Cortical plasticity of spatial stimulus-response associations: electrophysiological and behavioral evidence

Alessandro Angrilli,CA Marco Zorzi,[1],CA Mariaelena Tagliabue, Luciano Stegagno and Carlo Umiltà

Department of General Psychology, University of Padova, Via Venezia 8, 35131 Padova; [1]Faculty of Psychology, University S. Raffaele, Via Olgettina 58, 20132 Milano, Italy

CACorresponding Authors

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Right-handed subjects tend to respond faster to stimuli presented in the visual hemifield that spatially corresponds to the responding hand. In a typical Simon task, response is based on a non-spatial salient feature of the stimulus (e.g. color) whereas its position must be ignored. However, the spatial position of the stimulus interferes with the processing of the salient characteristic. Subjects are significantly faster when stimulus side and response side correspond (corresponding condition) than when they do not (non-corresponding condition). We have previously shown with behavioral experiments that, when subjects practice reversed contingencies (that is, spatially incompatible trials) in a session preceding the Simon task, they show a long-term retention of these associations, resulting in the disappearance of the latency cost typically observed in non-corresponding trials. Here we show, by means of the lateralized readiness potential, that the neural correlate of such behavioral plasticity is an increase in premotor cortex activation during preparation of non-corresponding responses. This effect showed a marked left–right asymmetry which suggests an important role of subjects' handedness. Our results demonstrate that humans can learn in a single session to reverse relatively stable stimulus-response associations. *NeuroReport* 12:973–977 © 2001 Lippincott Williams & Wilkins.

Key words: Cortical plasticity; Handedness; Laterality; Lateralized readiness potential; Simon effect; Spatial compatibility

INTRODUCTION

In a typical Simon task, subjects are asked to press one of two keys in response to a non-spatial attribute (e.g. color) of a lateralized stimulus. Even though stimulus position is not relevant for response selection, reaction times (RTs) are faster and responses are more accurate when stimulus side and response side correspond (corresponding trials) than when they do not (non-corresponding trials). The RT difference between non-corresponding and corresponding conditions (usually in the range 20–40 ms) is referred to as the Simon effect (see [1] for a review). A widely accepted explanation of the effect is that, in the Simon task, a spatial code is automatically generated for the irrelevant stimulus locational attribute, and this produces interference at the level of response selection [1,2]. More direct evidence for automatic activation of response codes has been found in several psychophysiological studies, using the lateralized readiness potential (LRP) [3–5] or electromyographic measures [6].

The Simon effect, like other response interference phenomena (e.g. the Stroop effect), is thought to be very robust and relatively impermeable to the influence of practice or strategies. However, the results of two recent studies revealed that performing a task, prior to the Simon task, in which the spatial dimension is task relevant, alters the Simon effect in a dramatic way [7,8]. In Tagliabue *et al.* [7], subjects performed the Simon task after a task that included just 72 trials of a spatially compatible or a spatially incompatible condition. Results showed a regular Simon effect after the spatially compatible task and a null or reverse Simon effect after the spatially incompatible task. Even more striking was that the size of the Simon effect, after the incompatible task, depended on the interval between the two tasks: there was no Simon effect with delays of 5 min and of 24 h, whereas after an interval of 7 days there was a reverse Simon effect.

These results were interpreted on the basis of dual-route models. Dual-route models, in their various versions [2,3,9], maintain that the onset of the imperative stimulus activates two parallel pathways. One pathway, referred to as conditional (or controlled) route, codes the non-spatial, task-relevant stimulus dimension and leads to the selection of the correct response on the basis of task instructions. The other pathway, referred to as unconditional (or automatic) route, codes the spatial, task-irrelevant stimulus dimension, becoming active irrespective of stimulus identification or task instructions. Barber and O'Leary ([10], see also [11]) distinguished these two pathways on the basis of their reliance upon short-term memory associations (STM links; i.e. the conditional route) or long-term memory associations (LTM links; i.e. the unconditional route).

This approach predicts that the magnitude of the Simon effect should depend on the relative strength of activation of the two routes. When the imperative stimulus appears, its position activates the LTM-based, unconditional route, thus priming the corresponding response. At the same time, the STM-based, conditional route activates the correct response depending on the non-spatial information. If both routes converge onto the same response, RT is fast; if not, the incorrect response must be inhibited, and selection of the correct response requires extra time (see [2] and [7] for computational models).

