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Cerebellum and spatial cognition: A connectionist approach

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Abstract. A large body of experimental and theoretical work has investigated the role of the cerebellum in adaptive motor control, movement coordination, and Pavlovian conditioning. Recent experimental findings have also begun to unravel the implication of the cerebellum in high-level functions such as spatial cognition. We focus on behavioural genetic data suggesting that cerebellar long-term plasticity may mediate the procedural component of spatial learning. We present a spiking neural network model of the cerebellar microcomplex that reproduces these experimental findings. The model brings forth a prediction on the interaction between the neural substrates of procedural and declarative spatial learning.

1 Introduction

Complementing the extensive research on *declarative* spatial memory (which concerns the ability to learn abstract contextual representations), another class of works has investigated the *procedural* component of spatial cognition, which involves the acquisition of adaptive sensorimotor couplings relevant to optimal goal-directed behaviour [1]. Declarative spatial learning is likely to be mediated by the anatomo-functional interaction between hippocampal and neocortical (mainly parietal and prefrontal) areas [2]. Procedural mnemonic processes permitting the fine tuning of navigation trajectories seem to involve the interaction between subcortical structures and the cerebellum [3]. We study procedural spatial learning via a computational neuroscience approach. The work presented here focuses on the behavioural genetic findings reported by Burguière et al. (2005) [3] suggesting that cerebellar long-term plasticity plays a significant role in learning efficient goal-directed trajectories.

We model the main information processing components of the cerebellar microcomplex (Fig. 1). Afferent information enters the cerebellum via two neural pathways: *(i)* mossy fibres (MFs) convey multimodal sensorimotor signals and project excitatory efferents to both the granular layer of the cerebellar cortex and the subcortical deep cerebellar nuclei; *(ii)* climbing fibres, which originate in the inferior olivary (IO) nucleus, are likely to transmit error-related information to the cerebellum by projecting strong excitatory connections to Purkinje cells (PCs) [4]. PCs receive also excitatory projections via the parallel fibres (PFs), which are the axons of the granule cells (GCs). PFs are believed to transmit to PCs an optimal account, in terms of information content, of the multimodal signals conveyed by the MFs [5]. Therefore, optimal sensorimotor representations and error-related signals converge onto the PC synapses, whose long-term modifications (i.e., long -term potentiation, LTP, and depression, LTD) constitute a suitable cellular mechanism for learning

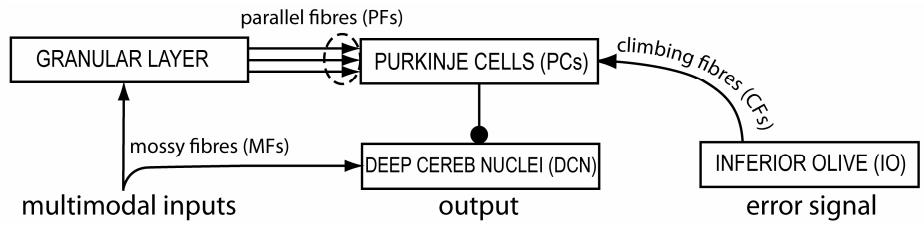

Figure 1. The model cerebellar microcomplex circuit. Arrows and filled circles are excitatory and inhibitory synapses, respectively. The dashed circle denotes the main learning site.

adaptive input/output associations. LTD between the PFs and PCs is thought to be the main synaptic mechanism enabling this mnemonic process [5]. PCs send inhibitory connections to the deep cerebellar nuclei, which form the main output of the cerebellar microcomplex.

Burguière et al. (2005) [3] employed L7-PKCI transgenic mice, which present an LTD inactivation at the PF – PC synapses. The learning performances of L7-PKCI mice were compared with those of control mice in two spatial tasks: the Morris water maze (MWM) [6] and the Starmaze task [7] (Fig. 2). In both setups mice had to swim from random departure locations toward a platform hidden below the surface of opaque water. Both tasks required the declarative capability of building a spatial representation of the environment. Yet, in contrast to the MWM task, the Starmaze alleys guided mice movements, which eventually reduced the procedural demand of the task. Thus, the use of these two tasks made it possible to dissociate the relative importance of the declarative and procedural components of navigation [3]. Compared to their control littermates, L7-PCKI mice were impaired to learn efficient goal-directed trajectories (see Methods for the measured parameters), which made the authors claim that cerebellar LTD may be relevant to the procedural component of spatial cognition [3].

