Thèse d'Habilitation à Diriger des Recherches, Université Grenoble Alpes

Solving the Exercise Paradox: A Neuro-Behavioral Approach

Matthieu P. Boisgontier

COMMITTEE		
	Stephan P. Swinnen	KU Leuven, Belgium
	Vincent Nougier	Université Grenoble Alpes, France
	Julie Duqué	Université Catholique de Louvain, Belgium
	Matthew W. Miller	Auburn University, USA
	Aïna Chalabaev	Université Grenoble Alpes, France
	Stéphane Cullati	Université de Genève, Switzerland

June 25, 2019

TABLE OF CONTENTS

1. CURRICULUM VITAE

MATTHIEU P. BOISGONTIER

EDUCATION & TRAINING

2008 – 2012	**PhD in Movement Sciences, Neuroscience, and Aging,** *Université de Grenoble, France.* Supervisor: Vincent Nougier
2008 – 2009	**Certificate of Advanced Study in Physical Therapy**, *MGH Institute of Health Professions, Boston, USA*. Supervisor: Maura D. Iversen
2006 – 2007	**Master of Science in Movement, Performance, Health, & Engineering**, *Université Grenoble 1, France.* Supervisors: Nicolas Vuillerme & Yohan Payan
2003 – 2006	**Bachelor and Master of Physical Therapy**, *Université Grenoble 1 & Institut de Formation en Masso-Kinésithérapie ASSAS, France*
1997 – 2003	**Bachelor and Master of Science in Kinesiology**, *Université Grenoble 1, France*

PROFESSIONAL ACTIVITIES

2016 – 2019	**Senior Researcher***, University of Geneva, Switzerland.*
2017 – 2018	**Visiting Researcher**, *University of British Columbia (UBC), Canada.*
2012 – 2018	**Postdoctoral Researcher**, *KU Leuven, Belgium*.
2011 – 2012	**Lecturer** (ATER), *Université Savoie Mont Blanc, France*
2010	**Physical Therapist**, *Les Granges Medical Centre, Echirolles, France*
2009 – 2010	**Physical Therapist**, *Home Care, La Tronche, France*
2008	**Physical Therapist,** *Hand Rehabilitation Centre, Grenoble, France*
2007	**Physical Therapist**, *Private Practice, Moirans, France*
2006 – 2007	**Physical Therapist**, *Rocheplane Medical Centre, Grenoble, France*

FELLOWSHIPS & GRANTS

2108	*European Research Council (**ERC**) Starting Grant interview – Rejected (~~1,500,000 EUR~~)*
2018	**Neurorehabilitation Seed Fund***, University of British Columbia (5,000 CAD)*
2018 – 2020	**Research Grant**, *Scientific Fund for Research – Flanders* (40,000 EUR)
2017 – 2020	**Post-Doctoral Fellowship**, *Scientific Fund for Research – Flanders*, ranked 1st (200,000 EUR)
2017 – 2018	**Grant for a Long Stay Outside Europe**, *Scientific Fund for Research – Flanders* (20,000 EUR)
2016 – 2018	**Research Grant**, *KU Leuven* (87,000 EUR)
2015 – 2018	**Research Grant**, *Scientific Fund for Research – Flanders* (40,000 EUR)
2014 – 2017	**Post-Doctoral Fellowship**, *Scientific Fund for Research – Flanders*, ranked 2nd (190,000 EUR)
2009 – 2012	**PhD Fellowship**, *French Ministry of Higher Education and Research* (90,000 EUR)
2009	**Healthcare Professional Award**, *SOFPEL* (2,000 EUR)
2008 – 2009	**Scholarship**, *Massachusetts General Hospital Institute of Health Professions* (10,000 USD)
2006 – 2007	**Scholarship***, French Ministry of Higher Education and Research* (7,000 EUR)

CERTIFICATES & DIPLOMAS

2019	**Qualification** for assistant professor positions in Movement Sciences (section **74**), Neuroscience (section **69**), and Psychology (section **16**), *France*
2018	Authorization to register for the **"Habilitation à Diriger des Recherches"** (HDR), *France*
2017	Authorization to act as a **medical imaging technologist**, *Belgium*

2016	Authorization to practice **physical therapy**, *Belgium*
2013	**Qualification** for assistant professor positions in Movement Sciences (section **74**) and Neuroscience (section **69**), *France*
2006	**Physical therapy license** (Diplôme d'Etat en Masso Kinésithérapie), *France*
2003	**Certificate of pre-professionalization to careers in teaching**, *France*
2000	**State Certificate of Sport Educator**, *France*

FIRST-AUTHOR ARTICLES (n = 22)

58-Cheval B*, **Boisgontier MP***, Bacelar MFB, Feiss R, Miller MW (**2019**) Opportunities to sit and stand trigger equivalent reward-related brain activity. International Journal of Psychophysiology. 141:9-17.
57-**Boisgontier MP**, Cheval B, van Ruitenbeek P, Cuypers K, Leunissen I, Sunaert S, Meesen R, Zivari Adab H, Renaud O, Swinnen SP (**2018**) Cerebellar grey matter explains bimanual coordination performance in children and older adults. Neurobiology of Aging. 65:109-120.
56-Cheval B*, **Boisgontier MP***, Orsholits D, Sieber S, Guessous I, Gabriel R, Stringhini S, Blane D, Courvoisier DS, Kliegel M, Burton-Jeangros C, Cullati S (**2018**) Association of early- and adult-life socioeconomic circumstances with muscle strength in older age. Age & Ageing. 47:398-407.
55-**Boisgontier MP**, Cheval B, Chalavi S, van Ruitenbeek P, Leunissen I, Levin O, Nieuwboer A, Swinnen SP (**2017**) Individual differences in brainstem and basal ganglia structure predict postural control and loss of balance in young and older adults. Neurobiology of Aging. 50:47-59.
54-**Boisgontier MP**, Serbruyns L, Swinnen SP (**2017**) Physical activity predicts performance in an unpracticed bimanual coordination task. Frontiers in Psychology. 8:249.
53-**Boisgontier MP**, Cheval B (**2016**) The anova to mixed model transition. Neuroscience & Biobehavioral Reviews. 68:1004-1005.
52-**Boisgontier MP**, Cheval B, van Ruitenbeek P, Levin O, Renaud O, Chanal J, Swinnen SP (**2016**) Whole-brain grey matter density predicts balance stability irrespective of age and protects older adults from falling. Gait & Posture. 45:143-150.
51-**Boisgontier MP**, van Ruitenbeek P, Leunissen I, Chalavi S, Sunaert S, Levin O, Swinnen SP (**2016**) Nucleus accumbens and caudate atrophy predicts longer action selection times in young and old adults. Human Brain Mapping. 37:4629-4639.
50-**Boisgontier MP** (**2015**) Motor aging results from cerebellar neuron death. Trends in Neurosciences. 38:127-128.
49-**Boisgontier MP** (**2015**) Commentary: cerebellar direct current stimulation enhances on-line motor skill acquisition through an effect on accuracy. Frontiers in Human Neuroscience. 9:578.
48-**Boisgontier MP**, Swinnen SP (**2015**) Age-related deficit in a bimanual joint position matching task is amplitude dependent. Frontiers in Aging Neuroscience. 7:162.
47-**Boisgontier MP**, Swinnen SP (**2014**) Proprioception in the cerebellum. Frontiers in Human Neuroscience. 8:212.
46-**Boisgontier MP**, Van Halewyck F, Corporaal SHA, Willacker L, Van den Bergh V, Beets IAM, Levin O, Swinnen SP (**2014**) Vision of the active limb impairs bimanual motor tracking in young and older adults. Frontiers in Aging Neuroscience. 6:320.
45-**Boisgontier MP**, Wittenberg G, Fujiyama H, Levin O, Swinnen SP (**2014**) Complexity of central processing in simple and choice multilimb reaction-time tasks. Plos One. 9:e90457.
44-**Boisgontier MP**, Beets IAM, Duysens J, Nieuwboer A, Krampe RT, Swinnen SP (**2013**) Age-related differences in attentional cost associated with postural dual tasks: increased recruitment of generic cognitive resources in older adults. Neuroscience & Biobehavioral Reviews. 37:1824-1837.
43-**Boisgontier MP**, Nougier V (**2013**) Ageing of internal models: from a continuous to an intermittent proprioceptive control of movement. Age. 35:1339-1355.
42-**Boisgontier MP**, Nougier V (**2013**) Proprioception: bilateral inputs first. Neuroscience Letters. 534:96-100.
41-**Boisgontier MP**, Olivier I, Chenu O, Nougier V (**2012**) Presbypropria: the effects of physiological ageing on proprioceptive control. Age. 34:1179-1194.

40-**Boisgontier MP**, Moineau B, Nougier V (**2012**) Superimposed electrical simulation comfortably improves the endurance of maximal voluntary contractions. The Journal of Sports Medicine & Physical Fitness. 52:558-562.

39-**Boisgontier M**, Mignardot J, Nougier V, Olivier I, Palluel E (**2011**) Attentional cost of the executive functions involved in postural control. Science & Motricité. 74:53-64.

38-**Boisgontier M**, Vuillerme N, Iversen M (**2010**) Superimposed electrical stimulation decreases maximal grip force. The Journal of Sports Medicine & Physical Fitness. 50:152-158.

37-**Boisgontier M**, Vuillerme N, Thomas D, Pinsault N, Emprin M, Caillat-Miousse J (**2009**) Effects of neuromuscular electrical stimulation on the range of motion recovery in hand proximal interphalangeal sprain. Science & Sports. 24:192-195.

LAST-AUTHOR ARTICLES (n = 15)

36-Cheval B, Orsholits D, Sieber S, Courvoisier D, Cullati S, **Boisgontier MP** (**2019**) Age-related decline of cognitive resources precedes the decline in physical activity. Mayo Clinic Proceedings. [Under Review – Major Comments]. doi: 10.31236/osf.io/pagx6

35- Cheval B, Rebar AL, Miller MW, Siever S, Orsholits D, Baranyi G, Courvoisier D, Cullati S, Sander D, Chalabaev A, **Boisgontier MP** (**2019**) Cognitive resources moderate the adverse impact of poor perceived neighborhood conditions on self-reported physical activity in older age. Preventive Medicine. 126:105741.

34-Cheval B, Chabert C, Orsholits D, Sieber S, Guessous I, Blane D, Kliegel M, Janssens JP, Burton-Jeangros C, Pison C, Courvoisier DS, **Boisgontier MP***, Cullati S* (**2019**) Disadvantaged early-life socioeconomic circumstances are associated with low respiratory function in older age. The Journals of Gerontology. Series A, Biological Sciences & Medical Sciences. 74:1134-1140.

33-Cheval B, Tipura E, Burra N, Frossard J, Chanal J, Orsholits D, Radel R, **Boisgontier MP** (**2018**) Avoiding sedentary behaviors requires more cortical resources than avoiding physical activity: an EEG study. Neuropsychologia. 119:68-80.

32-Cheval B, Radel R, Neva JL, Boyd LA, Swinnen SP, Sander D, **Boisgontier MP** (**2018**) Behavioral and neural evidence of the rewarding value of exercise behaviors: a systematic review. Sports Medicine. 48:1389-1404.

31-Cheval B, Sieber S, Guessous I, Orsholits D, Courvoisier DS, Kliegel M, Stringhini S, Swinnen SP, Burton-Jeangros C, Cullati S, **Boisgontier MP** (**2018**) Impact of early- and adult-life socioeconomic circumstances on level of physical inactivity. Medicine & Science in Sports & Exercise. 50:476-485.

30-Zivari Adab H, Chalavi S, Beets IAM, Gooijers J, Leunissen I, Cheval B, Collier Q, Sijbers J, Jeurissen B, Swinnen SP, **Boisgontier MP** (**2018**) White matter microstructural organization of interhemispheric pathways predicts different stages of bimanual coordination learning in young and older adults. European Journal of Neuroscience. 47:446-459.

29-Corporaal SHA, Gooijers J, Chalavi S, Cheval B, Swinnen SP, **Boisgontier MP** (**2017**) Neural predictors of motor control and impact of visuo-proprioceptive information in youth. Human Brain Mapping. 38:5628-5647.

28-Maes C, Gooijers J, Orban de Xivry JJ, Swinnen SP, **Boisgontier MP** (**2017**) Two hands, one brain, and aging. Neuroscience & Biobehavioral Reviews. 75:234-256.

27-Moineau B, **Boisgontier MP** (**2014**) Superimposed electrical stimulation improves mobility of pre-stiff thumbs after ulnar collateral ligament injury of the metacarpophalangeal joint: a randomized study. Annals of Physical & Rehabilitation Medicine. 57:373-380.

26-Vuillerme N, **Boisgontier M** (**2010**) Changes in the relative contribution of each leg to the control of quiet two-legged stance following unilateral plantar-flexor muscles fatigue. European Journal of Applied Physiology. 110:207-213.

25-Vuillerme N, **Boisgontier M** (**2009**) Effectiveness of a tongue-placed electrotactile biofeedback to improve ankle force sense following plantar-flexor muscles fatigue. Gait & Posture. 30:556-559.

24-Vuillerme N, **Boisgontier M** (**2008**) Muscle fatigue degrades force sense at the ankle joint. Gait & Posture. 28:521-524.

CO-AUTHOR ARTICLES (n = 23)

23-Sieber S, Cheval B, Orsholits D, Van der Linden BW, Guessous I, Gabriel R, Kliegel M, Aartsen MJ, **Boisgontier MP**, Courvoisier D, Burton-Jeangros C, Cullati S (**2019**) Welfare regimes modify the association of disadvantaged adult-life socioeconomic circumstances with self-rated health in old age. International Journal of Epidemiology. doi: 10.1093/ije/dyy283

22-Cheval B, Orsholits D, Sieber S, Stringhini S, Courvoisier DS, Kliegel M, **Boisgontier MP**, Cullati S (**2019**) Early-life socioeconomic circumstances explain health differences in old age, but not their evolution over time. Journal of Epidemiology & Community Health. doi: 10.1136/jech-2019-212110

21-Cheval B, Chabert C, Sieber S, Orsholits D, Cooper R, Guessous I, Blane D, Kliegel M, Courvoisier DS, Kelly-Irving M, **Boisgontier MP**, Cullati S (**2019**) The association between adverse childhood experiences and muscle strength in older age. Gerontology. doi: 10.1159/000494972

20-Neva JL, Ma JA, Orsholits D, **Boisgontier MP**, Boyd LA (**2019**) The effects of acute exercise on visuomotor adaptation, learning, and inter-limb transfer. Experimental Brain Research. 237:1109-1127.

19-Bolmont M, Bianchi-Demicheli F, **Boisgontier MP**, Cheval B (**2019**) The woman's (not the man's) body is used to evaluate sexual desire: an eye-tracking study of automatic visual attention. Journal of Sexual Medicine. 16:195-202.

18-Landös A, von Arx M, Cheval B, Sieber S, Kliegel M, Gabriel R, Orsholits D, van der Linden BWA, Blane D, **Boisgontier MP**, Courvoisier DS, Guessous I, Burton-Jeangros C, Cullati S (**2019**) Childhood socioeconomic circumstances and disability trajectories in older men and women: a European cohort study. European Journal of Public Health. 29:50-58.

17-Bonifazi P, Erramuzpe A, Diez I, Gabilondo I, **Boisgontier MP**, Pauwels L, Stramaglia S, Swinnen SP, Cortes J (**2018**) Structure-function multi-scale connectomics reveals a major role of the fronto-striato-thalamic circuit in brain aging. Human Brain Mapping. 39:4663-4677.

16-Corporaal SHA, Bruijn SM, Hoogkamer W, Chalavi S, **Boisgontier MP**, Duysens J, Swinnen SP, Gooijers J (**2018**) Different neural substrates for precision stepping and fast online step adjustments in youth. Brain Structure & Function. 223:2039-2053.

15-Chalavi S, Zivari Adab H, Pauwels L, Beets IAM, van Ruitenbeek P, **Boisgontier MP**, Santos Monteiro T, Maes C, Sunaert S, Swinnen SP (**2018**) Anatomy of subcortical structures predicts age-related differences in skill acquisition. Cerebral Cortex. 28:459-473.

14-Lavrysen A, Levin O, **Boisgontier MP**, Elliott D, Helsen WF (**2018**) Effects of wrist tendon vibration and eye movements on manual aiming. Experimental Brain Research. 236:847-857.

13-Cheval B, Sarrazin PG, **Boisgontier MP**, Radel R (**2017**) Temptations toward behaviors minimizing energetic costs (BMEC) automatically activate physical activity goals in successful exercisers. Psychology of Sport & Exercise. 30:110-117.

12-Santos Monteiro T, Beets IAM, **Boisgontier MP**, Gooijers J, Pauwels L, Chalavi S, King B, Albouy G, Swinnen SP (**2017**) Relative cortico-subcortical shift in brain activity but preserved training-induced neural modulation in older adults during bimanual motor learning. Neurobiology of Aging. 58:54-67.

11-Helsen WF, Van Halewyck F, Levin O, **Boisgontier MP**, Lavrysen A, Elliott D (**2016**) Manual aiming in healthy aging: does proprioceptive acuity make the difference? Age. 38:45.

10-Beets IAM, Gooijers J, **Boisgontier MP**, Pauwels L, Coxon JP, Wittenberg G, Swinnen SP (**2015**) Reduced neural differentiation between feedback conditions after training bimanual coordination with and without augmented visual feedback. Cerebral Cortex. 25:1958-1969.

9-Moineau B, **Boisgontier MP**, Gailledrat E, De Angelis M-P, Olivier I, Palluel E, Pérennou D, Nougier V (**2015**) Is postural control more impaired in hip-disarticulated patients compared to transfemoral amputees? A pilot study. Annals of Physical & Rehabilitation Medicine. 58:354-356.

8-Van Halewyck F, Lavrysen A, Levin O, **Boisgontier MP**, Elliott D, Helsen WF (**2015**) Factors underlying age-related changes in discrete aiming. Experimental Brain Research. 233:1733-1744.

7-Levin O, Fujiyama H, **Boisgontier MP**, Swinnen SP, Summers JJ (**2014**) Aging and motor inhibition: a converging perspective provided by brain stimulation and imaging approaches. Neuroscience & Biobehavioral Reviews. 43:100-117.

6-Moineau B, **Boisgontier MP**, Barbieri G, Nougier V (**2014**) A new method to assess temporal features of gait initiation with a single force plate. Gait & Posture. 39:631-633.
5-Théveniau N, **Boisgontier MP**, Varieras S, Olivier I (**2014**) The effects of clothes on independent walking in toddlers. Gait & Posture. 39:659-661.
4-Van Halewyck F, Lavrysen A, Levin O, **Boisgontier MP**, Elliott D, Helsen WF (**2014**) Both age and physical activity level impact on eye-hand coordination. Human Movement Science. 36C:80-96.
3-Vuillerme N, **Boisgontier M**, Chenu O, Demongeot J, Payan Y (**2007**) Tongue-placed tactile biofeedback suppresses the deleterious effects of muscle fatigue on joint position sense at the ankle. Experimental Brain Research. 183:235-240.
2-Vuillerme N, Chenu O, Pinsault N, **Boisgontier M**, Demongeot J, Payan Y (**2007**) Inter-individual variability in sensory weighting of a plantar pressure-based, tongue-placed tactile biofeedback for controlling posture. Neuroscience Letters. 421:173-177.
1-Vuillerme N, Pinsault N, Chenu O, **Boisgontier M**, Demongeot J, Payan Y (**2007**) How a plantar pressure-based, tongue-placed tactile biofeedback modifies postural control mechanisms during quiet standing. Experimental Brain Research. 181:547-554.

MENTORING & SUPERVISORY ACTIVITIES

Doctoral Supervisor	Dr Sharissa Corporaal	*(2012 – 2017, KU Leuven, Belgium)*
Doctoral Mentor	Dr Bastien Moineau	*(2011 – 2014, Université de Grenoble, France)*
	Dr Florian Van Halewyck	*(2010 – 2014, KU Leuven, Belgium)*
Doctoral Jury	Dr Jan Ruffieux	*(2018, University of Fribourg, Switzerland)*
Masters Supervisor	8 MSc theses	*(2010 – 2017, KU Leuven, Belgium)*

TEACHING ACTIVITIES – 237 hours

2011 – 2012	**Université Savoie Mont Blanc**, France
Biomechanics	Lectures (20 hours; ~80 MSc students)
Biomechanics	Labs (58 hours; ~15 MSc students),
Neurophysiology	Labs (28 hours; ~15 BSc students)
Sport Physiology	Labs (24 hours; ~15 MSc students)
Traumatology	Labs (20 hours; ~15 BSc students)
Neuroscience	Labs (12 hours; ~15 MSc students)
Training Methods	Labs (4 hours; ~15 MSc students)
2011 – 2012	**EFOM, Institut de Formation en Masso-Kinésithérapie**, France
Scientific Methods	Lecture (4 hours; ~60 BSc students)
Statistics	Lecture (4 hours; ~60 BSc students)
2010 – 2011	**Université Grenoble I**, France
Neuroscience	Labs (27 hours; ~30 BSc students)
Office Software	Labs (36 hours; ~30 BSc students)

REVIEWING ACTIVITIES – 162 articles, 48 journals**,** 2 projects

Projects United States – Israel Binational Science Foundation *(**BSF**; 2018; 150,000 USD)*
Fonds de Recherche du Québec – Nature et Technologies (***FRQ – NT**; 2018; 20,000 CAD*)

Articles *(number of articles reviewed)*

Archives of Physical Medicine & Rehabilitation (1) – BMC Musculoskeletal Disorders (1) – Brain & Cognition (1) – Brain Research (1) – Clinical Interventions in Aging (3) – Clinical Neurophysiology (2) – Cognition & Emotion (1) – European Journal of Applied Physiology (2) – European Journal of Public Health (5) – European Review of Aging and Physical Activity (1) –

*Experimental Aging Research (1) – **Experimental Brain Research** (11) – Experimental Gerontology (2) – Frontiers in Aging Neuroscience (10) – Frontiers in Behavioral Neuroscience (1) – Frontiers in Human Neuroscience (1) – Frontiers in Neurology (1) – Frontiers in Psychology (3) – **Gait & Posture** (14) – Gerontology (1) – GeroScience (1) – **Human Brain Mapping** (5) – International Journal of Neuroscience (1) – International Journal of Sports Medicine (10) – IEEE Transactions on Neural Systems and Rehabilitation Engineering (2) – **Journal of Applied Physiology** (1) – Journal of Experimental Psychology Human Perception & Performance (2) – Journal of Motor Behavior (6) – **Journal of Neurophysiology** (21) – Journal of NeuroEngineering and Rehabilitation (2) – Journal of Neuroscience Methods (5) – Journal of Sports Sciences (2) – Journal of Sport Rehabilitation (3) – **Journals of Gerontology. Series A, Biological Sciences and Medical Sciences** (1) – Knee (2) – **Medicine & Science in Sports & Exercise** (1) – **Neurobiology of Aging** (4) – **NeuroImage** (1) – **Neurorehabilitation & Neural Repair** (1) – Neuroscience Letters (3) – **Neuroscience & Biobehavioral Reviews** (1) – Parkinson's Disease (1) – **Physical Therapy** (5) – Plos One (11) – Psychology & Aging (1) – Reviews in the Neurosciences (1) – Scientific Reports (2) – **Sports Medicine** (1).*

EDITORIAL ACTIVITIES

2019	**Section Editor**	Registered Reports in Kinesiology
2019	**Section Editor**	Communications in Kinesiology
2018 – 2019	**Associate Editor**	Advances in Cognitive Psychology
2018 – 2019	**Review Editor**	Frontiers in Public Health
2016 – 2019	**Review Editor**	Frontiers in Psychology
2014 – 2019	**Review Editor**	Frontiers in Aging Neuroscience

ADMINISTRATIVE RESPONSIBILITIES IN OPEN SCIENCE

2018 – 2019	**Steering board member**, SportRχiv, the preprint repository for Movement Science research
2019	**Co-chair**, Society for Transparency, Openness, and Replication in Kinesiology (**STORK**)

MEDIA

2019

Belgium – De Morgen; RTBF – **Canada** – Centre for Active Living; Huffington Post Québec; The Thunderbird – **France** – Actu.fr; Cerveau & Psycho; France Info; Ouest France; Psychologies; Science & Vie; Slate; Sud Ouest; Université Grenoble Alpes; Yahoo! Actualités – **India** – Thenga Kola – **Italy** – MSD Salute – **Switzerland** – La Chronique des Sciences – **UK** – Institute for Optimal Nutrition – **USA** – FiveThirtyEight; Runner's World.

