## TMS-based neurofeedback facilitates motor imagery of different hand actions

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*Introduction:* Non-invasive brain-computer interfaces (BCIs) enable users to modulate brain activity in a goal-directed manner. Most non-invasive BCIs can decode only gross movements but many daily tasks require finer finger and hand control. We developed a novel BCI using motor imagery (MI) and transcranial magnetic stimulation (TMS)-based neurofeedback (NF) training to reinforce representations of complex hand actions in the brain. This proof-of-concept study investigates the utility of this BCI for training hand function via MI.

*Material, Methods and Results:* 12 participants (6 males, age  $32.0 \pm 2.7$  years) completed 4 (1 motor execution and 3 motor imagery (MI)) sessions of TMS-based NF training on 3 right-hand actions (holding a bottle, turning a key, and opening the hand). There were 4 blocks in each session. The MI sessions comprised 1 no NF and 3 NF blocks but Session 4 had an additional no NF block as ending. During the training, a personalized, adaptive support vector machine (SVM) ensemble was used to classify coming MI trials and provide NF accordingly. An SVM classifier with leave-one trial-out cross-validation was used to derive block-wise average classification accuracy as an outcome measure to assess the training effect. We used a linear mixed-effect model with MI without NF data and noted that the accuracy of the final block (60.5%) showed nearly significant improvement compared to the first block (53.3%;  $\beta = 0.091$ , t<sub>33</sub> = 1.974, p = 0.057; Figure 1). We used another linear mixed-effect model with MI+NF data to evaluate the learning effect and found that Session 3 accuracy (59.3%) was significantly higher than Session 2 (53.3%,  $\beta = -0.080$ , t<sub>88</sub> = -3.208, p = 0.006) and Session 4 accuracy (58.2%) was marginally significantly higher than Session 2 ( $\beta = -0.060$ , t<sub>88</sub> = -2.421, p = 0.053).

*Conclusion:* We developed and tested a novel, personalized, and adaptive MI and TMS-based BCI for complex hand actions. Our findings suggest that healthy adults could modulate brain activities for complex hand actions with the guidance of NF. This demonstrates that TMS-based BCI could be used for hand function training in individuals who are unable to produce overt motor output.

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Figure 1: Average cross-validation (CV) accuracy of all MI blocks. Overall, the CV accuracy increased with the training, indicating that participants could benefit from NF and retain the learning without NF immediately after the training as seen in Session 4.