, 2000](#); [Swinnen et al., 1998b](#)). In the 90° phase offset mode, an even more complex movement pattern, all studies showed consistent results with OA exhibiting lower accuracy and higher variability than YA ([Sparrow et al., 2005](#); [Swinnen et al., 1998b](#); [Wishart et al., 2002](#)). This finding suggests that OA experience more difficulties in overcoming or suppressing the tendency to fall into the preferred coordination modes while adopting the 90° phase offset mode. This may be indicative of reduced inhibitory control to overcome or reduce neural crosstalk.

Similar age-related effects were reported in the **multi-frequency tracking task** when complexity increased. More specifically, the increased error in conditions requiring a frequency decoupling between the hands (non-isofrequency vs. isofrequency) and without (vs. with) visual feedback ([Moes et al., 1995](#)) was higher in OA than YA. Although [Serbruyns et al. \(2015a\)](#) similarly reported an increased error rate in the non-isofrequency mode relative to the isofrequency mode, this effect was not higher with advancing age. However, participants in the latter study always received online augmented visual feedback.

The importance of complexity in the age-related decrement of performance is also stressed in **bimanual force tasks**. For example, [Fling and Seidler \(2012\)](#) introduced a bimanual force task requiring force production of both index fingers. They included one condition in which both the left and right finger had to produce the same amount of constant force (bimanual simultaneous condition), and one in which the right hand maintained a certain force level, whereas the left hand followed a 1 Hz sine wave (bimanual independent condition). Results revealed no group differences in the bimanual simultaneous condition, but when the complexity increased (i.e., the hands were uncoupled), greater variability in performance was found in OA relative to YA ([Fling and Seidler, 2012](#)). Similar findings were reported by [Spirduso and Choi \(1993\)](#). Participants were required to trace a triangular template on the screen by applying and releasing forces on spring levers with either bilateral index fingers or with the left index finger and right thumb. In general, OA deviated more from the required trajectory and took longer to trace the complete triangle. Importantly, the effects of age were largest on two sides of the triangle requiring decoupling of the left index finger and right thumb (i.e., flexion of the one and extension of the other). That is, bilateral movements away from the more intrinsic synergies were performed worse in OA than in YA ([Spirduso and Choi, 1993](#)).

Finally, three studies have investigated the impact of aging on continuous bimanual movements by means of a **juggling task**. Results showed a decline in movement speed and accuracy with advancing age in two studies ([Boyke et al., 2008](#); [Voelcker-Rehage and Willimczik, 2006](#)), whereas one study showed similar performance levels of OA compared to YA ([Perrot and Bertsch, 2007](#)).

4.2.2. Task difficulty

Using **cyclical 1-degree-of-freedom movements**, [Wishart et al. \(2000\)](#) showed that the effects of age on upper limb performance in both in-phase and anti-phase modes were dependent on movement frequency. Particularly, accuracy and variability of the relative phase was similar in YA and OA at low movement frequencies (0.5–1 Hz), but OA became less accurate and more variable than YA at higher movement frequencies (1.5–2 Hz). Along the same lines,

other studies showed that the maximum movement frequency at which subjects can maintain the anti-phase mode was lower in OA than YA (Goble et al., 2010; Greene and Williams, 1996; Lee et al., 2002; Temprado et al., 2010; Wishart et al., 2000). Nevertheless, other studies showed no interaction between age and task difficulty (Leinen et al., 2016; Temprado et al., 2010). Leinen et al. (2016) used a continuous 1:2 wrist coordination task under three different load conditions (0, 0.5, and 1 kg) and showed no interaction between age and load condition. Temprado et al. (2010) showed that the age-related decline in accuracy and variability was independent of task complexity (in-phase vs. anti-phase) and difficulty (0.5 vs. 1 vs. 1.5 vs. 2 vs. 2.5 Hz) during cyclical pronation-supination wrist coordination. This discrepant result may emerge from another type of complexity referring to musculo-skeletal features. As such, the pronation-supination movement the latter group used may be underused and/or more complex compared to tasks used in the other studies (i.e., mainly flexion-extension movements) and could therefore result in an age-related deficit, even in the in-phase mode and at low movement frequencies.

4.2.3. Visual feedback

The literature is inconsistent regarding the interaction between the effects of age and visual feedback. Some studies showed a lower ability of OA to benefit from visual feedback compared to YA (Boisgontier et al., 2014a; Ren et al., 2015). In the study of Ren et al. (2015), participants were instructed to track the 90° offset **cyclical movement** of two target dots. The targets were tracked using joysticks in haptic and haptic + visual feedback conditions. Results showed that YA, but not OA, benefited from the visual feedback. Furthermore, when actively tracking the cyclical movement of a passively driven wrist with the other wrist, vision of the active limb impaired performance more in OA than YA (Boisgontier et al., 2014a). In contrast, during a cyclical movement task with 90° phase offset, Swinnen et al. (1998b) showed that the relative phase was more accurate and less variable in an augmented visual feedback condition than in normal and no-vision conditions, irrespective of age group. Finally, in a **multi-frequency tracking task**, Moes et al. (1995) showed that OA exhibited more and larger errors than YA in both vision and non-vision conditions.