2018

Argentina – Bioguía; Clarín; Infobae; LM Neuquén; LV12 Radio; MDZ online; Orfeo FM; Sanjuan8 – **Australia** – Mind Food; Nine; Science Alert; Ten Daily – **Austria** – Die Presse; Kronen Zeitung – **Belgium** – KU Leuven News – **Bolivia** – Diario Opinión; Eju! – **Bosnia and Herzegovina** – The Bosnia Times – **Brasil** – BBC News; Bem Estar; BOL;CicloVivo; Estadão; HuffPost; Mega Curioso; Rádio 92FM; Site Miséria; Superinteressante; Terra Brasil; Tivinet; Veja – **Canada** – 660News; 770 CHQR; Aldergrove Star; As It Happens; Black Press; CBC; CFAX1070; Crag & Canyon; CTV; Daily Hive; Digital Journal; Edmonton Journal; Great Lakes Ledger; HuffPost; Les éclaireurs; L'actualité; La Presse; MétéoMédia; Métro Montréal; Ontario Morning; OZFM; Phare Ouest; Radio Canadá Internacional; Research2Reality; The Loop; The Star; The Whig-Standard; UBC News; Vancouver is Awesome; Yahoo News – **Chile** – Página 7 – **China** – Sohu; Yangtse – **Columbia** – Opinión Caribe; W Radio – **Croatia** – PRVI – **Cuba** – Cubahora; Radio Angulo – **Dominican Republic** – Acento – **Egypt** – Scientific American – **El Salvador** – La Noticia – **Finland** – Ilta-Sanomat; MTV – **France** – Futura Sciences; Le Bonbon; Numerama; Santé log; Slate; Terrafemina; Vital – **Germany** – aio; Fit For Fun; Focus Online – **Greece** – El; HuffPost; Mother –

Honduras – HRN – **Hong Kong** – Ezone – **Hungary** – 24HU; Nepszava – **India** – Business Standard; DNA; Financial Express; Indiatimes; Reporter; The Hindu; The Indian Express; The Times of India; Yahoo News – **Indonesia** – Liputan6; Suara – **Israel** – IsraLand – **Italy** – AgoraVox; ANSA; Il Secolo XIX; La Repubblica; La Stampa; OggiScienza; Sky tg24; Televenezia; TiscaliNews; Vanity Fair; Wired – **Japan** – The Mainichi – **Kenya** – Daily Nation – **Lebanon** – Al Mayadeen Español – **Mexico** – Cambio Digital; Colimanoticias; Diario de Yucatán; El Semanario; El Siglo de Torreón; New York Times en Español; Noticieros Televisa; Periódico Central – **Netherlands** – Famme; Welingelichte Kringen – **Norway** – Forskning.no; National Geographic – **Peru** – El Comercio – **Philippines** – MSN – **Poland** – Rzeczpospolita; Zet News; TVN Meteo; Nauka w Polsce; Aleteia; Chillizet; Onet – **Russia** – Вести.Ru – **Singapore** – The Business Times; The Independent – **Slovakia** – Denník N; Info.sk; Živé – **South Africa** – Independent Online – **Spain** – Amazings; La Razon; La Verdad; Tendencias21; TICbeat; Ideal; MUY Interesante; Yahoo Actualidad – **Switzerland** – Avis d'experts; Interpharma; La Tribune de Genève; Le Matin Dimanche; Léman Bleu; RTS; Swissinfo; UNIGE News – **Taiwan** – Cast Net; ETtoday; TechNews – **Turkey** – Bilim ve Ütopya; Sabah; Sözcü – **UK** – 2 New Things; BBC News Mundo; Daily Mail – **United Arab Emirates** – Gulf News – **USA** – Aaptiv; Aleteia; Arkansas Democrat Gazette; Big Think; BioSpace; Biz Women; Bustle; BYUradio; Care2; CBS Boston News; CBS Minnesota; Duowei News; Elite Daily; ENN Environmental News Network; Inverse; KABC; KOMO; EurekAlert!; KREM 2 News; Medical Daily; Medical Xpress; MSN; Neuroscience News; New York Times; PR News; Psych Central; PsychScience; Reader's Digest; Sac Business Journal; Science Daily; Slash Gear; The Good Men Project; The Mission; thirdAGE; Tonic; Treehugger; Washington Post; WRAL News – **Venezuela** – Actualidad y Gente; Diario Panorama; Globovisión; Televen; Tenemos Noticias – **Vietnam** – Báo điện tử VTV; Soha.

KNOWLEDGE TRANSLATION

1-Cheval B**, Boisgontier M** (**2019**) Tous paresseux ? Cerveau & Psycho.
2-**Boisgontier M**, Cheval B (**2019**) Are we lazy, or just being efficient? The brain's struggle to avoid sedentary behaviours. WellSpring.
3-**Boisgontier M**, Cheval B (**2019**) Enquête aux sources de la paresse. Sport & Vie.
4-Cheval B, **Boisgontier M**, Sarrazin P (**2019**) Nous sommes programmés pour la paresse. The Conversation.

SKILLS

Brain Imaging	Voxel-Based Morphometry (VBM) Vertex Analysis (FSL FIRST) Diffusion Tensor Imaging (DTI)
Statistics	Hierarchical Models (Linear Mixed Models) Multilinear Logistic Regression Multiple Mediation Analysis Spline Analysis

LANGUAGES

French	Native
English	Working proficiency

BOOK CHAPTERS

4-**Boisgontier M**, Olivier I, Nougier V (**2012**) Effets d'une contrainte cognitive sur le contrôle proprioceptif des mouvements de la cheville des adultes jeunes et âgés. In: Defebvre L, Lacour M, eds. Du contrôle postural à l'exécution du mouvement (Coll. posture & équilibre). Marseille, France;Solal:pp175-188.

3-Théveniau N, **Boisgontier M**, Varieras S, Olivier I (**2012**) L'acquisition de la marche chez l'enfant : impact du port d'une tenue vestimentaire. In: Defebvre L, Lacour M, eds. Du contrôle postural à l'exécution du mouvement (Coll. posture & équilibre). Marseille, France;Solal:pp347-355.

2-**Boisgontier M**, Chenu O, Payan Y, Vuillerme N (**2011**) Le système nerveux central est-il capable d'intégrer une information artificielle linguale pour compenser une altération proprioceptive de la cheville induite par une fatigue musculaire ? In: Defebvre L, Lacour M, eds. Posture et Locomotion (Coll. posture & équilibre). Marseille, France;Solal:pp227-237.

1-Vuillerme N, **Boisgontier M** (**2010**) Impact de la fatigue musculaire des fléchisseurs plantaires sur le contrôle de la posture bipédique et les capacités proprioceptives de la cheville. In: Julia M, Perrey S, Dupeyron A, et al., eds. Fatigue musculaire (Coll. pathologie locomotrice & médecine orthopédique). Paris, France;Masson Elsevier:pp36-45.

INVITED PRESENTATIONS

2-**Boisgontier MP** (**2019**) Paradoxe de l'activité physique – Approche neuroscientifique. *Université Catholique de Louvain*, Belgium.

1-**Boisgontier MP** (**2019**) A neuro-psycho-epidemiological approach to the exercise paradox. *Ben Gurion University*, Israel.

CONFERENCE PRESENTATIONS

31-Cheval B, **Boisgontier MP** (**2019**) Avoiding sedentary behaviors requires more brain resources: an EEG study. Association des Chercheurs en Activités Physiques et Sportives (ACAPS).

30-Bonifazi P, Erramuzpe A, Diez I, Gabilondo I, **Boisgontier MP**, Pauwels L, Stramaglia S, Swinnen SP, Cortes J (**2019**) Structure–function multi-scale connectomics reveals a major role of the fronto-striato-thalamic circuit in brain aging. *Organization for Computational Neurosciences* (OCNS).

29-Schmidt RE, Sieber S, Cheval B, **Boisgontier MP**, Kliegel M, Blane D, Courvoisier DS, Kelly-Irving M, Kraehenmann R, Guessous I, Burton-Jeangros C, Stéphane Cullati S (**2019**) Early parental loss predicts late life sleep problems: evidence from the Longitudinal Survey of Health, Aging, and Retirement in Europe. *World Congress of Behavioural Cognitive Therapies* (WBCBCT).

28-Cheval B, **Boisgontier MP**, Bacelar M, Feiss R, Zona V, Miller M (**2019**) Does lower energy expenditure increase reward pursuit and reward-related cerebral cortical activity? *The North American Society for the Psychology of Sport and Physical Activity* (NASPA).

27-Cheval B, **Boisgontier MP** (**2019**) Are we wired to sit? Automatic neuro-behavioral reactions to exercise-related stimuli. *The European Federation of Sport Psychology* (FEPSAC).

26-Peters S, Neva JL, Brown KE, **Boisgontier MP**, Boyd LA (**2018**) Acute exercise modulates excitability of M1 interneurons indexed by anterior-to-posterior induced current. *Society for Neuroscience* (SfN).

25-Cheval B, Courvoisier DS, Cullati S, **Boisgontier MP** (**2018**) Effect of early- and adult-life socioeconomic circumstances on the risk of physical inactivity in older age. *Société Française de Psychologie du Sport* (SFPS).

24-Cheval B, Sarrazin P, **Boisgontier MP**, Radel R (**2018**) Temptations toward sedentary behaviors automatically activate physical activity goals in successful exercisers. *Société Française de Psychologie du Sport* (SFPS).

23-Cheval B, Chabert C, Orsholits D, Sieber S, Guessous I, Blane D, Kliegel M, Janssens JP, Burton-Jeangros C, Pison C, Courvoisier DS, **Boisgontier MP**, Cullati S (**2018**) Disadvantaged early-life socioeconomic circumstances are associated with low respiratory function at older ages. *Society for Longitudinal and Life Course Studies* (SLLS).

22-Cheval B, Orsholits D, Sieber S, Guessous I, Blane D, Kliegel M, Burton-Jeangros C, Courvoisier DS, Kelly-Irving M, **Boisgontier MP**, Cullati S (**2018**) The gendered effect of adverse childhood experiences on muscle strength. *Society for Longitudinal and Life Course Studies* (SLLS).

21-von Arx M, **Boisgontier MP**, Cheval C, Sieber S, Kliegel M, Gabriel R, Blane D, Courvoisier D, Guessous I, Burton-Jeangros C, Cullati S (**2018**) Disadvantageous childhood socioeconomic circumstances are associated with higher levels of depression in old age. *Congrès International Francophone de Gérontology et Gériatrie* (CIFGG).

20-**Boisgontier MP**, Cheval B, Chalavi S, van Ruitenbeek P, Leunissen I, Levin O, Nieuwboer A, Swinnen SP (**2017**) Brainstem and basal ganglia structure predicts postural control and balance loss in young and older adults. Society for the Neural Control of Movement (NCM).

19-**Boisgontier MP**, Levin O, van Ruitenbeek P, Swinnen SP (**2017**) Aging in the motor system and the reward pathway: on the role of the nucleus accumbens in action selection. *The European Cognitive Aging Society* (EUCAS).

18-Cheval B, Gourlan M, Sieber S, **Boisgontier MP**, Courvoisier DS, Cullati S (**2017**). Predictive value of childhood and adulthood socioeconomic position on physical activity. *European Health Psychology Association* (EHPS).

17-Cheval B, Sieber S, Guessous I, Gabriel R, Stringhini S, Blane D, Courvoisier DS, **Boisgontier MP**, Kliegel M, Burton-Jeangros C, Cullati S (**2017**) The predictive value of childhood socioeconomic position on grip strength: the mediating role of education and main occupation class. *Society for Longitudinal Studies and Life Course Studies International* (SLLS).

16-**Boisgontier MP**, Cheval B, van Ruitenbeek P, Chalavi S, Leunissen I, Renaud O, Levin O, Nieuwboer A, Swinnen SP (**2016**) Structures cérébrales prédictives de la performance posturale des adultes jeunes et âgés. *Société Francophone Posture Equilibre Locomotion* (SOFPEL).

15-**Boisgontier MP**, Cheval B, van Ruitenbeek P, Levin O, Renaud O, Chanal J, Swinnen S (**2015**) Matière grise et contrôle de l'équilibre au cours du vieillissement. Association des Chercheurs en Activités Physiques et Sportives (ACAPS).

14-Levin O, Van Halewyck F, Lavrysen A, **Boisgontier MP**, Elliott D, Helsen W (**2015**) Do sedentary older adults "play it safe"? Evidence from studies on manual aiming in active and sedentary older adults. *Active Healthy Aging* (AHA).

13-Moineau B, **Boisgontier M**, Gailledrat E, Olivier I, Palluel E, De Angelis MP, Pérennou D, Nougier V (**2014**) Comportement postural chez les amputés transfémoraux et désarticulés de hanche. *Société Française de Médecine Physique et de Réadaptation* (SOFMER).

12-**Boisgontier M**, Olivier I, Nougier V (**2012**) Aging of ankle proprioceptive control. *International Society for Posture and Gait Research* (ISPGR).

11-**Boisgontier M**, Olivier I, Nougier V (**2012**) Effects of ageing on attentional cost and internal models of proprioceptive control of movement. *Society for the Neural Control of Movement* (NCM).

10-**Boisgontier M**, Olivier I, Nougier V. Presbyproprioception ? (**2011**) Les effets du vieillissement sur les aspects comportementaux et attentionnels de la proprioception. *Journées Annuelles de la Société Française de Gériatrie et Gérontologie* (SFGG).

9-**Boisgontier M**, Olivier I, Chenu O, Nougier V (**2011**) Les effets du vieillissement physiologique sur le contrôle proprioceptif. *Association Posture-Equilibre* (APE).

8-**Boisgontier M**, Nougier V (**2010**) Superimposed neuromuscular electrical stimulation to recover range of motion at the hand. *European Society for Physical and Rehabilitation Medicine* (ESPRM).

7-**Boisgontier M**, Moineau B, Cuisinier R, Pinsault N, Nougier V (**2010**) Effects of electrical stimulation superimposed to voluntary muscular contraction on muscular endurance. *European Society for Physical and Rehabilitation Medicine* (ESPRM).

6-**Boisgontier M**, Emprin M, Vuillerme N, Iversen MD (**2010**) Superimposed neuromuscular electrical stimulation effects on maximal voluntary contraction. *European Society for Physical and Rehabilitation Medicine* (ESPRM).

5-Pinsault N, Chenu O, **Boisgontier M**, Payan Y, Demongeot J, Vuillerme N (**2008**) Improving weight bearing asymmetry in unilateral lower limb amputees by use of an insole pressure sensor-based electro-tactile biofeedback system. *International Posture Symposium*.

4-Vuillerme N, **Boisgontier M** (**2010**) Impact de la fatigue musculaire des fléchisseurs plantaires sur le contrôle de la posture bipédique et les capacités proprioceptives de la cheville. *Société Française de Médecine Physique et de Réadaptation* (SOFMER).

3-**Boisgontier M**, Vuillerme N (**2009**) Altération des capacités proprioceptives au niveau de la cheville induite par un exercice musculaire fatigant les fléchisseurs plantaires. Association Posture-Équilibre (APE).

2-Vuillerme N, **Boisgontier M**, Pinsault N (**2007**) Effets d'une fatigue musculaire unilatérale des fléchisseurs plantaires sur le contrôle de la posture bipédique. *Association des Chercheurs en Activités Physiques et Sportives* (ACAPS).

1-Vuillerme N, Pinsault N, **Boisgontier M**, Chenu O, Demongeot J, Payan Y (**2007**) Suppléance perceptive par électrostimulation linguale pour la correction de l'asymétrie posturale chez la personne amputée du membre inférieur. *Association Posture-Equilibre* (APE).

2. RESEARCH AND SUPERVISION

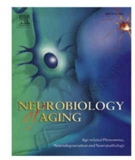
2.1. OVERVIEW

Research

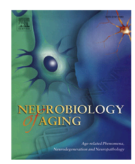
e

To provide an overview of my postdoctoral research, I have selected 10 representative articles published in peer-reviewed international journals during the past 5 years. I describe how these articles demonstrate the skills and knowledge I have developed during these years.

Article 1: Boisgontier MP, Cheval B, Chalavi S, van Ruitenbeek P, Leunissen I, Levin O, Nieuwboer A, Swinnen SP (**2017**) Individual differences in brainstem and basal ganglia structure predict pos tural control and loss of balance in young and older adults. Neurobiology of Aging. 50:47–59.

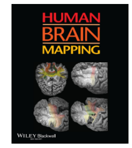


Article 2: Boisgontier MP, Cheval B, van Ruitenbeek P, Cuypers K, Sunaert S, Meesen R, Zivari Adab H, Renaud R, Swinnen SP (**2018**) Cerebellar grey matter explains bimanual coordination performance in children and older adults. Neurobiology of Aging. 65:109-120

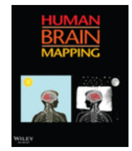


These articles demonstrate my ability to run state-of-the-art imaging and statistical analyses. I used the FreeSurfer automated segmentation, Voxel-Based Morphometry protocol (FSL VBM), a spatially unbiased atlas template of the cerebellum and brainstem (SUIT), and the FMRIB's Integrated Registration Segmentation Toolkit (FSL FIRST), which was specifically designed to provide accurate and robust segmentation of the basal ganglia. From a theoretical point of view, the results highlighted the importance of the brainstem (**Article 1**) and the cerebellum (**Article 2**) in postural control and bimanual coordination, respectively.

Article 3: Boisgontier MP, van Ruitenbeek P, Leunissen I, Chalavi S, Sunaert S, Levin O, Swinnen SP (**2016**) Nucleus accumbens and caudate atrophy predicts longer action selection times in young and old adults. Human Brain Mapping. 37:4629-4639.



Article 4: Corporaal SHA, Gooijers J, Chalavi S, Cheval B, Swinnen SP, **Boisgontier MP** (**2017**) Neural predictors of motor control and impact of visuo-proprioceptive information in youth. Human Brain Mapping. 38:5628-5647.



In these articles, I combined imaging results based on FSL FIRST and VBM analyses with linear mixed models. Results of **Article 3** showed that inward deformation (i.e., local atrophy) of the basal ganglia were predictive of longer action selection times, thereby suggesting that these grey matter nuclei were not only associate with the reward value of a stimulus but also with the brain processes preparing actions towards (or away from) this stimulus. Results of **Article 4**, which is first-authored by my former PhD student, Dr. Sharissa Corporaal, showed that manual tracking performance in youth does not solely rely on brain regions involved in sensorimotor processing, but also on prefrontal regions involved in attention and working memory.

Article 5: Boisgontier MP, Cheval B (**2016**) The anova to mixed model transition. Neuroscience & Biobehavioral Reviews. 68:1004–1005.

This commentary demonstrates my willingness to adopt the most appropriate methods, question the traditional approaches, and encourage the scientific community to be dynamic and follow the same path. Specifically, we urge neuroscientists to operate a transition towards mixed models because the requirements for using traditional analyses of variances are often not met and mixed models clearly provide a better framework.

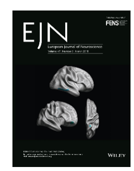
Article 6: Boisgontier MP (**2015**) Motor aging results from cerebellar neuron death. Trends in Neurosciences. 38:127–128.

This opinion article demonstrates my ability to propose novel ideas and conceptual approaches on timely topics. Specifically, I report consistent neurobehavioral evidence from animals and humans supporting the hypothesis that motor aging is primarily determined by an early death of neurons in the cerebellum.

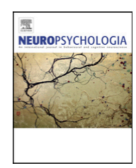
Article 7: Maes C, Gooijers J, Orban de Xivry JJ, Swinnen SP, **Boisgontier MP** (**2017**) Two hands, one brain, and aging. Neuroscience & Biobehavioral Reviews. 75:234-256.

Article 8: Cheval B, Radel R, Neva JL, Boyd LA, Swinnen SP, Sander D, **Boisgontier MP** (**2018**) Behavioral and neural evidence of the rewarding value of exercise behaviors: a systematic review. Sports Medicine. 48:1389-1404.

These review articles demonstrate my ability to synthesize the existing literature to produce additional knowledge. In **Article 7**, we show that aging is associated with cortical hyper-activity and subcortical hypo-activity during performance of bimanual tasks. In **Article 8**, we review studies testing the automatic reactions triggered by stimuli associated with different types of exercise behavior (i.e., physical activity, sedentary behaviors). We also examined evidence supporting the hypothesis that behaviors minimizing energetic cost are rewarding.



Article 9: Zivari Adab H, Chalavi S, Beets IAM, Gooijers J, Leunissen I, Cheval B, Collier Q, Sijbers J, Jeurissen B, Swinnen SP, **Boisgontier MP** (**2018**) White matter microstructural organization of interhemispheric pathways predict different stages of bimanual coordination learning in young and older adults. European Journal of Neuroscience. 47:446-459.



Article 10: Cheval B, Tipura E, Burra N, Frossard J, Chanal J, Orsholits D, Radel R, **Boisgontier MP** (**2018**) Avoiding sedentary behaviors requires more cortical resources than avoiding physical activity: an EEG study. Neuropsychologia. 119:68-80.

These articles show my ability to mentor postdoctoral researchers. In **Article 9**, we used diffusion weighted imaging and probabilistic constrained spherical deconvolution-based tractography to explain bimanual coordination learning in young and older adults. In **Article 10**, we used electroencephalography (EEG) to investigate the brain processes underlying the automatic attraction to sedentary behaviors.

Supervision

I have been fortunate to supervise one **PhD student** at KU Leuven (Belgium), Dr Sharissa Corporaal, who was a doctoral fellow of the Research Foundation – Flanders (FWO). She successfully defended her thesis publicly on December 8, 2017. Her thesis was a two-folded project investigating the brain correlates of gait and bimanual coordination. Based on her work, Dr Sharissa Corporaal published articles in highly-ranked and recognized journals.

- **Corporaal SHA** (2017) Brain substrates of sensorimotor control during upper and lower limb coordination in youth.

Although not officially, I have been significantly involved in the **doctoral theses** of Dr Florian Van Halewyck (KU Leuven, Belgium; 4 co-authored articles) and Dr Bastien Moineau (Université Grenoble Alpes, France; 4 co-authored articles).

- **Moineau B** (2014) Analyses des pressions à l'interface moignon-emboiture de la prothèse chez le patient amputé fémoral.
- **Van Halewyck F** (2014) Active aging and visuomotor control of manual aiming movements.

I supervised the thesis of **8 master's students** in the field of sensorimotor control of movements in children, young adults, and older adults.

- **Beelprez J, Albers M** (2017) Effects of amplitude on the age-related proprioceptive deficit
- **Bels L** (2015) Age-related changes in central processing of simple and choice multilimb reaction-time tasks in children and adolescence aged 8 to 18 years old.
- **Buttiens L** (2014) Effects of destabilization frequencies on postural stability in young and older adults.
- **Rolly C** (2014) Are visual and proprioceptive controls of movement equally affected by aging?
- **Ternest J, Rossaert L** (2015) The evolution of the perception-action cycle in children and adolescence aged 8 to 18 years old: evidence from a bimanual sensory tracking task.
- **Van Empten B** (2016) Effects of limb dominance on the perception-action cycle in bimanual tracking movements.

2.2. BIMANUAL COORDINATION

Many activities of daily living require moving both hands in an organized manner in space and time. In everyday functioning, bimanual movements occur twice as often as unimanual movements (Rinehart et al., 2009) and they serve as a critical marker of functional independence. This importance of bimanual skills in daily activities calls for a better understanding of how bimanual performance changes over the lifespan. Because these bimanual skills develop spontaneously during childhood, we consider them as easy and take them for granted. However, these skills depend on sophisticated neural interactions between brain hemispheres that are affected by aging. Bimanual coordination tasks (Figure 1) are a unique vehicle for investigating these interactions and prolonging functional independence and well-being in older adults.