We simulated the experimental protocols employed by Burguière et al. (2005), and we used our model to emulate the lack of LTD plasticity at PF – PC synapses of L7-PKCI mice. The following sections provide first a brief account of the simulated behavioural tasks and modelling methods, then present our results, and finally discuss them in relation to the experimental findings.

2 Methods

2.1 Simulated behavioural tasks

Figs. 2a,b display the simulated MWM and Starmaze paradigms, respectively. Similar to the experimental protocol used by Burguière et al. (2005), we let two groups of simulated mice (n=10 controls and mutants) undertake 40 training trials (i.e., 10 training days with 4 trials/day) for each of the two tasks. At the beginning of each trial the simulated animal was placed at a starting location randomly drawn from a set of four possible locations. Each trial ended when the subject had reached the hidden platform (small grey circles in Figs. 2a,b).

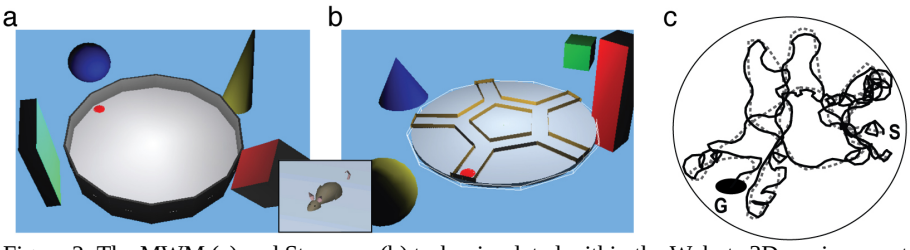

Figure 2: The MWM (a) and Starmaze (b) tasks simulated within the Webots 3D-environment. Inset: simulated mice. (c) Sample of desired (dashed grey line) and actual (black line) navigation trajectories in the MWM from a starting point (S) to the platform (G).

Five parameters were measured [3]: *(i)* the mean "escape latency" (i.e., the average time to reach the platform); *(ii)* the mean speed; *(iii)* the mean angular deviation between the optimal direction to the target and the actual motion direction of the animal (i.e., heading); *(iv)* the ratio between the time spent in the target quadrant and the trial duration; *(v)* the mean distance swum by the animal. These measurements were averaged over all the trials performed in one day by all the subjects of the same group. An ANOVA analysis was performed to assess the statistical significance of the results (significant threshold $=10^{-2}$, i.e. 0.01 was considered significant).

In order to isolate the procedural component of spatial navigation, we endowed control and mutant simulated mice with identical and effective declarative spatial learning. A set of goal-directed trajectories was algorithmically pre-computed and unimpaired declarative capabilities were emulated by generating more directed trajectories as training proceeded. At each trial, the cerebellar model was given a sequence of motor commands forming a global desired trajectory (assumed to be planned upstream the cerebellum). Local errors in the execution of these motor commands were simulated to account for unpredictable drifts during swimming locomotion (Fig. 2c). The procedural adaptation process accomplished by the cerebellar model aimed at minimising these local execution errors online.