4.2.4. Motor learning

Results regarding learning of **cyclical movement tasks** are equivocal. Studies report that in more demanding cyclical movements with a 90° phase offset trained over 2 or 3 days, OA improved more than YA (Swinnen et al., 1998b; Wishart et al., 2002). Although YA showed a more pronounced improvement of accuracy and consistency between blocks on day 1, only OA continued to improve on day 2 and 3 of practice (Swinnen et al., 1998b; Wishart et al., 2002). Following 3 days of practice, OA could perform the 90° phase offset mode as accurately and at the same speed as YA, but not as consistently (Wishart et al., 2002). Hence, OA can diminish the difference in performance with YA and sometimes improve more compared to YA. Conversely, no age-related difference was observed in the rather simple in-phase and anti-phase modes of a continuous forearm coordination task performed over 2 days of practice (Swinnen et al., 1998b). These results are, however, not in line with a study of Ren et al. (2015) investigating 90° phase offset cyclical movements trained over the course of 5 days. In this study, YA improved more than OA.

The learning effect in YA and OA has also been studied in a **continuous bimanual force task**. Spirduso and Choi (1993) demonstrated that when practicing (3 days) a complex bimanual force task that requires the coupling and decoupling of the right and left index finger and thumb to trace a triangular template, both YA and OA improved their accuracy scores and to speed up their movements. Although practice was equally beneficial for

both age groups, OA did show a larger decrease in movement time than YA from day 1 to day 2. Adopting a **multi-frequency tracking task**, Pauwels et al. (2015) demonstrated that practicing non-isofrequency complex bimanual movements introduces performance increments, and even more so in OA than in YA. OA improved more than YA over a period of 3 days with 6 practice sessions per day. However, retention performance was better in YA than in OA (Pauwels et al., 2015). Finally, Voelcker-Rehage and Willimczik (2006) demonstrated that OA were still able to improve on a new, complex motor skill such as a **juggling task**. More specifically, although learning gains were comparable to those of YA across 6 training sessions of 15 min each, absolute performance levels were lower in OA than in YA. In another juggling study, however, the learning rate over 12 sessions of 20 min each was faster for YA as compared to OA (Perrot and Bertsch, 2007).

In conclusion, it is fair to state that the effect of aging on continuous bimanual performance interacts with task-related factors. Firstly, considering task complexity, a recurrent finding is the increase/appearance of age effects in more complex conditions. Secondly, with respect to task difficulty, results are less consistent. Whereas some observed larger age effects at higher cycling frequencies, others revealed no interaction between age and difficulty level. Conflicting results probably emerge from the type of tasks performed and the corresponding degree of complexity. It seems that during relatively simple tasks (e.g., cyclical flexion-extension movements) age effects increase when speeding up the movement, whereas during more complex tasks (e.g., 1:2 coordination or pronation-supination) age effects do not further increase when making the task more difficult. Thirdly, when visual feedback interacts with age, this appears to be at the cost of OA. These results can possibly be linked to an underlying age-related cognitive overload (Boisgontier et al., 2013) becoming visible when additional feedback processing is required. Finally, with respect to bimanual motor learning in OA in comparison to YA the results are inconclusive. Although it is clear from multiple studies that OA can learn bimanual coordination tasks, the diversity in tasks leads to a disagreement in the literature regarding the pattern of learning within a given timeframe between OA and YA. Moreover, we should be cautious when comparing performance changes between YA and OA as higher initial performance levels in YA make them more likely to face a ceiling effect sooner and baseline performance is often different across the two age groups.

4.3. Dual-tasking

In dual-tasking, participants are instructed to perform two different tasks simultaneously (dual-task condition) and their performance is compared to when the same participants perform these same tasks individually (single-task condition). Dual-tasking serves to examine executive functions and more specifically, the attentional resources allocated to a task of interest. This is another presumed metric of functional independence in OA. The differences observed between the single and dual-task conditions are used to extrapolate potential differences in the ratio of attentional capacity to a task cost or a supply/demand discrepancy. In a study of Lee et al. (2002) where participants were instructed to perform cyclical bimanual upper-limb movements at 1 or 2 Hz with or without the addition of a serial addition task, the dual-task condition had generally no detrimental effect on accuracy and consistency of the relative phase. However, in the in-phase condition, OA were not able to maintain the frequency at 2 Hz, when performing a concurrent task. This result suggested a very low level of available attentional resources in the group of OA under investigation. Furthermore, OA showed an impaired consistency in the anti-phase pattern at 2 Hz under the single-task but not dual-task condition. This result appears to demonstrate that removing attention from

the coordination task in a difficult condition (2 Hz) allowed OA to maintain a level of performance in the anti-phase pattern similar to the one of the YA. This result is consistent with the fact that the anti-phase pattern can still be considered a relatively stable pattern (i.e., an attractor) that can be efficiently performed under automatic control and that may not necessarily benefit from increased cognitive control. The effects of dual tasking on bimanual coordination in YA and OA have been investigated in other studies (Sommervoll et al., 2011; Sparrow et al., 2005), but it is difficult to draw strong conclusions from these as either the coordination task or the secondary task was not tested in complementary single-task conditions.

In sum, only one single study reported interpretable results related to the effect of dual-tasking on bimanual coordination performance in the context of aging. Additional studies are warranted to further validate the results of this study and to further investigate the extent to which cognition, and the neural resources it requires, is linked to the age-related decline of bimanual coordination performance.