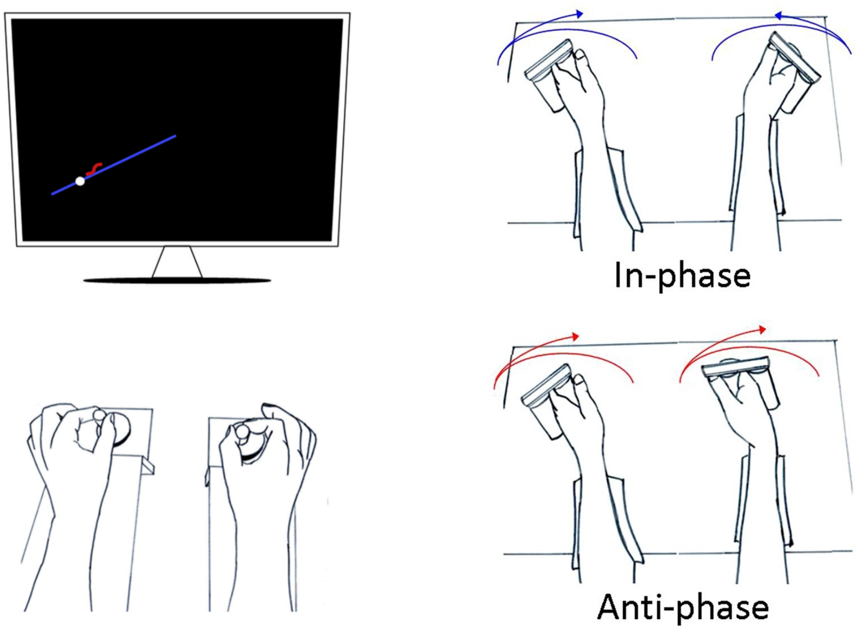


Figure 1. Bimanual coordination tasks. Left Panel: Participants are instructed to track a white target dot moving along a blue line on a screen by rotating the dials with the thumb and index finger according to specific coordination patterns and frequency ratios without vision of the upper limbs. As they rotated the dials, a red cursor moves on the screen to provide online visual feedback. Right Panel: 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.

Bimanual coordination and brain activity

In a review article, we noticed that aging may be associated with cortical hyper-activity and subcortical hypo-activity during performance of bimanual tasks (Maes et al., 2017). This age-related subcortico-cortical activation shift suggested that age-related cortical hyper-activity compensated for subcortical hypo-activity to prevent bimanual performance decline (Figure 2). In addition to these local activation changes, which were later supported by one of our experimental articles (Santos Monteiro et al., 2017), the results of the review article suggested that an age-related increase of functional connectivity in the resting brain could explain the age-related decline in bimanual coordination. This suggestion was confirmed one year later by King et al. (2018), who showed that stronger internetwork resting state connectivity observed as a function of age was significantly related to worse motor performance.

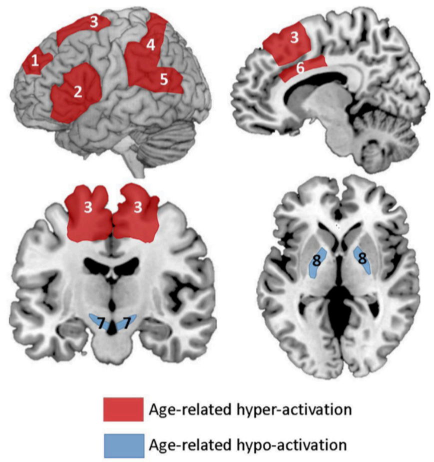


Figure 2. Age-related subcortico-cortical activation shift. Older adults show functional hyper-activation of the dorsolateral prefrontal cortex (1), inferior frontal gyrus (2), supplementary motor area (3), secondary somatosensory area (4), Inferior parietal cortex (5) and cingulate cortex (6), and functional hypo-activation of the subthalamic nucleus (7) and globus pallidus (8).

Bimanual coordination and the cerebellum

In an experimental article (Boisgontier et al., 2018), we investigated whether, as hypothesized earlier (Boisgontier, 2015), the cerebellum was a stronger predictor of bimanual coordination performance than other regions of interest in 109 participants aged 10 to 80 years. The regions of interest (Figure 3) were determined based on a separate dataset collected in studies of our group, where participants performed a similar bimanual coordination task (Beets et al., 2015; Chalavi et al., 2018; Santos

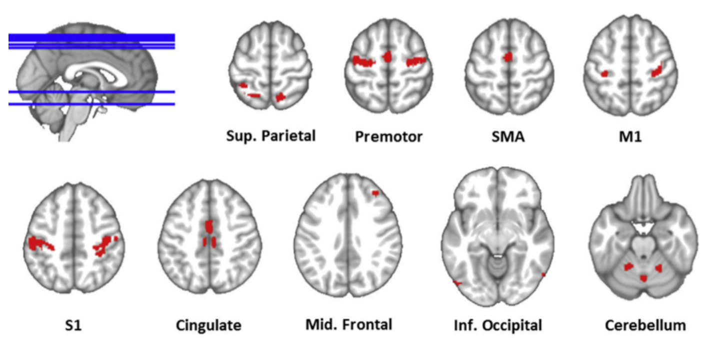


Figure 3. Regions of interest. Cerebellum = lobule VI; Inf. Occipital = bilateral inferior occipital cortex; M1 = bilateral primary motor cortex; Mid. Frontal = right middle frontal cortex; S1 = bilateral primary somatosensory cortex; SMA = supplementary motor area; Sup. Parietal = superior parietal cortex.

Monteiro et al., 2017). Results showed that in participants aged 10 to 20 years, the cerebellum was the only significant brain predictor of bimanual coordination performance. In participants aged 60 to 80 years, the cerebellum, together with the M1 and S1, also formed a group of the strongest predictors of performance. From a behavioral perspective, this study also revealed that bimanual coordination performance starts declining from the age of 40 years (Figure 4).

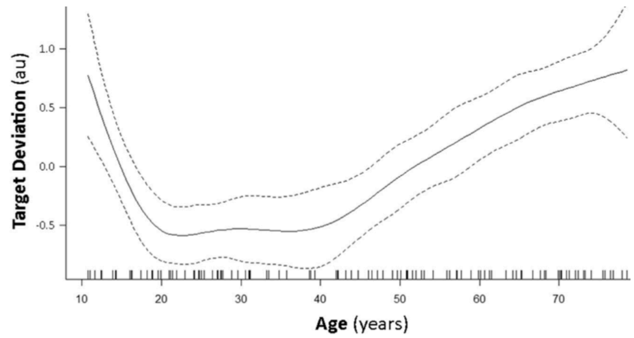


Figure 4. Effect of age on bimanual coordination performance over the lifespan. The effect and 95% confidence interval of continuous age on the Box-Cox transformed target deviation aggregated over the conditions were tested using spline smoothing. au = arbitrary unit.

Bimanual coordination learning and white matter microstructural organization

The ability to learn new motor skills is essential for activities of daily living, especially in older adults. Previous work in younger adults has indicated fast and slow stages for motor learning that were associated with changes in functional interactions within and between brain hemispheres. However, the impact of the structural scaffolds of these functional interactions on different stages of bimanual coordination learning were missing. In an experimental study (Zivari Adab et al., 2018), we used diffusion-weighted imaging and probabilistic constrained spherical deconvolution-based tractography to reconstruct transcallosal white matter pathways (Figure 5) between the left and right primary motor cortices (M1– M1), left dorsal premotor cortex and right primary motor cortex (LPMd–RM1) and right dorsal premotor cortex and left primary

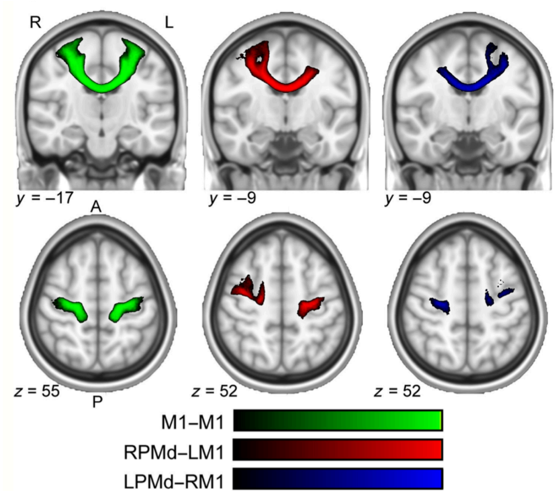


Figure 5. White matter microstructural organization of pathways of interest. Sagittal and axial slices of population maps across young and older adults for M1–M1 (left panel), RPMd–LM1 (middle panel) and LPMd–RM1 (right panel) pathways are overlaid on the MNI T11mm template. Color bars indicate the number of subjects (n) showing overlap of the individual pathways. For visualization purposes, images were thresholded to show only voxels common to at least 10 participants.

motor cortex (RPMd–LM1) in younger and older adults trained in a set of bimanual coordination tasks (Figure 1, left panel, and Figure 6). We used fractional anisotropy to assess microstructural organization of the reconstructed white matter pathways. Results showed that age determines the learning gains in the fast and slow learning stages with larger absolute performance improvement in older adults during the fast stage and in young adults during the slow learning stage. Results also showed that higher fractional anisotropy of the M1–M1 pathway predicted larger performance gain in the fast stage of bimanual learning, whereas higher fractional anisotropy of the RPMd–LM1 pathway predicted higher gain in the slow stage, irrespective of age. These results suggest that, in both young and older adults, the M1–M1 and RPMd–LM1 pathways are important for the fast and slow stage of bimanual learning, respectively.

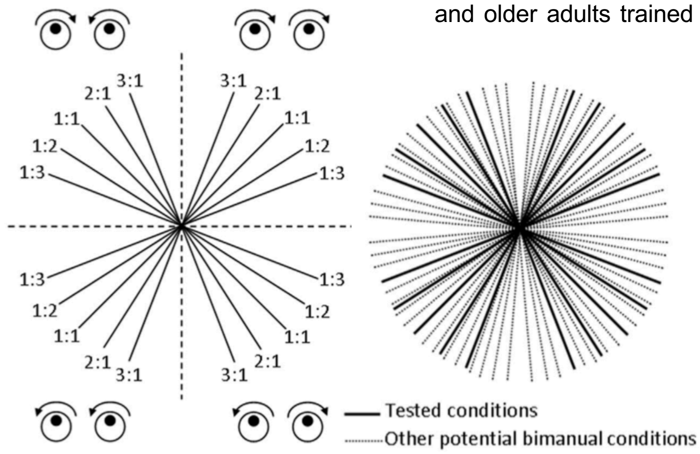


Figure 6. Coordination conditions. Left panel: Bimanual coordination patterns corresponding to the target line direction were tested: inward, outward, clockwise, and counter-clockwise hand rotation. The left hand and the right hand controlled movements on the ordinate axis and abscissa axis, respectively. Each pattern was performed according to 5 frequency ratios: 1:1, 1:2, 1:3, 2:1, and 3:1 (left hand : right hand), resulting in 20 different conditions. Right panel: Treating conditions as random in the linear mixed models allows to generalize the results to all potential conditions (grey lines), not only to the conditions that were actually tested (black lines).

Bimanual coordination and linear mixed models

When investigating bimanual coordination, the number of coordination modes that can be tested is limited. In the task illustrated in Figure 1 (left panel), participants were tested in 20 conditions. Linear mixed models (also known as hierarchical models) allow to treat both participants and conditions as random effects, thereby generalizing the results not only to the population of participants but also to the population of conditions. A transition towards mixed models is underway in science (Figure 7). This transition started up because the requirements for using analyses of variances are often not met

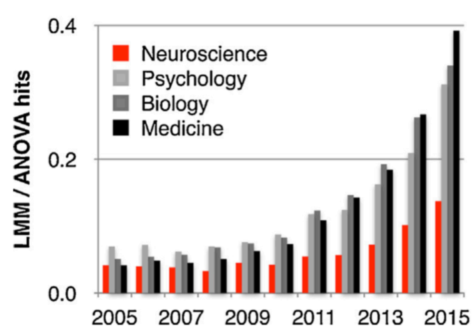


Figure 7. Ratio of “mixed effect” or “mixed model” over “ANOVA” hits when associated with “neuroscience”, “psychology”, “biology”, or “medicine” in a Google Scholar search.

and mixed models clearly provide a better framework. Neuroscientists have been slower than others in changing their statistical habits and are now urged to act (Boisgontier and Cheval, 2016).

References

Beets IAM, Gooijers J, Boisgontier MP, Pauwels L, Coxon JP, Wittenberg G, Swinnen SP (2015) Reduced neural differentiation between feedback conditions after training bimanual coordination with and without augmented visual feedback. Cerebral Cortex. 25:1958-1969.

Boisgontier MP (2015) Motor aging results from cerebellar neuron death. Trends in Neurosciences. 38:127-128.

Boisgontier MP, Cheval B (2016) The anova to mixed model transition. Neuroscience & Biobehavioral Reviews. 68:1004-1005.

Boisgontier MP, Cheval B, van Ruitenbeek P, Cuypers K, Leunissen I, Sunaert S, Meesen R, Zivari Adab H, Renaud O, Swinnen SP (2018) Cerebellar grey matter explains bimanual coordination performance in children and older adults. Neurobiology of Aging. 65:109-120.

Chalavi S, Zivari Adab H, Pauwels L, Beets IAM, van Ruitenbeek P, Boisgontier MP, Santos Monteiro T, Maes C, Sunaert S, Swinnen SP (2018) Anatomy of subcortical structures predicts age-related differences in skill acquisition. Cerebral Cortex. 28:459-473.

King BR, van Ruitenbeek P, Leunissen I, Cuypers K, Heise KF, Santos Monteiro T, Hermans L, Levin O, Albouy G, Mantini D, Swinnen SP (2018) Age-related declines in motor performance are associated with decreased segregation of large-scale resting state brain networks. Cerebral Cortex. 28:4390-4402.

Maes C, Gooijers J, Orban de Xivry JJ, Swinnen SP, Boisgontier MP (2017) Two hands, one brain, and aging. Neuroscience & Biobehavioral Reviews. 75:234-256

Rinehart JK, Singleton RD, Adair JC, Sadek JR, Haaland KY (2009) Arm use after left or right hemiparesis is influenced by hand preference. Stroke. 40:545-550.

Santos Monteiro T, Beets IAM, Boisgontier MP, Gooijers J, Pauwels L, Chalavi S, King B, Albouy G, Swinnen SP (2017) Relative cortico-subcortical shift in brain activity but preserved training-induced neural modulation in older adults during bimanual motor learning. Neurobiology of Aging. 58:54-67.

Zivari Adab H, Chalavi S, Beets IAM, Gooijers J, Leunissen I, Cheval B, Collier Q, Sijbers J, Jeurissen B, Swinnen SP, Boisgontier MP (2018) White matter microstructural organization of interhemispheric pathways predicts different stages of bimanual coordination learning in young and older adults. European Journal of Neuroscience. 47:446-459.

Mentoring and supervision

- Mentoring of 1 postdoctoral researcher: Zivari Adab H.
- Mentoring of 1 PhD student: Maes C.
- Supervision of 3 master students: Ternest J, Rossaert L (2013 – 2015) The evolution of the perception-action cycle in children and adolescence aged 8 to 18 years old: evidence from a bimanual sensory tracking task; Van Empten B (2013 – 2016) Effects of limb dominance on the perception-action cycle in bimanual tracking movements.

2.3. ACTION SELECTION

Reaction time (RT) refers to the time elapsing between a stimulus and a physical change occasioned by the occurrence of the stimulus. RT is traditionally described by a Stimulus-Processing-Response framework whereby the brain's processing capacity mediates the relationship between the stimulus and the response, including stimulus identification, appropriate response selection, and response programming. RT is therefore considered to be an index of speed and efficiency of central processing. Three main types of RT can be differentiated. Simple RT tasks require the participant to respond to the presence of a single stimulus. Recognition RT tasks require the participant to respond when one specific stimulus appears and to withhold his response when other types of stimuli are presented. Choice RT tasks require distinct responses for each type of stimulus. Although cognitive aspects associated with RT have been studied intensively, only few studies have tested whether the particular combination of limbs affects task performance.

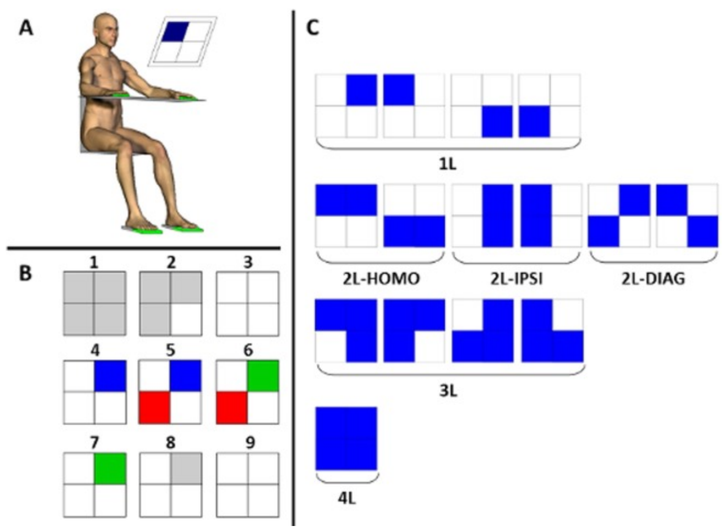


Figure 6. Multilimb reaction-time task. Panel A. Participants are seated in front of a PC screen, their forearms resting on a table and their fingers and forefeet on tablets with capacitive proximity switches (in green). Panel B. Example of a trial sequence represented on the PC screen. The right and left upper squares represent the right and left hands, respectively, whereas the right and left lower squares represent the right and left feet, respectively. (1) Squares are grey when limbs are not in contact with the tablets. (2) The squares turn white as soon as a limb contacts the corresponding tablet. (3) A trial starts as soon as all limbs are in contact with the tablets. (4) When a square on the PC screen turns blue, this is the stimulus for the participant to release contact with the corresponding tablet as quickly as possible. (5) If the participant lifts the incorrect limb(s), the corresponding square(s) turn(s) red. (6) If the participant lifts the correct limb(s), the corresponding square(s) turn(s) green. (7) A trial is not validated until the response is fully correct, i.e., without any red squares on the screen. (8) As soon as the trial is validated, the green squares turn back to grey. (9) The participant has to reposition all limb segments on the tablets to start a new trial. Panel C. Coordination modes and clusters. The 15 possible coordination modes grouped according to 5 clusters (1L, 2L-HOMO, 2L-IPSI, 2L-DIAG, 3L, 4L) based on the number of limbs to be recruited (1, 2, 3, or 4) and limb configuration. L = limb; DIAG = diagonal; IPSI = ipsilateral; HOMO = homologous.

Action selection and basal ganglia

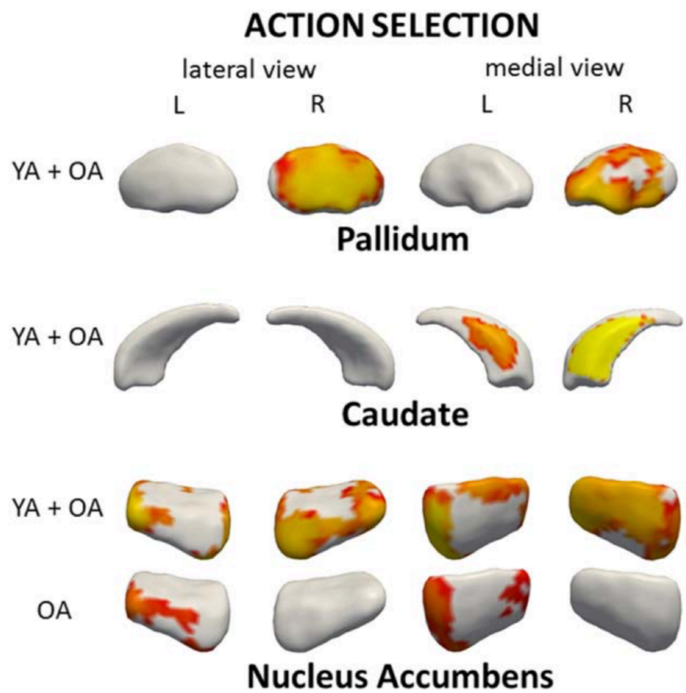


Figure 7. Association between performance in the most complex task conditions (normalized reaction time in 2L-DIAG and 3-L) and inward deformation (i.e., local atrophy) of the pallidum, caudate, and nucleus accumbens in young and old adults. YA = young adults; OA = older adults; L = left; R = right.

The selection of motor actions is fundamental to the survival of humans and other species. Therefore, action selection likely involves brain structures that were developed in primitive vertebrates and have been conserved throughout evolution, such as the basal ganglia. There is a convergence in the literature toward a critical role for the basal ganglia in action selection (Cisek and Kalaska, 2010). However, which substructures within the basal ganglia fulfill this role is still unclear. Young and older participants performed a multilimb RT tasks including the 15 possible configuration of limb recruitment (Figure 6; Boisgontier et al., 2016). We used shape analyses of structural magnetic resonance imaging data to determine the extent to which basal ganglia structures predict performance in easy and complex multilimb RT tasks in young and older adults. Behavioral results showed higher normalized RT and error rates in the 2L-DIAG and 3L conditions for both young and older adults. Moreover, the difference in performance between young and older adults, as assessed with normalized RT, was the largest in these two task conditions. These results suggested specific age-related impairment in processes underlying performance during these conditions. Imaging analyses and linear mixed models (Boisgontier and Cheval, 2016) revealed that local atrophy of the left caudate and left nucleus accumbens were predictive of performance in the most complex task conditions (Figure 7), but not in the easier conditions. This result suggested that the central processing dissociating the 2L-DIAG and 3L conditions from the other conditions was related to structural differences in caudate and nucleus accumbens grey matter.

Action selection and processing complexity in simple and choice multilimb reaction-times

Whether the relative weight of the selection process (i.e., which limb should react) and the recruitment process (i.e., how many limbs should react) in determining the overall complexity of a movement is dependent on the nature of the RT (simple vs. choice RT) was still unknown. Thirty-six young adults performed the multilimb RT task (Boisgontier et al., 2014). Simple, choice, and normalized (choice RT – simple RT) RT were analyzed. Simple and normalized RT were respectively assumed to be indicative of the recruitment and selection processes. Results in the different coordination modes suggested that recruitment complexity decreased as follows: 3 limbs = 4 limbs > 2 limbs (homologous, ipsilateral and diagonal) > 1 limb, and selection complexity as follows: 2 diagonal limbs > 3 limbs > 2 ipsilateral limbs.1 limb = 2 homologous limbs > 4 limbs. Based on these ordinal scales of recruitment and selection complexity, we extrapolated the overall processing complexity of the simple and choice multilimb RT. This method was efficient in reproducing the absolute results we obtained on a ratio scale (ms) and demonstrated that processing complexity in simple RT was mainly governed by the 'recruitment principle' (the more limbs recruited the lower the performance), whereas contributions of recruitment and 'selection principle' (nature of the coordination determines performance) to overall processing complexity were similar in choice RT (Figure 8).

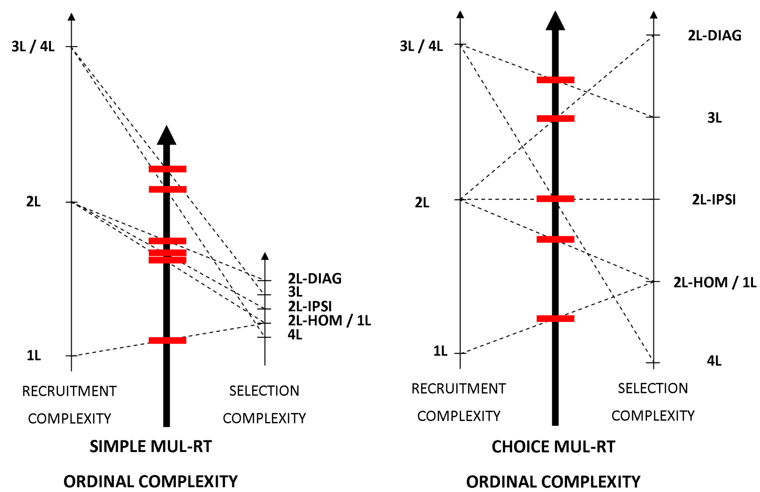


Figure 8. Relative contribution of the recruitment complexity and selection complexity to the overall complexity of simple (left panel) and choice RT (right panel). Overall ordinal complexity (middle bold arrow) is extrapolated from the association of the recruitment (left regular arrow) (4L=3L>2L>1L) and selection ordinal complexity (right regular arrow) (2L-DIAG>3L>2L-IPSI>1L=2L-HOM>4L). The arrows indicate the direction of increased complexity. The length of the arrows represents the relative contribution of each composite complexity to the overall complexity. This relative contribution determines the overall complexity of the different coordination conditions as indicated by red horizontal bars where dotted lines cross the bold arrow. In simple RT, the recruitment complexity contributes more than selection complexity. Accordingly, overall ordinal complexity in simple RT matches the pattern of recruitment complexity (4L=3L>2L>1L). In choice RT, the contribution of selection complexity increases (increased length of the selection complexity arrow). Accordingly, overall complexity in the choice RT (3L>2L-DIAG>4L = 2L-IPSI>2L-HOM>1L) is no longer solely governed by recruitment complexity but reflects a similar contribution from both composite complexities (similar length of the recruitment and selection arrows). The extrapolated overall complexity of the different coordination conditions matches the observed data observed (i.e., absolute RT measured in simple and choice RT). These results suggested that the overall complexity of a given coordination condition can be explained by a weighted combination of the recruitment and selection complexity. L = limb; DIAG = diagonal; IPSI = ipsilateral; HOM =

References

Boisgontier MP, Cheval B (2016) The anova to mixed model transition. Neuroscience & Biobehavioral Reviews. 68:1004-1005.