Tagliabue *et al.* [7] used computer simulations and time-course analyses of the RT data to contrast two different hypotheses regarding how previous practice with a spatially incompatible task might change the cognitive architecture to produce a reverse Simon effect. The first hypothesis was that previous practice produces a modification of LTM links (i.e. the unconditional route); the second hypothesis was that the STM links set up to perform the spatially incompatible task (i.e. a conditional pathway) are still active when the Simon task is later performed. The data supported the latter hypothesis.

In the present study, we aimed at investigating the electrophysiological correlates of the behavioural plasticity observed in our previous RT study [7]. Similar to that behavioural study, the Simon task was administered to two groups of subjects, which had previously performed either the compatible or the incompatible version of the spatial compatibility task. Based on previous electrophysiological studies [3–5], we focussed on the lateralized readiness potential (LRP) as an index of the processes related to the response selection stage [12,13]. In particular, we asked whether, after the compatibility tasks, the two groups would show different LRP patterns during the Simon task.

MATERIALS AND METHODS

Twenty-two students of the University of Padova participated in the experiment (13 females, nine males; mean age 23.6, range 21–30 years) after giving informed consent. All subjects were 100% right handed according to the Edinburgh Handedness Inventory [14]. Subjects were randomly assigned to one of two groups: 11 performed the compatible version of the spatial compatibility task (Group C) and 11 performed the incompatible version of the task (Group I). One subject was discarded from Group C because of excess in EEG artifacts during recording, thus resulting in $10 + 11$ subjects. Subjects of Group C had to respond as fast as possible with the hand (e.g. left hand) corresponding to the side of the target stimulus (e.g. left hemifield); subjects of Group I performed a reversed contingency: they had to respond with the hand placed on the side opposite to the position of the target stimulus. The session consisted of 144 trials (two conditions: left and right stimuli, 72 trials each).

Five minutes after the spatial compatibility task, both groups performed the Simon task. Thus, the only difference between the two groups was the nature of the first session (spatially compatible or spatially incompatible task). The Simon task consisted of 288 trials divided into four conditions and presented in randomized order. Each trial started with a fixation cross presented in the center of the screen together with a 300 ms beep; the cross persisted for other 1500 ms after which the target (a green or red square) was presented for 100 ms either on the left or on the right of fixation point. Subjects responded to the color of the stimulus (within 1000 ms) by pressing one of two keys with the index fingers of the left and right hands, respectively. The mapping between color of the stimulus and responding hand was balanced between subjects. The inter-trial interval was 1000 ms. The four experimental conditions derive from the combination of response hand (Lx *vs* Rx) and spatial correspondence between stimulus and response (corresponding *vs* non-corresponding). Thus, the conditions were: Lx–corresponding, Lx–non-corresponding, Rx–corresponding, Rx–non-corresponding.

EEG was recorded by means of 19 tin electrodes, mounted on an ElectroCap and placed at international standard positions. Linked mastoids were used as reference. In addition, two electrodes above and two below the eyes were placed to detect eye movements. Electrophysiological data were recorded by means of a SynAmp and Scan 4 software (NeuroSoft) in DC mode, low-pass set to 50 Hz, sampling rate 250 Hz, and resolution of 0.084 μV. Raw data were analysed off-line by epoching, linear detrend to remove slow DC drifts, eye blinks correction using eye electrodes as reference, manual rejection of trials with residual artifacts, response-locked averaging of all accepted trials for each condition. The final averaged epoch included 800 ms before and 200 ms after the response (total 1000 ms). The average of the first 100 ms was subtracted from the whole epoch. According to previous studies, the readiness potential is mainly generated in premotor areas [15–17]. For the LRP [18,19] the difference between C3 and C4 (C3−C4 for left hand response and C4−C3 for right hand response) amplitudes was computed in two intervals preceding the response: −400 to 200 ms and −200 to 0 ms (Fig. 2). Thus, positive values of the C3/C4 difference are associated with greater readiness potential (negativity), and therefore premotor cortical activation of the expected response (either with left or right hand), while negative deflections indicate preparation of the opposite incorrect response. Statistics on the LRPs were done by multifactorial analysis of variance including the following factors: group (C *vs* I), response (right *vs* left), condition (corresponding *vs* non-corresponding), interval (−400 to 200 ms *vs* −200 to 0 ms). Analyses of the behavioral data (RTs) did not include the interval factor.

