Enhanced somatosensory inhibition sharpens hand representation and sensorimotor skills in pianists

Masato Hirano, Yudai Kimoto, Sachiko Shiotani, and Shinichi Furuya

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19th Sep 2024

Dear Dr. Hirano:

Thank you for submitting your manuscript to The Journal of Neuroscience.

We have received the reviews of your paper, "Enhanced somatosensory inhibition sharpens hand representation and sensorimotor skills in pianists" (JN-RM-1486-24), which are appended to this email. Based on the reviewers' comments and our editorial assessment, we would like to reconsider your manuscript at The Journal of Neuroscience following major revisions. We hope that you will be able to address the reviewers' concerns in full and resubmit the manuscript, along with a point-by-point reply to the reviews that indicates your response to each concern. Before we make a decision about publication, we will have your revision reviewed by the reviewers and our editorial team.

Your revision must include the manuscript with new text highlighted, as well as a clean copy of the manuscript. Please carefully review your paper at this time for any corrections in style or substance. Please consult our Revised Submission Checklist for details on preparing your revision: https://www.jneurosci.org/sites/default/files/files/JN_Revised_Submissions_Checklist.pdf.

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Please return your revision within 3 months of this decision. If you need more time, please contact jn@sfn.org. When you are ready to submit your revision, log in using the link below and click on the manuscript number to create your revision.

Thank you for giving us the opportunity to consider your paper for publication in The Journal of Neuroscience. Please let us know if you have any questions or concerns.

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Yours sincerely,
James Bisley
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Editor-in-Chief
The Journal of Neuroscience

Manuscript Instructions

Reviewer #1 (Rationale for Significance Rating for Authors):

The study links somatosensory inhibition of finger digits during a task (not just rest) to concurrent perceptual and motor task performance - to my knowledge, this first time in humans.

Reviewer #1 :

Hirano et al. conducted a series of experiments to investigate the enhanced somatosensory inhibition of finger digits in pianists compared to non-musicians. They characterised the relationship between this inhibition and cortical representation of digits, perceptual acuity to passive movement, and skilled motor control. This study provides valuable insights into somatosensory inhibitory function and its relevance to skilled motor control.

I was particularly impressed by how the authors linked somatosensory inhibition of finger digits during a task (not just rest) to concurrent perceptual and motor task performance - to my knowledge, this first time in humans.

I have a few comments and suggestions:

1. Exp. 4 shows an increase in finger digit uniqueness 108-132 ms after the onset of the passive movement and particularly when the passive movement coincided with ulnar stimulation. Since the finger-specific distance measures were obtained from whole head EEG signals, it would be useful to see where they were most pronounced on the EEG topography (topoplot). This would allow the authors to test the hypothesis that the observed effect on digit distance is mediated by contralateral S1/M1. The localisation is briefly mentioned in the MS, but it would be useful to both plot and quantify it across the whole scalp. Despite expected distortions of the spatial patterns in EEG due to volume conduction, we can expect activity in contralateral/left sensorimotor areas to be picked up well by C3 and surrounding electrodes. If sceptical of the EEG surface results, the authors could delve deeper and run this analysis on source reconstructed data. My impression is that this analysis is central to the claims made based on results in Exp. 4.

2. Similar to the above, please supply topoplots for Sensory evoked potentials.

3. Cortical somatosensory inhibition is a sluggish process: The uniqueness of the digit-related patterns is most pronounced 110-300 ms after the onset of the passive movement. Considering that following the latter there would be a 50-60 ms delay due to motor adaptation/processing and cortico-spinal conduction before a response can be observed, the observed mean IKI in the sequence production task (~105 ms between finger presses) would not allow for somatosensory inhibition to take effect. Could the authors please comment on the role of open and closed loop control in the production of fast and skilled sequences like the ones used in the last experiment in the context of somatosensory inhibition? This is essential for interpreting the effect on skilled motor control.

4. Was there an overlap between participants across any of the experiments? I could not find a statement on this. If yes, are there any limitations, such as effects of plasticity across stimulations sessions/task generalisation?