Boisgontier MP, van Ruitenbeek P, Leunissen I, Chalavi S, Sunaert S, Levin O, Swinnen SP (2016) Nucleus accumbens and caudate atrophy predicts longer action selection times in young and old adults. Human Brain Mapping. 37:4629-4639.

Boisgontier MP, Wittenberg G, Fujiyama H, Levin O, Swinnen SP (2014) Complexity of central processing in simple and choice multilimb reaction-time tasks. Plos One. 9: e90457.

Cisek P, Kalaska JF (2010) Neural mechanisms for interacting with a world full of action choices. Annual Review of Neuroscience. 33:269–298.

Supervision

- Supervision of 1 master student: Bels L (2013 – 2015) Age-related changes in central processing of simple and choice multilimb reaction-time tasks in children and adolescence aged 8 to 18 years old.

2.4. POSTURAL CONTROL AND FALLS

Falls are a leading cause of injury, affecting all age groups but older adults have higher mortality and hospitalization rates than young adults (Kennedy et al., 2001). In 2000, the incidence of fatal and nonfatal fall injuries in adults aged over 65 years in the United States was estimated at 10,300 and 2.6 million, respectively (Stevens et al., 2006). Accordingly, a better understanding of the neurobiological factors that underlie poor postural control that may result in falls is needed. Postural control is fundamental for preventing falls, for both young and older adults (Boisgontier et al., 2016). This becomes increasingly critical with aging, especially for prolonging functional independence and preventing falls that cause catastrophic injuries (Corso et al., 2015). Postural control involves a set of mechanisms (e.g., sensory integration, motor command generation, and muscle contraction) that stabilize the center of the total body mass relative to the support base. Balance is the state of equilibrium resulting from the ability of the postural control system to keep the vertical projection of the center of mass within the support base. The better controlled the posture, the less likely that balance will be lost.

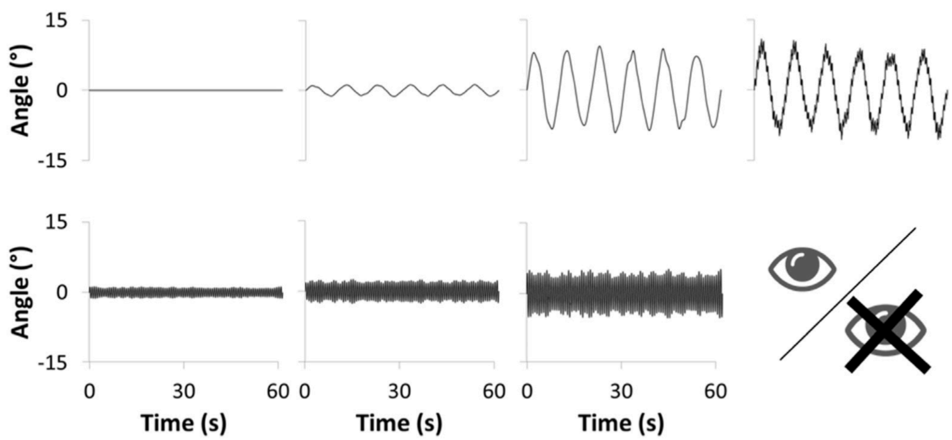


Figure 9. Balance disturbance patterns used in eyes open and eyes closed condition. Standing balance is tested on an Equitest balance platform. This dynamic postural system consists of a force platform (46×46 cm) that moves around a mediolateral axis and is equipped with force transducers to measure X, Y, and Z forces (Fx, Fy, and Fz) and X, Y, and Z moments (Mx, My, and Mz). Participants stand barefoot, with the medial malleoli of the ankles vertically aligned with the platform's axis of rotation. A safety harness is worn to prevent falls due to loss of balance. To fully assess balance performance, 7 balance disturbance conditions with different platform frequencies and mean amplitudes are tested in eyes open and eyes closed conditions. The 0.0 Hz – 0.0 deg couple (static) is the least challenging condition. The 0.1 Hz – 5.0 deg couple (very slow movement) is the most challenging condition in terms of movement perception. The 0.1 + 1.5 + 6.0 Hz – 5.0 deg couple is the most challenging condition in terms of triggering rapid corrective responses. The 4 remaining couples (0.1 Hz – 0.7 deg, 1.5 Hz – 0.7 deg, 1.5 Hz – 1.3 deg, and 1.5 Hz – 2.7 deg) are used to link the previously mentioned extreme couples: the challenge increased progressively with increasing amplitude and frequency.

Postural control and attentional resources

Dual-task designs have been widely used to study the degree of automatic and controlled processing involved in postural stability of young and older adults. However, several unexplained discrepancies in the results weakened this literature. To resolve this problem, a careful selection of dual-task studies that met specific methodological criteria were considered with respect to reported interactions of age (young vs. older adults) × task (single vs. dual task) in stable and unstable postural conditions. Our review article showed that in stable conditions older adults' performance in a postural dual task is similar to the ones of younger adults (Boisgontier et al., 2013). However, when the complexity of the postural task increases in dynamic conditions (surface and surround), performance in postural, concurrent, or both tasks is more affected in older compared to young adults. These results suggested an age-related increase in the recruitment of higher-level neural resources indicative of cognitive processing of posture during standing. The results also suggested that the sensitivity of a dual-task design to aging is increased when the challenges imposed by either the manipulation of the support surface condition or both the surface and the visual conditions increased.

Postural control, falls, and whole-brain grey matter

Functional and structural imaging studies have demonstrated the involvement of the brain to control standing balance. However, whether whole-brain grey matter density and white matter microstructural organization can explain balance stability in young and older adults remained unclear. Standing balance was tested on a platform moving at different frequencies and amplitudes (Figure 9) in 30 young and 30 older adults, with eyes open and with eyes closed. Centre of pressure variance was used as an indicator of balance instability. When a participant fell (held by the safety harness) or took a step to regain balance, the trial was recorded as a fall. The mean density of grey matter and mean white matter microstructural organization were measured using voxel-based morphometry and diffusion tensor imaging, respectively. Mixed-effects models (Boisgontier and Cheval, 2016) were built to analyze the extent to which age, grey matter density, and white matter microstructural organization predicted

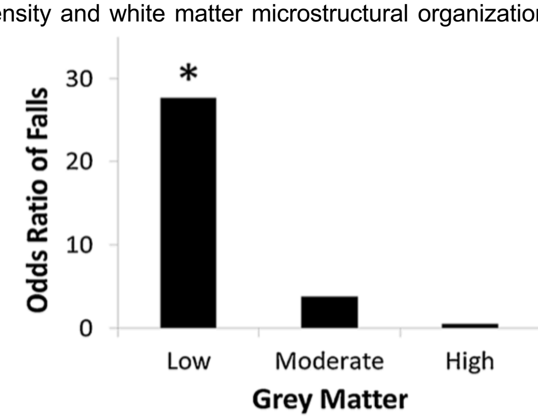


Figure 10. Odds ratio of falls between younger old adults and older old adults (mean age −1 SD; mean age +1 SD, respectively) as a function of brain grey matter density: low, moderate, and high (GM mean −1 SD; GM mean; GM +1 SD, respectively). *p < 0.05; GM = grey matter density; SD = standard deviation.

balance instability. Results showed that brain grey matter had a protective against falls in older adults with age increasing the probability of losing balance in older adults with low, but not moderate or high grey matter density (Figure 10; Boisgontier et al., 2016). Results also showed that both whole-brain grey matter density and age independently predicted balance instability (Figure 11). These predictions were reinforced when the level of difficulty of the conditions increased. Furthermore, grey matter predicted balance instability beyond age and at least as consistently as age across conditions. In other words, for balance stability, the level of whole-brain grey matter density is at least as decisive as being young or old. Finally, no such results were observed for white matter microstructural organization, thereby reinforcing the specificity of the grey matter findings.

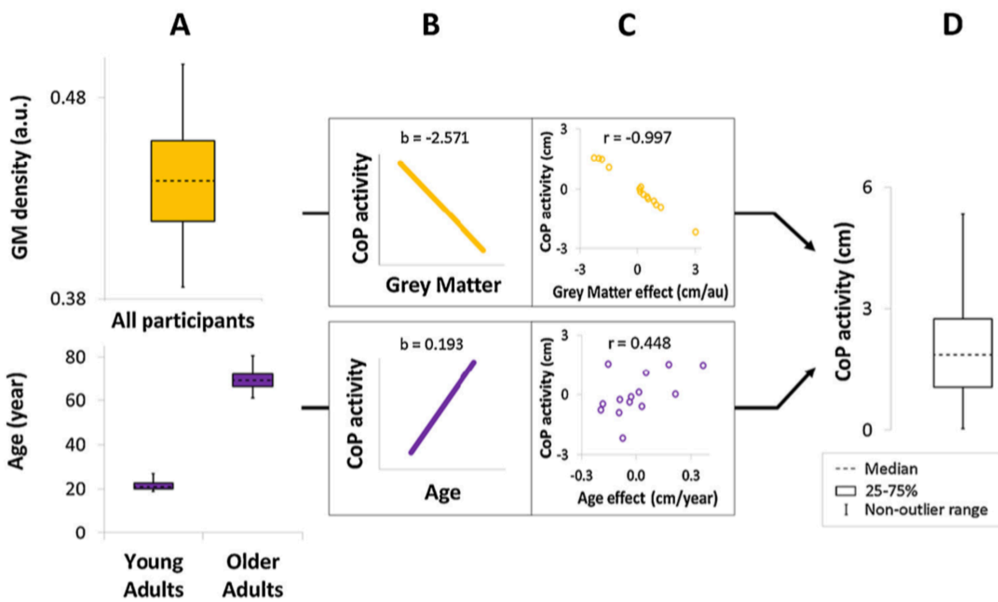


Figure 11. Fixed and random effects of age and grey matter density on postural stability. (A) Distributions of the whole-brain grey matter mean density (yellow box plot) and age (purple box plot) within the study sample. (B) Prediction of the fixed effect of grey matter (yellow line) and age (purple line). (C) Prediction of the random effect of grey matter (yellow circles), and age (young vs. older adults; purple circles) plotted against the random intercept of conditions, i.e., the predicted value of the center of pressure (CoP) activity. Each circle represents a condition (7 platform × 2 vision conditions). Both the negative effect of grey matter density and the positive effect of age on CoP activity were reinforced when the intercepts of the conditions increased, i.e., when the difficulty of the task increased. (D) Distribution of the CoP activity within the sample.

Postural performance, brainstem, and basal ganglia

It remained unclear which specific brain regions were the most critical for human postural control and balance. Therefore, we examined associations between postural performance and cortico-subcortical brain regions (Figure 12) in young and older adults using multiple structural imaging and linear mixed models (Boisgontier et al., 2017; Boisgontier & Cheval, 2016). Results showed that of the regions involved in posture, the brainstem was the strongest predictor of postural control and balance: lower brainstem volume predicted larger center of pressure deviation and higher odds of balance loss. Analyses of white and gray matter in the brainstem showed that the pedunculopontine nucleus area appeared to be critical for postural control in both young and older adults (Figure 13, left panel). In addition, the brainstem mediated the effect of age on postural control, underscoring the brainstem's fundamental role in aging. Conversely, lower basal ganglia volume predicted better postural performance, suggesting an association between greater neural resources in the basal ganglia and greater movement vigor, resulting in exaggerated postural adjustments (Figure 13, right panel). Finally, results showed that practice, shorter height and heavier weight (i.e., higher body mass index), higher total physical activity, and larger ankle active (but not passive) range of motion were predictive of more stable posture, irrespective of age.

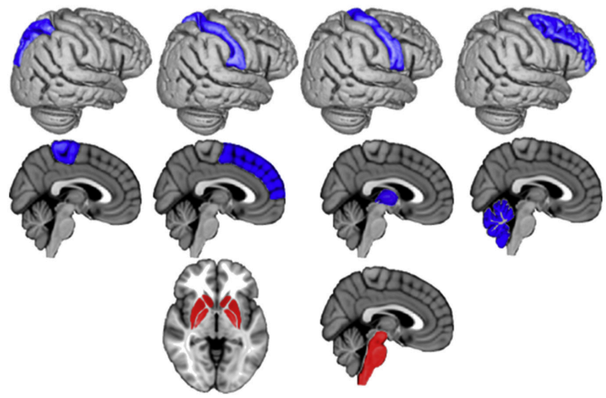


Figure 12. Brain regions that have been associated with postural performance in the literature and that were included in the linear mixed models. Structures that were predictive of the root mean square of the center of foot pressure time series on the anteroposterior axis (CoP RMSD) and of balance are in red (brainstem and basal ganglia). Structures that were not predictive are in blue.

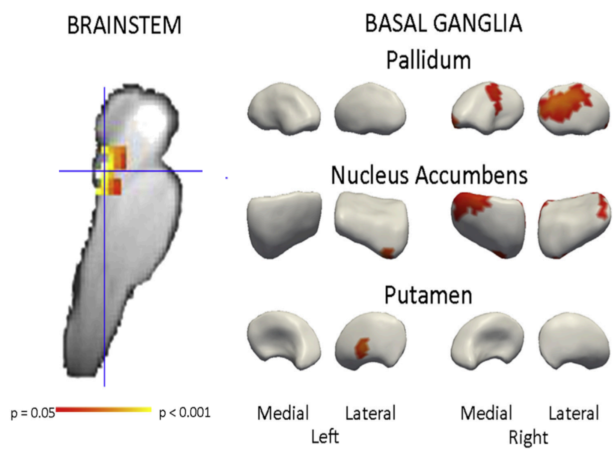


Figure 13. Brain imaging results. Left panel: Results of the voxelwise analysis based on the SUIT high-resolution atlas template of the brainstem showed a significant 110 voxel cluster associated with the center of pressure time series on the anteroposterior axis (CoP RMSD). Peak clusters were located in the area of the pedunculopontine nucleus. Right panel: Results of the vertex analysis testing the extent to which local deformations of the basal ganglia were predictive of CoP RMSD. Local expansion of the vertices was predictive of CoP RMSD in the right pallidum, bilateral nucleus accumbens, and left putamen. CoP = center of pressure; RMSD = root mean square deviation.

References

Boisgontier MP, Beets IAM, Duysens J, Nieuwboer A, Krampe RT, Swinnen SP (2013) Age-related differences in attentional cost associated with postural dual tasks: increased recruitment of generic cognitive resources in older adults. Neuroscience & Biobehavioral Reviews. 37:1824-1837.

Boisgontier MP, Cheval B (2016) The anova to mixed model transition. Neuroscience & Biobehavioral Reviews. 68:1004-1005.

Boisgontier MP, Cheval B, Chalavi S, van Ruitenbeek P, Leunissen I, Levin O, Nieuwboer A, Swinnen SP (2017) Individual differences in brainstem and basal ganglia structure predict postural control and loss of balance in young and older adults. Neurobiology of Aging. 50:47-59.

Boisgontier MP, Cheval B, van Ruitenbeek P, Levin O, Renaud O, Chanal J, Swinnen SP (2016) Whole-brain grey matter density predicts balance stability irrespective of age and protects older adults from falling. Gait & Posture. 45:143-150.

Kennedy RL, Grant PT, Blackwell D (2001) Low-impact falls: demands on a system of trauma management, prediction of outcome, and influence of comorbidities. Journal of Trauma. 51:717-724.

Stevens JA, Corso PS, Finkelstein EA, Miller TR (2006) The costs of fatal and non-fatal falls among older adults. Injury Prevention. 12:290-295.

Supervision

- Supervision of 1 master student: Buttiens L (2012 – 2014) Effects of destabilization frequencies on postural stability in young and older adults.

2.5. PROPRIOCEPTION

Perception is an interpretation of physical reality. Proprioception is the perception of our body state in the absence of vision (Boisgontier and Swinnen, 2014). This state is defined by position, movement, and muscle force. Interpretation of this state is based on the processing of information from peripheral receptors and motor efference copies. The proprioception that interprets body segment position and movement are called joint position or movement sense. Joint position sense has been widely investigated in the context of aging and the inability of the proprioceptive system to accurately interpret actual limb position or movement due to physiological aging has been named "presbypropria" (Boisgontier et al., 2012).

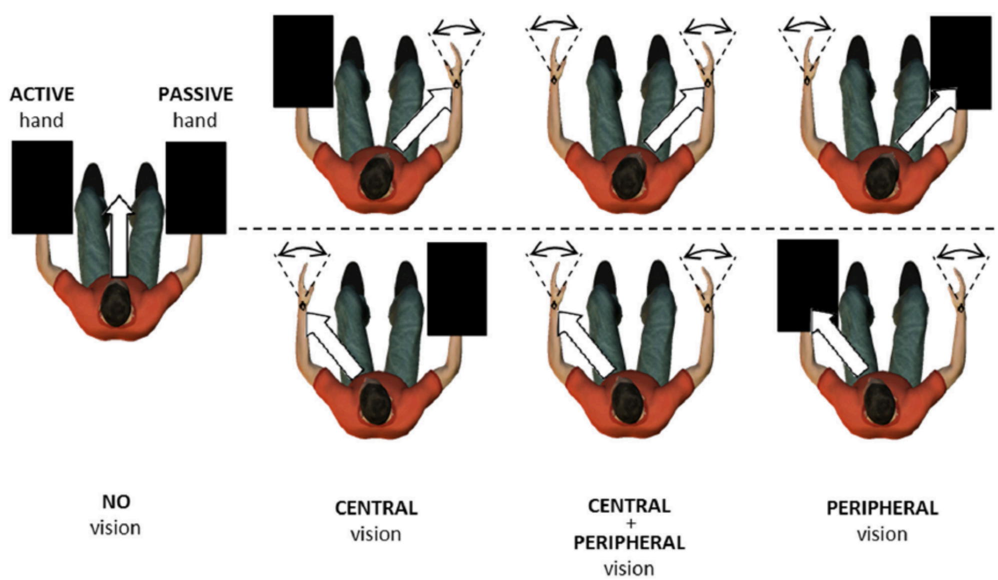


Figure 14. Contralateral movement matching task. Experimental conditions: No vision, Central vision, Central + Peripheral vision, and Peripheral vision. Participants are instructed to match a motor-driven right-hand movement (passive) with their left hand (active). Wrist movements range from 30° flexion to 30° extension (dashed lines). In some conditions, upper limbs are occluded by opaque boxes, here presented as black rectangles. White arrows indicate the gaze direction toward the right passive wrist (upper row) and left active wrist (lower row).

Proprioception and gaze direction

Despite the intensive investigation of proprioception, it remained unclear how directing vision toward either upper limb influenced performance and whether this influence was affected by age. Therefore, we assessed the performance of young and older adults on a contralateral movement matching task in which they matched motor-driven movements of their right passive hand with their left active hand according to in-phase and anti-phase patterns. Performance in six visual conditions involving central vision of the active or passive limb was compared to performance in a no vision condition (Figure 14). Results indicated that directing central vision to the active limb consistently impaired performance, with higher impairment in older than young adults (Figure 15). Conversely, directing central vision to the passive limb improved performance in young adults, but less consistently in older adults. These results indicated that the locus of visual attention influenced joint movement sense in young and older adults, with older adults being either more impaired or less able to benefit from a given visual condition.

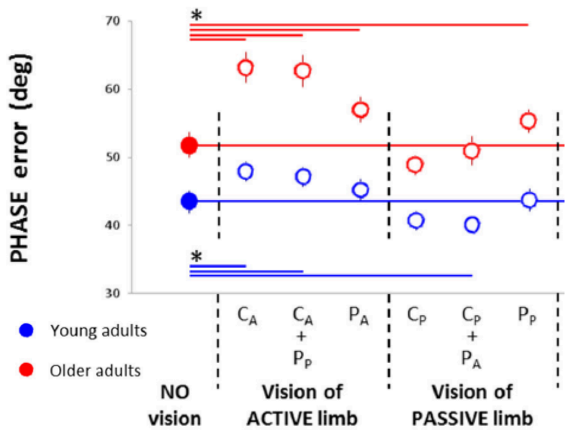


Figure 15. Root mean square of the relative phase (phase error) in the in-phase condition in young and older adults as a function of vision condition. No vision; central vision of the active wrist (CA), central vision of the active wrist and peripheral vision of the passive wrist (CA + PP), peripheral vision of the active wrist (PA), central vision of the passive wrist (CP), central vision of the passive wrist and peripheral vision of the active wrist (CP + PA), and peripheral vision of the passive wrist (PP).

Proprioception and movement amplitude

It was still unclear whether the amplitude of a movement affected the ability to accurately perceive it and whether this effect interacted with age. To test this hypothesis, young and older adults performed a bimanual wrist joint position matching task. Results revealed an age-related deficit when the target limb was positioned far from the neutral position (25°), but not when close to the neutral joint position (15°, 5°), irrespective of the direction. These results suggested

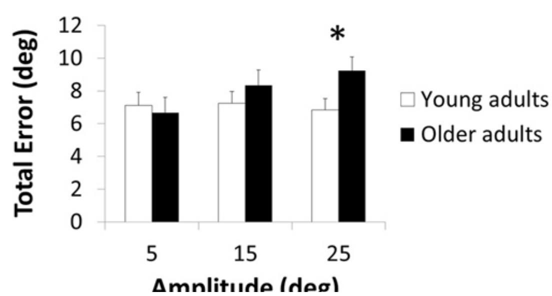


Figure 16. Total error as a function of the amplitude of the target position in young and older adults. *p < .05

that the difficulty associated with the comparison of two musculoskeletal states increases towards extreme joint amplitude and that older adults are more vulnerable to this increased difficulty.

Brain substrate of visuo-proprioceptive weighting

Motor control relies on the information from the environment and the body state, which is provided by vision and proprioception, respectively. In a study using magnetic resonance imaging, we investigated the relative contribution of visual and proprioceptive information to upper limb motor control and the extent to which structural brain measures predict this performance in youth (age range 9–18 years; n = 40; Corporaal et al., 2017). Participants performed the contralateral movement tracking task (Figure 14), adopting in-phase and anti-phase coordination modes (Figure17). Results showed that, in contrast to older participants, younger participants performed the task with lower accuracy in general and poorer performance in anti-phase than in-phase modes. However, a proprioceptive advantage was found at all ages: Tracking accuracy was higher during both in-phase and anti-

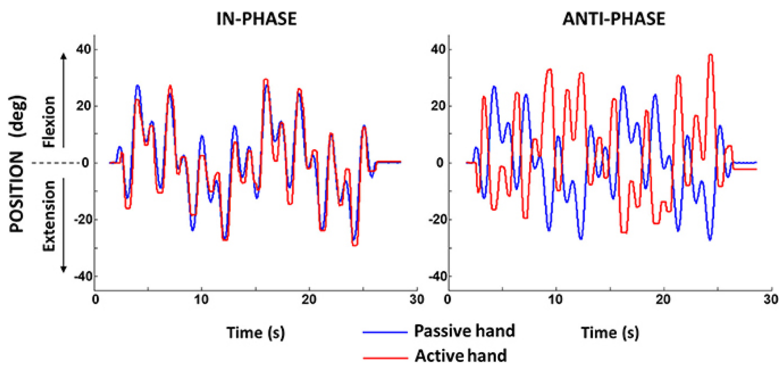


Figure 17. Sample of motor-generated motion in the passive hand (blue line) and tracking motion of the active hand (red line) for in-phase and anti-phase conditions.