5. Aging brain and bimanual coordination

5.1. Effects of aging on brain structure and function

Some of the studies mentioned in the previous section extended their investigation into the neural correlates of bimanual coordination. This neuroscientific approach is crucial to fully capture the underlying mechanisms of bimanual coordination in aging. Aging impacts brain structure and function. Studies have shown widespread age-related volume decreases in grey and white matter volume, together with volume increases in cerebro-spinal fluid in ventricles, fissures, and sulci (e.g., Giorgio et al., 2010; Salat, 2011; Sullivan and Pfefferbaum, 2007). Since the introduction of diffusion MRI (dMRI), enabling the characterization of microstructural tissue properties, numerous studies have reported microstructural disruptions of white matter fibers with advancing age (Sullivan and Pfefferbaum, 2007). Regionally, white matter in the frontal brain areas is often most affected (Sullivan and Pfefferbaum, 2007). In addition to structural degeneration, functional brain changes are evident in OA. In general, functional MRI (fMRI) and positron emission tomography (PET) studies in aging have revealed regional hyper-activations in cognitive, perceptual, and motor circuits (Cabeza, 2001; Cabeza et al., 2002; Calautti et al., 2001; Grady et al., 1994; Heuninckx et al., 2008; Li and Lindenberger, 1999; Logan et al., 2002; Mattay et al., 2002; Naccarato et al., 2006; Park et al., 2004; Riecker et al., 2006; Sala-Llanch et al., 2015; Van Impe et al., 2011; Ward and Frackowiak, 2003). Such hyper-activations are generally reflected by increased (including bilateral) activation. Two hypotheses and variations thereof have been proposed to explain such hyper-activations with advancing age: *dedifferentiation* and *compensation*. While the dedifferentiation hypothesis emphasizes a decrease in functional specificity during task performance in elderly (Grady et al., 1994; Li and Lindenberger, 1999; Logan et al., 2002; Park et al., 2004; Sala-Llanch et al., 2015), possibly as a consequence of reduced inhibitory processes, the compensation hypothesis states that additional recruitment of brain areas is a compensatory mechanism for functional and/or structural deficits in these or other more distributed brain areas (e.g. Calautti et al., 2001; Heuninckx et al., 2008; Mattay et al., 2002; Naccarato et al., 2006). When the age-related hyper-activations are beneficial at lower task demands, but fall short at higher task demands, the compensation-related utilization of neural circuits hypothesis is an appropriate account (CRUNCH; Grady, 2012; Reuter-Lorenz and Cappell, 2008; Schneider-Garces et al., 2010). Age-related changes in brain function have also been investigated using electroen-

cephalography (EEG). EEG-studies have revealed an enlarged alpha and beta desynchronization together with a decline in functional hemispheric asymmetry in OA (Labyt et al., 2004, 2006; Rossiter et al., 2014; Schmiedt-Fehr et al., 2016; Vallesi and Stuss, 2010). These changes might reflect a loss of selectivity that does not serve behavioral improvements (Inuggi et al., 2011; Labyt et al., 2006; Yordanova et al., 2004). Lastly, there is a growing body of literature pertaining to the effect of aging on functional connectivity (FC), which captures interactions between local or distributed brain regions. Both during a state of (awake) rest (resting-state FC) and during task performance (task-related FC), changes in interactions between distinct brain areas have been demonstrated with aging. A common finding in the field of resting-state FC is a reduction in functional connectivity across a variety of brain networks when people age (Sala-Llanch et al., 2015). Regarding task-related FC, mainly tested during cognitive task performance, studies have revealed both increases and decreases in FC with advancing age (Sala-Llanch et al., 2015). Studies investigating age-related FC changes by means of EEG are unfortunately very limited. One study by Vecchio et al. (2014) used a graph theoretical network approach (GTNA) to investigate the degree of global connectedness among distant brain areas with advancing age. Results revealed that OA have a shorter normalized characteristic path length than YA in the higher alpha band, indicative of reduced efficiency in communication between distant brain areas.

From here, we proceed with outlining the specific interaction between age-related functional/structural brain changes and bimanual motor performance. Results are primarily arranged according to the techniques applied (EEG, MRI, and TMS).

5.2. Brain function underlying the effect of age on bimanual coordination

5.2.1. Small timescale (electroencephalography)

EEG is a method used to record electrical activity of the brain (i.e., brainwaves) at rest or during task performance, using recordings from electrodes placed along the scalp. Its main advantage is the temporal resolution that is much better than fMRI but the spatial resolution is lower. In the following section, we review findings in the EEG literature in relation to bimanual motor control in OA. Merely discrete bimanual movement tasks are discussed since there is no EEG work available on continuous bimanual movements in OA.

5.2.1.1. Power and time analyses. One study using EEG during bimanual finger tapping in in-phase, anti-phase, or intermediate-phase coordination mode, showed an increased neural desynchronization in the alpha frequency band over parietal regions and in the beta frequency band over sensorimotor regions in OA relative to YA (Blais et al., 2014). These results are considered being indicative of age-related hyper-activations in sensorimotor areas and areas involved in attentional processing. These findings were amplified during the performance of the more complex (non in-phase) bimanual movements, suggesting that less stable coordination modes are instrumental in revealing larger age-related declines. No significant associations were observed between task performance and EEG findings.

