Neural control of balance in increasingly difficult standing tasks

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Appendices

NEURAL CONTROL OF BALANCE IN INCREASINGLY DIFFICULT STANDING TASKS

For almost 150 years, standing balance has been regarded as a window into neuromuscular control. Difficult tasks, which involve sensory or mechanical manipulations of quiet standing, are particularly useful for revealing fundamental neural control strategies. We now know that several brain areas, including the cortex are involved in standing balance control. However, much is yet to be learnt about how cortical inputs tune muscle activation in increasingly difficult standing tasks. This thesis addressed three major questions related to cortical control of standing balance.

First, we examined what cortical neurophysiological processes contribute to standing balance control and whether they correlate with postural sway dynamics. To this aim, transcranial magnetic stimulation (TMS) was used to examine the neural excitability of single muscles - tibialis anterior (**chapter 2**) and peroneus longus (**chapter 3**). Corticospinal excitability is correlated with sway velocity; however, though cortical inhibition and facilitation are modulated in response to increasing task difficulty, they are independent of sway velocity. We conclude that corticospinal excitability tunes current muscle activation and consequently sway velocity, whereas task difficulty related changes in cortical inhibition and facilitation likely reflect other aspects of postural control like planning and preparation for potential perturbations.

Next, we examined how the cortex contributes to the co-ordination between multiple lower extremity muscles comprising functional synergies. To this aim, EMG-EMG coherence was used to examine cortical common inputs to groups of lower extremity muscles (**chapter 4**). Agonist-agonist coherence would support a reciprocal control strategy in which agonist and antagonist activation is temporally alternated, while agonist-antagonist coherence would support a stiffness strategy in which agonists and antagonists are activated simultaneously. We found that task difficulty related increases in cortical inputs favor reciprocal control. Additionally, the common inputs to specific pairs of muscles are in line with the biomechanical demands of each task.

Lastly, we examined factors contributing to individual differences in the neural control of standing. Individual cognitive attributes like confidence are known to influence balance but the neural processes mediating these effects are poorly understood. In **Chapter 5**, we found that task difficulty related modulation of intracortical facilitation (ICF) is correlated with the participants' self-reported balance confidence, suggesting that ICF can mediate the effects of confidence on muscle activation in standing. On a different note, intrinsic neural excitability, driven by factors like neurotransmitter concentration, synaptic strength etc., can drive individual differences in TMS outcomes. Supplementary analysis of data from **chapter 3** provides preliminary evidence that intrinsic neural excitability influences task difficulty related modulation of cortical excitability and can consequently account for individual differences in neural control of standing balance.

Chapter 6 summarizes our main findings regarding the role of cortical inputs to lower extremity muscles in the control of standing balance. Corticospinal excitability of single muscles is directly associated with sway velocity. However, task difficulty changes in cortical excitability likely contribute to other postural goals, besides sway control. Additionally, we found that cortical inputs to multiple muscles favor reciprocal control which is inherently more complex than stiffness control. Finally, the effects of cognitive attributes like confidence on motor performance are likely mediated by cortical neurophysiological processes. The main conclusion is that the cortex plays a role in the higher order planning and processing required for determining muscle activation patterns in increasingly difficult standing tasks.

NEURALE CONTROLE VAN BALANS TIJDENS STEEDS MOEILIJKERE BALANS TAKEN

Al 150 jaar wordt de staande balans gezien als een taak die inzicht geeft in neuromusculaire controle. Vooral moeilijke taken waarbij de staande balans sensorisch of mechanisch gemanipuleerd wordt, kunnen fundamentele neurale controle strategieën bloot te leggen. We weten nu dat verschillende hersengebieden, inclusief de cortex, betrokken zijn bij de controle van de staande balans. Er is echter nog veel onbekend over hoe de corticale input de spieractiviteit bijstelt wanneer de taak moeilijker wordt. Dit proefschrift gaat in op drie belangrijke vraagstukken met betrekking tot de corticale controle van de staande balans.