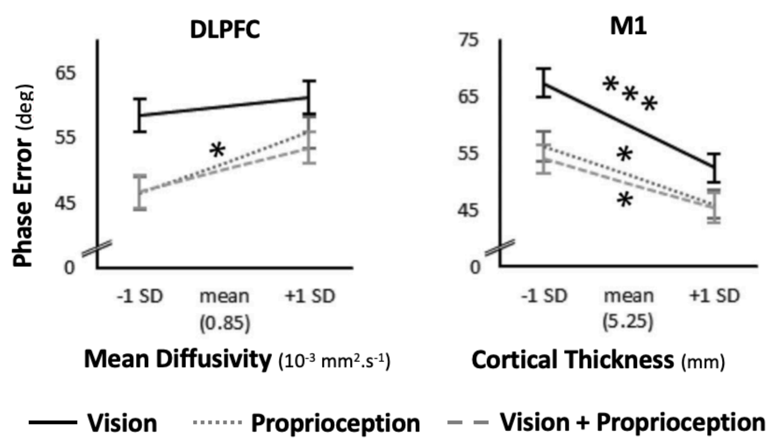


Figure 18. Neural predictors of tracking performance. Left panel: Increasing MD in Dorsolateral prefrontal cortex (DLPFC) tracts was associated with larger phase errors only in the proprioception conditions. Right panel: Larger cortical thickness of the precentral cortex (M1) was associated with lower phase errors in all sensory conditions. ***p < .001, *p < .05.

phase modes when proprioceptive information was available. The microstructural organization of interhemispheric connections between homologous dorsolateral prefrontal cortices as well as the cortical thickness of the primary motor cortex were associated with sensory-specific accuracy of tracking performance (Figure 18). Overall, these findings suggested that movement tracking performance in youth did not only rely on brain regions involved in sensorimotor processing, but also on prefrontal regions involved in attention and working memory.

References

Boisgontier MP, Olivier I, Chenu O, Nougier V (2012) Presbypropria: the effects of physiological ageing on proprioceptive control. Age. 34:1179-1194.

Boisgontier MP, Van Halewyck F, Corporaal SHA, Willacker L, Van den Bergh V, Beets IAM, Levin O, Swinnen SP (2014) Vision of the active limb impairs bimanual motor tracking in young and older adults. Frontiers in Aging Neuroscience. 6:320.

Boisgontier MP, Swinnen SP (2015) Age-related deficit in a bimanual joint position matching task is amplitude dependent. Frontiers in Aging Neuroscience. 7:162.

Corporaal SHA, Gooijers J, Chalavi S, Cheval B, Swinnen SP, Boisgontier MP (2017) Neural predictors of motor control and impact of visuo-proprioceptive information in youth. Human Brain Mapping. 38:5628-5647.

Supervision

- Supervision of 1 PhD student: Corporaal S (2012 – 2017) Brain substrates of sensorimotor control during upper and lower limb coordination in youth.
- Supervision of 3 master students: Beelprez J, Albers M (2014 – 2017) Effects of amplitude on the age-related proprioceptive deficit; Rolly C (2012 – 2014) Are visual and proprioceptive controls of movement equally affected by aging?

2.6. PHYSICAL (IN)ACTIVITY

Physical activity, defined as any bodily movement produced by the contraction of skeletal muscles that requires energy expenditure (Centers for disease control and prevention, 2015), is central to health protection. However, the advent of modern technology has produced an environment where opportunities to adopt sedentary behaviors are ubiquitous. The outcome of this environment is a population that intend to be active but fails to reach the guidelines of at least 150 min of moderate-to-vigorous physical activity per week. As a result, the World Health Organization has set regular physical activity as a global health priority (WHO, 2013).

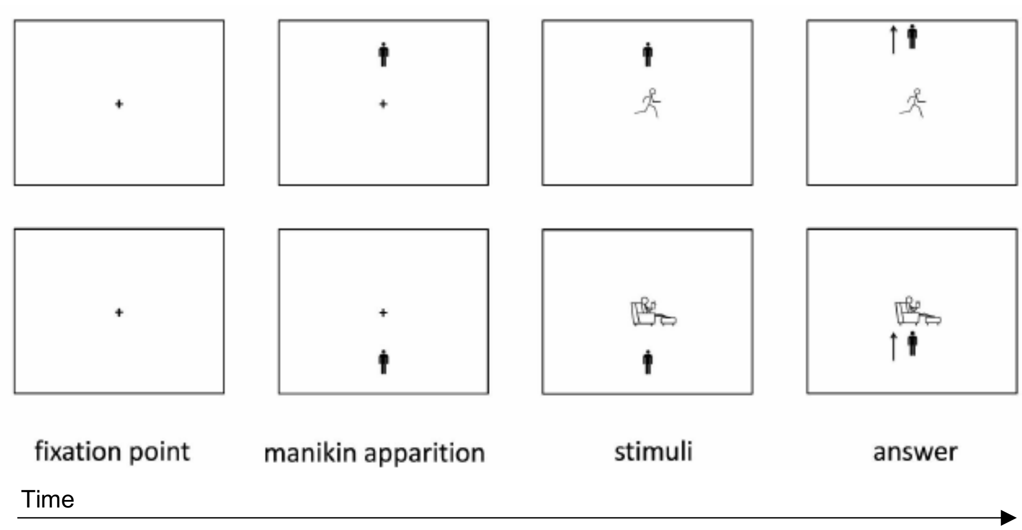


Figure 19. Approach-avoidance task. The contextual approach-avoidance task is used to measure automatic approach and avoidance tendencies toward physical activity and sedentary behaviors. Participants are asked to move a manikin (i.e., an avatar) on the screen "toward" (approach condition) and "away" (avoidance condition) from images depicting physical activity or sedentary behaviors by pressing keys on a keyboard. Each trial starts with a black fixation cross presented randomly for 250–750 ms in the center of the screen with a white background. Then, the manikin appears in the upper or lower half of the screen. Concurrently, a stimulus depicting "movement and active lifestyle" (i.e., physical activity) or "rest and sedentary lifestyle" (i.e., sedentary behavior) is presented in the center of the screen. Participants are instructed to quickly move the manikin "toward" a stimulus (approach) depicting physical activity and "away" from a stimulus (avoidance) depicting sedentary behaviors, or vice versa. After seeing the manikin in its new position for 500 ms, the screen is cleared. In case of an incorrect response, an error feedback (i.e., a cross) appears at the center of the screen. A neutral approach-avoidance task is used as a control. In this task, the stimuli depicting physical activity and sedentary behaviors are replaced by stimuli with circles or squares matching the number and size of information in the contextual stimuli (Figure 20).

Automatic processes and rewards in physical (in)activity

In a time of physical inactivity pandemic, attempts to better understand the factors underlying the regulation of exercise behavior are important. The dominant neurobiological approach to exercise behavior considers physical activity to be a reward. However, negative affective responses during exercise challenge this idea. The objective of our systematic review (Cheval et al., 2018a) was to test the automatic reactions triggered by stimuli associated with different types of exercise behavior (e.g. physical activity, sedentary behaviors). Three outcomes of automatic processes were tested in the literature: affective reactions, attentional capture, and approach tendencies. Behavioral results show that physical activity can become attention-grabbing, automatically trigger positive affect, and elicit approach behaviors. These automatic reactions explained and predicted exercise behaviors. Brain imaging results were scarce but showed that stimuli associated with physical activity and, to a lesser extent, sedentary behaviors activated regions involved in reward processes.

Brain substrates of the automatic attraction to sedentary behaviors

Why do individuals fail to exercise regularly despite knowledge of the risks associated with physical inactivity? Automatic processes regulating exercise behaviors may partly explain this paradox. Yet, these processes have only been investigated with behavioral outcomes (i.e., based on reaction times). In a study using EEG, we investigated the cortical activity underlying automatic approach and avoidance tendencies toward stimuli depicting physical activity, sedentary behaviors, and neutral figures (Figure 19 and 20) in 29 young adults who were physically active or physically inactive but with the intention of becoming physically active (Cheval et al., 2018b). Behavioral results showed faster reactions when approaching physical activity compared to sedentary behaviors and when avoiding sedentary behaviors compared to physical activity. Yet, faster reactions when avoiding sedentary behaviors compared to physical activity were also associated with higher conflict monitoring (larger early and late N1 event-related potentials) and higher inhibition (larger N2 event-related potentials), irrespective of the usual level of physical activity (Figure 21).

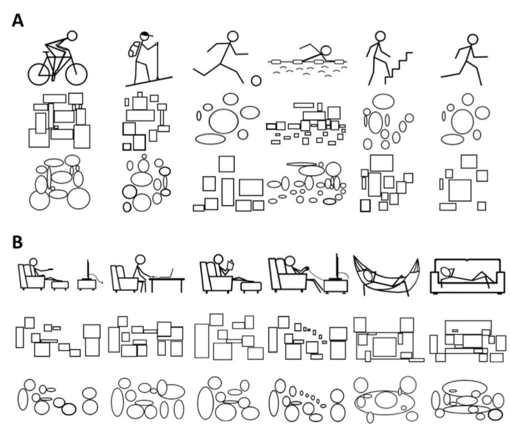


Figure 20. Contextual and neutral stimuli used in the approach-avoidance task. Panel A. Stimuli depicting physical activity and neutral stimuli built with circles and squares based on the amount of information (i.e., same number and same size) in the stimuli depicting physical activity. Panel B. Images depicting sedentary behaviors and neutral stimuli built with circles and squares based on the amount of information in the stimuli depicting sedentary behaviors.

These results suggested that additional cortical resources were required to counteract an attraction to sedentary behaviors.

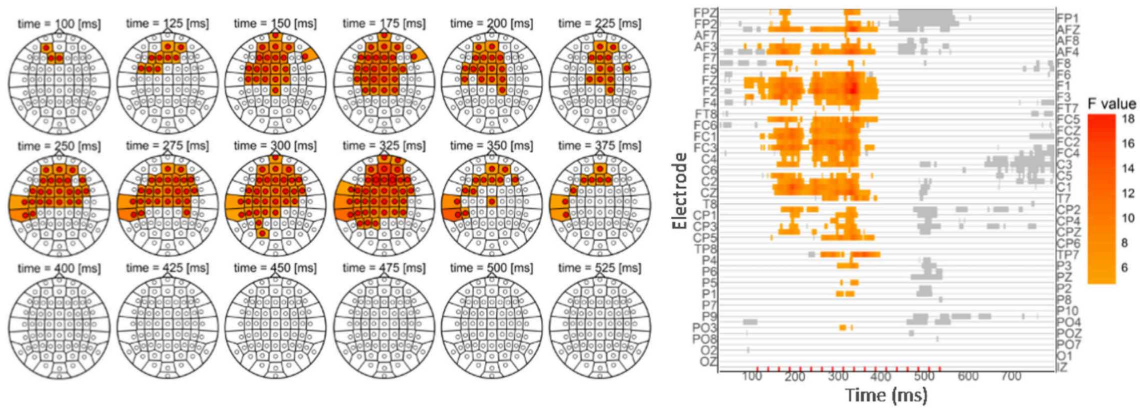


Figure 21. Event-related potential (ERP) results of the whole-scalp analysis. Two-way interaction between action (approach vs. avoid) and stimuli (physical activity vs. sedentary behaviors) for all electrodes in the 0–800 ms range. Results were based on a cluster-mass analysis using non-parametric permutation test and the family-wise error rate correction.

Physical activity and childhood socioeconomic circumstances

Along with factors such as age and sex, socioeconomic circumstances (SEC) in adulthood have been found to be a major determinant of physical activity. The objective of our study (Cheval et al., 2018c) was to investigate the associations between early-life and adult-life socioeconomic circumstances and physical inactivity (level and evolution) in aging using large-scale longitudinal data (Figure 22). This study used the Survey of Health Ageing and Retirement in Europe (SHARE), a 10-year population-based cohort study with repeated measurements in five waves, every 2 years between 2004 and 2013. Self-reported physical inactivity, household income,

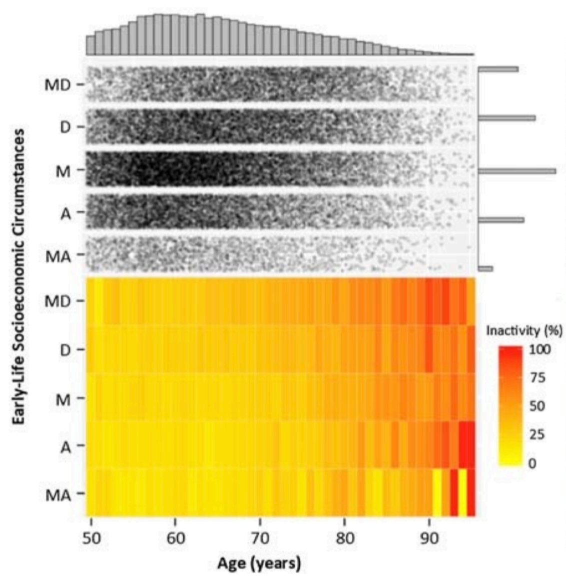


Figure 22. Physical inactivity dataset. Distribution and percentages across age as a function of early-life SEC at baseline. Upper panel: each dot represents an observation of a physically inactive participant stratified by early-life SEC and age. Lower panel: color coding indicates the relative prevalence of physical inactivity stratified by early-life SEC and age. A = advantaged; D = disadvantaged; M = middle; MA = most advantaged; MD = most disadvantaged.

educational attainment, and early-life socio-economic circumstance were collected in 22,846 individuals 50 to 95 year of age. The risk of physical inactivity was higher for women with the most disadvantaged early-life socioeconomic circumstances (Figure 23). With aging, the risk of physical inactivity increased for both sexes and was strongest for those with the most disadvantaged early-life socioeconomic circumstances, with the former effect being more robust than the latter one. The association between early-life socioeconomic circumstances and physical inactivity was mediated by adult-life socioeconomic circumstances, with education being the strongest mediator. In sum, early-life socioeconomic circumstances predicted high levels of physical inactivity at older ages, but this effect was mediated by socioeconomic indicators in adult life. This finding has implications for public health policies. Their actions should continue to promote education to reduce physical inactivity in people at older ages and to ensure optimal healthy aging trajectories, especially among women with disadvantaged early-life socioeconomic circumstances.

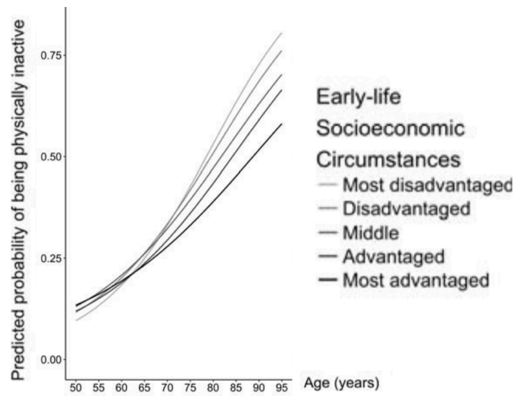


Figure 23. Predicted probability of being physically inactive across age depending on early-life socio-economic circumstances (SEC) in women.

Physical activity and cognitive resources

Cognitive resources may be critical to counteract an automatic attraction to effort minimization and increase the engagement in physical activity (Cheval et al., 2018a). To test this hypothesis, data from 105,206 adults aged 50 to 90 years from SHARE were used in adjusted linear mixed models to examine whether the engagement in physical activity and its evolution across aging was dependent on cognitive resources (Cheval et al., 2018d). Cognitive resources and physical activity were measured 5 times over a 12-year period. Delayed recall and verbal fluency were used as indicators of cognitive function and cognitive reserve was assessed based on the level of education. The frequency of engagement in moderate and vigorous physical activity was self-reported. Results showed that lower cognitive resources were associated with lower levels and steeper decreases of physical activity across aging. The associations between inter-individual cognitive differences and the engagement in moderate physical activity increased across aging (Figure 24). These findings suggest that, after 50 years old, the level of engagement in physical activity and its trajectory over the years depend on the level of cognitive resources still available.

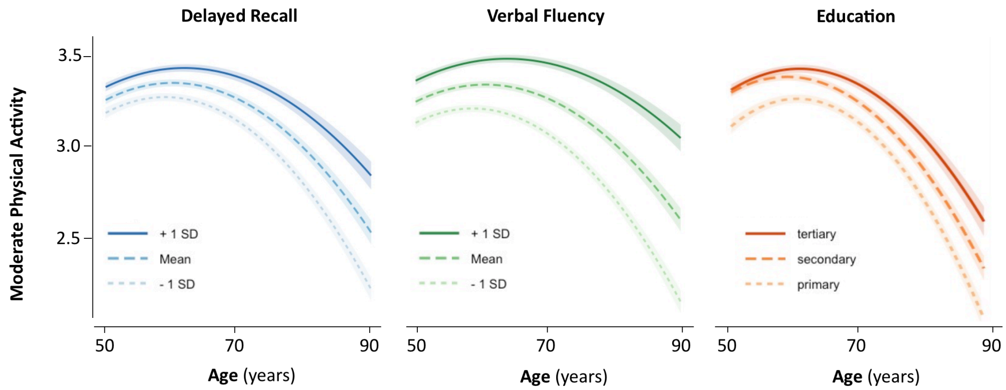


Figure 24. Associations of cognitive resources with the trajectories of moderate physical activity across aging. For delayed recall and verbal fluency, the variables were standardized. The coefficients are interpreted as the effect of an increase of one standard deviation.

Cognitive resources moderate the adverse impact of poor perceived neighborhood conditions on physical activity

Poor neighborhood conditions are associated with lower levels of physical activity in older age, but socio-ecological models put forth that physical activity is dependent on both environmental and individual factors. Older adults' abilities to overcome environmental physical activity barriers may partially rely on cognitive resources. However, evidence on the moderating role of these cognitive resources in environmental barrier and physical activity behavior associations is still lacking. We analyzed cross-national and longitudinal data on 28,876 adults aged 50 to 96 years in SHARE survey (Cheval et al., 2019). Lack of access to local services and neighborhood nuisances were used as indicators of poor neighborhood conditions. Delayed recall and verbal fluency were used as indicators of cognitive resources. Confounder-adjusted linear mixed models were conducted to test associations between neighborhood conditions and self-reported physical activity, as well as the moderating role of the cognitive resources. We found that poor neighborhood conditions, especially low access to local services, were associated with less frequent engagement in physical activity and with a steeper decline of engagement in physical activity across aging. Moreover, cognitive resources robustly reduced the adverse influence of poor neighborhood conditions on physical activity (Figure 25). These findings suggest that cognitive resources can temper the detrimental effect of poor neighborhood conditions on physical activity. Public policies should target both individual and environmental factors to tackle the current pandemic of physical inactivity more comprehensively.

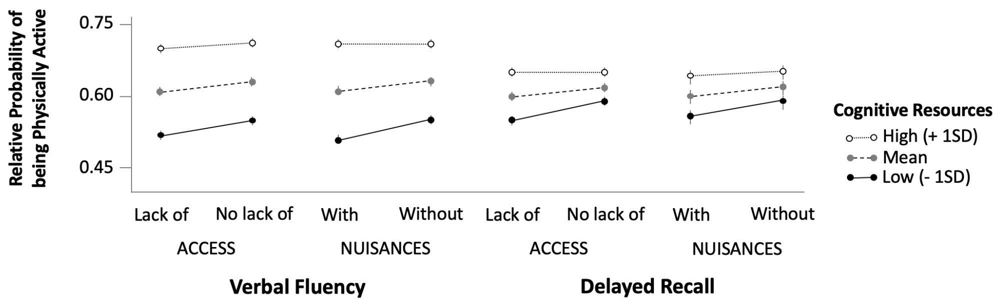


Figure 25. Relative probability of being physically active as a function of cognitive resources (verbal fluency; delayed recall) and neighborhood conditions (lack of access to local services; nuisances). Error bars = 95% confidence interval; SD = standard deviation.

Physical activity cancels the negative impact of adverse childhood experiences and depression on functional dependence

Adverse childhood experiences, depression, and functional dependence are inter-related. However, mechanisms underlying these relations remain unclear. We investigated the potential for depression to mediate the effect of adverse childhood experiences on functional dependence in older age and whether physical activity moderated this mediation (Boisgontier et al., 2019). Data from 25,775 adults aged 62±9 years from SHARE was used in adjusted linear mixed-effect models to test whether depression mediated the associations between adverse childhood experiences and functional dependence in activities of daily living (ADL) and instrumental activities of daily living (IADL) and whether physical activity moderated these mediations. As expected, adverse childhood experiences were positively associated with ADL and IADL. Both associations were mediated by depression. Physical activity reduced the effect of adverse childhood experiences on depression and tempered the effect of depression on functional dependence in ADL and IADL, thereby eliminating the effect of adverse childhood experiences on functional dependence through this pathway (Figure 26). In conclusion, physical activity tempered the impact of adverse childhood experiences on functional dependence. In inactive individuals, the effect of adverse childhood experiences on functional dependence (ADL and IADL) was mediated by depression.

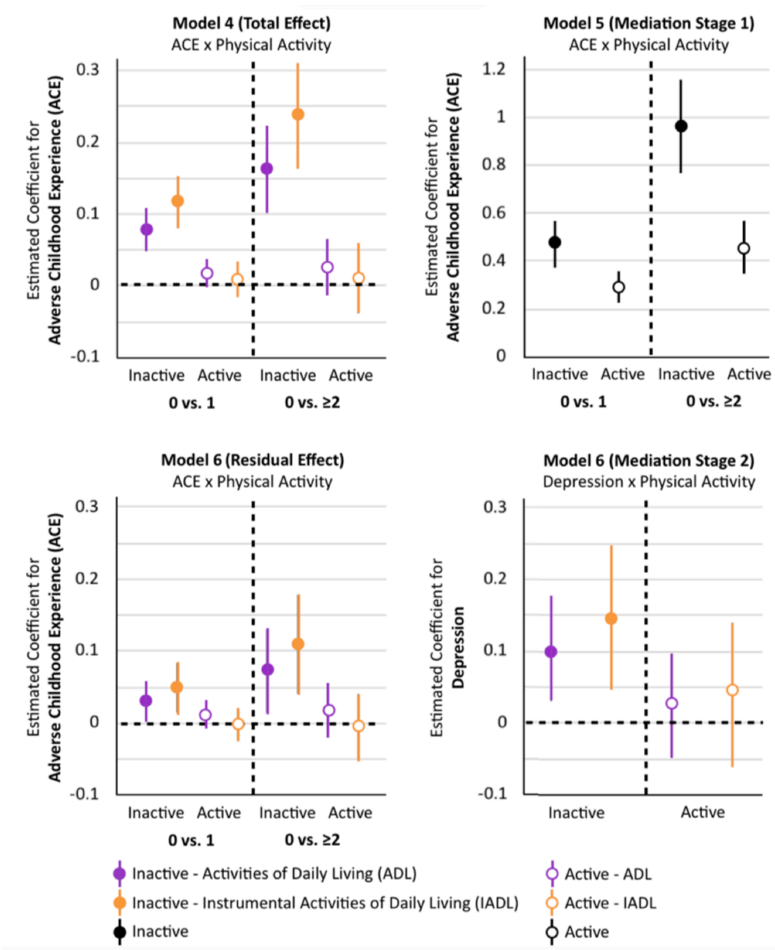


Figure 26. Conditional b coefficients and 95% confidence interval as a function of physical activity. Upper-left panel. Physical activity moderates the total effect of adverse childhood experiences (0 vs. 1 and 0 vs. ≥2 adverse childhood experiences) on functional dependence. Upper-right panel. Physical activity moderates the first stage of the mediation by depression. Lower-left panel. Absence of moderation by physical activity on the residual effect of adverse childhood experiences on activities of daily living (ADL) and the moderation effect on this effect on instrumental activities of daily living (IADL). Lower-right panel. Physical activity moderates the second stage of the mediation. Functional dependence in ADL and IADL are in orange and purple, respectively. Physically inactive and active participants are illustrated by filled and empty circles, respectively.

Physical activity and bimanual coordination

Practice of a given physical activity is known to improve the motor skills related to this activity. However, whether unrelated skills are also improved is still unclear. To test the impact of physical activity on an unpracticed motor task, twenty-six young adults completed the international physical activity questionnaire (IPAQ) and performed a bimanual coordination task they had never practiced before

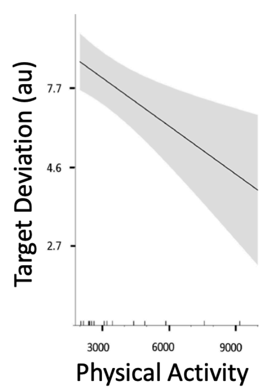


Figure 27. Fixed effect and 95% confidence interval of the effect of total physical activity (IPAQ) on target deviation. This effect was significant while controlling for all the other factors included in the model. The scale of target deviation was back transformed. IPAQ = International Physical Activity Questionnaire; ∗∗p < 0.01.

(Figure 1 and 6; Boisgontier et al., 2017). Results showed that higher total physical activity predicted higher performance in the bimanual task when controlling for multiple factors such as age, sedentary behaviors, music practice, and computer games practice (Figure 27). This finding runs counter to the notion that generalized motor abilities do not exist and supports the existence of a “learning to learn” skill that could be improved through physical activity and that impacts performance in tasks that are not necessarily related to the practiced activity.