Minor comments:
5. The manuscript is generally easy to follow, but the Methods section is lacking clarity of argument. It harder to understand the utility of the multiple experiments, presumably because the Results and Methods sections have appeared initially in a different order (as common for a lot of other journals). It would be beneficial if each Methods sub-section could feature one or two sentences on what the experiment is aiming to test and why a particular analysis has been chosen. It is present in some sub-sections, but not in all.

6. There are a variety of abbreviations, some standard (EEG, ISI) and some less so (PT, P, NM). Although they are explained, consider reducing the abbreviation load as much as possible to make the manuscript more accessible to a less specialised audience, e.g. animal model motor neuroscientists.

7. Fig, 4b -The colour axis in Figure 4b (RDMs) is difficult to read due to the similarity between blue (low values) and blue-green (medium values). Please adjust the colours for better clarity.

Reviewer 2 has declined to share their comments.

We appreciate the editors and two expert reviewers for their extremely helpful and constructive comments on our manuscript. Based on these pertinent comments, we made our best effort to revise and elaborate the manuscript so as to reflect the concerns raised by the editor and reviewers. Below, we provide responses to the individual comments based on our observation and interpretation, along with indications of a list of changes made in the revised manuscript.

Reviewer 1

1. Exp. 4 shows an increase in finger digit uniqueness 108-132 ms after the onset of the passive movement and particularly when the passive movement coincided with ulnar stimulation. Since the finger-specific distance measures were obtained from whole head EEG signals, it would be useful to see where they were most pronounced on the EEG topography (topoplot). This would allow the authors to test the hypothesis that the observed effect on digit distance is mediated by contralateral S1/M1. The localisation is briefly mentioned in the MS, but it would be useful to both plot and quantify it across the whole scalp. Despite expected distortions of the spatial patterns in EEG due to volume conduction, we can expect activity in contralateral/left sensorimotor areas to be picked up well by C3 and surrounding electrodes. If sceptical of the EEG surface results, the authors could delve deeper and run this analysis on source reconstructed data. My impression is that this analysis is central to the claims made based on results in Exp. 4.

A. We thank the reviewer for the valuable comment. We agree with the reviewer that providing the cortical topography of the digit distance can facilitate the understanding of the origin where the dissimilarity of ERP patterns between digits and the stimulation effect on it is mediated by the contralateral sensorimotor cortices. Here, we calculated the dissimilarity of ERP patterns between digits by a searchlight-like method. First, we defined neighborhood electrodes for each EEG electrode based on the Euclidean distance of the 3D layout of the electrodes (3-8 neighboring electrodes). Then, we calculated the dissimilarity of ERP patterns across the center and neighbors for each electrode. The resultant dissimilarity values, each corresponding to each center electrode, were finally used to display the EEG topography (Fig. 5D). This shows that the dissimilarity was maximum around the CP3 electrode, meaning that the evoked activity in the contralateral sensorimotor cortices was the main source of the inter-digit dissimilarity. The electrical stimulation to the ulnar nerve increased the dissimilarity around the contralateral sensorimotor cortices, indicating that the stimulation enhanced the uniqueness of the evoked neural activities around the contralateral sensorimotor cortex.

   We have added the result of this analysis to the revised manuscript.

2. Similar to the above, please supply topoplots for Sensory evoked potentials.

A. Thanks for the comment. We have added the averaged waveforms and topographical map of the ERP evoked by the passive movement of each finger in experiment 4 in Figure 4. We performed a source localization analysis to identify the origin of ERP components. We used the dipole source modeling, that was implemented in EEGLAB (Delorme and Makeig, 2004), using the function “dipfit_erpeeg”. A standard boundary-element model was used for localization. We used the group-averaged ERP data for this analysis because we did not record the actual electrode position and individual MRI data on the head structure. The position of the estimated dipole on the early components (i.e., the latency of 80 ms and 124 ms) is located around the sensorimotor cortex. By contrast, the vertex showed the most significant activity for the late component (i.e., the latency of 300 ms). This suggests that the somatosensory information, which is first processed in the somatosensory cortex, would propagate across the other cortical areas. We have added this result to the revised manuscript.