Eerst onderzochten we welke corticale neurofysiologische processen bijdragen aan de controle van de staande balans en of deze samenhangen met de dynamische beweging van het lichaamszwaartepunt. Transcraniële magnetische stimulatie (TMS) werd gebruikt om de neurale prikkelbaarheid van afzonderlijke spieren te onderzoeken – m. tibialis anterior (hoofdstuk 2) en m. peroneus longus (hoofdstuk 3). Hoewel corticale inhibitie en facilitatie wel gemoduleerd worden als gevolg van de moeilijkheid van de taak, blijken ze onafhankelijk van de snelheid van de beweging van het lichaamszwaartepunt. De corticospinale prikkelbaarheid bleek wel samen te hangen met de bewegingen van het lichaamszwaartepunt. Uit deze resultaten wordt geconcludeerd dat corticospinale prikkelbaarheid de spieractiviteit afstelt en daarmee ook de snelheid van de beweging van het lichaamszwaartepunt bepaald. Veranderingen in de corticale inhibitie en facilitatie die afhankelijk zijn van de moeilijkheid van de taak geven waarschijnlijk andere aspecten van de houdingscontrole weer, zoals planning en voorbereiding op mogelijke verstoringen.

Vervolgens werd onderzocht wat de bijdrage is van de cortex aan de coördinatie tussen verschillende spieren in de onderste extremiteit, in termen van functionele synergiën. De mate van EMG-EMG-coherentie werd gebruikt om corticale gemeenschappelijke input voor groepen spieren van de onderste extremiteit te onderzoeken (hoofdstuk 4). Agonist-agonist coherentie zou een controle strategie ondersteunen waarbij agonist en antagonist om en om geactiveerd worden. Agonist-antagonist coherentie zou een stijfheidsstrategie ondersteunen waarbij de agonist en de antagonist tegelijkertijd worden geactiveerd. Er werd gevonden dat de aan de moeilijkheid van de taak gerelateerde toename in de corticale input de controle strategie ondersteunt waarbij de agonist en de antagonist om en om geactiveerd worden. Bovendien is de gemeenschappelijke input van de specifieke spierparen in overeenstemming met de biomechanische eisen van elke taak.

Ten slotte werd onderzocht welke factoren bijdragen aan de individuele verschillenden in de neurale controle van de staande balans. Individuele cognitieve eigenschappen zoals vertrouwen, staan erom bekend dat ze de balans beïnvloeden. De neurale processen die deze effecten mediëren worden nog onvoldoende begrepen. In hoofdstuk 5 hebben we vastgesteld dat de aan de taakmoeilijkheid gerelateerde modulatie van de intracorticale facilitatie (ICF) gecorreleerd is aan het zelf gerapporteerde balansvertrouwen van de deelnemers. Dit suggereert dat ICF de effecten van balansvertrouwen op de spieractivatie kan regelen. Aan de andere kant zorgt ook de intrinsieke neurale prikkelbaarheid, aangedreven door factoren zoals de concentratie van neurotransmitters en de synaptische sterkte, voor individuele verschillen in TMS uitkomsten. Aanvullende analyse van de data uit hoofdstuk 3 levert voorlopig bewijs dat intrinsieke neurale prikkelbaarheid, invloed heeft op de aan de moeilijkheid van de taak gerelateerde modulatie van corticale prikkelbaarheid en daarmee individuele verschillen in de neurale controle van de balans kan verklaren.

Hoofdstuk 6 vat de belangrijkste bevindingen met betrekking tot de rol van de corticale input naar de spieren van de onderste extremiteit tijdens de controle van de staande balans samen. Corticospinale prikkelbaarheid van een enkele spier is direct geassocieerd met de beweging van het lichaamszwaartepunt. Echter, de aan de taakmoeilijkheid gerelateerde veranderingen dragen waarschijnlijk bij aan andere aspecten van de houdingscontrole, anders dan de snelheid van de beweging van het lichaamszwaartepunt. Bovendien bleek dat wanneer er corticale input naar meerdere spieren gaat de controle strategie wordt gebruikt die de agonist en de antagonist om en om activeert (reciproque controle),. Ten slotte worden de effecten van cognitive aspecten zoals vertrouwen op de motorische prestaties waarschijnlijk gemedieerd door corticale neurofysiologische processen. De belangrijkste conclusie is dat de cortex een rol speelt in de hogere orde planning en verwerking die nodig is voor het bepalen van spieractivatiepatronen in steeds moeilijkere staande balans taken.

ACKNOWLEDGEMENTS

This thesis would not have been possible without the support, guidance and patience of many people who have contributed directly and indirectly, over many years.

There is of course no question that I have learnt a great deal about science from all my academic advisors. I am grateful to each and every one of you for helping me to expand my horizons and develop my skills as a researcher. To some who have been most closely involved, I would like to say a special thank you for your kindness that went beyond the logical and objective confines of the research itself.