2.2 Cerebellar model

The microcomplex circuit of Fig. 1 was modelled as a network of populations of formal spiking neurons [8]. MFs were implemented as axons of a population of 10^3 leaky integrate-and-fire neurones [8]. Their input currents were determined by using radial basis functions spanning the motor command input space (target position and velocity) uniformly. MFs activated a population of 10^6 GCs, whose activity was regulated algorithmically to produce a sparse representation of the input state. This process provided an optimal encoding of the input signal [5]. MFs excited a population of 100 neurones in the deep cerebellar nuclei (DCN) layer of the model. Each GC drove on average a subset of 20 cells of a population of 200 PCs which send inhibitory projections onto the DCN neurones. In the model, GCs, PCs, and DCN neurones were modelled as conductance-based spiking neurones [9]. Finally, a population of 200 IO neurones was simulated to produce the climbing fibre projections targeting PCs (1 to 1 connections). The irregular firing of IO neurones was simulated by means of a Poisson spike-train generation model. Also, IO activity

was modulated to encode a teaching signal computed as a function of the ongoing angular and linear deviation of the actual path from the desired trajectory.

The firing of DCN neurons provided the motor correction output of the model. The firing rate of DCN units was mainly determined by the inhibitory action of PCs, which in turn were principally driven by PF activity. Therefore, modifying the strength of the synapses between PFs and PCs resulted in changes of the input-output relation characterising the cerebellar system. Bidirectional long-term plasticity (i.e., LTP and LTD) was modelled at the level of PF – PC synapses. LTP was implemented as a non-associative mechanism [10], such that every incoming PF spike triggered a synaptic efficacy increase. LTD was implemented as an associative mechanism, such that synapses were depressed following conjunctive inputs to the PCs from PFs and climbing fibres [4]. In our simulation, L7-PKCI mutant mice were emulated by inactivating the LTD between PF and PC synapses.

3 Results

Figs. 3a-d present our simulation results in the MWM. It is shown (Fig. 3a) that the mean escape latency of simulated L7-PKCI mice was significantly larger (ANOVA $F_{1,18}$ = 148.66, P<0.001) compared to control subjects over the entire training period (days 1 to 10). Fig. 3b shows that, on average, simulated mutants were significantly impaired (ANOVA $F_{1,18}$ = 19.277, P<0.001) in reducing the deviation between their locomotion orientation and the optimal direction to the platform. These results are consistent with experimental data [3], and they point towards a learning deficit of the simulated mutants in executing optimal goal-oriented behaviour. As also shown in the experimental study, we found that the difference of performance between the two groups of simulated animals was not due to a difference of swimming speed (Fig 3c, ANOVA $F_{1,18}$ = 9.4714, P>0.05).

It is worth recalling that we artificially provided both groups of subjects with identical declarative capabilities, which is reflected in the overall performance improvement of both mutant and control navigation behaviour. The significant learning differences observed in the MWM simulations were solely due to a procedural impairment of mutant subjects (i.e., they were prominently caused by the accumulation of local motor errors over time). Under this pure procedural scenario we did not observe any significant difference between the goal-searching behaviour of mutants and controls. Fig. 3d shows that the ratio R between the time spent within the platform quadrant and the duration of the trial increased over training for both simulated groups without any significant inter-group difference (ANOVA $F_{1,18}$ = 0.1150, P>0.5). This result is in contrast to the experimental data showing that controls increased the ratio R significantly faster than L7-PKCI mice over training [3]. The interpretation of this discrepancy between simulation and experimental results will be discussed in Sec. 4. Figs. 3e-g show the results of our Starmaze task simulations. Consistent with the experimental data, simulated mutants and controls exhibited comparable performances in this task. No statistically significant difference was observed in the mean escape latencies of the two groups nor in the mean distance swum to reach the target (Fig. 3f, ANOVA $F_{1,18}$ = 0.1177, P>0.5), and nor in the heading parameter (Fig. 3g, ANOVA $F_{1,18}$ = 0.3381, P>0.5).