Another EEG study showed that, when compared to unimanual finger tapping, bimanual tapping movements were associated with an increased power in the beta band in the superior parietal lobule (SPL) and decreased power in the left occipital lobe in OA, whereas YA showed no power modulation (Sallard et al., 2014). These results suggested that OA switched from somatosensory to visual imagery mechanisms to control bimanual coordination, likely due to a decline in distinct sensory processing abilities. No

direct correlations were observed between task performance and EEG power.

5.2.1.2. EEG-based functional connectivity (coherence). As there is no work available on EEG-based resting-state functional connectivity in relation to bimanual performance in the OA, this paragraph focuses on task-based functional connectivity. Effective connectivity is the influence of one neural system on another (Büchel and Friston, 1997). Loehrer et al. (2016) investigated the age-related alterations of effective connectivity of the motor network. YA and OA performed a bilateral tapping task with both hands either spatially coupled (i.e., tap same sequence with both hands) or uncoupled (i.e., tap different sequence with left and right hand). Using dynamic causal modeling (DCM; method to assess effective connectivity), they showed that, relative to YA, OA demonstrated a) increased M1-M1 connectivity, b) lateralized increased prefrontal-premotor connectivity, and c) lateralized decreased prefrontal-supplementary motor area (SMA) connectivity. However, no associations between increased connectivity metrics and performance were observed. Therefore, it remains inconclusive whether these findings represent compensatory activations or rather fit with the dedifferentiation hypothesis or an expanded version of this.

In summary, these preliminary EEG studies show power decreases/increases, increased desynchronization, and inter- and intra-hemispheric connectivity changes during bimanual task performance. Strikingly, although such age-related alterations in EEG were particularly present at increased complexity levels, none of the studies reported significant associations with task performance. A major research effort is required in the coming years to address these issues.

5.2.2. Large timescale (functional magnetic resonance imaging)

fMRI is a neuroimaging technique detecting (localized) brain activity at rest or in response to task performance by identifying changes in blood oxygenation and flow in the brain.

5.2.2.1. fMRI activations. Adopting fMRI in OA and YA during cyclical in-phase and anti-phase cyclical bimanual wrist movements, Goble et al. (2010) revealed greater activations in OA than YA in a variety of brain areas (SMA, dorsolateral prefrontal cortex (DLPFC), inferior frontal gyrus, inferior parietal cortex, secondary somatosensory cortex (SII), and cingulate cortex). There were no cortical areas with significantly greater activation in YA compared to OA. Additionally, it was shown that the increased activation in SMA was even more pronounced when the cycling frequency increased (i.e., higher difficulty level). Additionally, a positive relationship between performance in the anti-phase coordination mode (but not the in-phase mode) and functional brain activation in SII and SMA was found in OA only. More specifically, OA who showed higher activity levels in SII and SMA demonstrated a better coordination performance. Please note that it required a more complex coordination mode to reveal such a relationship. The results of Goble et al. (2010) have been suggested to provide support for the ‘compensation hypothesis’, implying that (a) hyper-activation in an area that is more recruited or uniquely recruited by OA and that is (b) associated with a performance benefit, can be indicative of compensatory mechanisms in the aging brain. Similar effects have also been shown in different motor tasks (Heuninckx et al., 2008; Mattay et al., 2002; Naccarato et al., 2006; Ward and Frackowiak, 2003). During the performance of cyclical bimanual in-phase and anti-phase circular index finger movements, Coxon et al. (2010) revealed higher cortical activations in OA than YA in SMA, DLPFC, inferior frontal gyrus, and inferior parietal cortex when switching from one coordination mode to another. There were no cortical areas with significantly greater activations in YA compared to OA. However, OA did show less activation than YA in subcor-

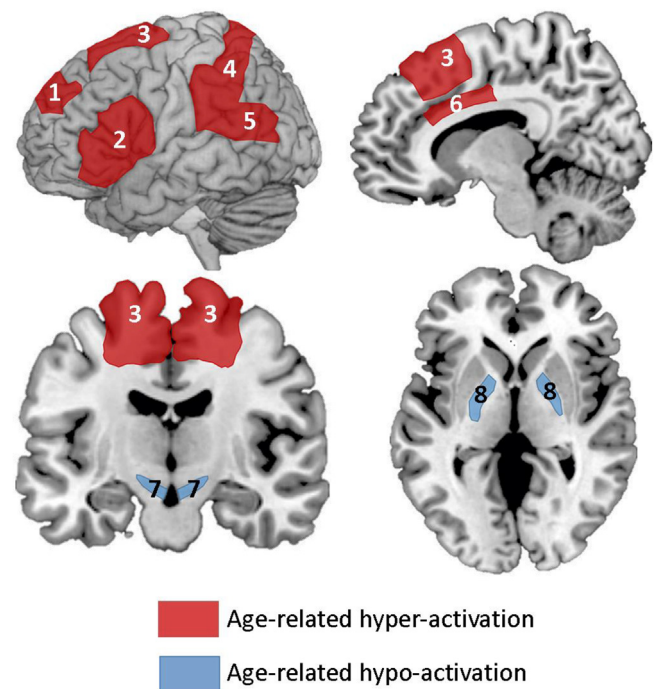


Fig. 3. Age-related subcortico-cortical activation shift (SUCAS). During a bimanual coordination task, older adults show functional hyper-activation of the dorsolateral prefrontal cortex (1), inferior frontal gyrus (2), supplementary motor area (3), Secondary somatosensory area (4), Inferior parietal cortex (5) and cingulate cortex (6) (Coxon et al., 2010; Goble et al., 2010), and functional hypo-activation of the subthalamic nucleus (7) and globus pallidus (8) (Coxon et al., 2010).