RESULTS

Behavioral data of the first task (the spatial compatibility task) showed a main effect of group ($F(1,19) = 12.3$, $p < 0.002$): subjects who performed the incompatible spatial associations were much slower than subjects who did respond to spatially compatible trials (402 ms and 304 ms, respectively).

The following statistics concern data collected during the Simon task. Analysis of the RT data showed a significant effect of response side ($F(1,19) = 4.5$, $p < 0.05$), indicating that subjects were faster with the right than the left hand (447 *vs* 458 ms). The effect of condition (i.e. the Simon effect) was only marginally significant ($F(1,19) = 4.28$, $p = 0.052$). There was, however, a clearly significant interaction between group and condition ($F(1,19) = 9.61$, $p < 0.01$): group C showed a significant 26 ms Simon effect (425 *vs* 451 ms; $p < 0.01$ Newman–Keuls) whereas group I showed a non-significant reversed effect of −5 ms (470 *vs* 465 ms; ns) (Fig. 1).

Statistical analysis of electrophysiological data showed two main effects. The condition factor (F(1,19) = 11.8, $p <$ 0.003) revealed greater cortical activation (positive values of LRP) for corresponding than for non-corresponding trials. The interval factor (F(1,19) = 162.8, $p < 0.0001$) showed the typical increased activation in the proximity of the response (see the time course of the LRP in Fig. 2).

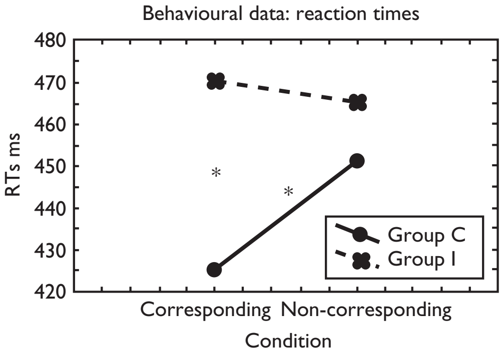

Fig. 1. Reaction times of compatible and incompatible groups collected during the second session (Simon task). *Significant *post-hoc* effect, $p <$ 0.01.

The three-way interaction group × response × condition was also significant (F(1,19) = 4.9, $p < 0.04$). *Post-hoc* analyses (Newman–Keuls) revealed that group C had greater LRP to corresponding than to non-corresponding trials, both for left and right responses ($p < 0.02$; Fig. 2a,b), whereas group I showed greater LRP for left responses ($p < 0.01$) but not for right responses (ns; Fig. 2c,d). The four-way interaction was also significant (F(1,19) = 6.7; $p < 0.02$), indicating that the effect was modulated by the interval (−400 to −200 ms *vs* −200 to 0 ms). Group C showed a significant effect of condition for both left and right responses at the first interval ($p < 0.01$) and for right responses at the second interval ($p < 0.01$). Group I showed a different pattern: the effect of condition for right responses was absent at both intervals.

It would seem therefore that a different pattern for the two groups is observed only for right responses. However, statistical tests performed by contrasting mean LRP against zero, revealed in group C a significant negative activation