References

Boisgontier MP, Orsholits D, von Arx M, Sieber S, Courvoisier DS, Iversen MD, Cullati S, Cheval B (2019) Physical activity cancels the negative impact of adverse childhood experiences and depression on functional dependence. SportRxiv. doi: 10.31236/osf.io/ms2u7

Boisgontier MP, Serbruyns L, Swinnen SP (2017) Physical activity predicts performance in an unpracticed bimanual coordination task. Frontiers in Psychology. 8:249.

Centers for disease control and prevention (2015). Division of nutrition, physical activity, and obesity: Glossary of terms. Retrieved from http://www.cdc.gov/ physicalactivity/basics/glossary/.10.

Cheval B, Orsholits D, Sieber S, Courvoisier DS, Cullati S, Boisgontier MP (2018d) Age-related decline of cognitive resources precedes and explaines the decline in physical activity. SportRxiv. doi: 10.31236/osf.io/pagx6

Cheval B, Radel R, Neva JL, Boyd LA, Swinnen SP, Sander D, Boisgontier MP (2018a) Behavioral and neural evidence of the rewarding value of exercise behaviors: a systematic review. Sports Medicine. 48:1389-1404.

Cheval B, Rebar A, Miller M, Sieber S, Orsholits D, Baranyi G, Courvoisier DS, Cullati S, Chalabaev A, Sander D, Boisgontier MP (2019) Cognitive resources moderate the adverse impact of poor perceived neighborhood conditions on physical activity. SportRxiv. doi: 10.31236/osf.io/ga3wue

Cheval B, Sieber S, Guessous I, Orsholits D, Courvoisier DS, Kliegel M, Stringhini S, Swinnen SP, Burton-Jeangros C, Cullati S, Boisgontier MP (2018b) Impact of early- and adult-life socioeconomic circumstances on level of physical inactivity. Medicine & Science in Sports & Exercise. 50:476-485.

Cheval B, Tipura E, Burra N, Frossard J, Chanal J, Orsholits D, Radel R, Boisgontier MP (2018c) Avoiding sedentary behaviors requires more cortical resources than avoiding physical activity: an EEG study. Neuropsychologia. 119:68-80.

World Health Organization (2013) Global action plan for the prevention and control of NCDs 2013–2020.

Mentoring

- Mentoring of 1 postdoctoral researcher: Cheval B.

3. PROJECT:

SOLVING THE EXERCISE PARADOX

ABSTRACT

What if the exercise paradox stemmed from a fundamental principle of evolution that has been neglected in exercise neuropsychology: Energetic cost minimization?

Individuals are increasingly aware of the positive effects of physical activity and most of them have the intention to exercise. Yet, the world population is becoming less active. I hypothesize that this exercise paradox results from brain processes supporting an automatic attraction to energetic cost minimization.

To test this hypothesis, I will ensure that the construct under investigation exclusively relates to energetic costs. Participants will be conditioned on a stationary bicycle to systematically associate neutral geometrical figures with different energetic cost patterns: Increasing, decreasing, and constant. The resulting conditioned stimuli will be used in behavioral tasks to test the effect of energetic cost variations on automatic approach tendencies, automatic affective associations, and attentional bias in children, adults, and older adults. Brain processes and regions underlying these automatic behaviors will be investigated using transcranial magnetic stimulation and magnetic resonance imaging. Then, I will test whether a bias-based training protocol can modify this automatic attraction.

The conceptual and methodological innovations of this project at the crossroad between psychology, neuroscience, and physiology have the potential to push the entire field of exercise psychology forward. Results are expected to show an automatic attraction to energetic cost minimization, at all ages, how cortical inhibition and brain activations support this behavior, and how dispositional and situational factors moderate these effects. Finally, results are expected to demonstrate that this automatic attraction can be reduced through training. This fundamental research will also improve interventions aiming to counteract a global health problem: The pandemic of physical inactivity.

3.1. INTRODUCTION

3.1.1. STATE OF THE ART

Context: the exercise paradox

During the past two decades, society has encouraged people to be more physically active [1-3]. As a result, most individuals are now aware of the positive effects of regular physical activity and have the intention to exercise [4]. Yet, this intention is not sufficient as plans are often not executed [5]. Despite gradually scaling up actions promoting physical activity across the years, we are actually becoming less active. From 2010 to 2016, the number of inactive adults has increased by 5% worldwide, now affecting more than 1 in 4 adults (1.4 billion people) [6,7]. This exercise paradox is also observed in Europe, where the situation is equally bad. Since the White Paper on sport [8], the European Union has invested ~€300 million to promote physical activity through preparatory actions [9] and Erasmus+ Sport [10]. Despite these investments demonstrating the urgency to increase population levels of physical activity, the number of people who *never* exercise or play sport in Europe has increased from 42% to 46% between 2013 and 2017 [11]. This context raised the question: Why are we unable to implement our intention to be physically active?

Why are we unable to implement our intention to be physically active?

I hypothesize that the exercise paradox is due to brain processes supporting an automatic attraction to energetic cost minimization. If the results of the project described in this thesis provide fundamental evidence supporting this hypothesis, the pandemic of physical inactivity [12] is driven by an automatic resistance to the reflective intention to engage in activities associated with higher energetic costs. Therefore, public health policies take the wrong approach. Part of the massive investment aiming at increasing reflective intentions to be active should be redirected towards the development of research projects aiming at understanding and counteracting the mechanisms underlying this automatic resistance.

Theoretical approaches in exercise psychology: the advent of automatic behaviors

Until recently, the dominant approaches to exercise behavior were based on theories focusing on how people reflect on their perceptions [13,14]. Yet, meta-analyses examining the effectiveness of exercise-related intervention based on these reflective approaches have shown small effect sizes [15,16] and high levels of unexplained variance [17]. These results have emphasized the impact of theoretical articles highlighting the importance of the automatic evaluation of exercise-related stimuli in exercise-related decision-making and behavior [18-20]. These theoretical articles are supported by multiple experimental studies [21-23] showing that exercise-related stimuli affect automatic reactions such as attentional capture [24-26], affective reactions [27-31], and approach tendencies [32-35]. The number of recent theoretical, experimental, and review articles on the topic suggests that the importance of automatic behaviors is about to be fully recognized in the field of exercise psychology. Yet, the reason why people fail to be physically active is still unclear.

Energetic cost minimization is positively valued: the hypothesis

Adaptation, a fundamental principle of evolution [36], can be defined as the dynamic process by which individuals improve their suitability to the environment. During evolution, adaptation has been vital and has defined the species constituting the world of living organisms as we know it. Energetic cost minimization is a specific type of adaptation postponing energy exhaustion [37], thereby increasing the odds of survival [38]. This automatic process aiming to achieve the most efficient behavior [32] has been widely evidenced in multiple fields, such as evolutionary biology [39] and biomechanics [40]. If we take the example of gait; On the evolutionary timescale, energetic cost of gait is lower in humans than in primates [41]. On the developmental timescale, children gradually increase the kinetic energy they are able to recover, thereby reducing energetic costs [42]. On a shorter timescale, energetic cost minimization determines the moment we switch from walking to running [43]. In sum, energetic cost is not only an outcome of movement, but also continuously shapes it [40] at multiple timescales.

Energetic cost minimization accounts for our behavior, our morphology, the physiology of our neural system [38], and has played a key role in their evolution. Therefore, I hypothesize that energetic cost minimization is positively valued and, as such, triggers automatic behaviors and brain processes that counters our intention to be physically active.

3.1.2. PROOF OF CONCEPT

The energetic cost minimization hypothesis has been formulated in a systematic review I published in June 2018 as last and corresponding author [21]. The concept of brain processes supporting an automatic attraction to this minimization is in line with the findings of an EEG experimental article I published in October 2018, also as last and corresponding author, that involved none of my PhD and postdoctoral advisors. In this study, all participants had the intention to be physically active and their actual level of physical activity was assessed. They were instructed to take control of an on-screen avatar to approach or avoid stimuli depicting physical activity, sedentary behaviors, or neutral figures (Figure 20). EEG signal was analyzed using a cluster-mass permutation test [44] that is appropriate for exploratory analyses [45,46]. Permutation F-tests were performed on reduce residuals [47] and familywise error rate was controlled using the cluster-mass test [44]. As expected, results showed that participants were faster at avoiding stimuli depicting sedentary behaviors compared to stimuli depicting physical activity, and more so in physically active participants, which supported the fact that participants had the intention to be physically active. However, as evidenced by a spatiotemporal interaction between action (approach vs. avoid) and stimuli (physical activity vs. sedentary behaviors), these faster reaction times were associated with larger evoked-related potentials in the medial frontal cortex and frontocentral cortex, which have been related to conflict monitoring and inhibition, respectively. These results suggested that avoiding stimuli depicting sedentary behaviors required higher brain resources to monitor a conflict between the intention to be physically active and an automatic attraction to sedentary behaviors. In September and October 2018, this research has been featured worldwide in more than 45 countries and 200 media including the New York Times [48] and the Washington Post [49].

3.1.3. CAVEATS IN THE LITERATURE

Humans are wired for laziness: a simplistic view

The results of the proof-of-concept study clearly demonstrate the potential of my hypothesis. However, they are insufficient. In this study, I used stimuli depicting physically active and inactive avatars. Therefore, I tested a dichotomic concept that do not fit the theoretical framework of the current project. Energetic cost minimization is a dynamic process involving a variation of energetic expenditure across time. A pictogram depicting an individual swimming refers to a level of energetic cost but does not account for any cost variation, be it a decrease or an increase. The same stands for a pictogram of an individual playing video game. Results of the proof-of-concept study may have suggested that humans are “wired to sit” [48]. Yet, as explained above, I contend that humans are wired for efficiency. I hypothesize that the automatic attraction to energetic cost minimization can be observed at all levels of energetic expenditure. The only solution to test this hypothesis, is to switch from a discrete to a continuous approach. The hypothesis of sedentary behaviors being inherently positively valued is simplistic and lacks theoretical ground. I hypothesize that energetic cost minimization is attractive at any level of energetic expenditure and should therefore be conceptualized on a continuum.

Time: the missing dimension

Thus far, investigations in the field of exercise psychology have relied on a discrete approach based on levels of energetic costs, dichotomizing lower (sedentary behaviors) and higher levels (physical activity). However, energetic costs are dependent on time dimensions that cannot be ignored, especially in exercise-related behaviors. There is an imperative to include this dimension in the theoretical framework of exercise psychology. In this project, I introduce this dimension in two ways. First, I focus on energetic cost variations by encapsulating variations of energetic costs across time into neutral geometrical figures through associative conditioning. Second, I investigate how the automatic evaluation of exercise-related stimuli varies across time. As yet, theories of exercise behavior have relied on a discrete approach based on levels of energetic costs. Here, I introduce a continuous approach taking time into account.

Physiological state: the missing control

The attraction force of a stimulus associated with energetic cost minimization may also depends on dispositional (e.g., cardiovascular fitness) and situational factors (e.g., level, variation, or duration of energetic expenditure during the experiment). Yet, previous studies never controlled for the physiological state before and during the experiment [21]. Moreover, participants have always been tested in a sitting or reclining position, which may have biased the results. This lack of control is an issue as in other contexts the value that individuals assign to stimuli is influenced by their physiological state [50-53]. For instance, participants show stronger attention and faster automatic approaches to food-related stimuli when they are hungry [54,55].

Stimulus purity: the issue

The systematic review I published in June 2018 revealed a major issue. As yet, studies have focused on specific exercise behaviors (e.g., running, dancing, or swimming) and/or sedentary behaviors (e.g., watching television or reading). However, these specific behaviors can be positively valued due to the energy cost they are associated with, but they can also be positively valued due to other factors. Therefore, it is difficult to infer strong conclusions from studies using an approach based on stimuli related to specific exercise behaviors. For example, the pleasure associated with a picture of an individual playing soccer may reflect the pleasure felt when watching this sport on TV, not the energetic cost required to play soccer.

3.2. OBJECTIVES

An automatic attraction to behaviors minimizing energetic cost may explain why individuals fail to reach the recommended amount of physical activity despite conscious intentions to exercise. However, the value assigned to this minimization has never been investigated.

The objective of this project is to examine whether and how energetic cost minimization triggers automatic behaviors and brain processes counteracting our intention to exercise. This main objective will be addressed in five work packages (WP).

In WP1, I will investigate whether stimuli associated with energetic cost minimization trigger automatic regulatory processes, including attention capture, affective reactions, and approach tendencies. In WP2, I will examine whether dispositional (e.g., cardiovascular fitness) and situational factors (e.g., level, variation, or duration of energetic expenditure during the experiment) moderate the automatic attraction to energetic cost minimization. In WP3, I will use transcranial magnetic stimulation (TMS) to test whether inhibition processes in the primary motor cortex (M1) underlie the automatic reactions to energetic cost minimization when individuals avoid stimuli associated with decreasing energetic cost and when they need to withhold their movement towards these stimuli, as compared to neutral stimuli and stimuli associated with increasing costs. In WP4, I will use functional magnetic resonance imaging (fMRI) to test whether brain regions related to reward or emotional arousal are more activated when reacting to a conditioned stimulus associated with decreasing versus constant and increasing energetic costs. I will also use structural MRI to test whether the shape and volume of the regions of interest (ROIs) revealed by the fMRI studies predict which individuals are successful at implementing their intention to be physically active. In WP5, I will investigate whether the automatic attraction to energetic cost minimization can be reduced through a bias-based training using a bimanual setup applying different physical resistance to the motor responses and whether this retraining affects intracortical inhibition processes.

3.3. METHODS

3.3.1. PARTICIPANTS

Participants aged 18-25 years will be recruited through a poster campaign. In the lifespan study (WP2, Study 2.3), children and older adults will also be recruited. To investigate the conflict between conscious intentions to be physically active and the hypothesized automatic attraction to energetic cost minimization, a prerequisite is that participants have the intention to be physically active. This intention will be tested using the state-of-change questionnaire [56] to ensure that participants are in the preparation (i.e., low level of physical activity with a strong intention to start) or maintenance stage of physical activity (i.e., high level of physical activity for at least 6 months). Individuals with diabetes, a history of alcohol or drug abuse, or receiving treatment for psychiatric disorder will be excluded from the study. Participants will be asked to refrain from consuming psychostimulants, to have a normal sleep time (6-9h per night) and food intake, and to complete a diary on the last two days preceding the experimental sessions to check for compliance with these constraints. Sociodemographic information, reflective motivation to exercise regularly (scale of motivation for sports [57]), personality (10-item personality inventory [58]), and impulsivity (brief self-control scale [59]) will also be assessed. All studies will be conducted after agreement from the appropriate ethical committees. All participants will sign an informed consent form after receiving a complete description of the study.

3.3.2. PROCEDURES

To address the purity issue raised in the state-of-the-art section of this project and ensure that the constructs under investigation are exclusively related to energetic cost variations, participants will be conditioned on a stationary bicycle to systematically associate neutral geometrical figures with different energetic cost patterns: increasing, decreasing, and constant (Figure 28). This conditioning procedure has already proven to be efficient with other types of stimuli [60-63]. The resulting conditioned stimuli will be used in reaction-time tasks to test the effect of energetic cost variations on automatic approach tendencies, automatic affective associations, and attentional bias. To determine if the conditioning procedure was successful, participants will complete a primed-lexical decision task to assess the degree of automatic association between each conditioned stimulus and words related to energy expenditure (e.g., active, energetic) versus energy conservation (e.g., inactive, rest) [33,64].

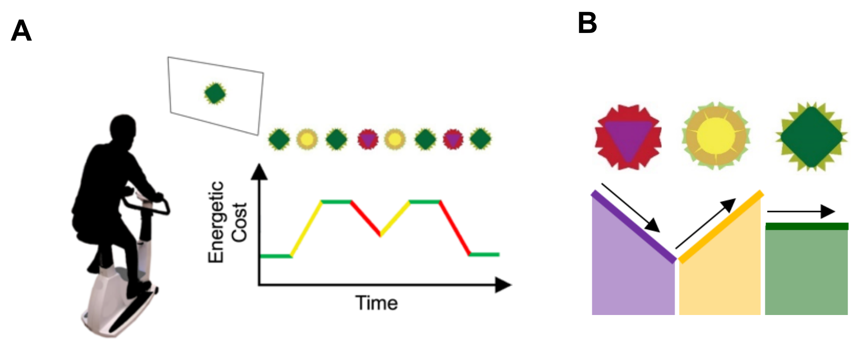


Figure 28. Associative conditioning. A. Procedure. Participants will be conditioned on a stationary bicycle to systematically associate neutral geometrical figures with increasing, decreasing, or constant energetic cost. The time of exposure to each conditioned stimulus will be identical and so will be the level of energy expenditure as the area under the curve is equal across stimuli. Multiple patterns will be used with the order of presentation of increasing and decreasing energetic costs being counterbalanced. B. Conditioned Stimuli. Each conditioned stimulus will be associated with a single energetic cost pattern: decrease, increase, or constant. The color and shape of these stimuli will be counterbalance across participants.

Physiological factors

As mentioned in the state-of-the-art section, the value assigned to a stimulus has been shown to depend on the physiological state of an individual [50,51]. For example, thirsty individuals show higher perceptual readiness to drinking-related stimuli [52] and hungry individuals show stronger automatic approach reactions towards food-related stimuli [53]. Therefore, the value assigned to energetic cost variations may depend on the participant's maximal exercise capacity and recent exercise history (e.g., did the participant come by bike or bus). To test this effect and control for it, all participants will perform a maximal exercise test at baseline to assess their peak O_2 consumption ($\dot{V}O_2$ peak) and physical activity will be monitored using a pedometer during the 24h preceding the experiment.

Maximal exercise test

At least 2 days before the other experimental sessions, participants will complete a graded maximal exercise test [65-67] on a cycle ergometer associated with a metabolic cart. The test will begin with a power output of 100W for men and 50W for women and will increase by 30 W increments every 2 min until volitional exhaustion. Participants will maintain a pedaling cadence of 70–90 rpm and remain seated throughout testing. The following measurements will be monitored throughout exercise testing: Expired O2 and CO2 concentrations and airflow via a metabolic cart, hear-rate, and Borg's 6–20 scale rating perceived exertion. $\dot{V}O_2$ peak criteria will include at least one of the following: A plateau in O2 uptake and heartrate with further increase in workload, perceived exertion greater than 17, an inability to maintain a cadence of 70 rpm, and volitional exhaustion [65-67]. The peak power output determined by the exercise test will be used to individualize the levels of wattage applied during the associative conditioning procedure.

3.3.3. STATISTICS

Statistical analyses

All data will be analyzed using linear mixed models. In several research fields, the use of linear mixed models is promoted as a better alternative than traditional statistical models [68]. Unlike traditional approaches (e.g., ANOVA), which requires averaging trials within each condition, linear mixed models preserve all the information (i.e., for each participant, these models keep the variability of the responses within each condition). Therefore, the number of data points in the model [69] and power increases [70]. Linear mixed models also allow incomplete and unbalanced data to be used. These models will be built using the R language. If necessary, the outcome will be normalized using the Box–Cox method [71,72]. The continuous variables will be scaled and centered on zero. The trial number will be included in the models to investigate the effect of time, which is only possible using linear mixed models, as traditional analyses of variance require to average across trials. I am already very familiar with the implementation of this type of statistical model [73-80].

The effect of age on performance in the reaction-time tasks testing automatic behaviors over the lifespan is expected to be nonlinear. While this nonlinearity is often modeled with the inclusion of a quadratic or cubic term in the equation, this approach presents several limitations [81], and nonparametric local smoothing has been shown to be more robust [82]. The lifespan dataset (WP2, Study 2.3) will therefore be analyzed using the spline smoothing method [83,84] that I have already apply in a previous study [75]. Using the R language mgcv package, I will implement smoothing splines to define age ranges for which the age effect was linear and apply linear mixed models on these age ranges.

Power analysis and sample size

Using power analysis to gauge an appropriate sample size in a linear mixed model approach is not possible here as variance at the level of the individuals and variance at the level of repeated trials is needed. Yet, this information is not available in the literature. Since the effects that will be investigated in the TMS and MRI studies have not been tested and because power analyses based on pilot data are biased [85], the experiments will follow a sequential analysis [86] including two planned analyses. One interim analysis will be performed after 50% data is collected and the other analysis after all data is collected. Based on the Pocock boundary [87], the threshold for significant p-values will be .0294. If the effect is significant at the first interim analysis the data collection will be terminated. The data collection will also be terminated if the observed effect size is smaller than a predetermined d-value based on the maximum number of subjects I am willing to collect for each experiment (e.g., $d = 0.44$ for a maximum $n = 40$ in the TMS experiment, as TMS experts agree that it is reasonable to set the maximal sample size to 40 participants [88]) and the fact that with one interim analysis, this maximum n provides 0.8 power [89] to detect an effect at the predetermined d-value. To secure the credibility of the results, the study designs will be pre-registered [90] when feasible, which is hardly the case for the exploratory fMRI studies (Study 4.1 and 4.2). To accelerate and facilitate knowledge dissemination, all articles will be pre-printed, and data and code shared on public repositories.

3.4. WORK PACKAGES

Five Work Package (WP) will be implemented to examine whether and how energetic cost minimization triggers automatic behaviors and brain processes counteracting the intention to be physically active.

3.4.1. DO STIMULI ASSOCIATED WITH ENERGETIC COST MINIMIZATION TRIGGER AUTOMATIC REGULATORY PROCESSES?

Objectives and hypotheses

In WP1, I will test whether stimuli that solely vary with respect to the energetic cost pattern they have been associated with (decrease, increase, constant) trigger automatic reactions. I hypothesize that due to the positive value the brain assigns to energetic cost minimization, stimuli associated with decreasing energetic costs will attract attention, produce automatic positive affective reactions, and trigger automatic approach tendencies (i.e., faster reactions to stimuli associated with decreasing compared to increasing energetic costs; Figure 29), to a greater extent than stimuli associated with constant and increasing energetic costs. I also hypothesize that withholding actions towards stimuli associated with decreasing energetic costs will require higher levels of inhibition than withholding actions towards increasing energetic costs.

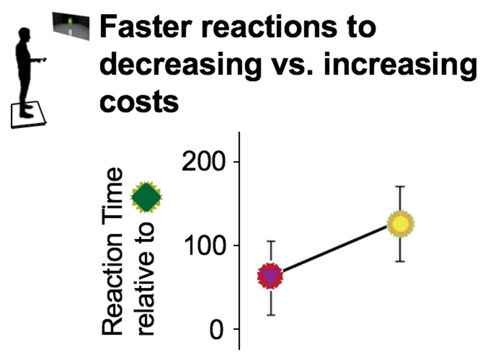


Figure 29. Expected results on the manikin task.

Behavioral assessment of automatic regulation processes

Attentional bias will be assessed using the *spatial cuing task* [91] (Figure 30A) to determine the initial attentional attraction to the conditioned stimulus and the difficulty in disengaging attention to reallocate it to another target. Automatic affective reactions will be assessed using the *evaluative priming task* [92,93] (Figure 30B) to determine the negative and positive affects automatically associated with each conditioned stimulus. Automatic approach tendencies will be assessed using the *manikin task* [94-96] (Figure 30C) to determine the tendency to approach rather than avoid each conditioned stimulus. Inhibition will be assessed using the *go/no-go task* [97] (Figure 30D) to determine the level of inhibition required to withhold actions towards each conditioned stimulus.