Dr. T. Hortobágyi, Tibor, I must start by thanking you for giving me the opportunity to come to Groningen and to enrich my life, both professionally and personally. Thank you, not only for sharing your immense knowledge, but also for always being accessible and approachable despite your packed schedule. It was always a comfort to know that I could knock on your door or email you and get a response within the hour! I must particularly mention the one evening (after all the equipment had given up!) when you called to reassure me that we would find a way to see the project through. This support and encouragement have been instrumental for bringing this book to completion.

Dr. C.J.C. Lamoth, Claudine, thank you for being a mentor I could always look up to for advice. I am inspired by your zest and enthusiasm both at and away from work. You have been an amazing role model and I am grateful for all the conversations about your experiences. You have truly helped me consider all the possibilities and envision where I want to be ten years from now. Also, I had no idea how much I could enjoy working with Matlab until I experienced the feeling of accomplishment from working with you till 7pm to get the code just right!

Dr. Salem, I can't believe it's been more than seven years since I walked into your office as a master's student! Thank you for always encouraging me to explore new avenues and push the boundaries. And, also, for teaching me to be practical – your advice to reserve two months when I thought I could get it done in two weeks, has saved me many a time! Your positivity and gentle encouragement really helped sustain my excitement for research, especially in the first couple years when I came to you with ideas, which in retrospect may not have been the best! But more importantly thank you for showing me how to find the right work-life balance; you have truly helped me to recognize priorities and maintain perspective.

Dr. Fisher, I must start by saying thank you for trusting me with the precious TMS equipment, even after I dropped the lab keys down the elevator shaft! Despite your many responsibilities, you were always there not only to guide the project, but also to help navigate the day to day hurdles of research. You made me feel like a part of your lab and gave me the opportunity to find my niche within Biokinesiology. But more importantly thank you for sharing your passion about caring for patients, and helping me to always remember the true aim and value of our research.

Dr. van Keeken, Helco, thank you helping me navigate to the CAREN system and always having innovative ideas to maximize the potential of our technology. Dr. Lewthwaite, thank you giving me the 'confidence' and support to explore topics outside my comfort zone. You showed me how to put research into practice by always finding the right approach to keep me 'motivated'! Dr. Powers, thank you showing me a great example of bringing research findings to clinical practice, and giving me the opportunity to observe this process closely at your clinic. I have always appreciated your direct (almost Dutch!) communication style and really enjoyed working with you over the years. Dr. Winstein, thank you for always pushing me to do better, and giving me the courage to believe that I could. You have helped me appreciate that our scientific beliefs can (and most likely will!) change with experience and see that I might be arguing against my own hypothesis 20 years from now! ! Dr. Baker, thank you for spending so many hours in the lab with me. Dr. Gregor, thank you for all the encouraging conversations that helped to find my way back when I was feeling a bit lost. Dr. Sigward thank you for infecting me with your enthusiasm for anatomy and teaching. Dr. Kulig, thank you for all the opportunities to improve my teaching skills, and for sharing your passion for research. The IT guys – Matt (USC), Emyl and Dirk (UMCG)! Thank you for being patient EVERY TIME I came to you with a new problem. All of you have taught me so many things that have helped me better appreciate both the possibilities and limitations of our technology.

The G9, G12 and 2nd floor peeps! Thank you all for helping me to navigate American and Dutch culture and making me feel at home. The evenings at Barbara's and Dog's have been just as instrumental as the lab meetings and seminars for bringing this project to completion. I must especially mention Andrea – I am amazed by your tenacity and optimism. It has always been so reassuring to know that I could reach out to you any time. Tom and Sigrid, you made me feel like I belonged here, right from the first day. And of course, thank you for teaching me the most important Dutch word, vrijdagmiddagborrel, and introducing me to Dutch music. I have been most fortunate to work in both LA and Groningen and get to know many more people I haven't been able to name individually. The most precious thing I have gained from this PhD is your friendship!

Akshara and Medha, I know I can call you after six months and pick up where we left off. I have been privileged to share important life events with both of you and you will always be my family, even if we are halfway across the world. Suma, it's been 12 years since you offered to help me navigate Manipal hospital, and the undergrad social life! Even though you don't live two floors away anymore, I still feel just as close to you. Leslie, Claire and Berber, I had not imagined I would find such a wonderful family when I decided to move here. I had never heard of Groningen, and now it feels like the home I will always want to return to. Thank you for the all the memories - Horst forever! Leslie, how could I have ever explored Bedum, Zuidhorn and Niehove without you?!

