Assessing the influence of age related changes in premotor-motor connectivity on action selection

Theoretical background

The global population is rapidly aging, calling for investigation of the consequences of age related changes on everyday life behaviors. In this regard, age related changes in cognitive functioning and affective and motivational processes have been related to suboptimal action selection, and decision making in general (Hess, Strough, & Löckenhoff, 2015; Samanez-Larkin & Knutson, 2015).

Crucially, motor processes also crucially influence action selection. In fact, the interaction between premotor and motor areas is not downstream of the action selection process, limited to mere kinematic coordination, but plays a causal role in driving action selection (Thura & Cisek, 2014). In this regard, changes in the connectivity of the cortical motor system have been identified in aging (Draganski, Lutti, & Kherif, 2013). Nevertheless, the consequences that these changes may have on action selection remain largely neglected.

Aims and Hypotheses

We will test the effect of age related changes in the connectivity of the motor system on action selection. We hypothesize older adults to have reduced premotor-motor (PM-to-M1) connectivity, which should be related to impairments in action selection, such that larger reductions in PM-to-M1 connectivity should be associated with more severe impairments.

Methods

Participants and sample. 18 young (~20-30 y) and 18 older (~65-80 y) healthy right-handed adults free from any contraindication to TMS (Rossi et al., 2009) will be recruited. Sample size based on power analysis: mixed factor ANOVA, effect size=.25; alpha=.05; power=.8.

Tools.

Action selection task. A validated task will be used to assess differences in action selection between young and older participants (Garofalo & di Pellegrino, 2015). It will include three consecutive phases:

1. Instrumental conditioning phase. Participants will learn to perform different actions, some leading to a food reward and others to no-reward (as control condition). Participants’ responses will be collected.

2. Pavlovian conditioning phase. We will test PM-to-M1 connectivity (see below), when no action is executed but motor activity is covertly elicited by the presented stimuli (Zhang, Mano, Ganesh, Robbins, & Seymour, 2016). Participants will learn the value of different visual stimuli. Some will be associated with a reward obtained during the Instrumental phase, i.e. “action-related” Pavlovian stimuli. Some will be associated with a reward never obtained during the Instrumental phase, i.e. “non-action-related” Pavlovian stimuli. Some will be associated with no-reward, i.e. control stimuli.

3. Action selection phase. We will test the influence of the acquired Pavlovian associations on action selection. Participants will make the instrumental actions, while the Pavlovian stimuli will be presented. Participants’ responses will be collected.

Transcranial Magnetic Stimulation (TMS). To assess PM-to-M1 connectivity during the Pavlovian conditioning phase, dual site TMS (dSTMS) will be performed using 2 Magstim 200 monophasic stimulators via 2 focal coils by recording motor-evoked potentials (MEPs) induced by a test TMS pulse over M1 preceded by a conditioning pulse over PM (Fiori, Chiappini, & Avenanti,
A neuronavigation system will be used to assist identification of PM and M1 areas over participant’s scalp.

**Skin conductance response (SCR).** To assess Pavlovian learning during the Pavlovian conditioning phase, SCR will be recorded and peak-to-peak SCR to Pavlovian stimuli will be computed as previously done in Starita, Kroes, Davachi, Phelps, & Dunsmoor (2019).

**Procedure.** The instrumental phase will be completed. Then, individual calibration of TMS stimulation parameters, localization of PM and M1 sites over the scalp and placement of SCR electrodes will be conducted. The Pavlovian phase will follow, during which dsTMS will be performed and SCR recorded. Finally, the action selection phase will be completed.

**Statistical analyses.** To assess instrumental conditioning, a mixed factor ANOVA (factors: group, response type) on total number of responses will be used. To assess Pavlovian conditioning and PM-to-M1 connectivity, a mixed factor ANOVA (factors: group, stimulus type) on mean SCR and mean MEP amplitude, respectively, will be used. To assess the influence of the Pavlovian stimuli on action selection, a mixed factor ANOVA (factors: group, stimulus type) on total number of responses will be used. Finally, to assess the relationship between premotor-motor connectivity and action selection, in each group, simple regressions will be performed between mean MEP amplitude in response to each CS during the Pavlovian conditioning phase and the respective number of responses during the action selection phase.

**Declaration of commitment to request ethical approval.** Ethical approval will be requested from the Ethics Committee of the University of Bologna.

**Expected results**

To confirm instrumental conditioning, we expect participants to perform more rewarded than non-rewarded actions. To confirm Pavlovian conditioning, we expect greater mean SCR in response to rewarded than non-rewarded stimuli. For the action selection phase, we expect the young group to show more responses in presence of the “action-” than the “non-action-related” Pavlovian stimuli and control stimuli. Compared to the young group, in the older group, we expect a reduced difference in responses between “action-” and “non-action-related” Pavlovian stimuli.

Crucially, during Pavlovian conditioning in the young group, we expect an inhibitory effect of PM over M1 during the presentation of control stimuli (similar to a resting condition). Instead, we expect an excitatory effect of PM over M1 during the presentation of “non-action-related” stimuli, which should be even greater during the presentation of “action-related” stimuli. This will result in greater mean MEP amplitude for “action-” than “non-action-related” stimuli and control stimuli. Compared to the young group, in the older group, we expect a reduced inhibition of PM over M1 during the presentation of control stimuli and a reduced excitation of PM over M1 during the presentation of “non-action-related” stimuli, which should be even greater during the presentation of “action-related” stimuli. This will be reflected in greater mean MEP amplitude for “action-” than “non-action-related” stimuli and control stimuli. Finally, in each group, we also expect mean MEPs amplitude to each CS to predict the respective total number of responses during action selection.

**Implications**

The study will highlight the functional role of PM-to-M1 connectivity in action selection and the extent to which age related changes in such connectivity affect action selection. This may have clinical implications for the design of neurostimulation procedures to improve action selection in healthy and pathological aging.
References


Plan of activities

Project and training activities

- Deepen theoretical knowledge regarding instrumental and Pavlovian learning, action selection, the role of the motor system in these processes and associated age related changes
- Acquire new methodological skills specific to the design and implementation of research studies concerning the investigation of instrumental and Pavlovian learning, and action selection
- Acquire new technical skills regarding the use of hardware and software to deliver visual stimuli and record behavioral response (e.g. Matlab), record psychophysiological measures (e.g. BIOPAC) and deliver transcranial magnetic stimulation
- Acquire new technical skills regarding data processing and analysis (e.g. SPSS)
- Improve scientific communication skills concerning the dissemination of results by participating at national and international conferences
- Improve scientific writing skills by writing up the results for peer-reviewed publication
- Acquire new skills concerning the translational application of the results in order to understand health aging and improve pathological aging

Timing of activities

Months 1-2: literature review, study design
Months 3-4: piloting and study refinement
Months 5-7: testing
Months 8-9: data analysis
Months 10-12: results writing and dissemination
Feasibility of the project

The study will be conducted at the Center for Studies and Research in Cognitive Neuroscience, where the equipment to carry out the study is already available.

Project: 6998 characters (including spaces)

References and plan of activities: 3118 characters (including spaces)