tical structures, namely the bilateral subthalamic nuclei and right globus pallidus, when switching to a more difficult coordination mode. Interestingly, age-related hyper-activations in DLPFC were positively correlated with the differential switch cost (i.e., reaction time difference between switch to in- or anti-phase coordination mode).

Overall, age-related hyper-activation has been shown in at least 6 regions of the brain during bimanual coordination: SMA, DLPFC, inferior frontal gyrus, inferior parietal cortex, SII, and cingulate cortex. Such results are partly consistent across different tasks, such as the previously addressed cyclical movement task (Goble et al., 2010) and switching task (Coxon et al., 2010). This raises the question whether candidate areas for age-related hyper-activation are independent of the type of (bimanual) motor task (i.e., whether cortical hyper-activation constitutes a more generic feature of the aging process). However, hypo-activation has also been observed in subcortical structures during bimanual task switching (Coxon et al., 2010) and this has received much less attention. Taken together, these results raise the hypothesis about whether hyper-activation of cortical regions in OA represents an attempt to counteract (subcortical) hypo-activation that may be associated with suboptimal processing of information for bimanual coordination. Additional studies are needed to test the extent to which this age-related subcortico-cortical activation shift (SUCAS; Fig. 3) is specific to bimanual coordination or represents a more generic feature of motor control and/or other behavioral functions.

5.2.2.2. FMRI-based functional connectivity. In addition to hyper-activity during the performance of (bimanual) motor tasks in OA, brain connectivity also undergoes changes in relation to bimanual motor performance. Functional connectivity methods estimate similarities between BOLD time series recorded in different regions of the brain. In other words, information exchange among isolated brain areas is measured, leading to distinct subnetworks represent-

ing functional modules. Generally, functional connectivity is either based on data at rest (resting-state networks), or during actual task performance (task-related networks).

5.2.2.2.1. Resting-state connectivity. While the most common trend across different resting-state networks (e.g., default mode, visual, auditory, salience, etc.) is reduced functional connectivity in OA as compared to YA (Sala-Llonch et al., 2015), the motor resting network (tailored to bimanual task performance by extraction of regions of interest based on task-related fMRI) has shown functional connectivity increases across the lifespan (20–80 years) (Soleisio-Jofre et al., 2014). Moreover, when correlating functional connectivity metrics with behavioral measures, the authors revealed that increased functional connectivity was associated with poorer performance (i.e., higher error score) on a multi-frequency tracking task (Soleisio-Jofre et al., 2014). More specifically, poorer performance was associated with higher functional connectivity between interhemispheric dorsal and ventral premotor areas. In line with other studies, the default mode network (DMN) serving as control, was anti-correlated with the motor network (Soleisio-Jofre et al., 2014). Moreover, no significant associations were observed between motor performance and functional connectivity in the DMN, adding specificity to the correlations between motor network functional connectivity and bimanual performance. These findings suggest that distinct resting state networks may be differentially affected by aging.

5.2.2.2.2. Task-related connectivity. In addition to the effect of aging on motor resting-state networks, changes in task-related networks have also been reported. Heitger et al. (2013) applied graph theoretical network analyses (GTNA) to fMRI BOLD signals during the performance of in-phase and anti-phase continuous wrist movements (based on Goble et al., 2010). Cycling frequency levels were adapted individually to ensure that experienced task difficulty levels were comparable among individuals with different ages. As a result of this, no significant differences in performance (coordination accuracy and consistency) were present between YA and OA, allowing inferences on functional connectivity free of performance differences (Goble et al., 2010). Connectivity metrics across several task-relevant motor subnetworks were different between OA and YA. Higher mean connectivity degree, connection strength, network density and efficiency, together with shorter mean communication path length between the network regions were reported. In other words, OA exhibited tighter functional connectivity and shorter communication path lengths between brain regions than YA but there were no significant associations between individual functional connectivity scores and bimanual performance (Heitger et al., 2013). Thus, it appears that OA not only exhibited increased brain activation (as discussed in the previous section) but also tighter functional communication between areas. Interestingly, functional connectivity was also higher during anti-phase than in-phase coordination in both YA and OA, suggesting a comparable connectivity modulation as a function of task difficulty. This increased connectivity in both groups, may result from an attempt to resist loss of coordinative stability and transitions from anti-phase to in-phase coordination.