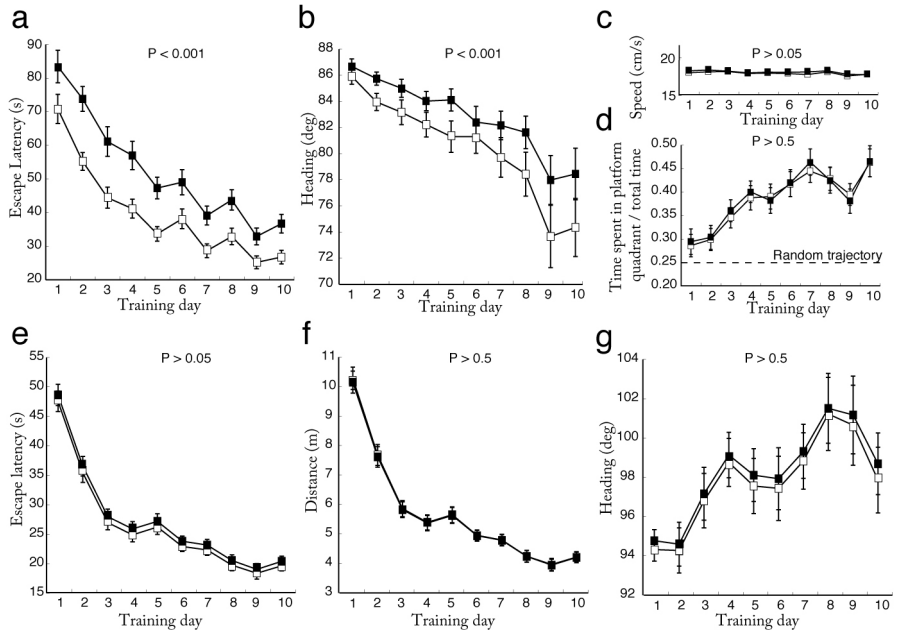

Figure 3. Simulation results for the MWM (top) and the Starmaze (bottom).

4 Discussion

Numerous computational models have been put forth to study the cerebellar role in adaptive motor learning (e.g., [11]). Although a large portion of these works called upon analogue firing-rate units, some of them proposed spiking neuronal models to investigate how timing information is processed within the cerebellum (e.g., [12]). Yet, to our knowledge, none of these works addressed the issue of the role of the cerebellum in high-level functions such as spatial cognition. We present a spiking neural network model of the cerebellar microcomplex that learns to optimise navigation trajectories, which is relevant to the procedural mnemonic component of spatial cognition. It is shown that the system can acquire closed-loop representations of the sensorimotor properties of a simulated mouse.

On the one hand, the model reproduces most of the experimental findings by Burguière et al. (2005) [3] on the spatial learning impairments of L7-PKCI mice (which have a LTD deficit at PF – PC synapses). Consequently, our results corroborate the interpretation drawn by Burguière et al. (2005) that cerebellar LTD plays a significant role in optimising goal-directed trajectories through a continuous adaptation process that minimises motor-command execution errors *locally*. Indeed, simulated L7-PKCI mice were impaired to acquire such a procedural capability, and their navigation trajectories were suboptimal due to cumulative motor execution errors over time. Thus, their learning performances in the MWM were significantly poorer than control subjects.

On the other hand, because our modelling approach permitted to isolate the procedural component of spatial cognition, we provide a slightly different

interpretation of a part of the experimental data. Since simulated controls and mutants were provided with the same desired navigation trajectories, we could verify the hypothesis that declarative spatial learning was unaffected in L7-PKCI subjects. In other words, we could challenge the hypothesis that the *entire* set of findings reported by Burguière et al. (2005) could be ascribed to a local procedural deficit only. Our preliminary findings may suggest that a purely procedural deficit cannot explain why real L7-PKCI mice exhibited coarser goal-searching behaviours than controls – i.e., they spent significantly less time within the target quadrant of the MWM, and showed larger searching zones during the entire training period. Could a more *global* spatial learning process (eventually taking place upstream the cerebellum) be responsible for such impairments? In order to corroborate or refute this hypothesis, a series of new simulations and new analyses of data from Burguière et al. (2005) are currently being performed. If these results were confirmed, this work would put forth the prediction that the lack of cerebellar LTD in L7-PKCI mice might also affect the declarative component of spatial cognition. A way to test this prediction experimentally would be for instance to perform electrophysiological recordings of pyramidal cells in the hippocampal formation (CA1-CA3 place cells and entorhinal grid cells) from L7-PKCI mice.

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