Unfortunately, we only recorded the EEG from the CP3 electrode (the reference electrode is the Fz) in experiments 2 and 3, so we cannot provide the topography of the SEP evoked by the peripheral nerve stimulation.

3. Cortical somatosensory inhibition is a sluggish process: The uniqueness of the digit-related patterns is most pronounced 110-300 ms after the onset of the passive movement. Considering that following the latter there would be a 50-60 ms delay due to motor adaptation/processing and cortico-spinal conduction before a response can be observed, the observed mean IKI in the sequence production task (~105 ms between finger presses) would not allow for somatosensory inhibition to take effect. Could the authors please comment on the role of open and closed loop control in the production of fast and skilled sequences like the ones used in the last experiment in the context of somatosensory inhibition? This is essential for interpreting the effect on skilled motor control.

A. Thank you for pointing out the critical issue. We regard that somatosensory inhibition is not a slow process; rather, it could influence the early somatosensory processes. In experiments 2 and 3, a preceding conditioning stimulus modulated the N20-P25 components of SEP evoked by a subsequent ulnar nerve stimulus in pianists when the inter-stimulus interval between the two stimuli was 10 ms. This means that the conditioning stimulus could modulate the neural activity in the somatosensory cortex just 30 ms after the onset of the conditioning stimulation (i.e., 10 ms ISI + 20 ms latency of the N20 component). This latency is sufficiently shorter than the average IKI in the sequence production task, even considering cortical processing and cortico-spinal conduction delay.

In experiment 4, the conditioning stimulus altered the inter-digit distance evoked by the passive movements 108-132 ms after the stimulation, suggesting that the effect of conditioning stimulus on somatosensory activities lasts for 100 ms. In experiment 5, we delivered the electrical stimulation to the ulnar nerve at 10 Hz in the sequence production task. Considering the long-lasting effect (i.e., ~100 ms) of a single conditioning stimulus, the 10 Hz stimulation would modulate the somatosensory activity while performing the task.

During the sequence production task, the somatosensory system must process incoming somatosensory afferents from different fingers. The processed somatosensory information is utilized to adjust motor commands (i.e., somatosensory-motor integration, closed-loop control). We previously demonstrated that the somatosensory-motor integration function, as indexed by a modulatory effect of passive movements on the corticospinal excitability, is associated with the fingertip force fluctuation during a tapping task (Hirano et al. 2020. Cereb.Cortex). In the fast multi-finger movements, abundant somatosensory afferents from different fingers are inputted into the somatosensory system. However, they interfere with each other due to the functional and structural overlap of somatosensory representation between fingers. This distorts not only the perception but also the somatosensory-motor integration processes during the fast multi-finger movements, which may lead to generating sub-optimal motor commands. We postulate that activating the somatosensory inhibition by the conditioning stimulation prevented this interference, facilitating the sequence production.

Although the present study cannot reveal the mechanism of the long-lasting effect of the conditioning stimulus, this effect was robust, as demonstrated by the behavioral test in experiment 3, that the stimulus improved the perceptual discrimination threshold for the sequence order of passive movements.

4. Was there an overlap between participants across any of the experiments? I could not find a statement on this. If yes, are there any limitations, such as effects of plasticity across stimulations sessions/task generalisation?

A. Thank you for the valuable comment. Yes, some pianists participated in several experiments. We listed the pianists in the table below. By contrast, there was no overlap between nonmusicians across experiments. We consider this overlap did not influence the results of this study because each experiment was separated by at least 3 months, the neurophysiological measurements in EXP2, EXP3, and EXP4 did not involve methods that could induce plasticity in the sensorimotor cortex, and the behavioral tasks in EXP1, EXP3, and EXP5 have been used to assess motor and perceptual abilities, not to induce learning effects. We have specified this in the method and discussion sections in the revised manuscript.