Using structural equation modeling to analyze fMRI BOLD responses during a bimanual in-phase and anti-phase four-finger coordination task in YA and OA, Kiyama et al. (2014) studied the basic sensorimotor network including bilateral SMA, PMd, M1, SPL, and primary somatosensory cortex (S1). Similar to earlier work (Grefkes et al., 2008; Walsh et al., 2008; Zhuang et al., 2005), they showed strong interhemispheric connections between bilateral motor regions in YA. Interestingly, intrahemispheric connectivity within the dominant hemisphere increased from in-phase to anti-phase coordination only in YA. In addition, they reported decreased functional connectivity between left PMd and other intra and interhemispheric regions in OA relative to YA (distant connectivity),

while functional connectivity between bilateral PMd pairs was equally strong in YA and OA (local connectivity). The age-related alterations in distant task-related connectivity appear partially consistent with other work in which effective connectivity (i.e., looking at the influence of one neural system on another (Büchel and Friston, 1997)) was studied using TMS (see next section). Local connectivity between the bilateral PMds was enhanced while their connectivity with more remote regions was reduced in OA (Rowe et al., 2006).

In summary, both resting-state and task-based functional connectivity was higher in OA relative to YA even though there was also evidence for a more differentiated perspective for local as compared to more distant network connections. At rest, increased functional connectivity was associated with poorer performance (i.e., indirect indications of functional dedifferentiation), whereas task-based changes were not associated with performance. Overall increased functional connectivity in the motor network appears apparent in aging but it remains unclear at this stage of knowledge whether and/or under what circumstances this is related to behavioral performance.

5.2.3. Transcranial magnetic stimulation

TMS is a non-invasive technique used to stimulate the brain. It can also be instrumental to study connectivity between pairs of brain areas. In the context of bimanual coordination, TMS has been applied to assess interhemispheric connections via the CC and intrahemispheric connections between motor or other areas. Using a dual-site TMS paradigm with a conditioning stimulus followed by a test stimulus to study interhemispheric interactions, Fujiyama et al. (2016b) examined the functional influence from either DLPFC or PMd to the contralateral M1 (left > right, right > left) during the preparation phase of a bimanual multi-frequency tracking task. This enabled them to relate pre-movement connectivity metrics (interhemispheric modulation) to subsequent motor performance. Participants had to perform the task with either the same (1:1) or different frequency ratios: left hand faster (3:1) or right hand faster (1:3). In both YA and OA, the left PMd-right M1 interaction became facilitatory when the left hand (controlled by right M1) had to move faster than the right hand, while inhibitory modulation was observed when the movement frequency arrangement was reversed. This suggested that the left PMd was primarily in charge of regulating or gating the motor output to the contralateral M1, in both YA and OA, to ensure differentiated movements between both limbs. The interhemispheric right PMd-left M1 interaction did not show this specific modulation as a function of task assignment to the left and right hand. The advantage of assigning hand-specific task modulation to the PMd of the left hemisphere may be that this helps overcoming or precluding competition between both PMds for task control. Moreover, individual differences in modulatory capability of this interhemispheric interaction during the planning phase of movement correlated with the quality of subsequent movement performance, i.e., modulation towards a facilitatory interaction for the 3:1 task and towards an inhibitory interaction for the 1:3 task was positively correlated with performance on these bimanual tasks and this was the case for participants in both age groups. With respect to the interhemispheric interaction between left and right DLPFC with the contralateral M1, a more general facilitatory interaction was observed in YA, implying that it was indifferent to the specific task assignment of each hand (faster or slower rotation) but also indifferent with respect to the connectivity direction (i.e., left DLPFC to right M1 versus right DLPFC to left M1). This facilitatory interaction appeared to be absent for the group of OA. That is, compared to YA, the OA group showed a reduced ability to regulate the interaction between DLPFC and M1 (Fujiyama et al., 2016b). This is an important observation in view of the more extensive recruitment of DLPFC in OA than YA

during bimanual (Coxon et al., 2010; Goble et al., 2010) and ipsilateral coordination (Heuninckx et al., 2005), and possibly many other motor tasks.

5.3. Brain structure underlying the effect of age on bimanual coordination

5.3.1. White matter analysis and bimanual coordination

Different approaches have been used to associate various white and grey matter measures with behavior. For example, diffusion weighted imaging is a magnetic resonance technique that determines the directionality of water diffusion in the brain to reveal the micro-structural organization of brain white matter. By means of DTI and the more recent high angular resolution diffusion imaging methods (HARDI), diffusion-weighted metrics across voxels are used to reconstruct white matter connections. One of the most prominent measures used for assessment of micro-structural organization of white matter is called fractional anisotropy (FA), referring to the degree of directionality of water diffusion in the brain.

One important white matter structure in the brain in the context of bimanual coordination is the CC (Gooijers and Swinnen, 2014). For instance, Fling et al. (2011) studied the relationship between CC size and microstructure on the one hand and bimanual performance on the other hand in both YA and OA. They observed a significant association between the size and microstructural properties of the CC (restricted to subregions of the CC connecting SMA, M1, and S1) and performance on an out-of-phase but not simultaneous finger tapping task (Fling et al., 2011). Importantly, whereas a larger corpus callosum size and more optimal microstructural properties were associated with poorer performance in YA, the same parameters were associated with better performance in OA. These results indirectly suggested an age-related switch in the impact of callosal properties on bimanual control. A study of Serbruyns et al. (2015a) demonstrated that a better microstructural organization (i.e., higher FA) in OA (restricted to the subregion of the CC connecting premotor areas) was associated with better performance on a tapping task in the simultaneous, but not alternating mode. Tapping performance in YA was not correlated with CC integrity. Higher values of anisotropy in the CC (restricted to the subregions connecting occipital, premotor, and S1 areas) were also associated with increased performance on the Purdue Pegboard Test and a choice reaction task, only in the group of OA. In a multi-frequency tracking task, better performance was correlated with better CC microstructural properties in YA (restricted to the subregion of the CC connecting S1) and OA (restricted to the subregion of the CC connecting M1) (Serbruyns et al., 2015a).