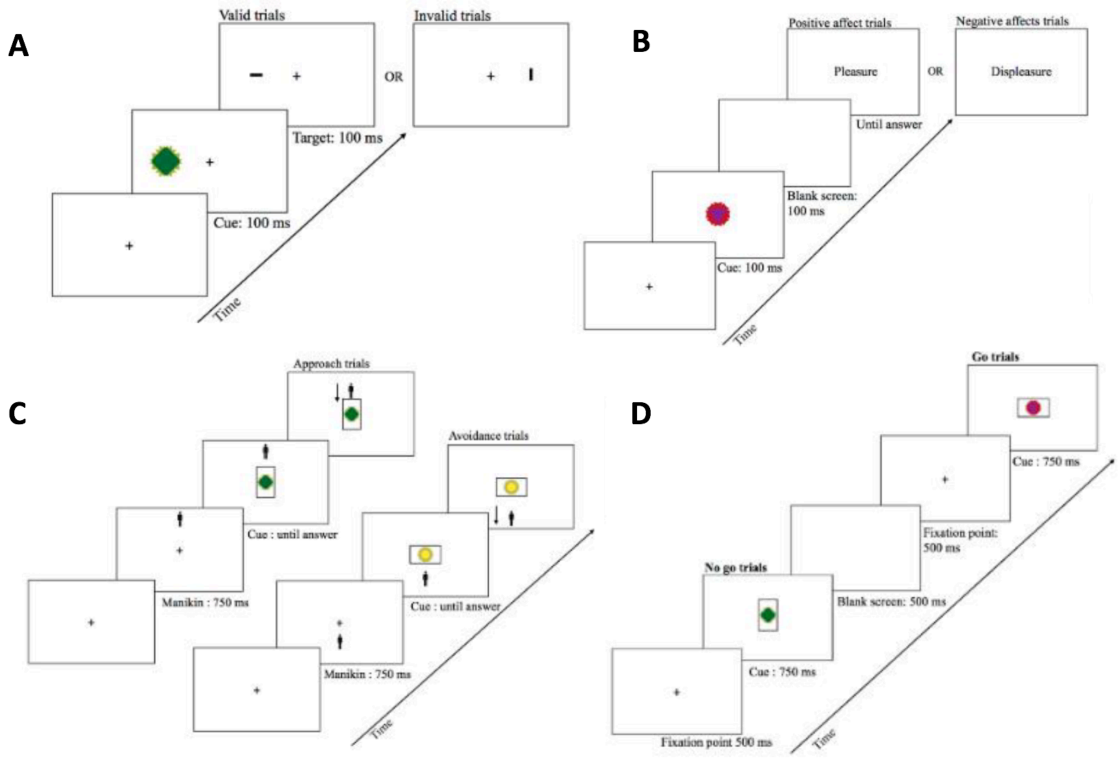


Figure 30. Reaction-time tasks used to investigate automatic regulatory processes. Panel A. Spatial cuing task. Panel B. Evaluative priming task. Panel C. Manikin task. Panel D. Go/no-go task.

Experiments

In WP1 (Study 1; n = 50), I will test whether stimuli associated with different pattern of energetic cost variations trigger different automatic reactions. All the tasks will use the conditioned stimuli. In the valid trials of the spatial cuing task, the target will appear in the same location as the stimulus. In the invalid trial, the target will appear in the opposite location to the stimulus. In the evaluative priming task, one of the three conditioned stimuli will briefly appear on the screen. Then, participants will determine whether the target word is related to a positive (e.g., pleasure) or a negative (e.g. displeasure) affect. In the manikin task, participants will take control of an on-screen avatar. In the approach trials, the stimuli will be presented in portrait format and participants will be asked to move the manikin towards the stimuli. In the avoidance trials, the stimuli will be presented in landscape format and participants will be asked to move the manikin away from the stimuli. This rule will be counterbalanced across participants. In the no-go trials of the go/no-go task, the stimuli will be presented in portrait format and participants will have to withhold any response. In the go trials, the stimuli will be presented in landscape format and participants will have to respond. The format of the go and no-go trials will be counterbalanced across participants and stimuli will be presented using an 80/20% go/no-go ratio. These tasks will be completed before and after the conditioning procedure, in a standing position on a force platform to control for physical activity over time using the displacements of the center-of-pressure under their feet.

3.4.2. WHICH FACTORS MODIFY THE AUTOMATIC ATTRACTION TO ENERGETIC COST MINIMIZATION?

Objectives and hypotheses

WP1 should have demonstrated that stimuli associated with energetic cost decreases trigger multiple automatic regulatory processes (i.e., attention capture, affective reactions, approach tendencies, and inhibition). In WP2, I will examine factors that can affect these reactions, such as time, age, cardiovascular fitness ($\dot{V}O_2$ peak), and the level or variation of energetic expenditure. As stressed in the state-of-the-art section, as yet, no study has controlled or manipulated the physiological state of the individual (e.g., energy previously consumed during the day, $\dot{V}O_2$ peak, age) or during the experiment (e.g., increasing or decreasing energetic costs, time), which is an important issue. WP2 will extend previous literature that has tested the effect of dispositional and situational factors on the value assigned to stimuli [50-55] and integrate this new knowledge in exercise psychology. I hypothesize that physical fitness ($\dot{V}O_2$ peak), the short-term history of energetic expenditure (number of steps 1h and 24h before the experiment), the level of energy expenditure associated with the task (sitting position, standing position, or cycling), the time spent on the task (Figure 31), and age modify the automatic attraction to the stimuli related to energetic costs.

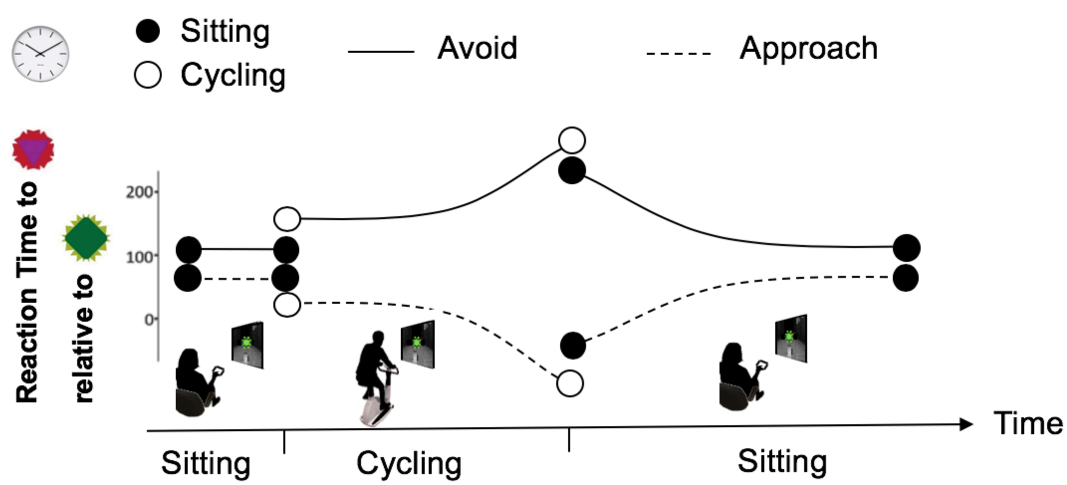


Figure 31. Expected effects of time and the level of energy expenditure on the automatic evaluation of the conditioned stimuli.

Experiments

The extent to which time and physical fitness modify automatic reactions in a standing position can already be investigated based on the WP1 dataset (n = 50) by including these factors as independent variables in the equations (Study 2.1). While I expect time to increase the positive value of the conditioned stimuli associated with energetic cost decreases in a standing position, this effect of time can also depend on the difference between recent energetic expenditure history and current energetic cost. To test this hypothesis, the effect of time will be investigated in the tasks described in WP1 while the participant is seated or cycling at different percentages of $\dot{V}O_2$ peak (Study 2.2; n = 50). The study will be composed of two counterbalanced experimental sessions differing in the order of the sitting and cycling position (sitting-cycling-sitting vs. cycling-sitting-cycling). Each session will be scheduled at the same hour of the day. I hypothesize that the automatic attraction to stimuli associated with decreasing energetic cost increases over the course of an active task (e.g., standing, cycling) and is more pronounced when the energetic cost of this task is higher (i.e., lower vs. higher percentage of $\dot{V}O2$ peak). To investigate whether the positive value assigned to energetic cost minimization depends on age, I will test automatic reactions to the conditioned stimuli in a sample of 105 participants aged 10 to 80 years with 15 subjects per 10-year slot (Study 2.3). Since my theory is based on evolution, I expect the attraction to decreasing energetic costs to be true irrespective of age.

3.4.3. WHICH BRAIN PROCESSES UNDERLIE THE AUTOMATIC REACTIONS TO ENERGETIC COST MINIMIZATION?

Objectives and hypotheses

WP1 and WP2 should have provided behavioral evidence supporting the positive value assigned to energetic cost decreases and its dependence on dispositional (i.e., different cardiovascular fitness) and situational factors (i.e., different level or duration of energetic expenditure). The results of the **proof-of-concept study** showed higher inhibition (larger N200 amplitude) when avoiding stimuli depicting inactive avatars (e.g., watching TV, lying on the sofa, or in a hammock) compared to avoiding physically active avatars (e.g., running, playing soccer, or swimming). These results suggested that avoiding the automatic attraction to lower energetic cost required higher levels of inhibition. In WP3, I will, for the first time, use TMS in a within-subjects design to investigate whether inhibition processes in the brain support an automatic attraction to energetic cost minimization. Based on the neurophysiological results of the EEG study, I hypothesize that inhibition processes will be higher when participants avoid stimuli associated with energetic cost decreases (compared to increases) in the manikin task (Figure 19) and when they withhold actions towards these stimuli in the go/no-go task. In addition, I hypothesize that this inhibition will be higher in participants with higher $\dot{V}O_2$ peak and higher usual level of physical activity as measured by the pedometer, i.e., participants who managed to implement their intention to be physically active.

Transcranial magnetic stimulation

TMS is a technique inducing a **localized electrical current** in the brain through **electromagnetism** [98]. This induced current is sufficient to **depolarize neuronal membranes**, to trans-synaptically activate corticospinal output neurons, and to generate motor evoked potentials (**MEPs**) [99]. MEPs elicited using TMS over M1 are used to assess **corticospinal excitability**. In WP3, I will be particularly interested in the **inhibition** processes underlying this excitability during the avoidance of stimuli associated with energetic cost decreases in the manikin task [94-96] and when withholding actions towards these stimuli in a go/no-go task [97]. Therefore, short- (**SICI**) and long-interval intracortical inhibition (**LICI**) will be tested through paired-pulse paradigms [100] in these two tasks.

Experiments

To decrease intra- and inter-tester variability and measurement error [101,102], TMS coil location and stimulation trajectory will be recorded and monitored in real-time through MRI-guided TMS neuronavigation (BrainSight) based on individual T1-weighted anatomical images. In WP3 (Study 3; n = 40), TMS-elicited MEPs will be recorded using surface electromyography (EMG) from participants' right first dorsal interosseous (FDI) muscle because MEPs are larger when the TMS probe is applied over the left M1 than over the right M1 [88]. The hotspot for eliciting MEPs in the FDI will be found by positioning the coil over the scalp region overlying the hand M1 representation [103]. FDI is chosen because the reaction-time tasks require index abduction to press the keys. The resting motor threshold will be defined as the lowest stimulus intensity that will elicit 5 out of 10 MEPs greater than or equal to a peak-to-peak amplitude of 50 µV [104]. SICI (2.5 ms inter-stimuli interval) and LICI (100-ms inter-stimuli interval) will be measured with a subthreshold (80% of the resting motor threshold) conditioning stimulus (CS) followed by a 120% suprathreshold (to produce a ~1 mV MEP) test stimulus (TS) and will be expressed and analyzed as a ratio of the MEP amplitude measured with paired stimuli (CS + TS) over the MEP measured with a single pulse stimuli (TS), where lower values represent more inhibition. The test stimulus will be at ~200 ms after presentation of the visual stimulus because our EEG proof-of-concept study and previous results [105] showed the highest inhibition present at ~200 ms. A pilot study will be performed to confirm this approach. The motor response for a typical two-choice reaction time is ~250 ms [106]. I will monitor EMG activity before and after the TMS stimulus to ensure no pre-stimulus muscle activity contaminates the recording of MEPs. In the first session, I will normalize the variations of excitability by expressing the amplitude of the MEPs measured after a single pulse under the experimental conditions (increasing cost, decreasing cost, constant cost) as a function of MEP baseline measured through 20 MEPs at a 120% suprathreshold intensity between each experimental block while participants are at rest. In the second session, I will test whether this altered corticospinal excitability is supported by processes of intracortical inhibition that have been related to $GABA_A$ and $GABA_B$-receptor using SICI [107] and LICI paired-pulse paradigm [108], respectively [109] (Figure 32).

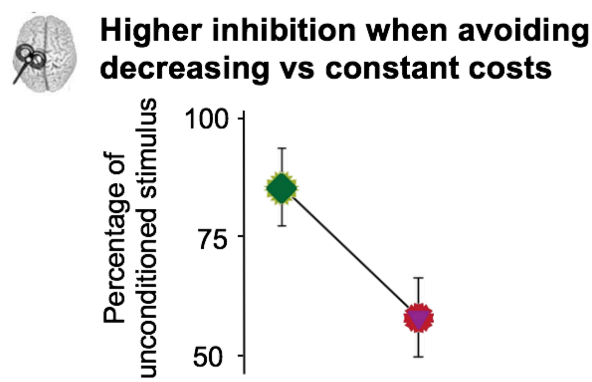


Figure 32. Expected results of the transcranial magnetic stimulation experiment testing intracortical inhibition in the manikin task.

3.4.4. WHICH BRAIN REGIONS UNDERLIE THE AUTOMATIC REACTIONS TO ENERGETIC COST MINIMIZATION?

Objectives and hypotheses

WP3 should have demonstrated that inhibitory brain processes support the automatic attraction to energetic cost minimization. In WP4, I will investigate which brain regions underlie this attraction. The key brain regions of reward and emotional arousal have been widely investigated in animals and humans [110-120]. Here, I will use fMRI to test whether these brain regions, such as the amygdala, nucleus accumbens, or the ventral striatum [110-120], are more activated when reacting to stimuli associated with decreasing versus constant of increasing energetic costs. Since the results of the proof-of-concept study showed higher inhibition when avoiding physically inactive compare to active avatars, I will also test whether brain regions involved in action inhibition, such as the right inferior frontal cortex, presupplementary motor area, and basal ganglia (striatum and subthalamic nucleus) (Figure 33) [121-123], are more activated when participants avoid stimuli associated with decreasing energetic cost than when they avoid stimuli associated with increasing energetic cost. I hypothesize that brain regions related to reward and emotional arousal are more activated when reacting to stimuli associated with decreasing than constant and increasing energetic cost. In addition, I hypothesize that these brain activations are higher in individuals with lower $\dot{V}O_2$ peak and lower usual level of physical activity as measured by the pedometer and the IPAQ, i.e., participants who failed to implement their intention to be physically active. To further test my hypotheses, structural MRI analyses will be performed to test whether the shape and volume of the significant regions revealed by the fMRI experiments explain the automatic reaction to the conditioned stimuli and whether they can predict which people are successful at implementing their intention to be physically active.

Magnetic resonance imaging

MRI is a non-invasive technique imaging technique that can be used to study both brain structure (T1 image) and brain function (T2 image) through the application of a magnetic field and a radio frequency pulse. fMRI is used to study brain activity. The most common fMRI approach uses the Blood Oxygenation Level Dependent (BOLD) contrast. BOLD fMRI measures the metabolic demands (i.e., oxygen consumption) of active neurons as an indicator of their activity. The spatial resolution of structural MRI images is higher than the T2 images and allows distinguishing different types of tissues (e.g., grey vs. white matter).

Figure 33. Expected results of WP4 testing brain activity that explains automatic reactions to stimuli related to energetic variations using functional magnetic resonance imaging.

Experiments

To investigate which brain regions underlie the automatic reactions to energetic cost minimization, I will use MRI to test whether activity and structure of reward-related brain regions explain behavioral reaction differences between conditioned stimuli associated with decreasing versus constant and increasing energetic cost. First, I will use a reactivity task [124] adapted to the conditioned stimuli to define ROIs among the key brain regions of reward and emotional arousal (Study 4.1; n = 20). Participants will be asked to look separately at each conditioned stimulus. The ROIs evidenced in this first fMRI experiment will be used in a second experiment (n = 40) based on the manikin task. To ensure that the regions involved in the attraction to energetic minimization are activated during scanning, participants will stand on a force plate for 3 × 5 min before being tested in the scanner. This second experiment (Study 4.2) will be based on 4 conditions: 1) approaching stimuli associated with increasing costs and avoiding stimuli associated with decreasing costs, 2) the opposite, 3) approaching stimuli associated with constant costs and avoiding stimuli associated decreasing costs, and 4) the opposite. Each condition will be tested in a run where each stimulus is presented 12 times and each run is repeated three times. Trials and runs will be randomly ordered. Each run will start with a cueing phase informing the nature of the run. Each trial will start a fixation cross, after 750 ms the stimulus and manikin will be presented concurrently, and the following trial will randomly start 4, 6, or 8 s after the presentation of the stimulus [124]. Because it is hardly possible to predict the setting that will be used during the analysis of the fMRI results, a third study (Study 4.3; n = 40) will be performed using identical analysis settings and published as a registered report to demonstrate their replicability. Functional images will be acquired using a research-devoted 3-Tesla MRI machine with a 32-channel head coil.

The volume of the ROIs explaining automatic behavioral reaction in the fMRI experiments will be included in linear mixed models to investigated whether the structure [73-75] of these ROIs explains automatic reactions to the conditioned stimuli and whether the structure of these ROIs predicts which people are successful at implementing their intention to be physically active. T1 images collected during study 3 (n = 40) and 4.1, 4.2, 4.3 (total n = 100) will be analyzed in Study 4.4.

fMRI analysis

After standard preprocessing (correction for slice acquisition, motion realignment, and co-registration to the individual anatomical image), I will use a first-level linear model implemented in SPM12 to estimate the activation for each type of the run. The design matrix will consist of a regressor for each condition and an intercept for each run. The regressor will be modelled as a boxcar function beginning with the first stimulus of the run, which will be convolved with a standard hemodynamic response function. From the estimated regression weights, I will compute the percentage signal change compared with the neutral condition. The cluster probability threshold will be set at $p < 0.05$ and familywise error will be controlled by calculating the critical size of the largest suprathreshold cluster that would be expected by chance using Gaussian field theory as implemented in the fmristat package. I have already performed such fMRI studies [125-126]. Based on my hypotheses, I will also conduct a ROI analysis. Additional ROIs may be added based on the results from the exploratory analysis (reactivity task). The average activity in these ROIs will be submitted to a linear mixed model to calculate differences between the 3 conditions.

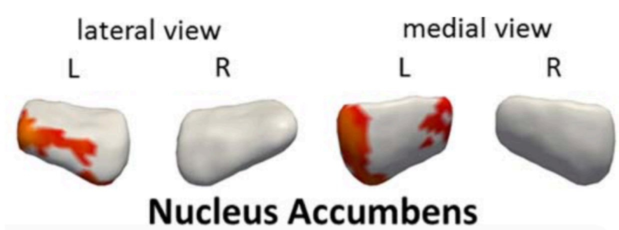


Figure 34. Expected results of analyses using the FMRIB's Integrated Registration Segmentation Toolkit (FSL FIRST) testing which brain structure can predict the automatic attraction to energetic cost minimization.

Structural MRI analysis

To support the fMRI results, complementary structural imaging techniques will be selected to address specific research questions as I already did in previous articles [73-75]. As a first step, the FreeSurfer automated segmentation [128] will be used to extract the volumetric measurement from cortical and subcortical structures identified with the fMRI analysis. The extracted volumes will be included as predictors of approach-avoidance tendencies in linear mixed models. Based on the results of the linear mixed models, I will perform additional imaging analysis to strengthen the fMRI results and refine spatial accuracy. To further investigate sub-regions of the basal ganglia, I will use the FMRIB's Integrated Registration Segmentation Toolkit (FSL

FIRST; Figure 34), which was specifically designed to provide accurate and robust segmentation of subcortical structures such as the basal ganglia [130]. To further investigate cortical ROIs, I will use the Voxel-Based Morphometry protocol (FSL VBM) [131] with registration to the MNI152 standard space because it has been demonstrated accurate for local cortical grey matter volume analysis.

3.4.5. CAN THE AUTOMATIC ATTRACTION TO ENERGETIC COST MINIMIZATION BE RETRAINED?

Objectives and hypotheses

Perceptual decisions have been shown to be biased by the physical resistance applied to the response [127]. In WP4 (Study 5.1; n = 50), I will use this bias to retrain participants' automatic attraction to stimuli associated with lower level of energetic costs by making their approach more effortful (i.e., increased resistance) compared to stimuli associated with higher level of energetic costs. In addition to allow the application of different resistive forces to movement, the KINARM Bilateral End-Point Lab (BKIN Technologies) will contribute to make the training task more entertaining as it allows the presentation of the stimuli in all directions on either the right or left hand. I hypothesize that, through a bias that has been evidenced in the literature [127], the automatic attraction to energetic cost minimization can be reduced (Study 5.1) and that this reduction is associated with increased inhibition (Study 5.2).

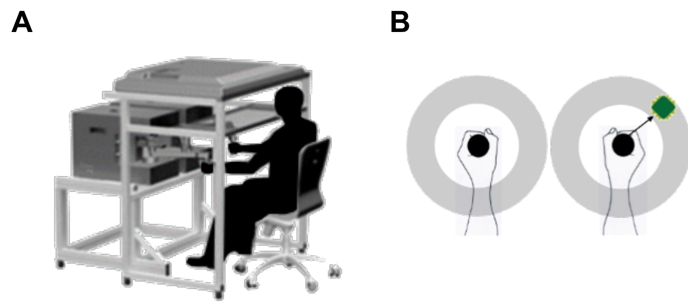


Figure 35. Bias-based training task. Panel A. KINARM Bilateral End-Point Lab set up. Panel B. Superior view of the hand and manipulanda. The participants will be instructed to approach or avoid stimuli associated with low and high energetic costs. A subliminal resistive force will be applied when participants will approach stimuli associated with lower energetic cost or avoid stimuli associated with higher energetic costs.

Experiments

This interventional study will consist of three phases. At pre-test (day 1), I will test baseline and $GABA_A$ and $GABA_B$ receptor related inhibition using SICI and LICI paired-pulse paradigms in a manikin task using the conditioned stimuli. From day 2 to day 4, participants will be trained on the approach-avoidance task in six 10-min blocks per day with 5-min rest between blocks. In a within design study, participants will be trained on the KINARM Bilateral End-Point Lab (Figure 35A), to approach the stimuli related to increasing energetic cost and avoid stimuli associated with decreasing energetic cost (Figure 35B). The posttest (day 5) will be identical to the pre-test. Feedback about reaction time performance and error rates will be provided.

Stimuli

To test the effect of training, the pre and post-test will use the conditioned stimuli. However, during the training, the objective is not to investigate the mechanisms underlying the automatic attraction to energetic cost minimization but to modifies this attraction. Therefore, the purity of the stimuli is not critical during the training sessions and may be inefficient due to a potential fading of the conditioned association across trials. Therefore, I will use actual pictures associated with low and high energetic costs. I will use a multitude of different pictures to prevent any bias due to information carried by pictures that is not relevant to energetic costs. In a pilot study, I will identify the pictures to be included in the approach-avoidance task. Thirty participants will be asked to rate the extent to which 250 pictures express “high energetic cost an active lifestyle” and “low energetic cost and sedentary lifestyle” (1 = not at all, 7 = a lot). For each stimulus, the “rest and sedentary lifestyle” score will be subtracted from the “movement and active lifestyle” score. The 100 stimuli with the largest positive and negative differences will be chosen as the stimuli depicting high energetic costs and low energetic cost in the training session, respectively.

3.5. CONCLUSION

The continuous approach to automatic exercise behavior introduced by this project will refine the theoretical framework of exercise psychology. The implementation of this approach through associative conditioning will provide results purely related to the construct of interest: energetic costs. This construct will allow to discover whether our behavior is attracted to energetic cost minimization, irrespective of age and of the reference level of energetic expenditure. The brain processes responsible for this behavior and underlying our inability to implement our intention to exercise will be identified and individuals will be trained to overcome this automatic attraction. In addition to providing new fundamental knowledge, the applied interest of the topic is evident as it taps into a global health problem: The pandemic of physical inactivity.

REFERENCES

[1] Chodzko-Zajko WJ. The World Health Organization issues guidelines for promoting physical activity among older persons. J Aging Phys Act. 1997;5:1–8.

[2] Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT; Lancet Physical Activity Series Working Group. Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet. 2012;380:219–229.

[3] WHO, 2010. Global recommendations on physical activity for health. World Health Organization, Geneva, Switzerland.

[4] Canadian Fitness and Lifestyle Research Institute, 2008. Physical activity monitor: facts and figures. http://www.cflri.ca/sites/default/files/node/95/files/PAM2008FactsFigures_Bulletin14_Intention_to_be_activeEN.pdf. Accessed October 11, 2018.

[5] Rhodes RE, Plotnikoff RC, Courneya KS. Predicting the physical activity intention-behavior profiles of adopters and maintainers using three social cognition models. Ann Behav Med. 2008;36:244–252.

[6] World Health Organization Global Health Observatory. Prevalence of insufficient physical activity. 2010. http://www.who.int/gho/ncd/risk_factors/physical_ activity/en/. Accessed September 6, 2018.