Ma-Baba and Dabhai-Dimma – you have stood by me and encouraged me through all the ups and downs, even when it seemed like this PhD would never end. I really won't attempt to express my gratitude here because any words will be inadequate. I love you! To the extended family – thank you for always being there for me.

Hans, you stuck by me through the rollercoaster of finishing the PhD and finding a job, it can only get better after this! You make me want to dance and to live in one place, and it's a first for both😆

ABOUT THE AUTHOR

Tulika Nandi was born in Indore, India on 8th January 1988 and grew up in Nagpur, India. In 2006, she moved to Manipal and in 2011 she obtained a Bachelor's in Physiotherapy from Manipal University, India. Subsequently, she moved to Los Angeles and in 2014 she obtained a Master's in Biokinesiology from the University of Southern California (USC), USA.

Tulika is interested in studying human movement, specifically balance, using a multi-dimensional approach that includes biomechanical, neural and cognitive assessments. She started her PhD in Los Angeles and moved to Groningen in 2016 to pursue a Sandwich PhD program funded by the Abel Tasman Scholarship. Her initial PhD work was conducted at the Jacquelin Perry Musculoskeletal Biomechanics Research Laboratory (at USC) and focused on the biomechanical aspects of standing balance. Later, she expanded her research to explore how brain activity, specifically in the motor cortex, relates to the postural sway observed in standing. This work was started at the Neuroplasticity and Imaging Laboratory (at USC) and continued at the University Medical Center Groningen. During her PhD, she published two papers that used a combined biomechanical and neurophysiological approach for studying standing balance. Additionally, Tulika was involved in teaching Anatomy courses in the Physical Therapy program (USC) for four years.

Currently, Tulika seeks to continue her career in human movement science, with a focus on clinical perspectives.

Journal Publications

- **Nandi, T.**, Lamoth, C. J., van Keeken, H. G., Bakker, L. B., Kok, I., Salem, G. J., Fisher, B. E., & Hortobágyi, T. (2018). In Standing, Corticospinal Excitability Is Proportional to COP Velocity Whereas M1 Excitability Is Participant-Specific. ***Frontiers in human neuroscience***, ***12***.
- **Nandi, T.**, Fisher, B. E., Hortobágyi, T., & Salem, G. J. (2018). Increasing mediolateral standing sway is associated with increasing corticospinal excitability, and decreasing M1 inhibition and facilitation. ***Gait & posture***, ***60***, 135-140.
- Hashish, R., Du Bois, A., Samarawickrame, S. D., **Nandi, T**., & Salem, G. J. (2017). Spatiotemporal characteristics of habitually shod runners change when performing barefoot running. ***Sport Sciences for Health***, 1-7.

Conference Contributions

- **Nandi T**, Lamoth CJC, van Keeken HG, Bakker LBM, Salem GJ, Fisher BE, Hortobágyi T. Task difficulty-related modulation of peroneus longus neural excitability during standing in young adults. ***Poster presentation at Annual Conference of the Society for the Neural Control of Movement, Santa Fe, NM, USA, May 2018.***
- **Nandi T**, Fisher BE, Hortobágyi T, Salem GJ. M1 inhibition and facilitation decrease when mediolateral standing balance is manipulated. ***Poster presentation at Annual Conference of the Society for the Neural Control of Movement, Dublin, Ireland, May 2017.***
- **Nandi T**, Fisher BE, Salem GJ. Association between motor cortical excitability and postural stability in standing. ***Poster presentation at Annual Conference of the American Society of Biomechanics, Raleigh, NC, USA, August 2016.***
- **Nandi T**, Fisher BE, Salem GJ. Modulation of cortical excitability with changes in base of support during standing. ***Poster presentation at Annual Conference of the Society for the Neural Control of Movement, Montego Bay, Jamaica, April 2016.***
- **Nandi T**, Du Bois A, Runkle N, Havens K, Salem GJ. Biomechanics of the functional reach test. ***Poster presentation at Annual Conference of the American Society of Biomechanics, Columbus, Ohio, USA, August 2015.***
- **Nandi T**, Salem GJ. Biomechanical Role of the hip in maintaining balance during standing forward reach. ***Poster presentation at Annual Conference of the American College of Sports Medicine, San Diego, California, USA, May 2015.***
- Du Bois A, **Nandi T**, Salem GJ. Validation of center of pressure measurements with artificial turf. ***Poster presentation at Annual Conference of the American College of Sports Medicine, San Diego, California, USA, May 2015.***

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