Using probabilistic white matter tractography, Fujiyama et al. (2016b) investigated structural properties of connections between DLPFC-contralateral M1 and PMd-contralateral M1, in relation to bimanual performance in both OA and YA. In OA only, significant positive associations between performance on the bimanual multi-frequency tracking task and fractional anisotropy values were reported. More specifically, higher anisotropy values in the tracts from left PMd to right M1 were correlated with higher performance (i.e., lower error scores) in OA, particularly in conditions where the left hand moved faster than the right hand (3:1 ratio). This left PMd-right M1 interhemispheric connection appeared to play a critical role in regulating the tasks assignments between both hands. Moreover, only in OA, a higher modulatory capability of the interhemispheric interaction, as assessed via dual-site TMS, was associated with higher fractional anisotropy in the subserving tracts (left PMd-right M1). Overall, this suggests interesting associations between interhemispheric functional interactions, microstructural organization of the underlying tracts mediating these interactions, and quality of bimanual movement

in OA. In other words, brain structure is predictive of brain function and behavior and this appears to be more so in OA than YA.

5.3.2. Grey matter analysis and bimanual coordination

The existing literature on the relation between grey matter data and bimanual performance in the aging population is less extensive. The association between grey matter, age and bimanual performance has been investigated using a multi-frequency tracking task (Van Ruitenbeek et al., 2017). Results of this study demonstrated that performance in the in-phase mode was negatively associated with age and grey matter in M1, SMA, S1, premotor cortex, and cingulate motor cortex. In line with these results, a study investigating the subcortical correlates of bimanual coordination in the context of aging showed that local inward deformation in the ventrolateral thalamic subregions subserving connectivity with M1, premotor, and somatosensory areas, mediated the effect of aging and performance on the Purdue Pegboard Test: the higher the volume reduction in this subregion of the thalamus, the lower the bimanual performance (Serbruyns et al., 2015b). This correlation was specific to this subregion (that exhibited an age-related reduction) and was neither found for other (non-motor) subregions of the thalamus nor for general thalamus volume.

Overall, structural alterations with advancing age, i.e., macro- and microstructural decreases in WM and GM tissue in OA relative to YA, correlate well with poorer bimanual performance. These findings support the deterministic role of brain structure for bimanual performance in OA specifically and possibly for motor performance in general. Unfortunately, besides the work of Fujiyama et al. (2016b), there is little evidence that such age-related structural brain alterations in the bimanual motor network play an important role in the previously reported functional activation and functional connectivity changes. Moreover, future studies should investigate whole brain structural connectivity in relation to bimanual performance deficits in elderly.

6. Discussion

Here we investigated the behavioral and neural determinants of bimanual coordination in aging. Results from continuous and discrete tasks were analyzed as a function of task complexity and difficulty. The surveyed functional and structural brain studies revealed some of the mechanisms underlying the effects of aging on bimanual coordination but also evidenced some caveats in the literature.

6.1. Aging triggers increased involvement of cognition in bimanual coordination performance

Results consistently showed an age-related decline in various bimanual movement tasks, whereas performance on static force coordination tasks did not seem to be affected by age. Overall, bimanual coordination actions met the typical hallmarks of motor aging exhibiting slower and/or less accurate as well as more variable movements which required more attention (Boisgontier, 2015). These effects of age became more pronounced at higher levels of complexity and/or difficulty, supporting results from unimanual task studies (Riviere and Thakor, 1996; Smith et al., 1999). The provision of feedback was found to be more detrimental or less beneficial to OA than YA, which supports some findings from the field of postural control (e.g., Dault et al., 2003). Moreover, dual-task paradigms demonstrated that complex bimanual tasks are cognitively more demanding for OA than YA. This age-related deficit supports previous results across a large variety of motor (e.g., Boisgontier et al., 2013) and non-motor tasks (Verhaeghen and Cerella, 2002; Verhaeghen et al., 2003).

Overall, these results suggest that cognition becomes increasingly critical for the control of bimanual coordination in aging adults, which becomes more obvious in difficult and/or complex conditions. This age-related penetration of cognition into the control of movement is not specific to bimanual coordination (e.g., Heuninckx et al., 2005), but is a more global process. These findings beg the question whether it is possible to overcome or reduce this cognitive penetration through motor and/or cognitive training. In this respect, the results of the present review are encouraging as they showed greater improvement of bimanual coordination in OA than YA as a result of practice. However, these results may be accounted for by lower initial performance levels in OA, leaving more room for gains. Nevertheless, learning capability appears generally preserved in OA. Future work should address how bimanual skill learning can be optimized in OA by improving organization of practice, by provision of various forms of information feedback, and by boosting neuroplasticity via noninvasive brain stimulation techniques such as transcranial direct and alternating current stimulation (Hardwick and Celnik, 2014; Orban de Xivry and Shadmehr, 2014; Zimerman et al., 2013) to upregulate local neuronal activity or distributed networks (i.e., neuro-enhancement of motor function).