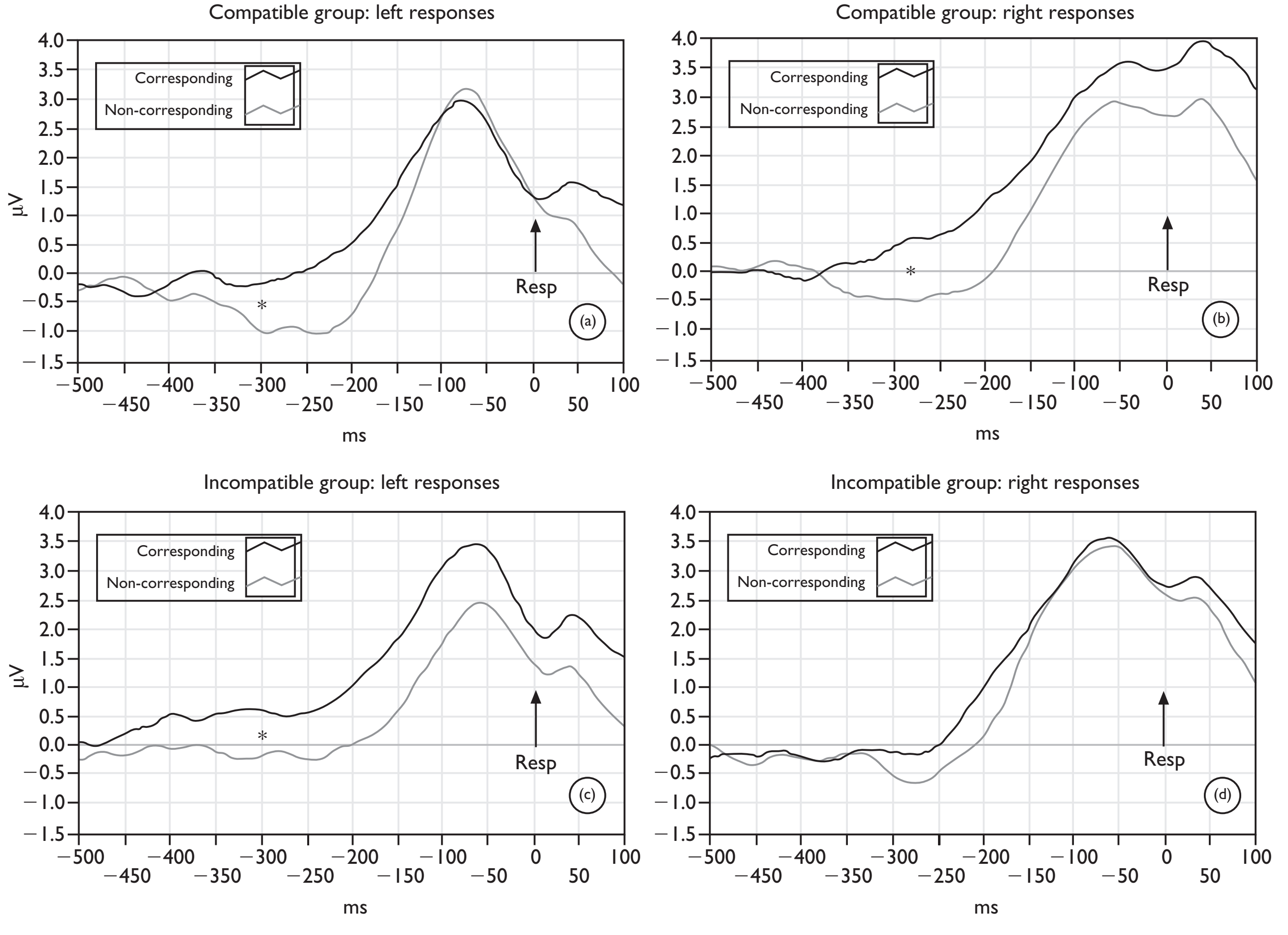

Fig. 2. Waveforms showing lateralized readiness potential of compatible (**a**,**b**) and incompatible (**c**,**d**) groups for left (a, c) and right responses (b,d). In each figure the time courses of corresponding vs non-corresponding conditions are compared. Cortical activation of the expected response is represented by positive values and activation of contralateral incorrect response by negative values. Every waveform is the difference between C3 and C4 electrodes (C3−C4 for left hand response and C4−C3 for right hand response). *Significant *post-hoc* effect, $p < 0.01$.

of left responses during the first interval of the non-corresponding trials ($t9 = 3.93$, $p < 0.01$), but this negativity did not appear in group I ($t10 = 0.55$, ns).