[7] Guthold R, Stevens GA, Riley LM, Bull FC. Worldwide trends in insufficient physical activity from 2001 to 2016: a pooled analysis of 358 population-based surveys with 1.9 million participants. 2018;6:e1077–e1086.

[8] Commission of the European communities. White paper on sport. 2017. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52007DC0391&from=EN. Accessed September 6, 2018.

[9] WelcomeEurope. Preparatory action in the field of sport and special annual events. https://www.welcomeeurope.com/european-funds/preparatory-action-field-of-sport-special-annual-events-732+632.html#tab=onglet_details. Accessed September 6, 2018.

[10] Erasmus+ Sport. Pourquoi un volet sport dans Erasmus+ ? http://site.erasmusplus-jeunesse.fr/sport-2.html. Accessed September 6, 2018.

[11] European Commission. Special Eurobarometer 472. Sport and physical activity. 2018. http://ec.europa.eu/commfrontoffice/publicopinion/index.cfm/ResultDoc/download/DocumentKy/82432. Accessed September 6, 2018.

[12] Kohl HW 3rd, Craig CL, Lambert EV, Inoue S, Alkandari JR, Leetongin G, Kahlmeier S, Lancet Physical Activity Series Working Group. The pandemic of physical inactivity: global action for public health. Lancet. 2012;380:294–305.

[13] Bandura A. Social foundations of thought and action: a social cognitive theory. 1986: Englewood Cliffs, Prentice-Hall.

[14] Deci EL, Ryan RM. Intrinsic motivation and self-determination in human behavior. 1985: New York, Plenum Publishing Co.

[15] Ekkekakis P, Zenko Z. Escape from cognitivism: exercise as hedonic experience. In Raab M, Wyllemann P, Seiler R, Elbe AM, Hatzigeorgiadis A (Eds). Sport and exercise psychology research. From theory to practice. 2016:389–414. Amsterdam: Elsevier.

[16] Rhodes RE, Dickau L. Experimental evidence for the intention-behavior relationship in the physical activity domain: a meta-analysis. Health Psychol. 2012;31:724–727.

[17] Hagger MS, Chatzisarantis NLD. Integrating the theory of planned behaviour and self-determination theory in health behaviour: a meta-analysis. Br J Health Psychol. 2009;14:275–302.

[18] Ekkekakis P. People have feelings! Exercise psychology in paradigmatic transition. Curr Opin Psychol. 2017;16:84–88.

[19] Brand R, Schweizer, G. Going to the gym or to the movies? Situated decisions as a functional link connecting reflective and automatic evaluations of exercise with exercising behavior. J Sport Exerc Psychol. 2015;37:63–73.

[20] Brand R, Ekkekakis P. Affective–reflective theory of physical inactivity and exercise. Ger J Exerc Sport Res. 2018;48:48–58.

[21] Cheval B, Radel R, Neva JL, Boyd LA, Swinnen SP, Sander D, Boisgontier MP. Behavioral and neural evidence of the rewarding value of exercise behaviors: a systematic review. Sports Med. 2018;48:1389–1404.

[22] Rebar AL, Dimmock JA, Jackson B, Rhodes RE, Kates A, Starling J, Vandelanotte C. A systematic review of the effects of non-conscious regulatory processes in physical activity. Health Psychol Rev. 2016;10:395–407.

[23] Schinkoeth M, Antoniewicz FF. Automatic evaluations and exercising: systematic review and implications for future research. Front Psychol. 2017;8:2103.

[24] Berry TR. Who's even interested in the exercise message? Attentional bias for exercise and sedentary-lifestyle related words. J Sport Exerc Psychol. 2006;28:4–17.

[25] Berry TR, Spence JC, Stolp SM. Attentional bias for exercise-related images. Res Q Exerc Sport. 2011;82:302–309.

[26] Calitri R, Lowe R, Eves FF, Bennett P. Associations between visual attention, implicit and explicit attitude and behaviour for physical activity. Psychol Health. 2009;24:1105–1123.

[27] Antoniewicz F, Brand R. Dropping out or keeping up? Early-dropouts, late-dropouts, and maintainers differ in their automatic evaluations of exercise already before a 14-week exercise course. Front Psychol. 2016;7:838.

[28] Bluemke M, Brand R, Schweizer G, Kahlert D. Exercise might be good for me, but I don’t feel good about it: do automatic associations predict exercise behavior? J Sport Exerc Psychol. 2010;32:137–153.

[29] Chevance G, Caudroit J, Romain AJ, Boiché J. The adoption of physical activity and eating behaviors among persons with obesity and in the general population: the role of implicit attitudes within the Theory of Planned Behavior. Psychol Health Med. 2017;22:319–324.

[30] Conroy DE, Hyde AL, Doerksen SE, Ribeiro NF. Implicit attitudes and explicit motivation prospectively predict physical activity. Ann Behav Med. 2010;39:112–118.

[31] Rebar AL, Ram N, Conroy DE. Using the EZ-diffusion model to score a single-category implicit association test of physical activity. Psychol Sport Exerc. 2015;16:96–105.

[32] Cheval B, Tipura E, Burra N, Frossard J, Chanal J, Orsholits D, Radel R, Boisgontier MP. Avoiding sedentary behaviors requires more cortical resources than avoiding physical activity: an EEG study. Neuropsychologia. 2018;119:68–80.

[33] Cheval B, Sarrazin P, Boisgontier MP, Radel R. Temptations toward behaviors minimizing energetic costs (BMEC) automatically activate physical activity goals in successful exercisers. Psychol Sport Exerc. 2017;30:110–117.

[34] Cheval B, Sarrazin P, Isoard-Gautheur S, Radel R, Friese M. Reflective and impulsive processes explain (in)effectiveness of messages promoting physical activity: a randomized controlled trial. Health Psychol. 2015;34:10–19.

[35] Cheval B, Sarrazin P, Pelletier L. Impulsive approach tendencies towards physical activity and sedentary behaviors, but not reflective intentions, prospectively predict non-exercise activity thermogenesis. PLoS One. 2014;9:e115238.

[36] Darwin C. On the origin of species, 1859. 2003: Routledge.

[37] Chin DD, Lentink D. How birds direct impulse to minimize the energetic cost of foraging flight. Sci Adv. 2017;3:e1603041.

[38] Alexander RM. Optima for animals. 1996: Princeton University Press.

[39] Niven JE, Laughlin SB. Energy limitation as a selective pressure on the evolution of sensory systems. J Exp Biol. 2008;211:1792–804.

[40] Selinger JC, O'Connor SM, Wong JD, Donelan JM. Humans can continuously optimize energetic cost during walking. Curr Biol. 2015;25:2452–2456.

[41] Rodman PS, McHenry HM. Bioenergetics and the origin of hominid bipedalism. Am J Phys Anthropol. 1980;52:103–106.

[42] Ivanenko YP, Dominici N, Lacquaniti F. Development of independent walking in toddlers. Exerc Sport Sci Rev. 2007;35:67–73.

[43] Srinivasan M, Ruina A. Computer optimization of a minimal biped model discovers walking and running. Nature. 2006;439:72–75.

[44] Maris E, Oostenveld R. Nonparametric statistical testing of EEG-and MEG-data. J Neurosci Methods. 2007;164:177–190.

[45] Groppe DM, Urbach TP, Kutas M. Mass univariate analysis of event-related brain potentials/fields I: a critical tutorial review. Psychophysiology. 2011;48:1711–1725.

[46] Luque D, Beesley T, Morris RW, Jack BN, Griffiths O, Whitford TJ, Le Pelley ME. Goal-directed and habit-like modulations of stimulus processing during reinforcement learning. J Neurosci. 2017;37:3009–3017.

[47] Kherad-Pajouh S, Renaud O. A general permutation approach for analyzing repeated measures ANOVA and mixed-model designs. Stat. Pap. 2015;56:947–967.

[48] Reynolds G. Are We Wired to Sit? The New York Times. 2018. https://www.nytimes.com/2018/09/26/well/move/are-we-wired-to-sit.html. Accessed October 11, 2018.

[49] Chiu A. You really, really want to go to the gym but still avoid it. New research may explain why. The Washington Post. 2018. https://www.washingtonpost.com/news/morning-mix/wp/2018/09/21/you-really-really-want-to-go-to-the-gym-but-still-avoid-it-new-research-may-explain-why/?utm_term=.025afb11c2e2. Accessed October 11, 2018.

[50] Robinson MJ, Berridge KC. Instant transformation of learned repulsion into motivational “wanting”. Curr Biol. 2013;23:282–289.

[51] Zhang J, Berridge KC, Tindell AJ, Smith KS, Aldridge, JW. A neural computational model of incentive salience. PLoS Comput Biol. 2009;5:e1000437.

[52] Aarts H, Dijksterhuis A, Vries P. On the psychology of drinking: being thirsty and perceptually ready. Br J Psychol. 2001;92:631–642.

[53] Seibt B, Häfner M, Deutsch R. Prepared to eat: how immediate affective and motivational responses to food cues are influenced by food deprivation. Eur J Soc Psychol. 2007;37:359–379.

[54] Pool E, Brosch T, Delplanque S, Sander D. Attentional bias for positive emotional stimuli: a meta-analytic investigation. Psychol Bull. 2016;142:79–106.

[55] Radel R, Clément-Guillotin C. Evidence of motivational influences in early visual perception: hunger modulates conscious access. Psychol Sci. 2012;23:232–234.

[56] Marcus BH, Selby VC, Niaura RS, Rossi JS. Self-efficacy and the stages of exercise behavior change. Res Q Exerc Sport. 1992;63:60–66.

[57] Brière NM, Vallerand RJ, Blais MR, Pelletier LG. Développement et validation d'une mesure de motivation intrinsèque, extrinsèque et d'amotivation en contexte sportif : l'échelle de motivation dans les sports (ÉMS). Int J Sport Psychol. 1995;26:465–489.

[58] Gosling SD, Rentfrow PJ, Swann WB. A very brief measure of the Big-Five personality domains. J Res Pers. 2003;37:504–528.

[59] Tangney JP, Baumeister RF, Boone AL. High self-control predicts good adjustment, less pathology, better grades, and interpersonal success. J Pers. 2004;72:271–324.

[60] Talmi D, Seymour B, Dayan P, Dolan RJ. Human Pavlovian–instrumental transfer. J Neurosci. 2008;28:360–368.

[61] Pool E, Brosch T, Delplanque S, Sander D. Where is the chocolate? Rapid spatial orienting toward stimuli associated with primary rewards. Cognition. 2014;130:348–359.

[62] Freeman SM, Razhas I, Aron AR. Top-down response suppression mitigates action tendencies triggered by a motivating stimulus. Curr Biol. 2014;24:212–216.

[63] Claes N, Crombez G, Vlaeyen JW. Pain-avoidance versus reward-seeking: an experimental investigation. Pain. 2015;156:1449–457.

[64] Fujita K, Sasota JA. The effects of construal levels on asymmetric temptation-goal cognitive associations. Soc Cogn. 2011;29:125–146.

[65] Mang CS, Snow NJ, Wadden KP, Campbell KL, Boyd LA. High-intensity aerobic exercise enhances motor memory retrieval. Med Sci Sports Exerc. 2016;48:2477–2486.

[66] Mang CS, McEwen LM, MacIsaac JL, Snow NJ, Campbell KL, Kobor MS, Ross CJD, Boyd, LA. Exploring genetic influences underlying acute aerobic exercise effects on motor learning. Sci Rep. 2017;7:12123.

[67] Mang CS, Snow NJ, Campbell KL, Ross CJ, Boyd, LA. A single bout of high-intensity aerobic exercise facilitates response to paired associative stimulation and promotes sequence-specific implicit motor learning. J Appl Physiol. 204;117:1325–1336.

[68] Boisgontier MP, Cheval B. The anova to mixed model transition. Neurosci Biobehav Rev. 2016;68:1004–1005.

[69] Ma Y, Mazumdar M, Memtsoudis SG. Beyond repeated-measures analysis of variance: advanced statistical methods for the analysis of longitudinal data in anesthesia research. Reg Anesth Pain Med. 2012;37:99–105.

[70] Judd CM, Westfall J, Kenny DA. Treating stimuli as a random factor in social psychology: a new and comprehensive solution to a pervasive but largely ignored problem. J Pers Soc Psychol. 2012;103:54–69.

[71] Box GEP, Cox DR. An analysis of transformations. J R Stat Soc Series B Stat Methodol. 1964;26:211–252.

[72] Osborne JW. Improving your data transformations: applying the Box–Cox transformation. Pract Assess Res Eval. 2010;15:1–9.

[73] Boisgontier MP, Cheval B, Chalavi S, van Ruitenbeek P, Leunissen I, Levin O, Nieuwboer A, Swinnen SP. Individual differences in brainstem and basal ganglia structure predict postural control and balance loss in young and older adults. Neurobiol Aging. 2017;50:47–59.

[74] Boisgontier MP, van Ruitenbeek P, Leunissen I, Chalavi S, Sunaert S, Levin O, Swinnen SP. Nucleus accumbens and caudate atrophy predicts longer action selection times in young and old adults. Hum Brain Mapp. 2016;37:4629–4639.

[75] Boisgontier MP, Cheval B, van Ruitenbeek P, Cuypers K, Leunissen I, Sunaert S, Meesen R, Zivari Adab H, Renaud O, Swinnen SP. Cerebellar grey matter explains bimanual coordination performance in children and older adults. Neurobiol Aging. 2018;65:109–120.

[76] Boisgontier MP, Serbruyns, L, Swinnen, SP. Physical activity predicts performance in an unpracticed bimanual coordination task. Front Psychol. 2017;8:249.

[77] Cheval B, Sieber S, Guessous I, Orsholits D, Courvoisier DS, Kliegel M, Stringhini S, Swinnen SP, Burton-Jeangros C, Cullati S, Boisgontier MP. Impact of early- and adult-life socioeconomic circumstances on level of physical inactivity. Med Sci Sports Exerc. 2018;50:476–485.

[78] Zivari Adab H, Chalavi S, Beets IAM, Gooijers J, Leunissen I, Cheval B, Collier Q, Sijbers J, Jeurissen B, Swinnen SP, Boisgontier MP. White matter microstructural organization of interhemispheric pathways predicts different stages of bimanual coordination learning in young and older adults. Eur J Neurosci. 2018;47:446–459.

[79] Corporaal SHA, Gooijers J, Chalavi S, Cheval B, Swinnen SP, Boisgontier MP. Neural predictors of motor control and impact of visuo-proprioceptive information in youth. Hum Brain Mapp. 2017;38:5628–5647.

[80] Boisgontier MP, Cheval B, van Ruitenbeek P, Levin O, Renaud O, Chanal J, Swinnen SP. Whole-brain grey matter density predicts balance stability irrespective of age and protects older adults from falling. Gait Posture. 2016;45:143–150.

[81] Davidian M, Giltinan DM. Nonlinear Models for Repeated Measurement Data. 1995: Chapman & Hall, London, UK.

[82] Fjell AM, Walhovd KB, Westlye LT, Østby Y, Tamnes CK, Jernigan, TL, Gamst A, Dale AM. When does brain aging accelerate? Dangers of quadratic fits in cross-sectional studies. Neuroimage. 2010;50: 1376–1383.

[83] Hastie TJ, Tibshirani RJ, Friedman JH, 2008. The Elements of statistical learning: data mining, inference, and prediction, second ed. Springer, USA.

[84] Wood S, 2006. Generalized additive models: an introduction with R. CRC Press, USA.

[85] Albers CJ, Lakens D. When power analyses based on pilot data are biased: Inaccurate effect size estimators and follow-up bias. J Exp Soc Psychol. 2018;74:187–195.

[86] Lakens D. Performing high-powered studies efficiently with sequential analyses. Eur. J. Soc. Psychol. 2014;44:701–710.

[87] Pocock SJ. Group sequential methods in the design and analysis of clinical trials. Biometrika 1977;64:191–199.

[88] Brown KE, Lohse KR, Mayer IMS, Strigaro G, Desikan M, Casula EP, Meunier S, Popa T, Lamy JC, Odish O, Leavitt BR, Durr A, Roos RAC, Tabrizi SJ, Rothwell, JC, Boyd, LA, Orth M. The reliability of commonly used electrophysiology measures. Brain Stimul. 2017;10:1102–1111.

[89] Cohen J, 1988. Statistical power analysis for the behavioral sciences. New York, NY: Routledge Academic.

[90] Nosek BA, Lakens D. Registered reports: a method to increase the credibility of published results. Soc Psychol. 2014;45:137–141.

[91] Posner MI, Cohen Y. Components of visual orienting. In Bouma H, Bouwhuis DG (Eds.), Attention and performance X: control of language processes (1984;32:531–556). Hillsdale: NJ: Erlbaum.

[92] Fazio RH, Sanbonmatsu DM, Powell MC, Kardes FR. On the automatic activation of attitudes. J Pers Soc Psychol. 1986;50:229–238.

[93] Fazio RH, Jackson JR, Dunton BC, Williams CJ. Variability in automatic activation as an unobtrusive measure of racial attitudes: a bona fide pipeline? J Pers Soc Psychol. 1995;69:1013–1027.

[94] Krieglmeyer R, Deutsch R. Comparing measures of approach-avoidance behaviour: the manikin task vs. two versions of the joystick task. Cogn Emot. 2010;24:810–828.

[95] Mogg K, Bradley BP, Field M, De Houwer J. Eye movements to smoking-related pictures in smokers: relationship between attentional biases and implicit and explicit measures of stimulus valence. Addiction. 2003;98:825–836.

[96] Rougier M, Muller D, Ric F, Alexopoulos T, Batailler C, Smeding A, Aubé B. A new look at sensorimotor aspects in approach/avoidance tendencies: the role of visual whole-body movement information. J Exp Soc Psychol. 2018;76:42–53.

[97] Gomez P, Ratcliff R, Perea M. A model of the go/no-go task. J Experimental Psychol Gen. 2007;136:389–413.

[98] Cabrera LY, Evans EL, Hamilton RH. Ethics of the electrified mind: defining issues and perspectives on the principled use of brain stimulation in medical research and clinical care. Brain Topogr. 2014;27:33–45.

[99] Hamilton R, Messing S, Chatterjee A. Rethinking the thinking cap: ethics of neural enhancement using noninvasive brain stimulation. Neurology. 2011;76:187–193.

[100] Kujirai T, Caramia MD, Rothwell JC, Day BL, Thompson PD, Ferbert A, Wroe S, Asselman P, Marsden CD. Corticocortical inhibition in human motor cortex. J Physiol. 1993;471:501–519.

[101] Sack AT, Cohen Kadosh R, Schuhmann T, Moerel, M, Walsh V, Goebel R. Optimizing functional accuracy of TMS in cognitive studies: a comparison of methods. J Cogn Neurosci. 2009;21:207–221.

[102] Klein PA, Duque J, Labruna L, Ivry RB. Comparison of the two cerebral hemispheres in inhibitory processes operative during movement preparation. Neuroimage. 2016;125:220–232.

[103] Yousry TA, Schmid UD, Alkadhi H, Schmidt D, Peraud A, Buettner A, Winkler P. Localization of the motor hand area to a knob on the precentral gyrus. A new landmark. Brain. 1997;120:141–157.

[104] Rossini PM, Burke D, Chen R, Cohen LG, Daskalakis Z, Di Iorio R, Di Lazzaro V, Ferreri F, Fitzgerald PB, George MS, Hallett M, Lefaucheur JP, Langguth B, Matsumoto H, Miniussi C, Nitsche MA, Pascual-Leone A, Paulus W, Rossi S, Rothwell JC, Siebner HR, Ugawa Y, Walsh V, Ziemann U. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. Clin Neurophysiol. 2015;126:1071–1107.

[105] Waldvogel D, van Gelderen P, Muellbacher W, Ziemann U, Immisch I, Hallett M. The relative metabolic demand of inhibition and excitation. Nature. 2000;406:995–998.

[106] Audiffren M, Tomporowski PD, Zagrodnik J. Acute aerobic exercise and information processing: energizing motor processes during a choice reaction time task. Acta Psychol. (Amst) 2008;129:410–419.

[107] Ziemann U, Lönnecker S, Steinhoff BJ, Paulus W. Effects of antiepileptic drugs on motor cortex excitability in humans: a transcranial magnetic stimulation study. Ann Neurol. 1996;40:367–378.

[108] McDonnell MN, Orekhov Y, Ziemann U. The role of $GABA_B$ receptors in intracortical inhibition in the human motor cortex. Exp Brain Res. 2006;173:86–93.

[109] Chen R, Cros D, Curra A, Di Lazzaro V, Lefaucheur JP, Magistris MR, Mills K, Rösler KM, Triggs WJ, Ugawa Y, Ziemann U. The clinical diagnostic utility of transcranial magnetic stimulation: report of an IFCN committee. Clin Neurophysiol. 2008;119:504–532.

[110] Gupta A, Mayer EA, Sanmiguel CP, Van Horn JD, Woodworth D, Ellingson BM, Fling C, Love A, Tillisch K, Labus JS. Patterns of brain structural connectivity differentiate normal weight from overweight subjects. Neuroimage Clin. 2015;7:506–517.

[111] Corbit LH, Balleine BW. The general and outcome-specific forms of Pavlovian-instrumental transfer are differentially mediated by the nucleus accumbens core and shell. J Neurosci. 2011;31:11786–11794.

[112] Gottfried JA, O'Doherty J, Dolan RJ. Encoding predictive reward value in human amygdala and orbitofrontal cortex. Science. 2003;301:1104–1107.

[113] Prévost C, Liljeholm M, Tyszka JM, O'Doherty JP. Neural correlates of specific and general Pavlovian-to-Instrumental Transfer within human amygdalar subregions: a high-resolution fMRI study. J Neurosci. 2012;32:8383–8390.

[114] Small DM, Jones-Gotman M, Dagher A. Feeding-induced dopamine release in dorsal striatum correlates with meal pleasantness ratings in healthy human volunteers. Neuroimage. 2003;19:1709–1715.

[115] Wyvell CL, Berridge KC. Intra-accumbens amphetamine increases the conditioned incentive salience of sucrose reward: enhancement of reward “wanting” without enhanced “liking” or response reinforcement. J Neurosci. 2000;20:8122–8130.

[116] Berridge KC. Food reward: brain substrates of wanting and liking. Neurosci Biobehav Rev. 1996;20:1–25.

[117] Knutson B, Adams CM, Fong GW, Hommer D. Anticipation of increasing monetary reward selectively recruits nucleus accumbens. J Neurosci. 2001;21:RC159.

[118] Murray EA. The amygdala, reward and emotion. Trends Cogn Sci. 2007;11:489–497.

[119] Roesch MR, Olson CR. Neuronal activity related to reward value and motivation in primate frontal cortex. Science. 2004;304:307–310.

[120] Schultz W, Tremblay L, Hollerman JR. Reward processing in primate orbitofrontal cortex and basal ganglia. Cereb Cortex. 2000;10:272–283.

[121] Aron AR, Durston S, Eagle DM, Logan GD, Stinear CM, Stuphorn V. Converging evidence for a fronto-basal-ganglia network for inhibitory control of action and cognition. J Neurosci. 2007;27:11860–11864.

[122] Aron AR, Robbins TW, Poldrack RA. Inhibition and the right inferior frontal cortex: one decade on. Trends Cogn Sci. 2014;18:177–185.

[123] Zandbelt BB, Vink M. On the role of the striatum in response inhibition. PLoS One. 2010;5:e13848.

[124] Wiers CE, Stelzel C, Gladwin TE, Park SQ, Pawelczack S, Gawron CK, Stuke H, Heinz A, Wiers RW, Rinck M, Lindenmeyer J, Walter H, Bermpohl F. Effects of cognitive bias modification training on neural alcohol cue reactivity in alcohol dependence. Am J Psychiatry. 2015;172:335–343.

[125] Santos Monteiro T, Beets IAM, Boisgontier MP, Gooijers J, Pauwels L, Chalavi S, King B, Albouy G, Swinnen SP. Relative cortico-subcortical shift in brain activity but preserved training-induced neural modulation in older adults during bimanual motor learning. Neurobiol Aging. 2017;58:54–67.

[126] Beets IAM, Gooijers J, Boisgontier MP, Pauwels L, Coxon JP, Wittenberg G, Swinnen SP. Reduced neural differentiation between feedback conditions after bimanual coordination training with and without augmented visual feedback. Cereb Cortex. 2015;25:1958–1969.

[127] Hagura N, Haggard P, Diedrichsen J. Perceptual decisions are biased by the cost to act. Elife. 2017;6: e18422.

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