6.2. Hyper-activation, hypo-activation, and compensation/dedifferentiation in OA

Studies investigating brain-behavior relationships in bimanual coordination tasks by means of fMRI showed an age-related cortical hyper-activation in several regions: SMA, DLPFC, inferior frontal gyrus, inferior parietal cortex, SII, and cingulate cortex (Coxon et al., 2010; Goble et al., 2010). This may reflect increased demands on sensory processing and penetration of cognition into action. Similar age-related hyper-activation has also been reported in other motor studies (Heuninckx et al., 2005, 2008; Van Impe et al., 2009, 2011; Ward, 2006; Ward and Frackowiak, 2003). These results demonstrate that the hyper-activation associated with aging is not specific to bimanual coordination but is a more generic signature of aging. The extent to which such cortical hyper-activation is compensatory in nature has been supported by several studies, including those using bimanual tasks (Coxon et al., 2010; Goble et al., 2010). Nevertheless, the story is more complicated because subcortical hypo-activity has also been observed (Coxon et al., 2010). This prompts questions about potential interactions between hyper and hypo-activity in the aging brain and, more generally, about the origin of these age-related activation changes. Particularly, this subcortico-cortical activation shift (SUCAS) may suggest that age-related cortical hyper-activity compensates for subcortical hypo-activity to prevent bimanual performance decline. Additional research is needed to determine the relationship between this activation shift and whether it supports mechanisms of compensatory recruitment or dedifferentiation in the aging brain.

6.3. Functional connectivity

Aging is associated with changes in the interaction between brain regions during rest and task performance, as determined by functional connectivity measures. When looking at the bimanual motor network during the resting state, an increase in functional connectivity was observed as a function of aging (Solesio-Jofre et al., 2014). Moreover, higher connectivity was associated with lower performance on a bimanual coordination task, suggesting that interactions among the motor network regions at rest do have implications for motor performance. Similar to resting state connectivity, higher functional connectivity in OA was also observed in task-related networks associated with bimanual wrist coordination (Heitger et al., 2013). In addition, we observed that both OA

and YA showed increased functional connectivity with higher task demands. This suggests that functional connectivity can be flexibly adapted as a function of task requirements. Future studies should investigate how resting state and task-related networks interact with each other and whether OA can flexibly shift between such networks. Moreover, whereas learning of bimanual tasks is associated with increases in task-related functional connectivity in YA (Heitger et al., 2012), very little is known about motor training-induced alterations in functional connectivity in OA.

6.4. Macro and microstructural changes in the aging brain affect bimanual coordination

Our review provides critical indications for the deterministic nature of brain structure in relation to bimanual coordination performance. Most studies have demonstrated that age-related declines in volume, size, and microstructural properties of grey and white matter are associated with poorer performance. Considering white matter, the CC including tracts connecting homotopic and heterotopic cortical motor regions contribute to bimanual performance, particularly when the complexity level of the task increases. Regarding grey matter, age-related volume decreases of the somatosensory cortex and subregional changes in thalamus were shown to be associated with bimanual performance declines. These grey matter alterations may have implications for brain activation as correlations between brain volume and brain activity have been observed (Qing and Gong, 2016). This reinforces the need for further research investment in the study of brain structure-function associations.

7. Conclusion

As we age, movements become slower and/or less accurate and more cognition-dependent. These hallmarks of motor aging apply to bimanual movements and are associated with age-related hyper-activation of distinct cortical structures, reflecting additional neural recruitment for cognitive and sensory processing functions. The bimanual literature appears to suggest that this cortical hyper-activation may be linked to the age-related hypo-activation of subcortical structures (SUCAS). In addition to increased recruitment of distinct brain areas, interactions among these areas are also exhibiting age-related changes, as suggested by tighter functional connectivity (both at rest and during task) with increasing age. Finally, manipulation of the complexity and difficulty of motor tasks appear critical to reveal these effects, to increasing their effect size and to facilitate their investigation.

8. Perspectives

Current developments in imaging neuroscience are increasingly marked by multimodal approaches that combine various techniques to study brain structure, function, connectivity, and neurochemical composition. Combining these techniques to reach a comprehensive multimodal imaging approach is challenging because it requires high-level expertise in various domains and sophisticated technologies. Nevertheless, if we wish to understand how aging affects motor behavior, we need to investigate the interactions between alterations in brain grey and white matter structure and how these interactions impact reorganization of the brain that triggers changes in brain function and connectivity. This is a particularly complex endeavor because biological systems do not passively undergo these age-related brain alterations but actively create functional solutions to the structural alterations that inevitably occur. The mounting evidence for lifelong neuroplasticity suggests that we may not yet have reached a full understanding

about the substantial potential of older adults to maximize and extend their functional independence by means of an active and healthy life. The use of bimanual skills may be very helpful in this research enterprise because such skills provide a unique window into age-related alterations in interhemispheric interactions that are of fundamental importance for understanding complex brain function.

Author contributions

Conceived and designed review: M.P.B., S.P.S. Searched articles: M.P.B. Analyzed results: M.P.B., J.G., C.M. Prepared and wrote manuscript: M.P.B., S.P.S., J.G., C.M., J.J.O.X.

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