DISCUSSION

Behavioral results reliably replicated our previous study [7]. Subjects who performed the incompatible version of the spatial compatibility task (Group I; reversed contingencies: right response to a left stimulus and left response to a right stimulus) prior to the Simon task showed no effect of spatial stimulus–response correspondence (i.e. no Simon effect). In contrast, a regular Simon effect was observed in subjects who performed the spatially compatible task prior to the Simon task (group C). This result was originally explained [7] with reference to the distinction between long-term memory (LTM) and short-term memory (STM) links (see also [11]). It has been suggested that the STM links set up to perform the spatial compatibility task, which are supposed to be brief and transient, are nonetheless still active when the Simon task is subsequently performed [7]. Therefore, in the case of the spatially incompatible task, STM links encoding reversed contingencies will affect the execution of the Simon task and cause the disappearance of the correspondence effect that is produced by the LTM links (see [7] for computer simulations with a connectionist model).

The present study provides evidence regarding the electrophysiological correlates of this phenomenon and can help in clarifying the mechanisms involved. First, our results show that, indeed, different LRP patterns can be observed in the two groups of subjects while they are performing the same task. This confirms a model which assumes that the phenomenon shows up at the level of response selection [7].

More specifically, the LRP data showed greater premotor activation for corresponding compared with non-corresponding trials (i.e. the LRP equivalent to the Simon effect) for the control group (Group C). This effect, however, was not present for the right responses of the other group (Group I). Thus, subjects who performed the spatially incompatible task failed to show a LRP Simon effect on the right side. It is somewhat striking, however, that left responses were not affected in the same way of right responses. This asymmetry between left and right responses can be perhaps understood with reference to handedness of the subjects. All our subjects were right-handed, so it seems plausible to assume that right-hand responses are somewhat more automatized than left-hand responses. In particular, spatial associations between stimulus position and response position might be stronger for the dominant hand because it is preferentially used to respond in everyday activities. In terms of the computational model of Zorzi and Umiltà [2,7], this can be implemented as weaker LTM links for left-side associations compared to right-side associations. When the stimulus appears on the left side, the weaker LTM link would produce less automatic priming of the left response, which in turn implies less inhibition of the right response (because the two responses are mutually inhibitory). This is compatible with the LRP data reported for group C. Left responses in non-corresponding trials are significantly inhibited in the first time interval, indicating that the incorrect right response is relatively stronger; this inhibition, however, is not significant for non-corresponding right responses. In group I, the inhibition of non-corresponding left responses disappears, suggesting that the activation of the incorrect right response is reduced (or blocked) as a result of practicing the spatially incompatible task.

The literature on the Simon effect has often neglected the possible asymmetries between left and right responses. However, in addition to the asymmetric effects described for the electrophysiological results, three lines of evidence from behavioural data argue in favour of handedness as the main source of the observed asymmetries. First, the dominant hand is typically faster than the non-dominant one (see Results). Second, it is also more efficient in responding to ipsilateral stimuli (that is, one of the effects observed in the Simon task). Third, the Simon effect is often, although not always, greater to right than to left responses: 33 ms *vs* 11 ms, respectively, in the present experiment. Indeed, the fastest, more efficient hand pays the greatest cost (slower RTs) when non-corresponding responses are requested. This greater efficiency of the dominant hand is probably related to ipsilateral long-term stimulus-response neural connections reinforced by experience (see [11] for discussion). That is, in the case of right-handed subjects, LTM links would produce greater preactivation of right than left responses. This preactivation is beneficial for corresponding responses (faster right-side RTs) but is detrimental for non-corresponding responses (greater right-side RTs cost).

Cortical plasticity is revealed in our data by two phenomena: first, practicing the spatially incompatible task reduces (or eliminates) the preactivation of right incorrect responses, as shown by the significant negative deflection for left non-corresponding responses found in group C. This early negative bump disappears in group I (Fig. 2a,c). Second, practicing the spatially incompatible task also eliminates LRP differences between corresponding and non-corresponding right responses (Fig. 2b,d).

CONCLUSION

A group of subjects who first performed a task with incompatible spatial associations was able to recover, in the subsequent Simon task, the typical cost (slower RTs, see responses of group C) paid for spatial mismatch between stimulus position and response side (non-corresponding condition). This effect was evident in both behavioral and electrophysiological measures. Our interpretation that the observed left-right asymmetry found at all measured levels is related to different strengths of long term memory links for dominant and non-dominant hand (and thus to the handedness of the sample of subjects) will be the focus of future investigations.

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