EXP1	EXP2	EXP3	EXP4	EXP5
1	2	27	37	16
2	16	2	38	44
3	17	28	8	37
4	18	15	39	45
5	15	29	10	46
6	19	4	34	47
7	20	10	40	10
8	4	30	16	48
9	21	31	35	49
10	22	32	41	50
11	23	33	42	51
12	24	34	43	52
13	25	35	3	53
14	26	36	13	54
15				

Table. Pianist's ID. The digit in each cell represents the unique pianist ID in this study. We colored the pianists who participated in multiple experiments.

Minor comments:

5. The manuscript is generally easy to follow, but the Methods section is lacking clarity of argument. It harder to understand the utility of the multiple experiments, presumably because the Results and Methods sections have appeared initially in a different order (as common for a lot of other journals). It would be beneficial if each Methods sub-section could feature one or two sentences on what the experiment is aiming to test and why a particular analysis has been chosen. It is present in some sub-sections, but not in all.

A. Thank you for the pertinent comment. We have added a brief explanation on what this experiment was aiming to examine at the beginning of each paragraph.

6. There are a variety of abbreviations, some standard (EEG, ISI) and some less so (PT, P, NM).

Although they are explained, consider reducing the abbreviation load as much as possible to make the manuscript more accessible to a less specialised audience, e.g. animal model motor neuroscientists.

A. We have carefully checked the abbreviations and reduced them.

7. Fig, 4b -The colour axis in Figure 4b (RDMs) is difficult to read due to the similarity between blue (low values) and blue-green (medium values). Please adjust the colours for better clarity.

A. We have changed the colormap used in the RDM image, accordingly.

Reviewer 2 has declined to share their comments.

29th Nov 2024

Dear Dr. Hirano:

Thank you for submitting your manuscript to The Journal of Neuroscience.

We have received the reviews of your paper, "Enhanced somatosensory inhibition sharpens hand representation and sensorimotor skills in pianists" (JN-RM-1486-24R1), which are appended to this email. Based on the reviewers' comments and our editorial assessment, we would like to reconsider your manuscript at The Journal of Neuroscience following a minor revision. As you will see, Reviewer 1 asks that the gist of your response to one of their issues be included in the manuscript. We hope that you will be able to address this issue and resubmit the manuscript, along with a reply that indicates your response. Before we make a decision about publication, we will have your revision reviewed by our editorial team.

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Yours sincerely,
James Bisley
Senior Editor

Angelika Lingnau
Reviewing Editor

Sabine Kastner
Editor-in-Chief
The Journal of Neuroscience

Manuscript Instructions

Reviewer #1 (Rationale for Significance Rating for Authors):

This study provides valuable insights into somatosensory inhibitory function and its relevance to skilled motor control.

Reviewer #1 :

I have reviewed the author's responses alongside the revised manuscript. I am happy with the revision, although I could not see whether my point 3 ("Could the authors please comment on the role of open and closed loop control in the production of fast and skilled sequences like the ones used in the last experiment in the context of somatosensory inhibition? This is essential for interpreting the effect on skilled motor control.") was only addressed in the response or also in the revised manuscript. A clarification in the manuscript would be beneficial, in my view.

Reviewer 2 has declined to share their comments.

We appreciate the editors and reviewers for their helpful and constructive comments on our manuscript. Based on the comments, we have revised and elaborated the manuscript to address the concerns raised by the editor and reviewers.

Reviewer #1

1. I have reviewed the author's responses alongside the revised manuscript. I am happy with the revision, although I could not see whether my point 3 ("Could the authors please comment on the role of open and closed loop control in the production of fast and skilled sequences like the ones used in the last experiment in the context of somatosensory inhibition? This is essential for interpreting the effect on skilled motor control.") was only addressed in the response or also in the revised manuscript. A clarification in the manuscript would be beneficial, in my view.

   Answer: Thanks for your comment. We have added the relevant sentences on this topic in the discussion section. We have also made minor changes to the discussion section to avoid exceeding the maximum word limit for the discussion.

Reviewer 2 has declined to share their comments.